University of Hamburg
Department of Chemistry

Synthesis of Novel 2-Alkoxy(aralkoxy)-4*H*-[1,2,4]triazolo[1,5-a] quinazolin-5-ones and Derivatives

Dissertation submitted in partial satisfaction of the requirements for the degree
Doctor of philosophy in pharmaceutical chemistry

by
Rashad Al-salahi
from
Yemen-Taiz

Hamburg 2009

Gutachter: Prof. Dr. Detlef Geffken
Prof. Dr. Hans-Jürgen Duchstein

Defense of doctoral thesis: 23. 01. 2009

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Finally, I am forever indebted to my wife for her understanding, endless patience and encouragement when it was most required.

Standard Abbreviations and Acronyms

aq	aqueous
Ar	aryl
Bn	benzyl
BrCN	cyanogen bromide
MTBE	methyl *tert*-butylether
^{o}C	degree Celsius
calcd.	calculated
cm^{-1}	wavenumber(s)
CS_2	carbon disulfide
Å	angstrom
Δ	reflux
δ	chemical shift in parts per million downfield from
d	doublet (spectral)
CDI	1,1′-carbonyldiimidazole
DMSO-d_6	dimethylsulfoxide-deuterated
DMF	dimethylformamide
e.g	for example
equiv	equivalent(s)
Et_3N	triethylamine
Et_2O	diethyl ether
EtOAc	ethyl acetate
EtOH	ethanol
FAB	fast atom bombardment
g	gram(s)
h	hour(s)
Hz	hertz

IR	infrared
J	coupling constant (in NMR spectrometry) in Hz
L	liter(s)
lit.	literature (abbreviation used with period)
m	multiplet (spectral)
Me	methyl
MeOH	methanol
min.	minute(s)
mmol	millimole(s)
M.p.	melting point
MS	mass spectrometry
MW	molecular weight
m/z	mass-to-charge ratio
NaOMe	sodium methoxide
NaOEt	sodium ethoxide
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	part(s) per million
i-Pr	isopropyl
q	quartet (spectral)
rt	room temperature
s	singlet (spectral); second(s)
t	triplet (spectral)
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	tetramethylsilane

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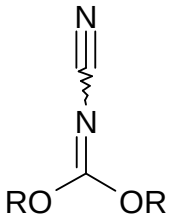
1 Introduction

1.1 Preface

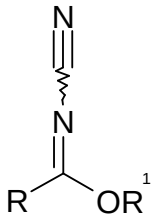
The present work deals with the synthesis of novel 1,2,4-triazolo[1,5-a]quinazoline derivatives and anellated derivatives thereof by employing *N*-cyanoimidocarbonates as building blocks.

N-Cyanoimidocarbonates **(I)**, first described by Allenstein et al. [1] in 1967, and *N*-cyanoimidates **(II)**, known since 1963, [2] are versatile reagents and play an important role as building blocks for bioactive compounds, containing a modified cyanoguanidine moiety [3, 4] and offer access to a great variety of heterocyclic systems.[5-7]



I

R : alkyl, aryl, aralkyl

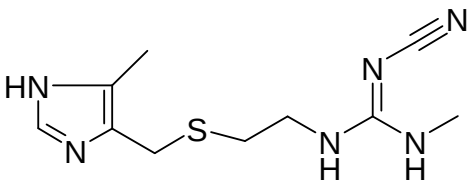


II

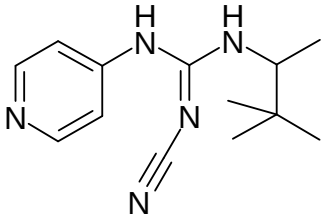
R : H, alkyl R^1 : alkyl

For example, synthesis of cyanoguanidine functionality of *cimetidine* **(III)**, a potent H_2-histamine antagonist [8-10], and preparation of *pinacidil* [a] (**IV**) has been effected by employing diphenyl *N*-cyanoimidocarbonate.[13]

[a] Pinacidil is a potassium channel opener, it has been found to exert similar effect as Minoxidil on cardiovascular system disease (antihypertensive).[11, 12]

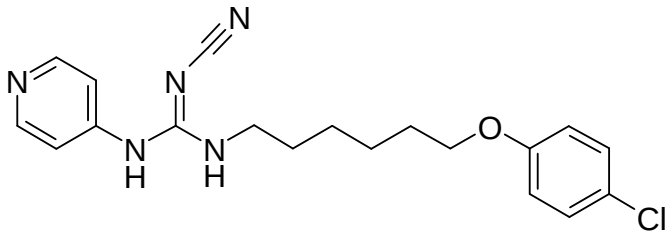


Cimetidine **III**

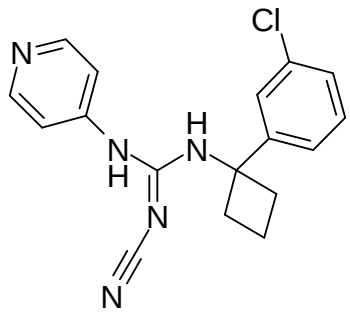


Pinacidil **IV**

The cyanoguanidine pharmacophore is also present in the development compound *CHS 828* **(V)** which has been reported to possess cytotoxic activity. [14, 15] The novel "lead" compound *PNU-99963* **(VI)**, is another example of a bioactive cyanoguanidine derivative that has been described as an inhibitor of glucose induced insulin secretion.[16, 17]



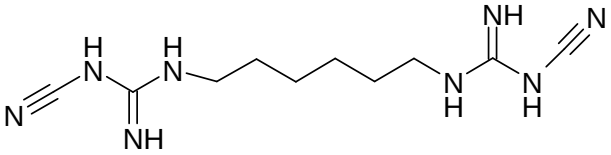
CHS 828 **V**



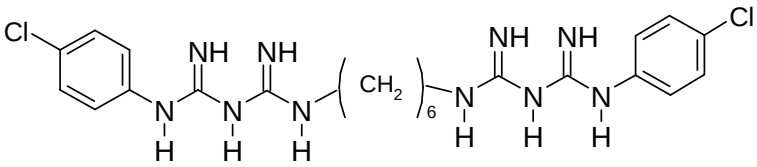
PUN-99963 **VI**

Two cyanoguanidine functionalities, linked by a C_6-spacer are embodied in compound **VII** which is used as a synthetic precursor of chlorhexidine **(VIII)**.[b] [18]

[b] Chlorhexidine is prescribed as an antiseptic agent and has antibacterial activity against a wide variety of gram positive and gram negative organisms.



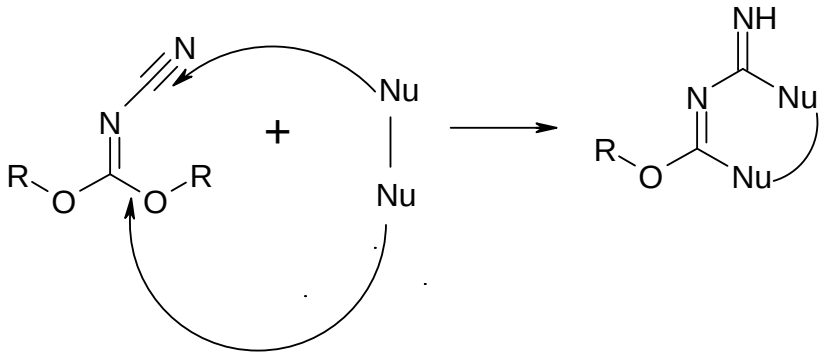
VII



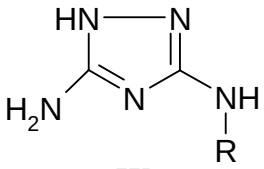
VIII

Reaction of *N*-cyanoimidocarbonates with "bi-nucleophiles" (Nu – Nu), may offer access to a great variety of bioactive heterocyclic compounds [19] with different ring-size, as generally outlined by (Scheme 1).

Scheme 1 *Reaction of N-Cyanoimidocarbonates with bi-nucleophiles*



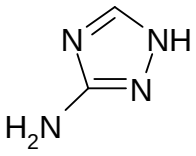
For example, 1,2,4-triazole derivatives **(IX)**, accessible according to Scheme 1, have recently received growing attention in drug and agricultural chemistry because of their wide biological activities.[20-25]



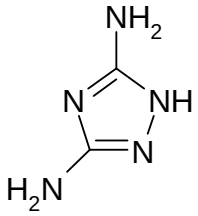
IX

R : alkyl, aryl

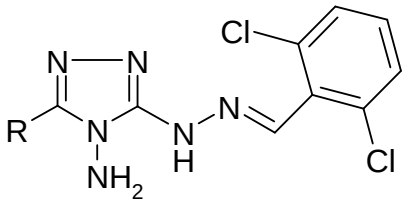
Some acclaimed examples, *amitrol* **(X)** [26], *guanazol* **(XI)** [27] are reported to exert cytotoxic activity whereas triazole derivatives of type **XII** [28] have shown antihypertensive activity and compound **XIII** [29] was found to exhibit antimalaria activity.



Amitrol **X**

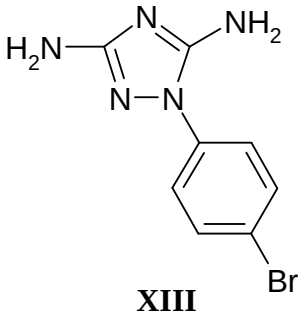


Guanazol **XI**



XII

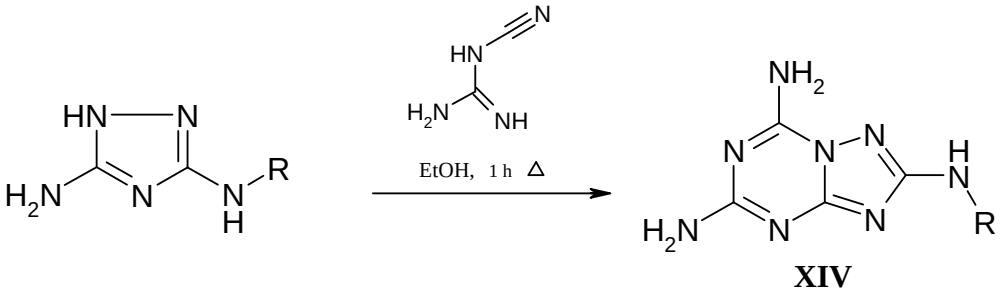
R : H, alkyl, aryl, aralkyl



XIII

2,5,7-Triaminosubstituted 1,2,4-triazolo[1,5-a][1,3,5]triazine derivatives **(XIV)**, prepared according to Scheme 2 by reaction of 3,5-diamino-1,2,4-triazole with cyanoguanidine, have been elaborated as dihydrofolate reductase (DHFR) inhibitors [c] and may become useful in the chemotherapy of cancer and bacterial infections.[30]

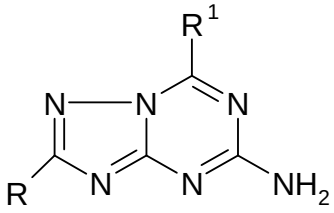
Scheme 2 *Synthesis of 2,5,7-Triamino-1,2,4-triazolo[1,5-a][1,3,5]triazine derivatives* **(XIV)**



XIV

R : alkyl, aryl, aralkyl

Replacement of the 5,7-diamino groups in **XIV** by organyl substituents furnished 1,2,4-triazolo[1,5-a][1,3,5]triazines of type **XV** that proved to be potent adenosine antagonists.[31]



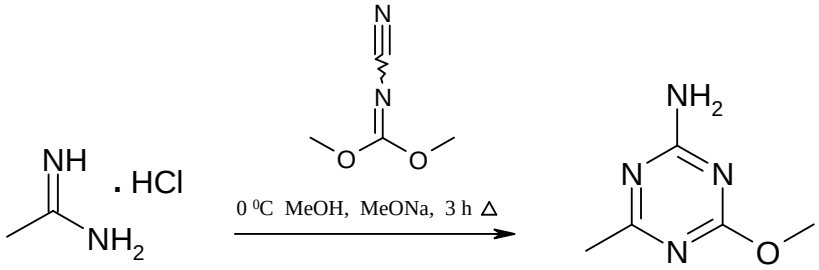
XV

R: alkyl, aryl, alkoxy, thioalkyl
R^1: alkyl, aralkyl

[c] Dihydrofolate reductase inhibitors are used for treatment of cancer and autoimmune diseases. They act by inhibiting the dihydrofolate reductase enzyme which converts dihydrofolate to the active tetrahydrofolate, that plays an important role in the biosynthesis of DNA and RNA nucleoside bases such as thymidine and purine.

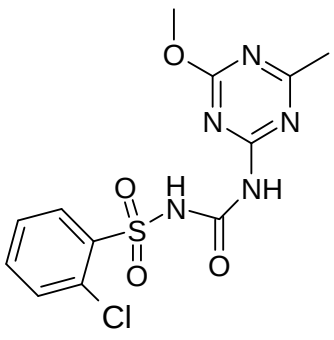
2-Amino-4-methyl-6-methoxy-1,3,5-triazine **(XVI)**, obtained from treatment of acetamidine hydrochloride with dimethyl *N*-cyanoimidocarbonate (Scheme 3) [32, 33], served as precursor for a variety of sulfonylurea compounds which are valuable herbicides.[34, 35]

Scheme 3 *Synthesis of 2-Amino-4-methyl-6-methoxy-1,3,5-triazine* **(XVI)**

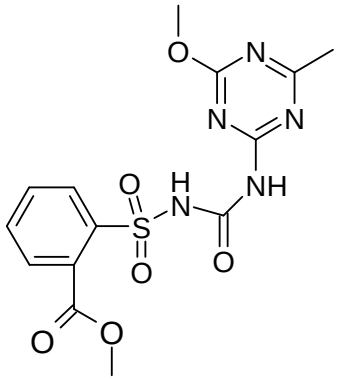


XVI

For example, *chlorsulfuron* **(XVII)** and *metsulfuron-methyl* **(XVIII)**, are systemic sulfonylurea herbicides for the selective pre- and post emergency control of broad-leaved and grass weeds in cereal crops. Their mode of action is founded upon inhibition of protein synthesis, by blocking acetolactate synthase (ALS)[d] in plants.[36, 37]



Chlorsulfuron **XVII**

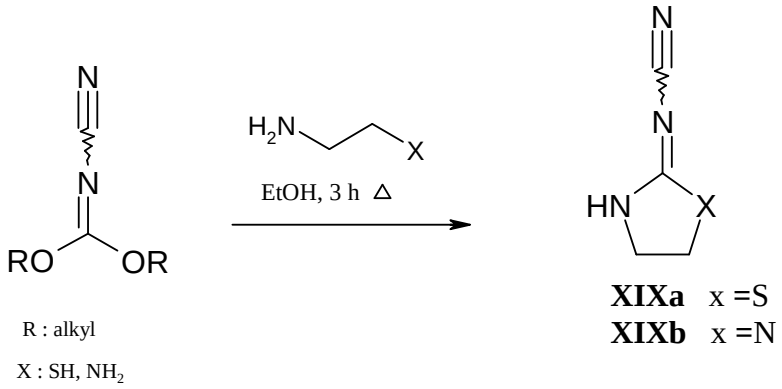


Metsulfuron-methyl **XVIII**

[d] Acetolactate synthase (ALS) is an enzyme of the biosynthetic pathway of branched amino acids (valine, leucine and isoleucine) in plants and micro-organism.

From the reaction of *N*-cyanoimidocarbonates with 2-aminoethanthiol and ethylenediamine resulted cleanly 2-cyanoiminothiazolidine **(XIXa)** and 2-cyanoiminoimidazolidine **(XIXb)** [38-40] (Scheme 4), which upon further derivatization provided neonicotinoid compounds as highly active insecticides. [41, 42]

Scheme 4 *Synthesis of 2-Cyanoiminothiazolidine* **(XIXa)** *and 2-Cyanoiminoimidazolidine* **(XIXb)**



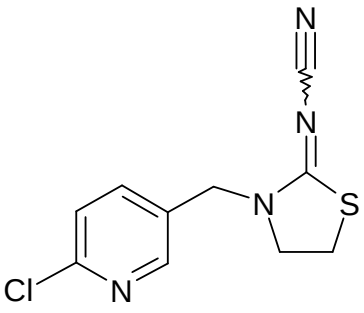
R : alkyl

X : SH, NH_2

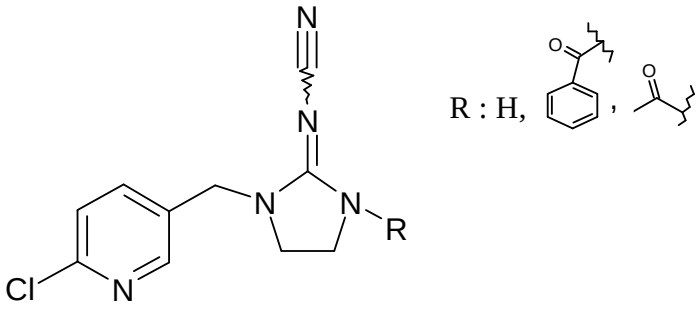
XIXa x =S

XIXb x =N

For example, *thiacloprid* **(XX)** [43] and the cyclic cyanoguanidines **XXI** [39]**,** exert their insecticidal activity by acting as an agonist on the nicotinic acetylcholine receptors (nAChRs) in the CNS of insects, giving rise to abnormal excitement, paralysis, and death of insects.[44, 45]



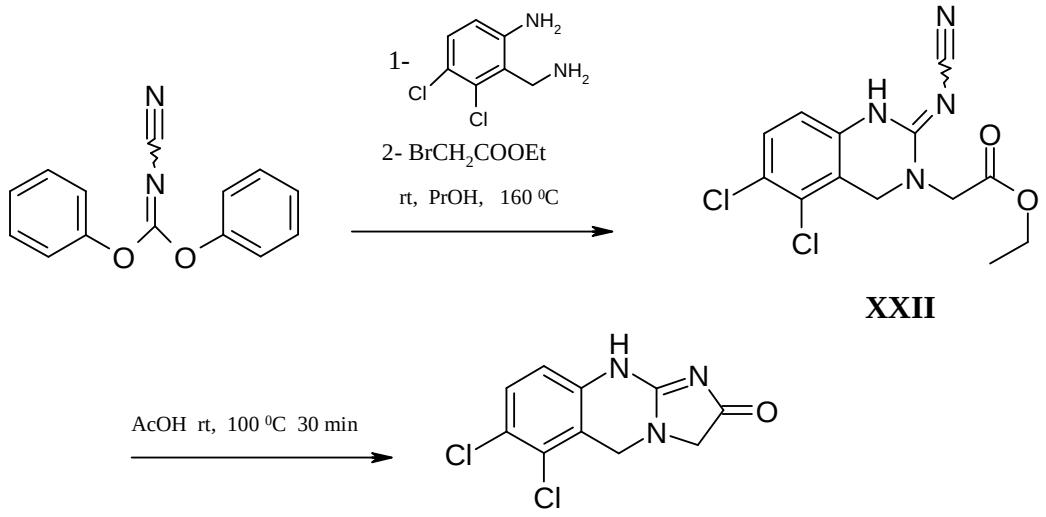
Thiacloprid **XX**



XXI

Ethyl (2-cyanoimino-5,6-dichloro-1,2,3,4-tetrahydroquinazoline-3-yl) acetate **(XXII**), prepared according to Scheme 5 by reaction of diphenyl *N*-cyanoimidocarbonate with 2-amino-5,6-dichloro-benzylamine [46], proved to be a valuable precursor of *anagrelide (agrylin*^{R}*)* [e] (**XXIII).**[47]

Scheme 5 *Synthesis of 6,7-Dichloro-1,5-dihydroimidazo-[2,1-b]quinazolin-2(3H)-one* **(XXIII)**



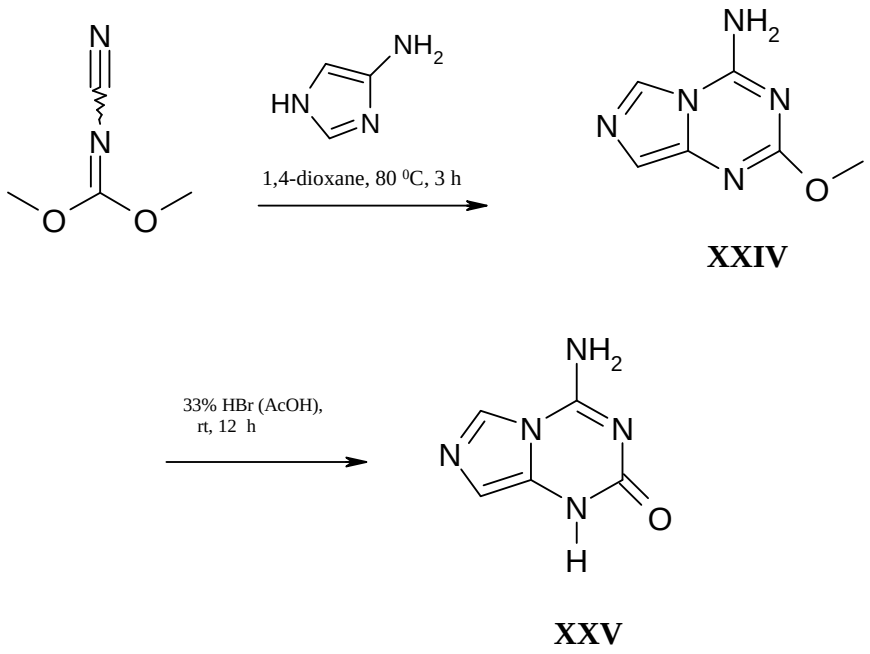
XXII

Anagrelide **XXIII**

[e] Anagrelide was launched recently by Roberts Pharmaceuticals Corporation as the first drug approved for oral treatment of essential thrombocythemia, a life threatening blood disorder, characterized by high blood platelet counts.

4-Amino-2-methoxy-imidazo-[1,5-a][1,3,5]triazine **(XXIV)**, obtained from treatment of 4-aminoimidazole with dimethyl *N*-cyanoimidocarbonate (Scheme 6) [48], acts an intermediate for isoguanine **(XXV**), a modified purine base, which is used in combination with isocytosine (a modified pyrimidine base) as a potent inducer of a stable parallel-stranded DNA duplex structure.[49-51]

Scheme 6 *Synthesis of 4-Amino-1H-imidazo-[1,5-a][1,3,5]triazin-2-one* **(XXV)**

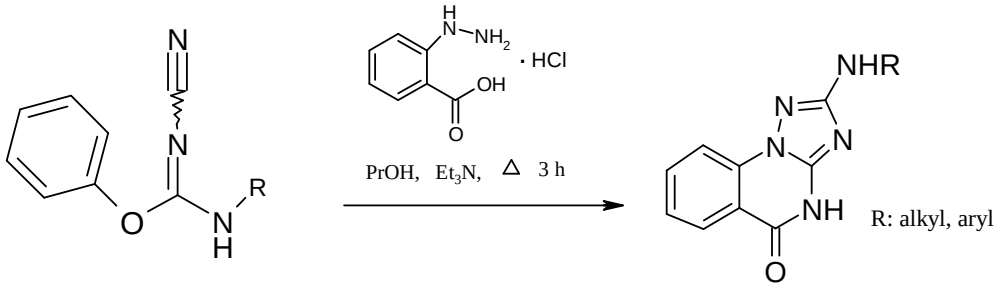


XXIV

XXV

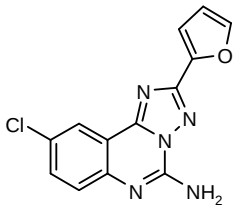
From treatment of *N*-cyano *N´*-(alkyl(aryl)amino)-*O*-phenyl isourea with 2-hydrazinobenzoic acid (Scheme 7), resulted very recently [1,2,4] triazoloquinazolines[f] of type **XXVI** which have been disclosed as potent proteinkinase inhibitor.[52]

Scheme 7 *Synthesis of 2-Alkyl(aryl)amino-[1,2,4]triazolo[1,5-a]quinazolin-5-ones* **(XXVI)**

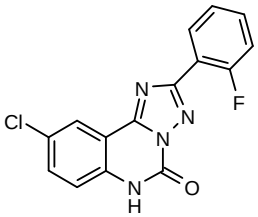


XXVI

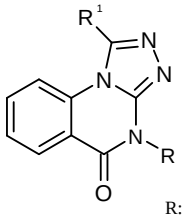
[f] Compounds with [1,2,4]triazoloquinazoline moiety have been shown to exhibit diverse biological activities. For example, the novel compound **XXVII** is effective *adenosine antagonist* whereas the related compound **XXVIII** was found to be *benzodiazepine receptor antagonist*. [53–61] The [1,2,4]triazoloquinazolines of type **XXIX** were reported as a new class of non sedative *H_1-histamine antagonists*.[62-64]



XXVII



XXVIII



R: alkyl, aryl
R^1: alkyl, aryl

XXIX

1.2 Aim of the Thesis

In view of the beforementioned biological activities of diverse heterocycles which originated from *N*-cyanoimidocarbonates as building blocks, my thesis focused first on the preparation of several dialkyl *N*-cyanoimidocarbonates **(2)** and second on their ability to react with 2-hydrazinobenzoic acids (**3**) to provide novel [1,2,4]triazolo[1,5-a]quinazolin-5-ones (**6**) (Scheme 8), which in turn should offer access to a variety of derivatives upon chemical transformations of the inherent lactam moiety and the 2-alkoxy group as outlined in (Fig. 1).

Scheme 8 *Synthesis of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-ones (**6a-g**)*[g]

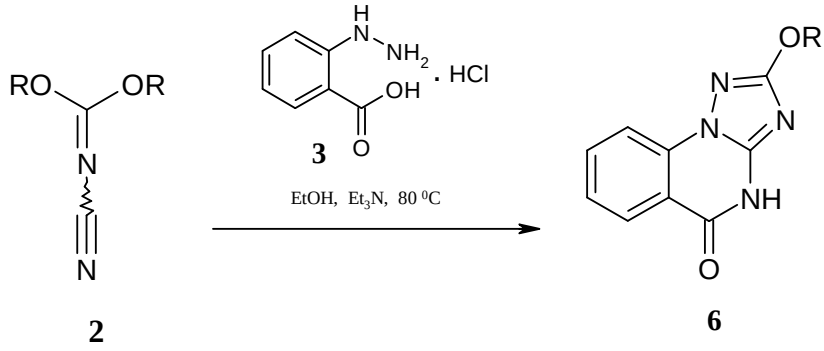
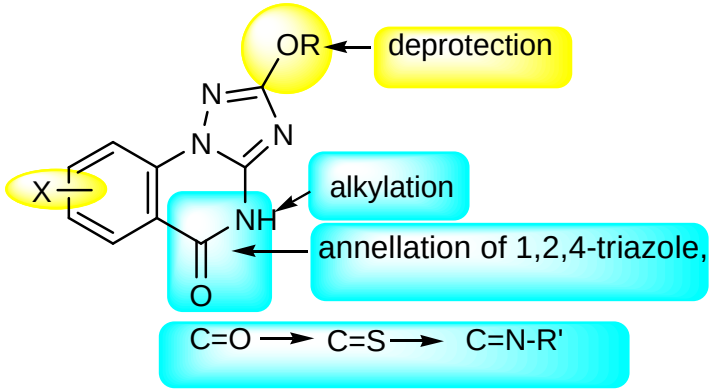


Fig . 1 *Planned structure modifications of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo-[1,5-a]quinazolin-5-ones* (**6**)



[g] The intermediates **4** and **5** are shown in Scheme 10 (page 24.

2 Synthesis

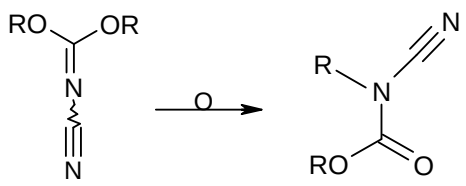
2.1 Synthesis of 2-Alkoxy(aralkoxy)-4*H*-[1,2,4]triazolo[1,5-a]quinazolin-5-ones (6a-g)

2.1.1 Synthesis of Dialkyl *N*-Cyanoimidocarbonates (2a-g)

Procedures for the preparation of dialkyl *N*-cyanoimidocarbonates have been reported in the literature. [65–69] For the present investigations a synthetic route developed by Michael et collaborators has been successfully applied. [70] Thus, reaction of cyanogen bromide with different alcohols in the presence of sodium hydroxide in methyl *tert*-butyl ether under ice cooling provided the non-isolable imidocarbonates **1** as intermediates that subsequently underwent reaction with an additional equivalent cyanogen bromide in the presence of triethylamine and a catalytic amount of sodium carbonate to produce the desired dialkyl *N*-cyanoimidocarbonates **2a-g** in 40-55% yield (Scheme 9).

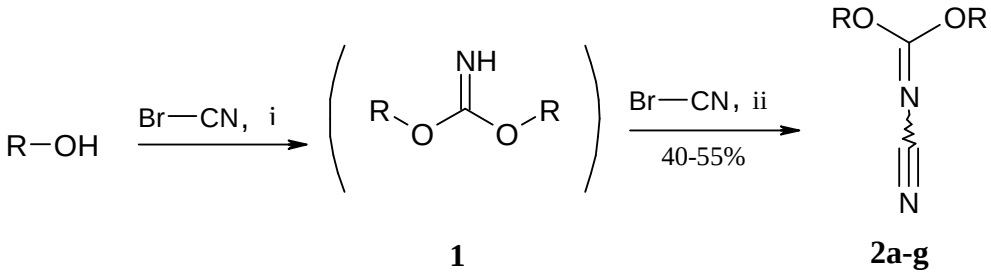
Due to their instability and tendency to rearrange, the compounds **2a-g** have to be stored in the refrigerator.[h] The IR spectra of **2a-g** are characterized by a weak absorption band at 2205-2219 cm^{-1} (C≡N) and a strong absorption band at 1611-1614 cm^{-1} (C=N) (Fig. 2). For ^{1}H NMR and ^{13}C NMR spectral data see experimental part.

[h] Dialkyl *N*-cyanoimidocarbonates undergo facile rearrangement to the isomeric alkoxycarbonyl cyanamide (**2B**) at elevated temperature.[1, 71]



2a-g **2B**

Scheme 9 *Preparation of Dialkyl N-Cyanoimidocarbonates* **(2a-g)**



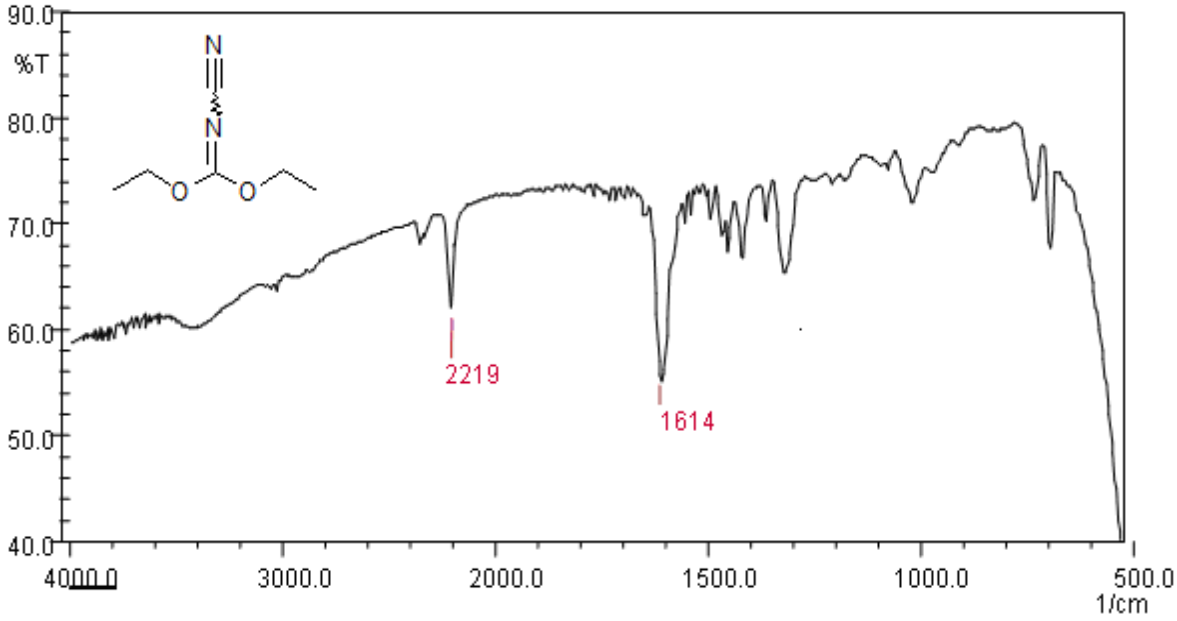
1 **2a-g**

i: NaOH, MTBE ii: Na_2CO_3, Et_3N

Table 1 *Prepared Dialkyl N-Cyanoimidocarbonates* **(2a-g)**

2	R	Yield [%]
a	CH_3	50
b	CH_3CH_2-	53
c	$(CH_3)_2CH$-	40
d	CH_2=$CHCH_2$-	48
e	$CH_3CH_2CH_2CH_2CH_2$-	50
f	$C_6H_5CH_2$-	55
g	$C_6H_5CH_2CH_2$-	52

Fig. 2 *IR Spectrum of Diethyl N-Cyanoimidocarbonate* **(2b)**

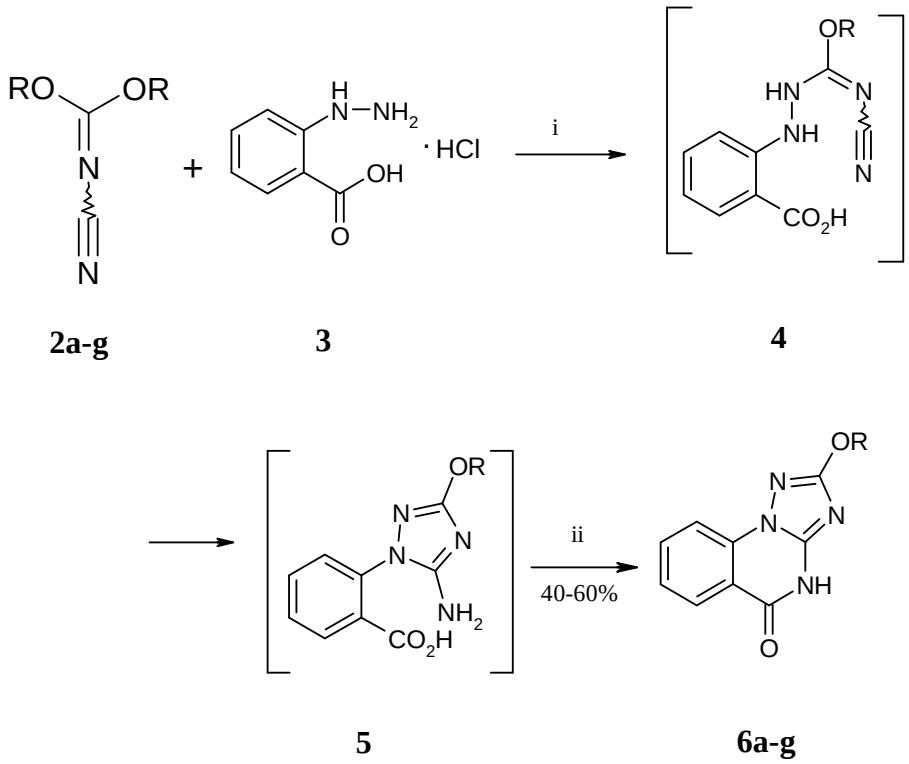


2.1.2 Condensation of Dialkyl *N*-Cyanoimidocarbonates 2a-g with 2-Hydrazinobenzoic Acid

Based on the high reactivity of *N*-cyanoimidocarbonates towards hydrazines to produce 1,2,4-triazole derivatives [72-76], it was anticipated that **2** would react with 2-hydrazinobenzoic acid **3** analogously to give the respective 1,2,4-triazoles **5** as primary condensation products which in turn were expected to deliver the targeted [1,2,4]triazolo[1,5-a]quinazolin-5-ones **6** by intramolecular condensation. As a matter of fact, reaction of **2** with **3** in ethanol under ice cooling in the presence of triethylamine provided the intermediate 1,2,4-triazole derivative **5**, which upon treatment with hydrochoric acid (36%) produced the tricyclic compounds **6a-g** in 40-60% yield (Scheme 10).[77]

The structure of the novel [1,2,4]triazoloquinazolin-5-ones **6a-g** was confirmed by IR, ^{1}H NMR, ^{13}C NMR spectra and microanalysis. The IR spectra of compounds **6** are characterized by a strong (C=O)-stretching band at 1685-1705 cm^{-1} (Fig. 3). Representative ^{1}H NMR and ^{13}C NMR spectra are shown in Fig. 4 and 5. In addition, the structure of compound **6f** has been unambiguously proven by X-ray crystallography (Fig. 6).

Scheme 10 *Preparation of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-ones* **(6a-g)**



i : Et_3N, EtOH ii : conc. HCl, 80 °C

Table 2 *Prepared 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-ones* **(6a-g)**

6	R	Yield [%]
a	CH_3	60
b	CH_3CH_2-	60
c	$(CH_3)_2CH$-	40
d	$CH_3CH_2CH_2CH_2CH_2$-	50
e	CH_2=$CHCH_2$-	55
f	$C_6H_5CH_2$-	58
g	$C_6H_5CH_2CH_2$-	56

Fig. 3 *IR Spectrum of 2-Ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(6b)**

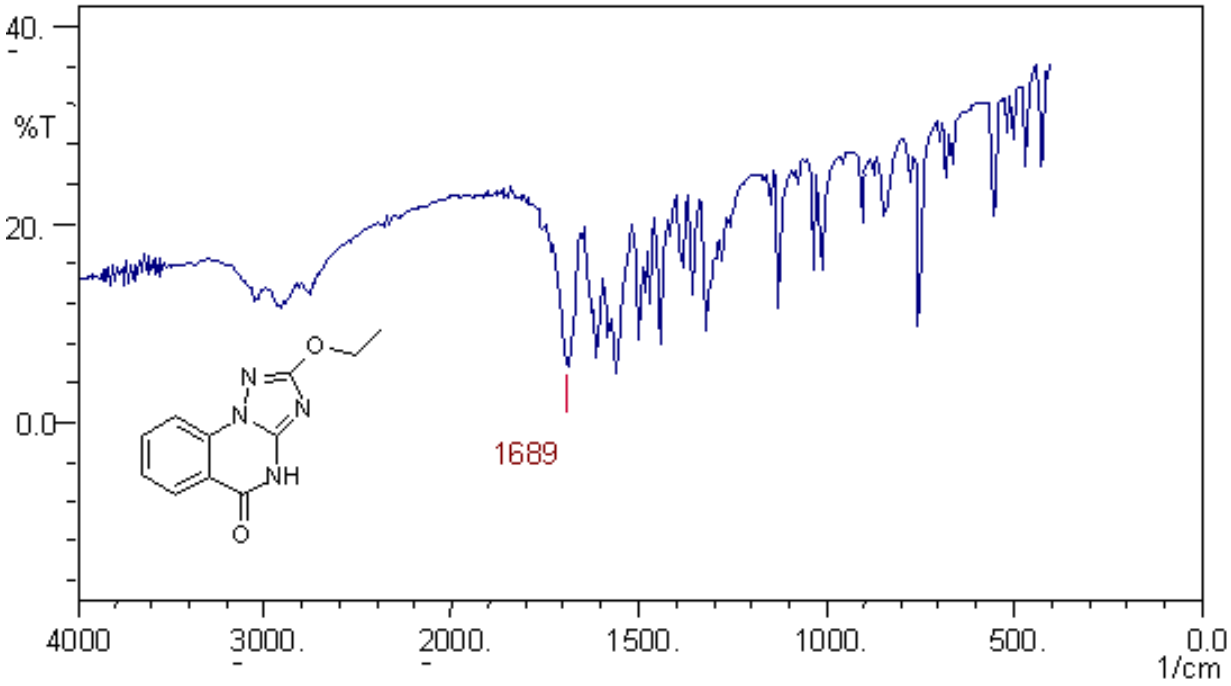


Fig. 4 *^{1}H NMR Spectrum of 2-Ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(6b)**

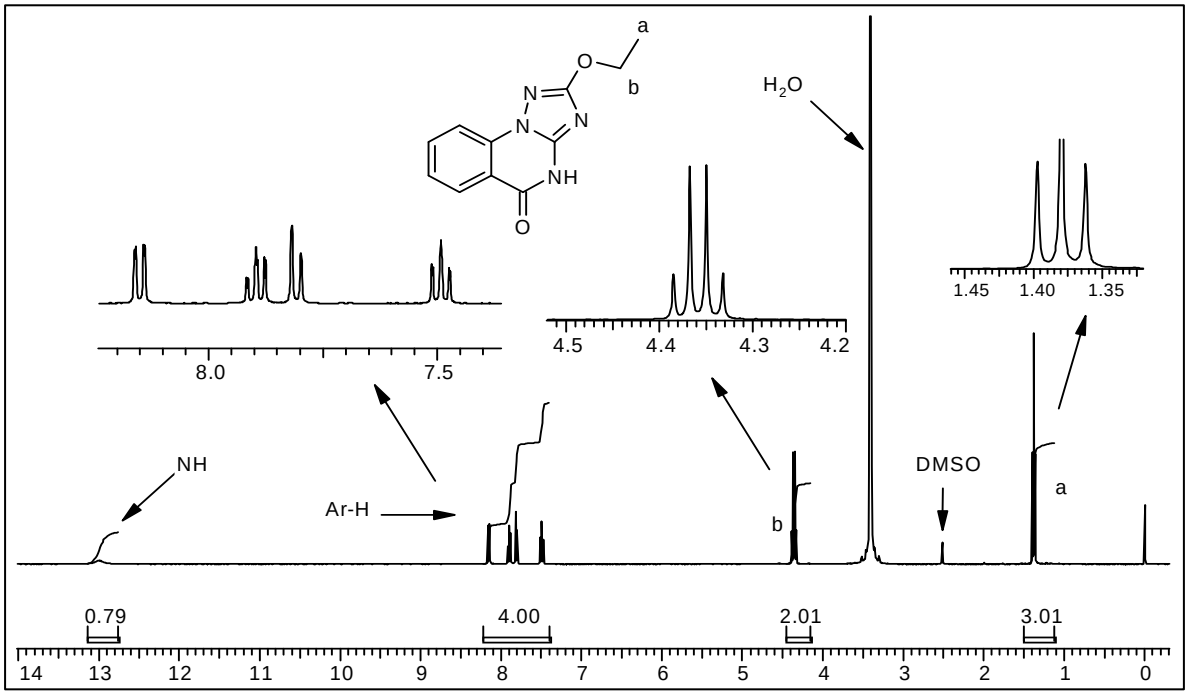


Fig. 5 *^{13}C NMR Spectrum of 2-Ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(6b)**

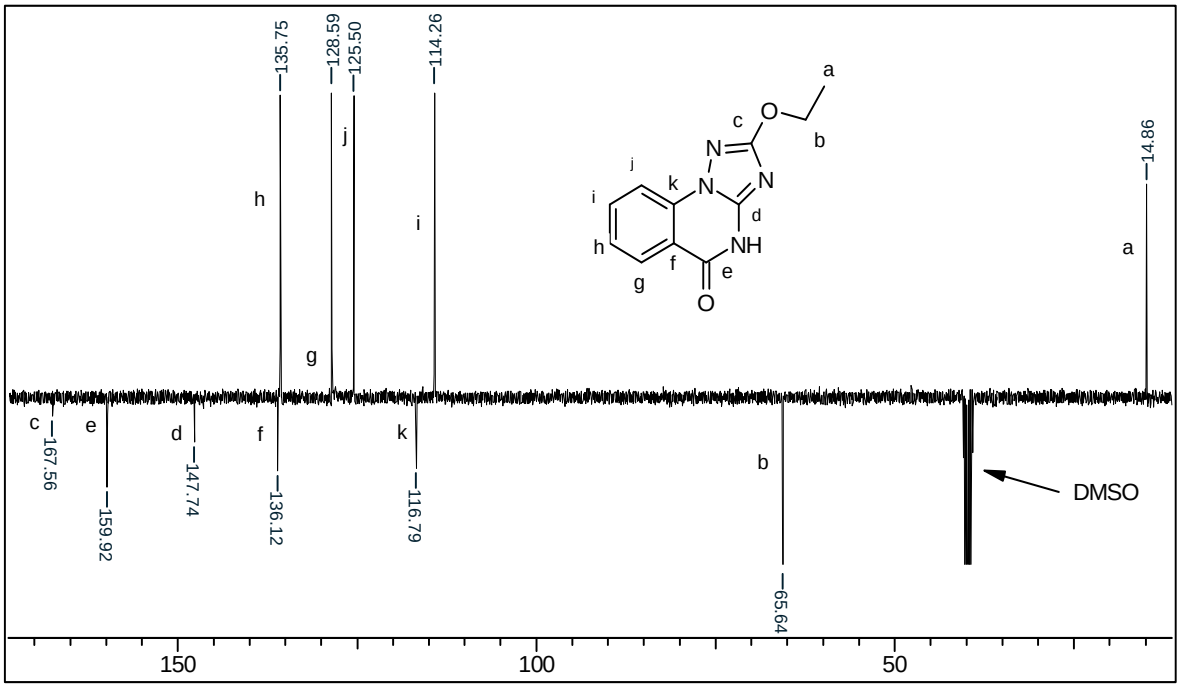
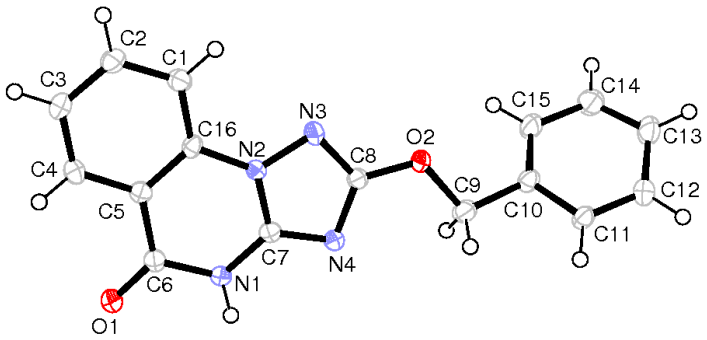
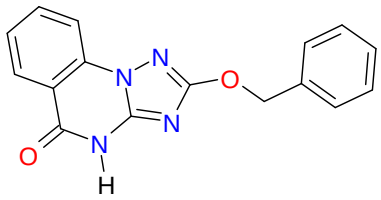


Fig. 6 Molecular structure *of 2-Benzyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(6f)** (diamond-visual crystal structure)





6f

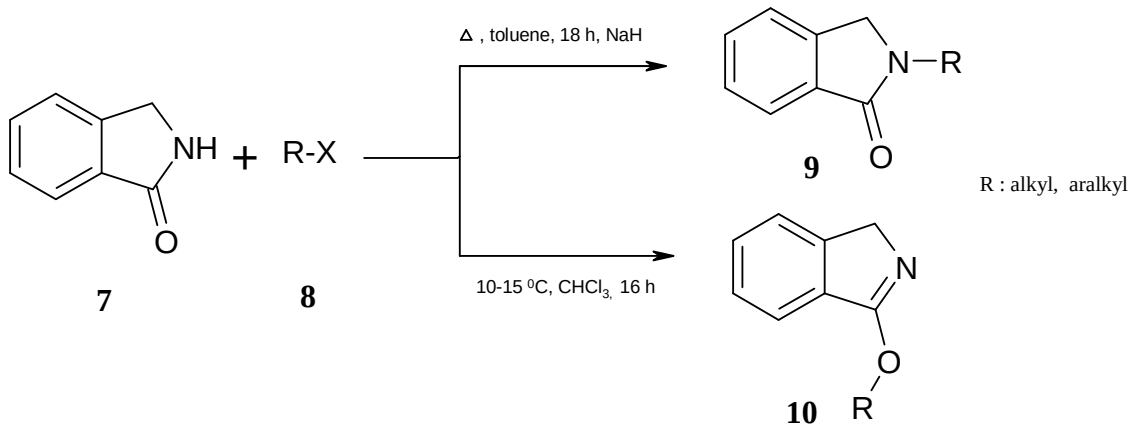
2.2 Reactions of [1,2,4]Triazolo[1,5-a]quinazolin-5-ones (6)

After the successful synthesis of the desired heterocyclic compounds **6**, their reactivity towards alkylation, reduction, thionation, chlorination, hydrogenolysis and nitration reactions was studied.

2.2.1 Alkylation of [1,2,4]Triazolo[1,5-a]quinazolin-5-ones (6) with Alkyl Halides

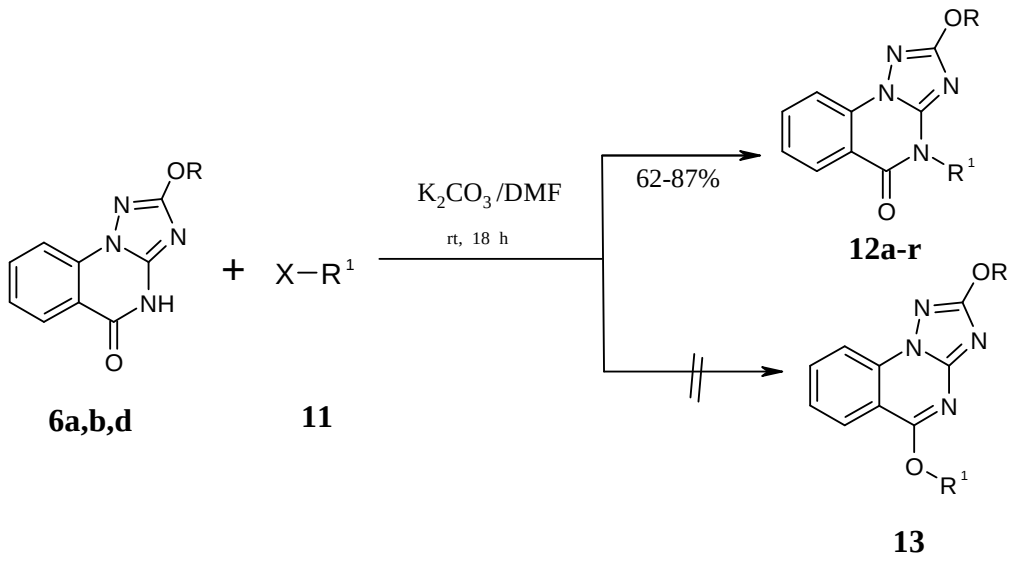
Alkylation of lactams with alkyl halides may give rise to N- or/and O-alkylated products, the outcome of the reaction being dependent on the pH of the reaction, temperature, the nature of solvents, and the reactivity of the alkylating agents [78-84]. For example, alkylation of isoindolinone **(7)** with alkyl halides **(8)** in toluene under refluxing conditions in the presence of a base afforded **9** [85], whereas O-alkylation to the corresponding lactim ether **10** occured when **7** was allowed to react with alkyl halides in chloroform at 10-15 ^{o}C for 1 h, followed by stirring at ambient temperature [86] (Scheme 11).

Scheme 11 N- *and* O-*Alkylation of the lactam group of Isoindolin-1-one* **(7)** [85, 86]



Accordingly, when the [1,2,4]triazoloquinazolin-5-ones **6a,b,d** were allowed to react with alkyl halides (**11)** in a molar ratio of 1:1.5 in absolute dimethyl formamide at room temperature in the presence of potassium carbonate [87], the corresponding 2-alkoxy(aralkoxy)-4-alkyl(aralkyl)-4*H*-[1,2,4]triazolo[1,5-a]quinazolin-5-ones **12** resulted in 62-87% yield (Table 3, Scheme 12). Under these conditions, formation of the isomeric lactim ethers **13** was not observed.

Scheme 12 *Preparation of 2-Alkoxy(aralkoxy)-4-alkyl(aralkyl)-4H-[1,2,4]triazolo-[1,5-a]quinazolin-5-ones* **(12a-r)**



The products **12a-r** were obtained as colored (yellow or pale brown) solid compounds and their structures were proved by ^{1}H NMR,^{13}C NMR, IR spectra and microanalysis. The IR spectra of **12a-r** display a strong (C=O)-absorption band at 1670-1685 cm^{-1} (Fig. 7). Representative ^{1}H NMR and ^{13}C NMR spectra are shown in Fig. 8 and 9.

Table 3 *Prepared 2-Alkoxy(aralkoxy)-4-alkyl(aralkyl)-4H-[1,2,4]triazolo[1,5-a]-quinazolin-5-ones* (**12a-r)**

12	R	R^1	Yield [%]
a	CH_3	4-Br-$C_6H_4CH_2$-	83
b	CH_3	$C_6H_5CH_2CH_2$-	85
c	CH_3	4-F-$C_6H_4CH_2$-	83
d	CH_3	$C_6H_5CH_2$-	82
e	CH_3	CH_3CH_2-	62
f	CH_3	CH_2=$CHCH_2$-	82
g	CH_3	HC≡CCH_2-	84
h	CH_3CH_2-	4-Br-$C_6H_4CH_2$-	85
i	CH_3CH_2-	4-OCH_3-$C_6H_4CH_2$-	71
j	CH_3CH_2-	$C_6H_5CH_2$-	81
k	CH_3CH_2-	HC≡CCH_2-	87
l	CH_3CH_2-	CH_2=$CHCH_2$-	83
m	CH_3CH_2-	$C_3H_5CH_2$-	70
n	CH_3CH_2-	CH_3CH_2-	65
o	CH_3CH_2-	2,4-diCl-$C_6H_3CH_2$-	73
p	CH_3CH_2-	$CH_3CH_2CH_2$-	66
q	CH_3CH_2-	4-F-$C_6H_4CH_2$-	81
r	$CH_3CH_2CH_2CH_2CH_2$-	4-Br-$C_6H_4CH_2$-	77

Fig. 7 *IR Spectrum of 4-Allyl-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(12l)**

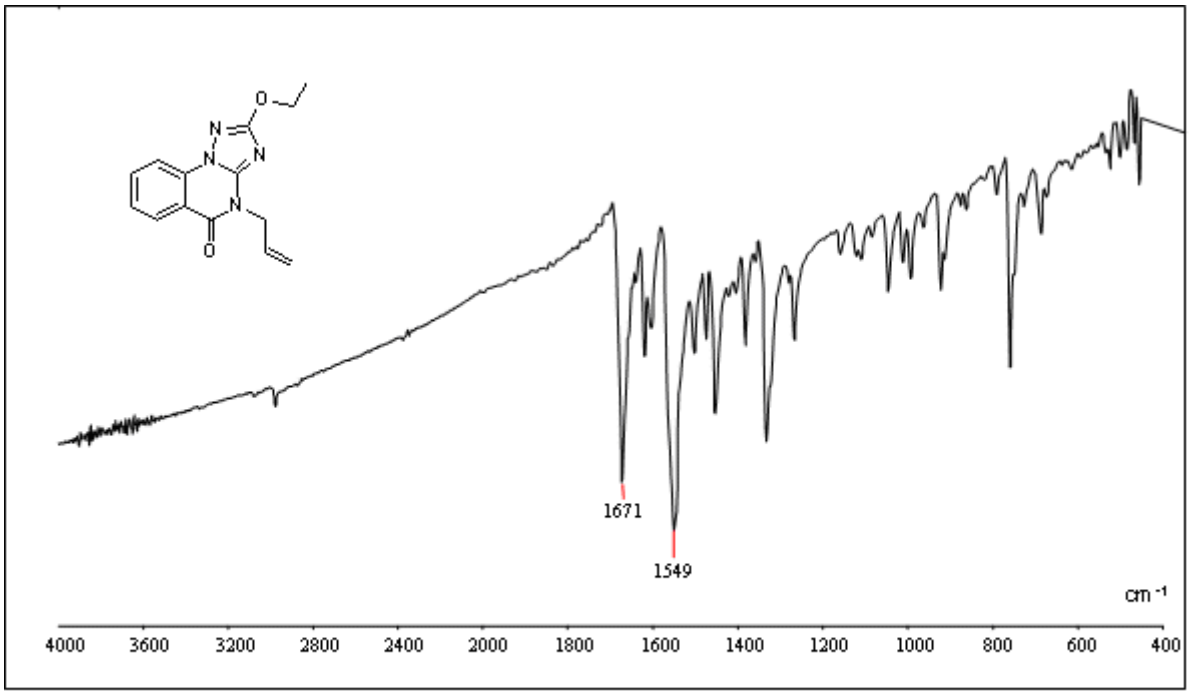


Fig. 8 *^{1}H NMR Spectrum of 2-Methoxy-4-phenethyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(12b)**

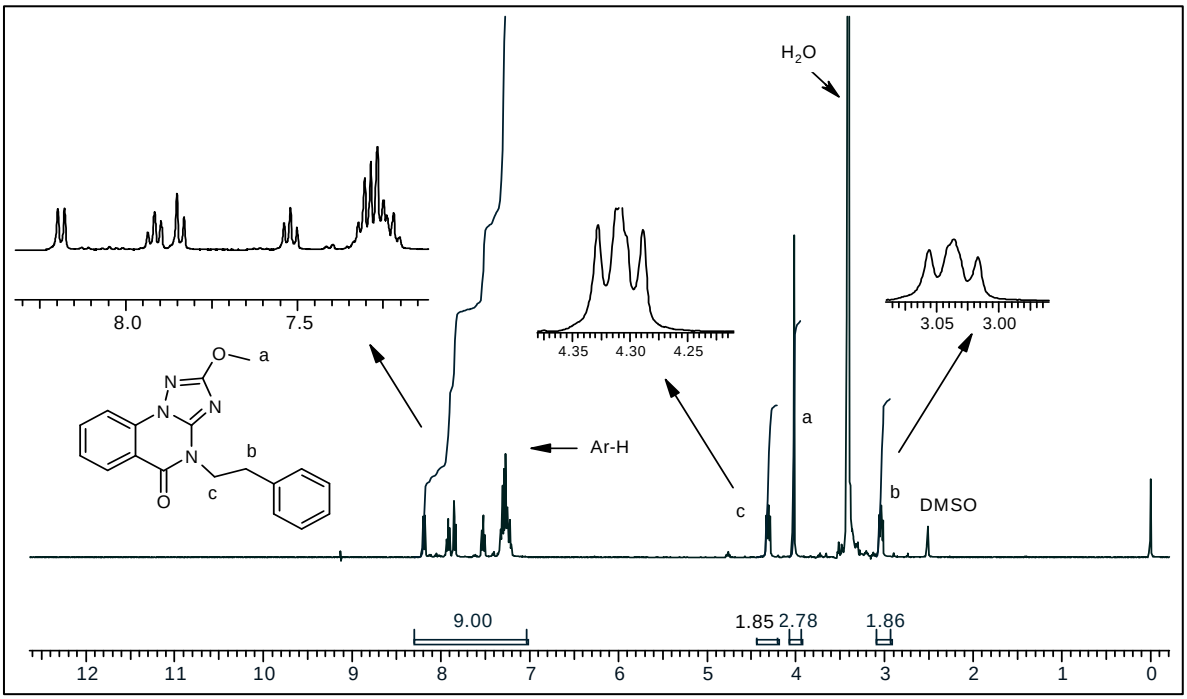
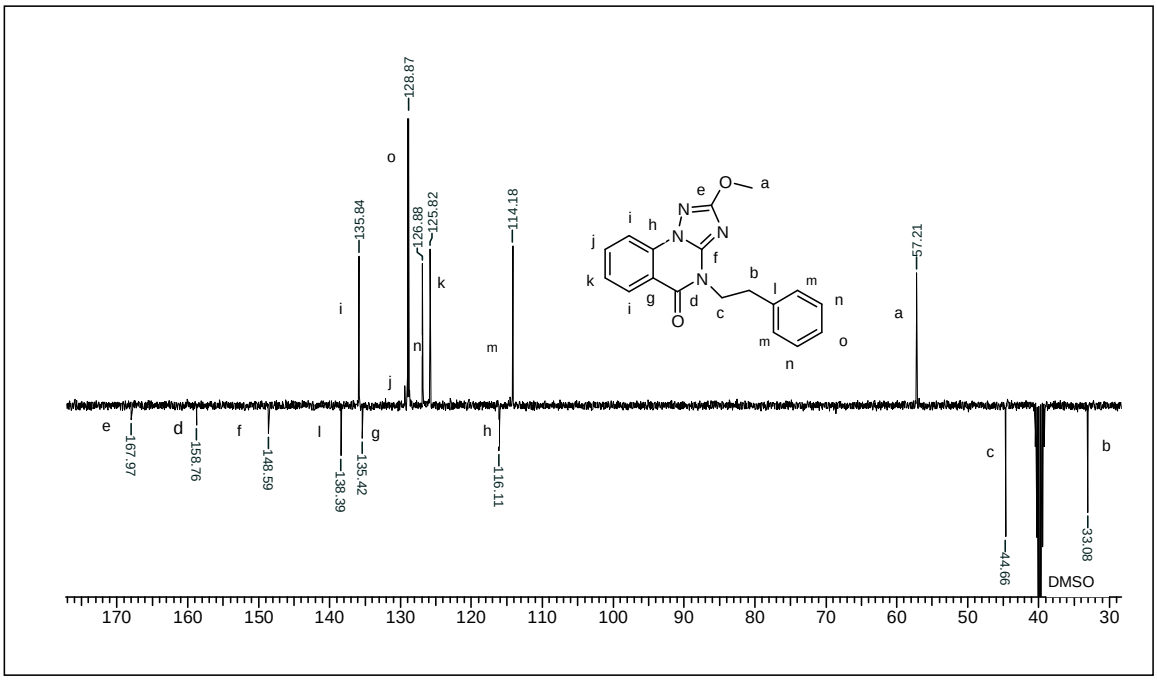


Fig. 9 *^{13}C NMR Spectrum of 2-Methoxy-4-phenethyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(12b)**

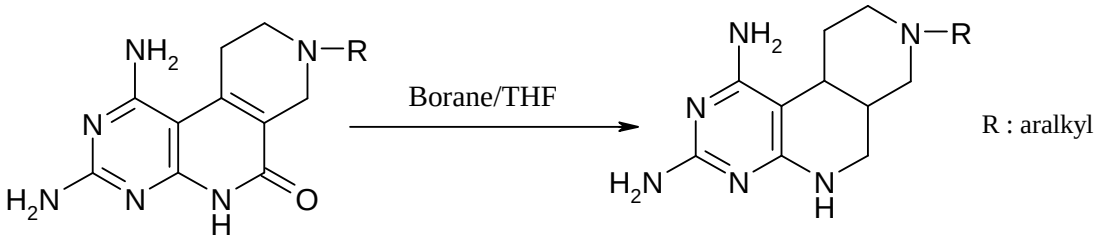


2.2.2 Hydrogenation of [1,2,4]Triazolo[1,5-a]quinazolin-5-ones (6)

2.2.2.1 Reduction of [1,2,4]Triazolo[1,5-a]quinazolin-5-ones (6) with Lithium Aluminium Hydride

The reduction of the lactam functionality offers an easy access to cyclic secondary or tertiary amines and plays an important role in alkaloid and drug chemistry [88, 94]. For instance, reduction of diamino-tetrahydropyrimido[4,5-c][2,7]naphthyridin-6(5H)-one (dihydrofolate reductase inhibitor (DHFR)[i]) **(14)** by borane-tetrahydrofuran, produced the analogue **15** which was found to bind towards DHFR more effectively. [95] (Scheme 13).

Scheme 13 *Reduction of Diamino-tetrahydropyrimido[4,5-c][2,7]naphthyridin-6(5H)-one* **(14)** [95]



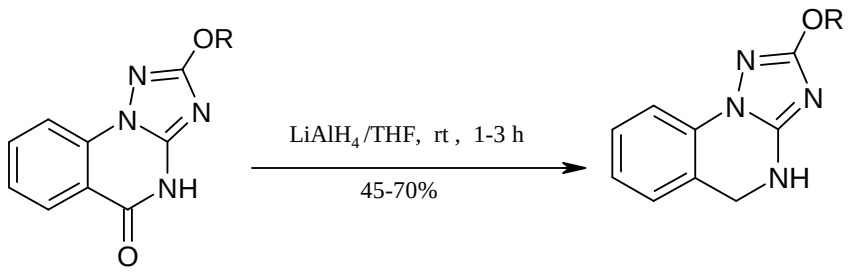
14 **15**

Reduction of lactams to amines may be performed by means of diisobutylaluminum hydride, [96] sodium borohydride, [97] lithium aluminum hydride, [98] alane, [99] sodium bis(2-methoxyethoxy)aluminum hydride, [100] rhodium-catalyzed hydrosilylation [101] and borane-tetrahydrofuran (BH_3-THF). [102]

[i] see the footnote in page 14

In this work, lithium aluminium hydride has been given preference for the reduction of the tricyclic compounds **6** in order to achieve (C=O)- to (CH_2)-conversion, thus providing the desired 4,5-dihydro-[1,2,4]triazoloquinazolines **16**. As a matter of fact, treatment of compounds **6a,b,d,f,e,g** with lithium aluminum hydride in absolute tetrahydrofuran at room temperature furnished the targeted 2-alkoxy(aralkoxy)-4,5-dihydro-[1,2,4]triazolo[1,5-a]quinazolines **16** in 45-70% yield (Table 4, Scheme 14). [103]

Scheme 14 *Preparation of 2-Alkoxy(aralkoxy)-4,5-dihydro-[1,2,4]triazolo[1,5-a]-quinazolines* **(16a-f)**



6a,b,d,f,e,g **16a-f**

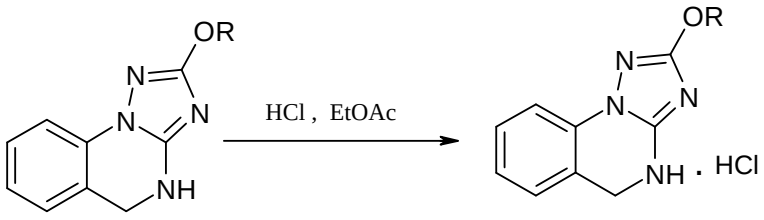
Table 4 *Prepared 2-Alkoxy(aralkoxy)-4,5-dihydro-[1,2,4]triazolo[1,5-a]quinazolines* **(16a-f)**

16	R	Yield [%]
A	CH_3	60
B	CH_3CH_2-	61
C	CH_2=$CHCH_2$-	55
D	$CH_3CH_2CH_2CH_2CH_2$-	45
E	$C_6H_5CH_2$-	70
F	$C_6H_5CH_2CH_2$-	64

The novel compounds **16a-f** were obtained after column chromatography as colorless solids and their structure was proven by IR, ^{1}H NMR, ^{13} C NMR spectra and microanalysis. The IR spectra of **16a-f** are characterized by a weak (NH)-band at 3167-3198 cm^{-1} and a (C=N)-absorption band at 1612-1645 cm^{-1} (Fig. 10). Representative ^{1}H NMR and ^{13}C NMR spectra of **16** are shown in Fig. 11 and 12.

Compared with the [1,2,4]triazoloquinazolin-5-ones **6**, the dihydro-[1,2,4]triazoloquinazolines **16** possess enhanced solubility in (dichloromethane, diethyl ether and ethyl acetate) and can be converted to the respective hydrochlorides (**17)** by treatment with hydrochloric acid (Scheme 15).

Scheme 15 *Preparation of 4,5-Dihydro-[1,2,4]triazolo[1,5-a]quinazoline Hydrochlorides* **(17)**



16 **17**

Fig. 10 *IR Spectrum of 4,5-Dihydro-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline* **(16f)**

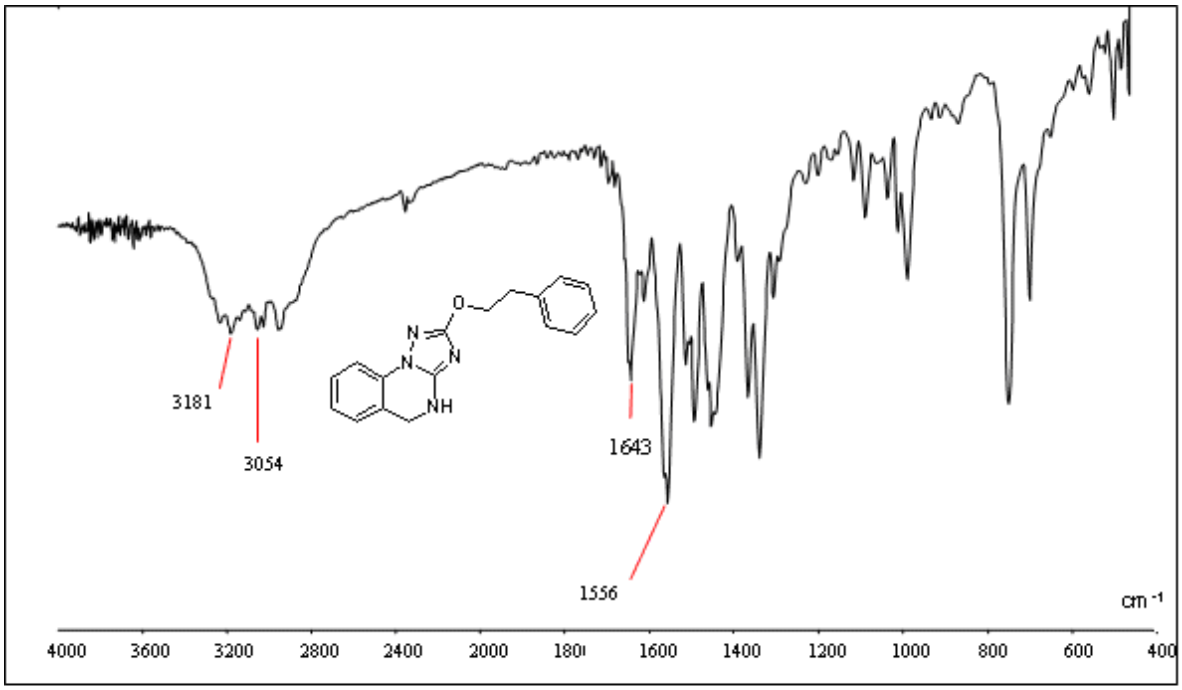


Fig. 11 *^{1}H NMR Spectrum of 4,5-Dihydro-2-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(16b)**

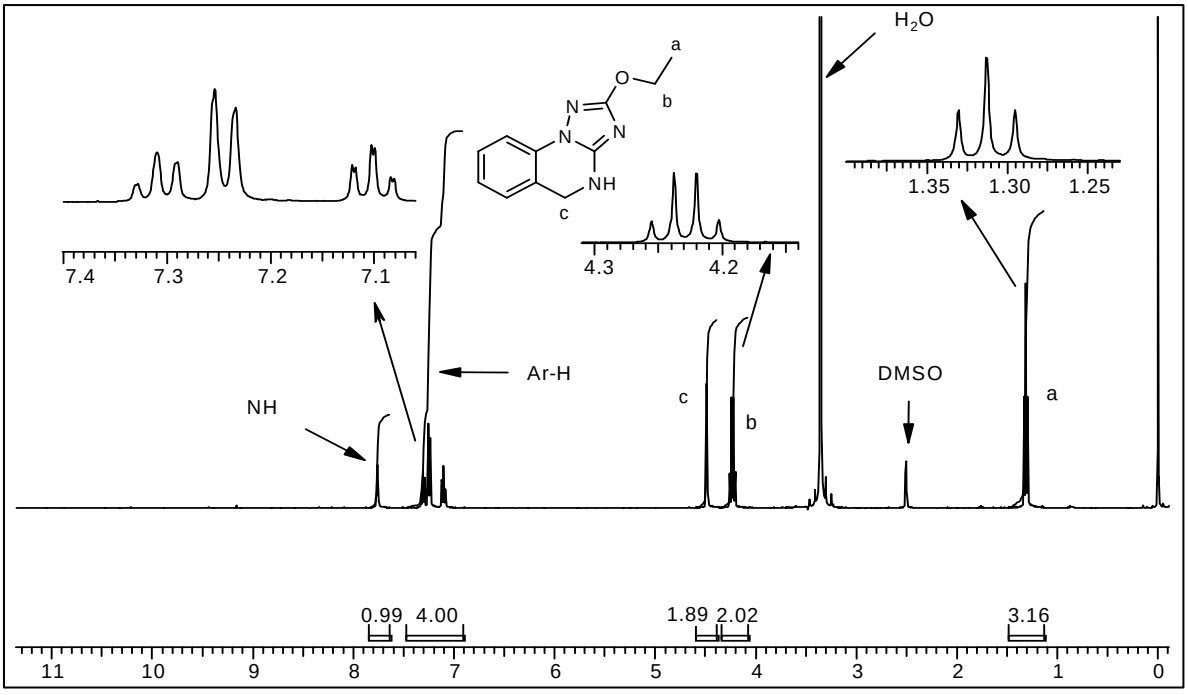
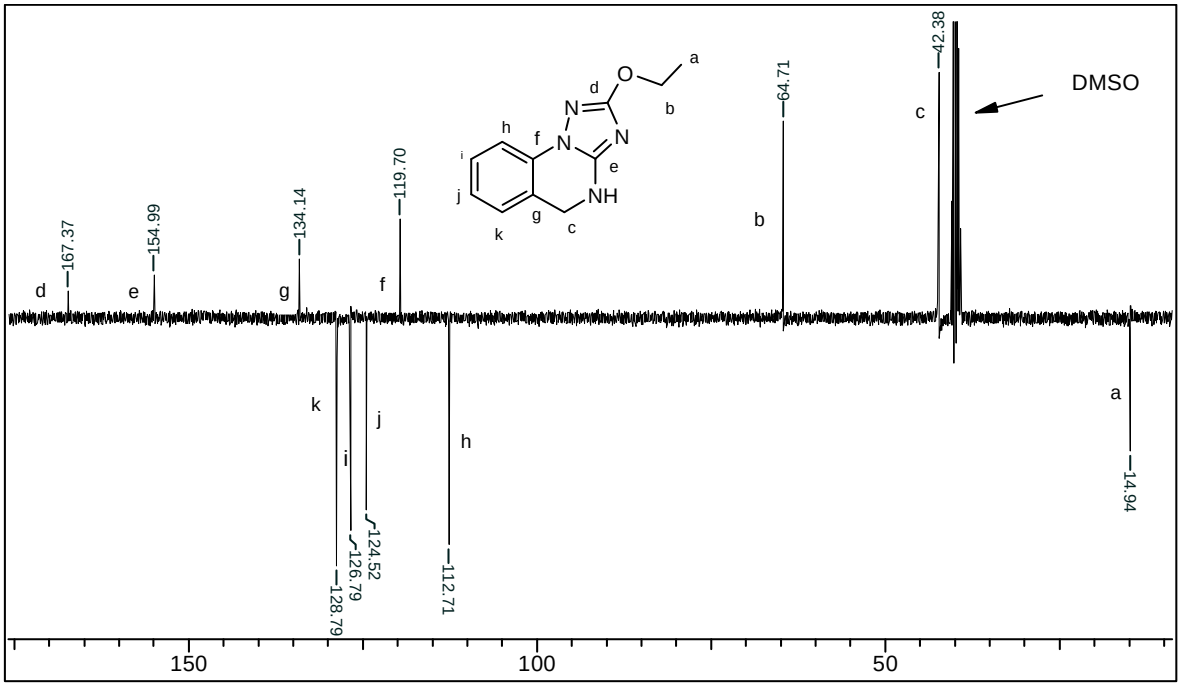


Fig. 12 *^{13}C NMR Spectrum of 4,5-Dihydro-2-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(16b)**

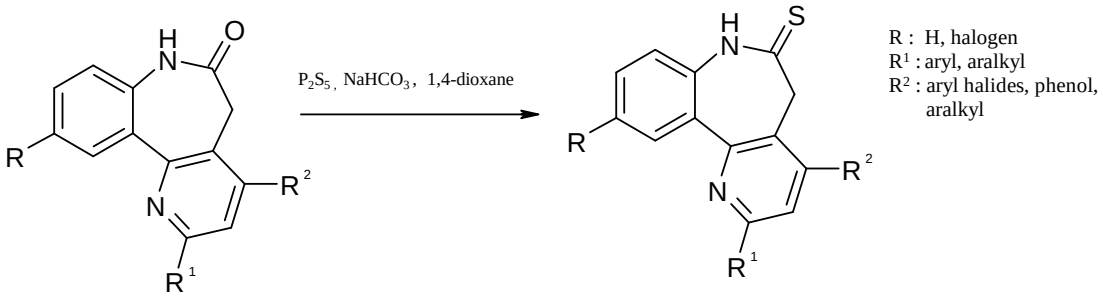


2.2.3 Thionation of [1,2,4]Triazoloquinazolin-5-ones (6) to [1,2,4]Triazolo-[1,5-a]quinazolin-5-thiones (27)

Thioamides/thiolactams are essential building blocks in organic synthesis and offer access to a plethora of diverse heterocyclic compounds.[104-110] Furthermore, thioamides/thiolactams deserve interest as bioactive compounds in agrochemsitry and medicinal chemistry. [111-115] Accordingly, there are numerous procedures for their preparation from amides and lactams. Of these methods, thionation of lactams with *Lawesson's reagent*[116] or phosphorous pentasulfide[117], have been preferentially applied. In addition, several thionating reagents, such as hydrogen sulphide (gas) [118], sulfur element [105] and hexamethyldisilathiane [106] were reported in literature .

For example, thionation of substituted pyrido[3,2-d][1]benzazepine-6(7H)-ones **(18)** with phosphorous pentasulfide in the presence of sodium hydrogencarbonate provided the corresponding thiolactam analogs (**19)** which were found to be highly active against renal cancer cell lines (Scheme 16). [119]

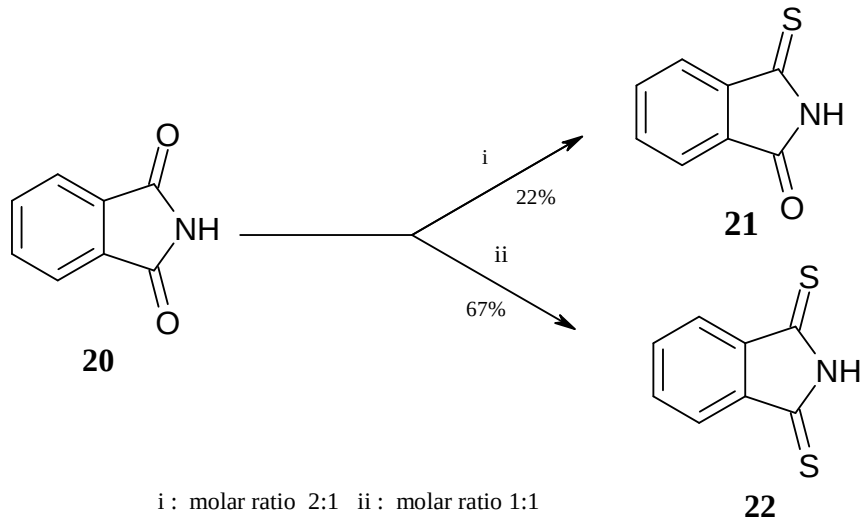
Scheme 16 *Thionation of Substituted Pyrido[3,2-d][1]benzazepine-6(7H)-ones* **(18)** *to Thiolactams* **(19)** [119]



18 **19**

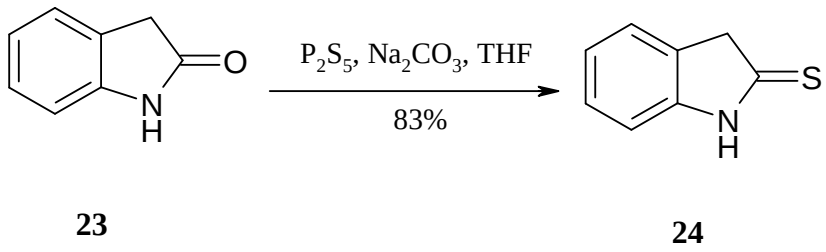
Depending on the molar ratio, phthalimide **(20)** was converted by Lawesson's reagent to either the monothionated analog (**21)** or dithionated derivative (**22)** in 22% or 67% yield, respectively [120] (Scheme 17).

Scheme 17 *Thionation of Phthalimide* **(20)** *with 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide* [120]



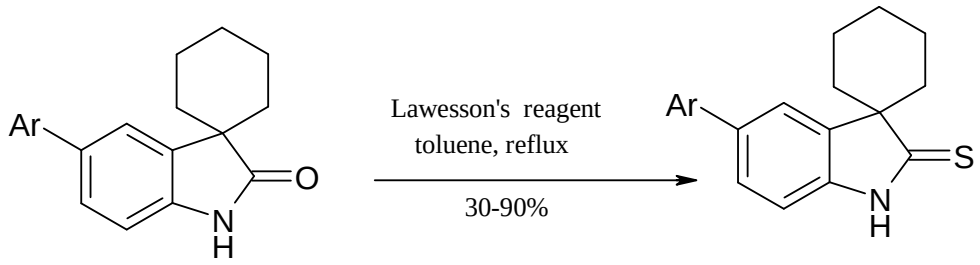
Conversion of oxindole **(23)** to 2-thioxoindoline (**24**), an important building block for tyrosine kinase inhibitors, has been achieved with phosphorous pentasulfide in the presence of sodium carbonate in excellent yield of 83% (Scheme 18). [121]

Scheme 18 *Thionation of Oxindole* **(23)** *to 2-Thioxoindoline* **(24)** [121]



Orally active progesterone receptor ***agonists*** of type **26** have been obtained from the appropriate oxindoles **(25)**[j] by treatment with Lawesson's reagent in moderate to excellent yield [122] (Scheme 19).

Scheme 19 *Synthesis of Spirocyclic Thioxoindolines* **(26)** *as Progesterone Receptor Agonists* [122]

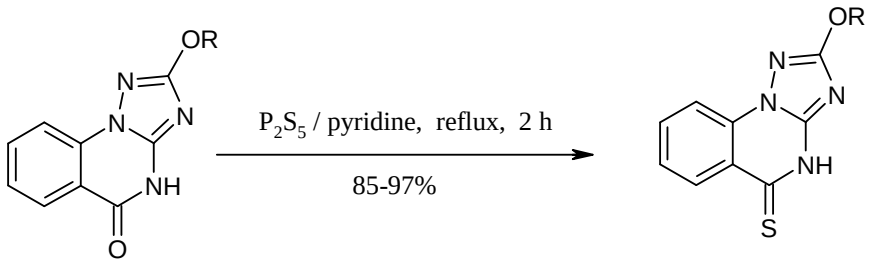


25 **26**

Based on these bioactive thiolactams, my interest arose whether the novel [1,2,4]triazoloquinazolin-5-thiones **27** could simply be obtained by thionation of the corresponding [1,2,4]triazoloquinazolin-5-ones **6**. Luckily, when equimolar amounts of [1,2,4]triazoloquinazolin-5-ones **6a,b,e,f,g** and phosphorous pentasulfide were allowed to react in absolute pyridine under reflux for 2 h, the targeted 2-alkoxy(aralkoxy)-4*H*-[1,2,4]triazolo[1,5-a]quinazolin-5-thiones **27** could be isolated in excellent yields of 85-97% as yellow solids (Table 5, Scheme 20). [123]

[j] The oxindoles of type **25** display progesterone ***antagonistic*** activity .[122]

Scheme 20 *Preparation of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thiones* **(27a-e)**



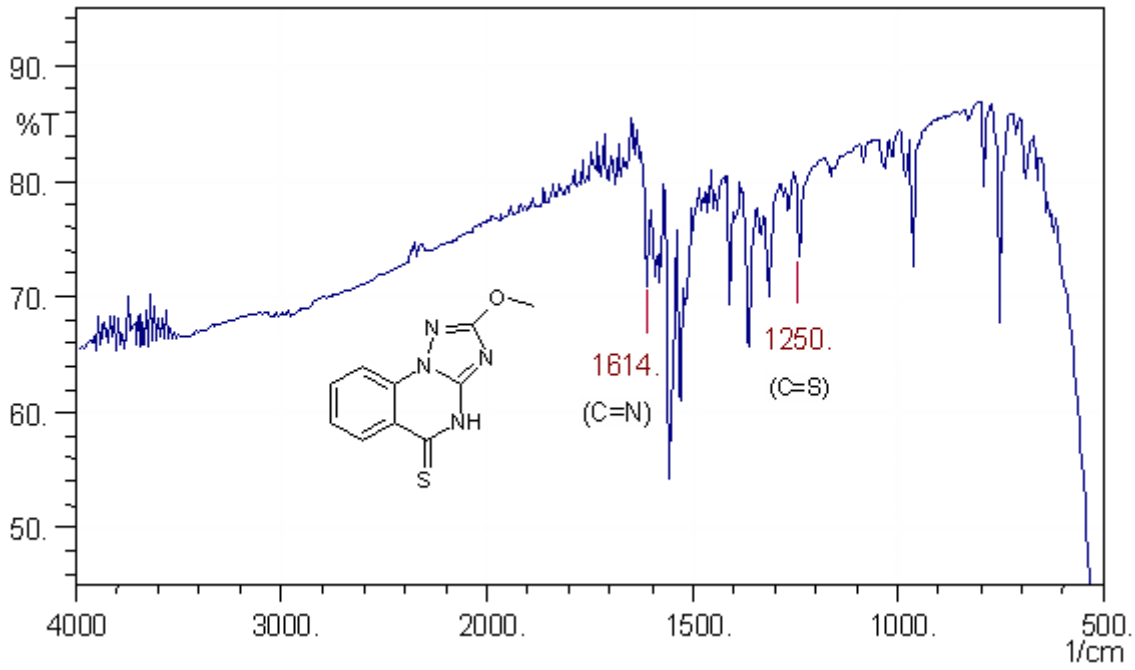
6a,b,e,f,g **27a-e**

Table 5 *Prepared 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thiones* **(27a-e)**

27	R	Yield [%]
A	CH_3	85
B	CH_3CH_2-	92
C	CH_2=$CHCH_2$-	95
D	$C_6H_5CH_2$-	97
E	$C_6H_5CH_2CH_2$-	89

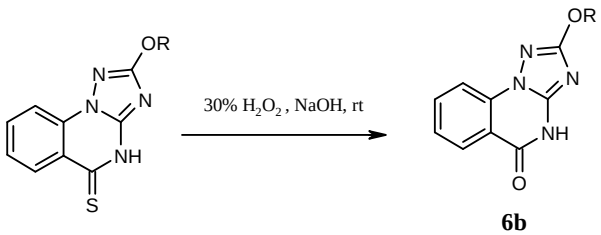
The structure of the compounds **27**[k] was proven by IR, ^{1}H NMR, ^{13}C NMR spectra (Fig. 13-15), and microanalysis. The IR spectra of **27a-f** display a weak absorption band at 1244-1257 cm^{-1} (C=S) and the ^{13}C NMR spectra are characterized by a (C=S) resonance at 184.9-185.6 ppm.

Fig. 13 *IR Spectrum of 2-Methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione* **(27a)**



[k] As exemplified by **27b**, the thioxo group could easily be desulfurized with 30% hydrogen peroxide in basic medium at ambient temperature to yield **6b** (Scheme 21). [124]

Scheme 21 *Desulfurization of Thiolactam* **(27b)** *to the corresponding Lactam* **(6b)**



27b **6b**

Fig. 14 *^{1}H NMR Spectrum of 2-Allyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione* **(27c)**

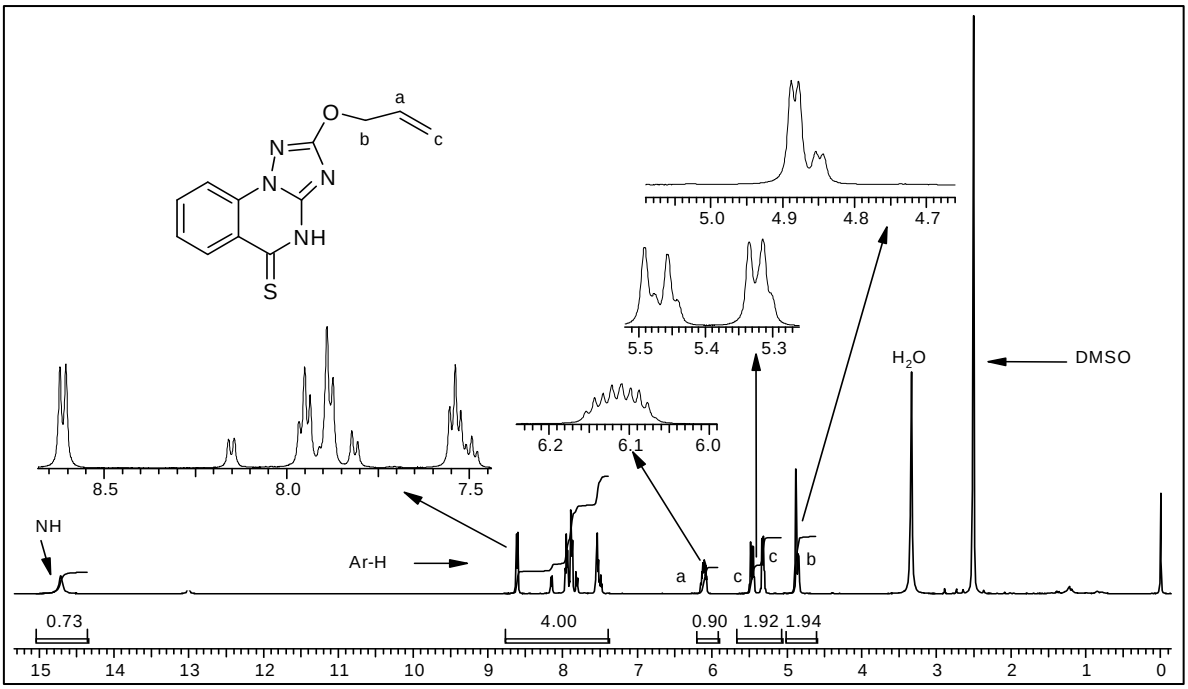
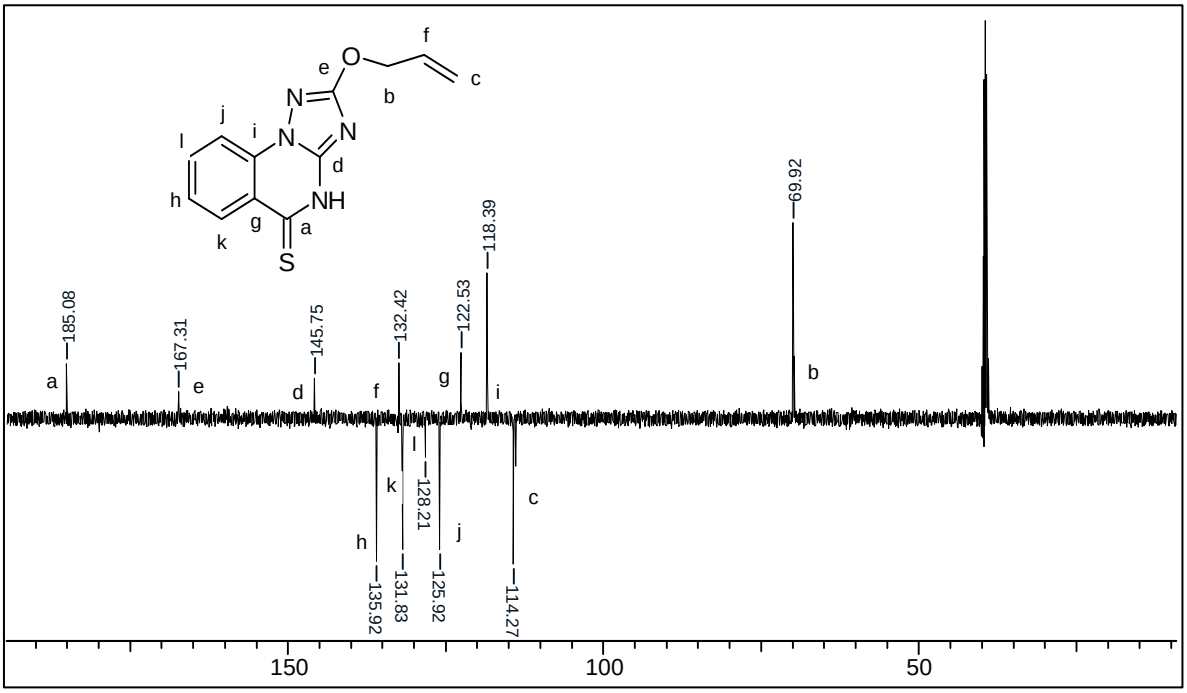


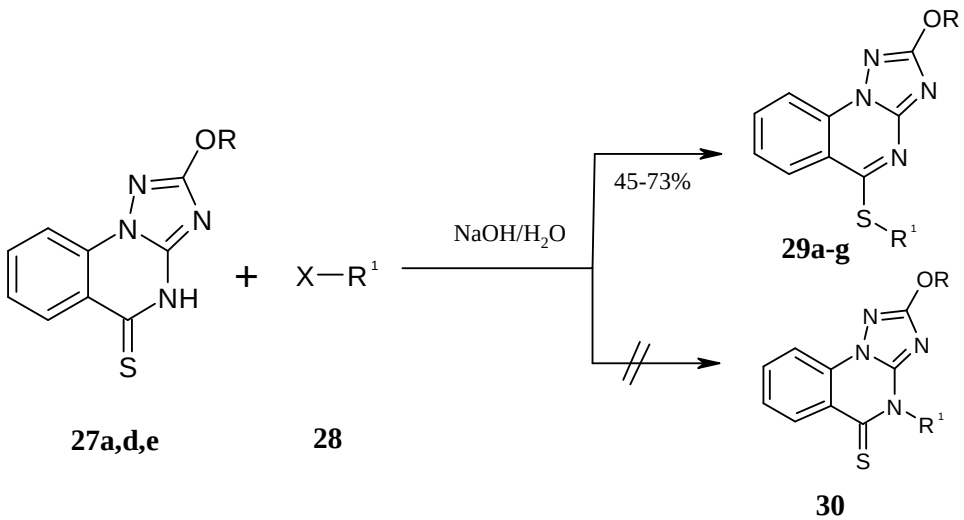
Fig. 15 *^{13}C NMR Spectrum of 2-Allyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione* **(27c)**



2.2.3.1 Alkylation of [1,2,4]Triazoloquinazolin-5-thiones (27) with Alkyl-Halides

Treatment of the [1,2,4]triazoloquinazolin-5-thiones **27a,d** with different alkyl halides **(28)** in aqueous 0.5 M sodium hydroxide solution afforded smoothly the expected thioethers **29a-e** in 58-73% yield [124] (Scheme 22). The analogous reaction of **27d** with 2-(chloromethyl)pyridine in methanol in the presence of sodium methoxide afforded **29f** in 45% yield [125] and alkylation of **27e** with bromoacetic acid in ethanol produced 2-phenethyloxy-[1,2,4]triazoloquinazolin-5-ylsulfanyl-acetic acid (**29g)** in 56% yield.[126]

Scheme 22 *Preparation of 2-Alkoxy(aralkoxy)-5-alkyl(aralkyl)sulfanyl-[1,2,4]triazolo-[1,5-a]quinazolines* **(29a-g)**



The thioethers **29a-g** were obtained as pure, colored (yellow or brown) solids after recrystallization from ethanol and their structure has been confirmed by IR, ^{1}H NMR,^{13}C NMR spectra (Fig. 16-18) and microanalysis.

Table 6 *Prepared 2-Alkoxy(aralkoxy)-5-alkyl(aralkyl)sulfanyl-[1,2,4]triazolo-[1,5-a]quinazolines* **(29a-g)**

29	R	R^1	Yield [%]
a	CH_3	CH_2=$CHCH_2$-	70
b	$C_6H_5CH_2$-	CH_3	73
c	CH_3	HC≡CCH_2-	61
d	CH_3	CH_3	60
e	CH_3	$C_6H_5CH_2$-	58
f	$C_6H_5CH_2$-	Pyridin-2-ylmethyl	45
g	$C_6H_5CH_2CH_2$-	$HCOOCH_2$-	56

Fig. 16 *IR Spectrum of 5-Allylsulfanyl-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(29a)**

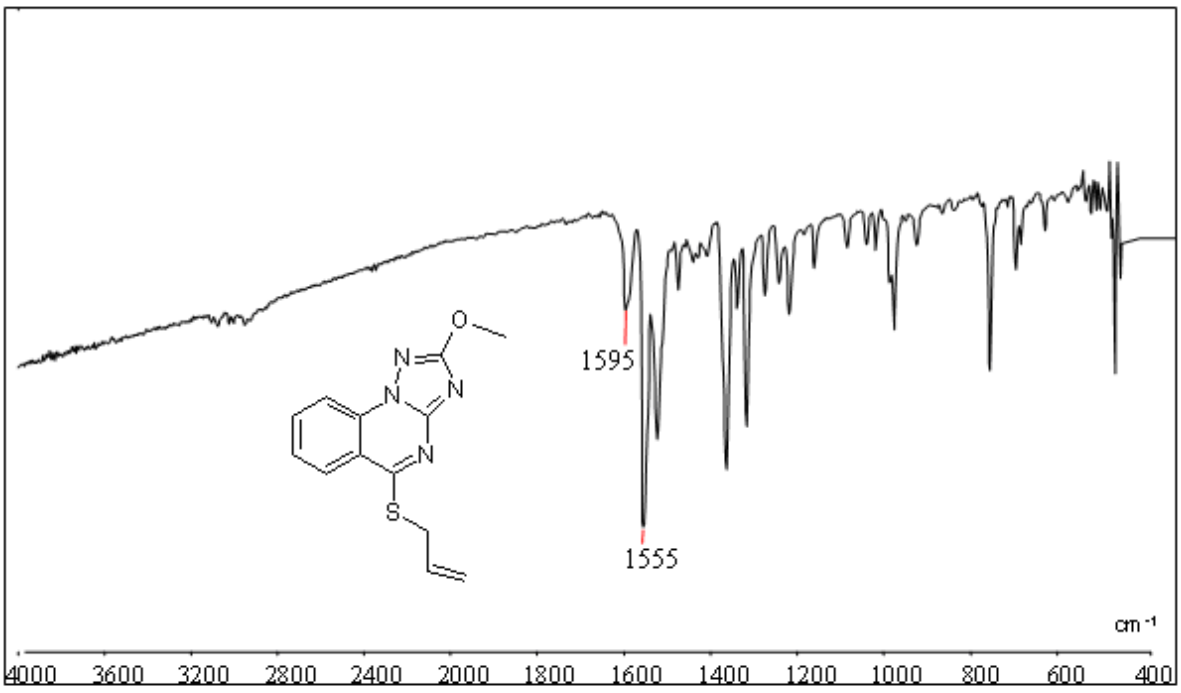


Fig. 17 *^{1}H NMR Spectrum of 5-Allylsulfanyl-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(29a)**

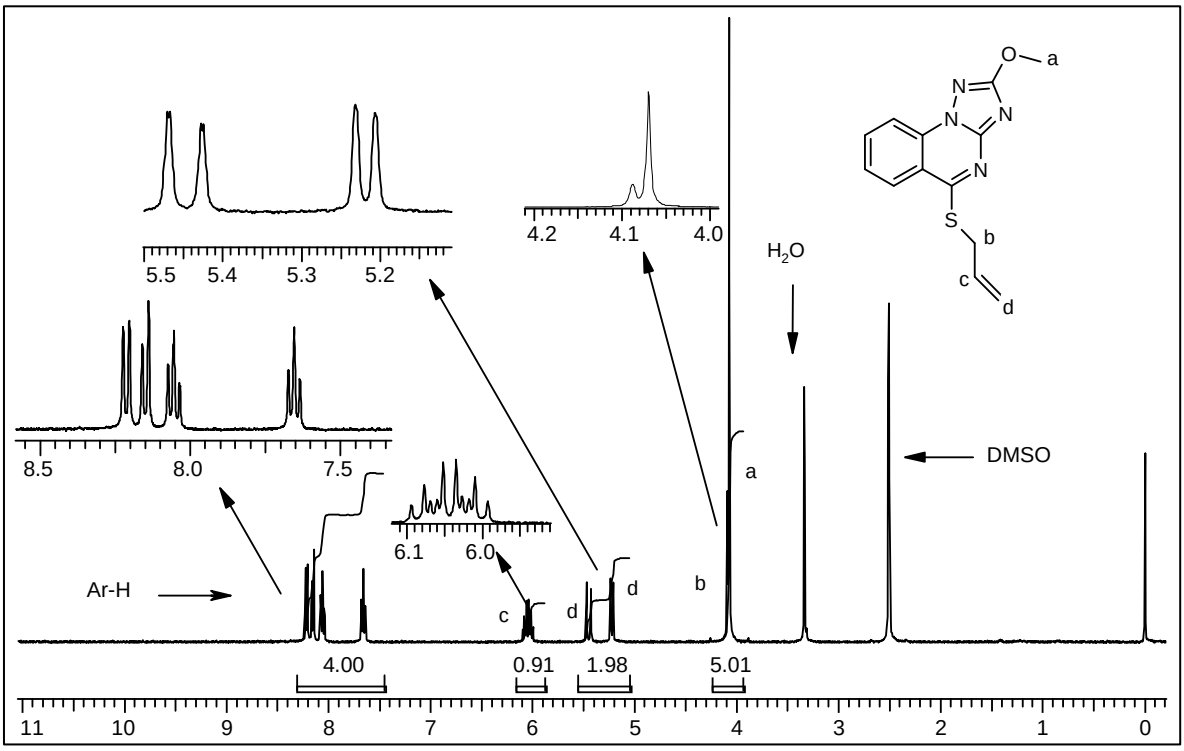
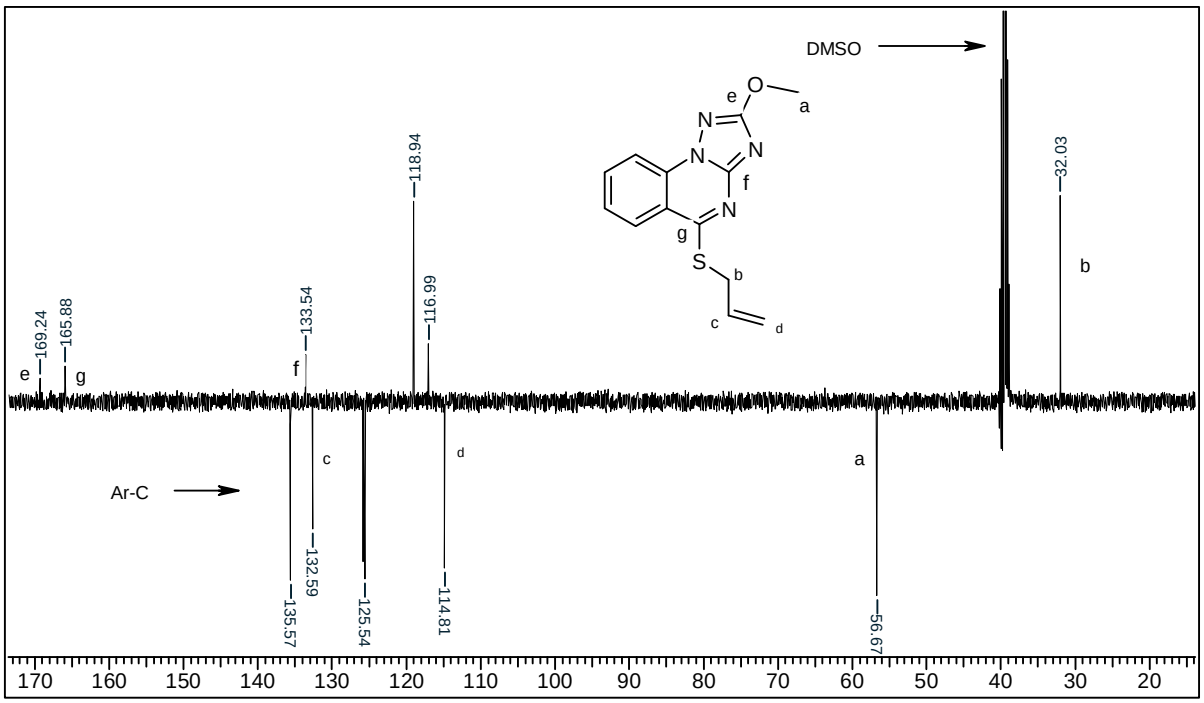


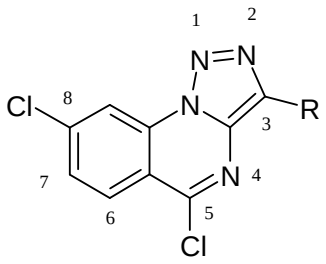
Fig. 18 *^{13}C NMR Spectrum of 5-Allylsulfanyl-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(29a)**



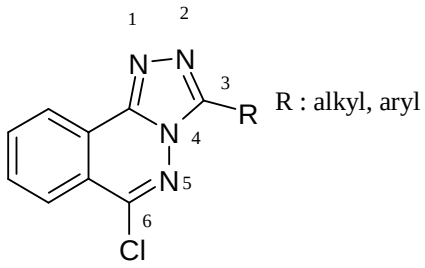
2.2.4 Chlorination of [1,2,4]Triazoloquinazolin-5-ones (6) with Oxalyl Chloride or Phosphorous Oxychloride to give 5-Chloro-[1,2,4]triazolo-quinazolines (31)

After having prepared successfully a number of [1,2,4]triazolo[1,5-a]quinazolin-5-thiones **27**, it was of interest to convert the lactam moiety in **6** into an imidoyl chloride functionality (**31**), which was not only expected to be a valuable compound for further nucleophilic displacement reactions but also may contribute as a pharmacophore to the bioactivity of **6**.

For example, it has been demonstrated that introduction of electron withdrawing atoms or groups in ring positions 5, 6 and 8 of the [1,2,3]triazolo[1,5-a]quinazolines (**XXX**) or [1,2,4]triazolo[3,4-a]phthalazine (**XXXI**) enhance strongly the binding affinity towards benzodiazepine and adenosine A_1, A_{2A} receptors.[127, 128]



XXX

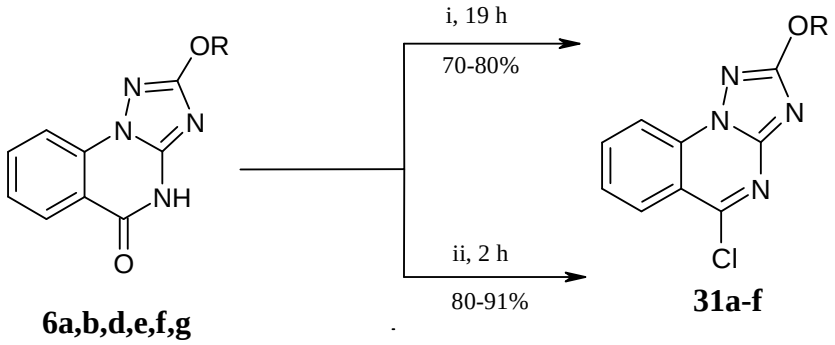


R : alkyl, aryl

XXXI

Within this thesis, conversion of [1,2,4]triazoloquinazolin-5-ones **(6)** into 5-chloro-[1,2,4]triazolo[1,5-a]quinazolines **31** has been successfully achieved by chlorination with either oxalyl chloride in boiling 1,1,2-trichloroethane for 19 h [77] or with phosphorous oxychloride in boiling benzene for 2 h, followed by trituration with a saturated solution of potassium carbonate (Scheme 23).[129]

Scheme 23 *Preparation of 2-Alkoxy(aralkoxy)-5-chloro-[1,2,4]triazolo[1,5-a]quinazolines* **(31a-f)**



6a,b,d,e,f,g **31a-f**

i : $C_2O_2Cl_2$, 1,1,2-trichloroethane ii : $POCl_3$, benzene

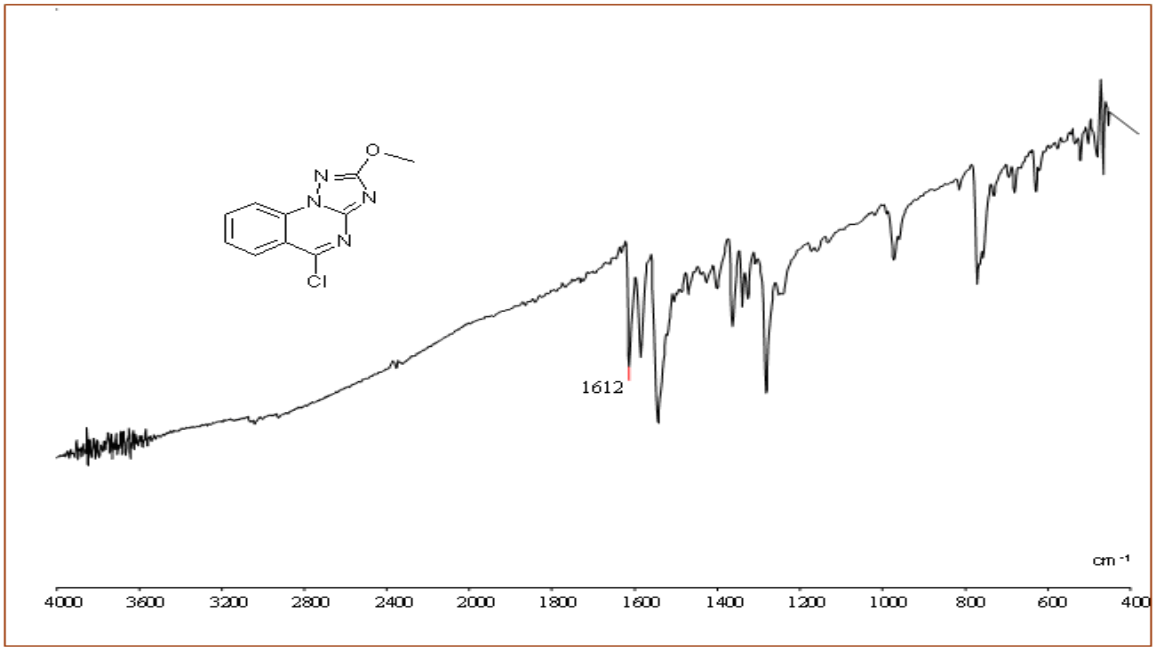
The synthesized 5-chloro-[1,2,4]triazoloquinazolines **31a-f** were obtained as colored (yellow or brown) solids and were purified by recrystallization from tetrahydrofuran.

Conversion of **6** into **31** could be monitored either by IR spectroscopy or thin layer chromatography. Samples were taken at various intervals of time and examined by IR spectroscopy. The formation of **31** was accompanied by the gradual disappearance of the characteristic (C=O) band of **6** at 1685-1705 cm^{-1} (Fig. 19). Representative ^{1}H NMR and ^{13}C NMR spectra of **31** are shown in Fig. 20 and 21.

Table 7 *Prepared 2-Alkoxy(aralkoxy)-5-chloro-[1,2,4]triazolo[1,5-a]quinazolines* **(31a-f)**[1]

31	R	Yield [%] with $C_2O_2Cl_2$	Yield [%] with $POCl_3$
a	CH_3	70	80
b	CH_3CH_2-	72	89
c	CH_2=$CHCH_2$-	70	87
d	$CH_3CH_2CH_2CH_2CH_2$-	60	81
e	$C_6H_5CH_2$-	80	90
f	$C_6H_5CH_2CH_2$-	75	91

Fig. 19 *IR Spectrum of 5-Chloro-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(31a)**



[1] Although both methods gave acceptable yields, the reaction of **6** with phosphorous oxychloride is more advantageous with regard to short reaction time and higher yields**.**

Fig. 20 *[1]H NMR Spectrum of 5-Chloro-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline* **(31f)**

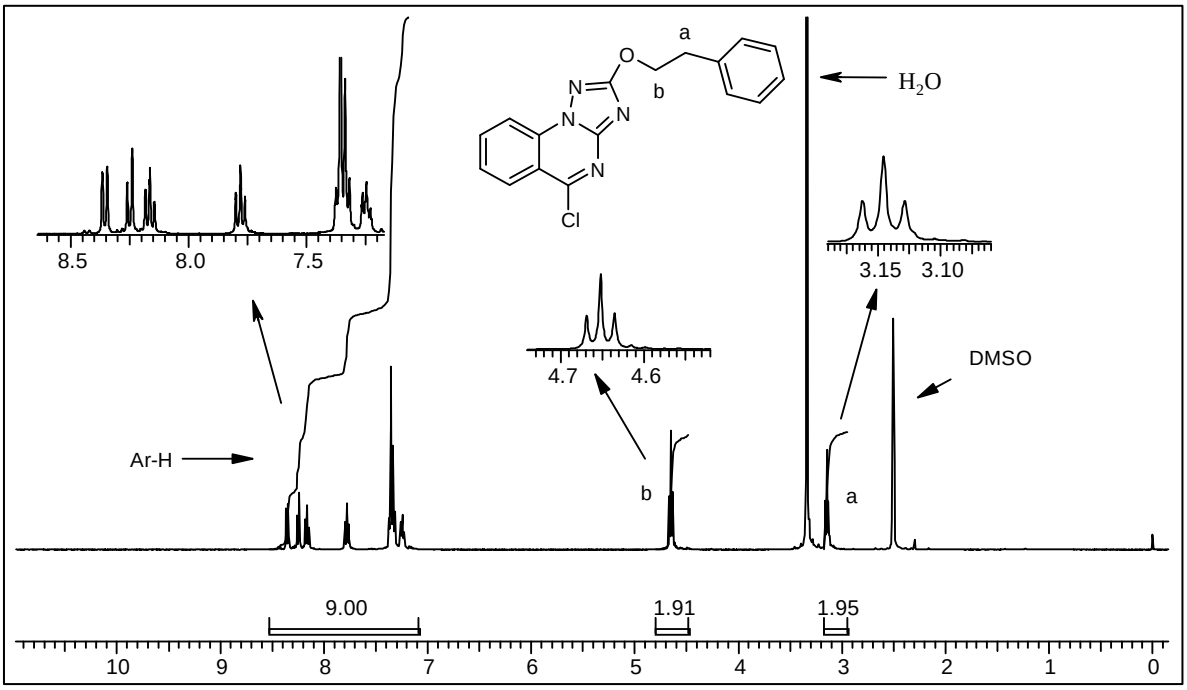
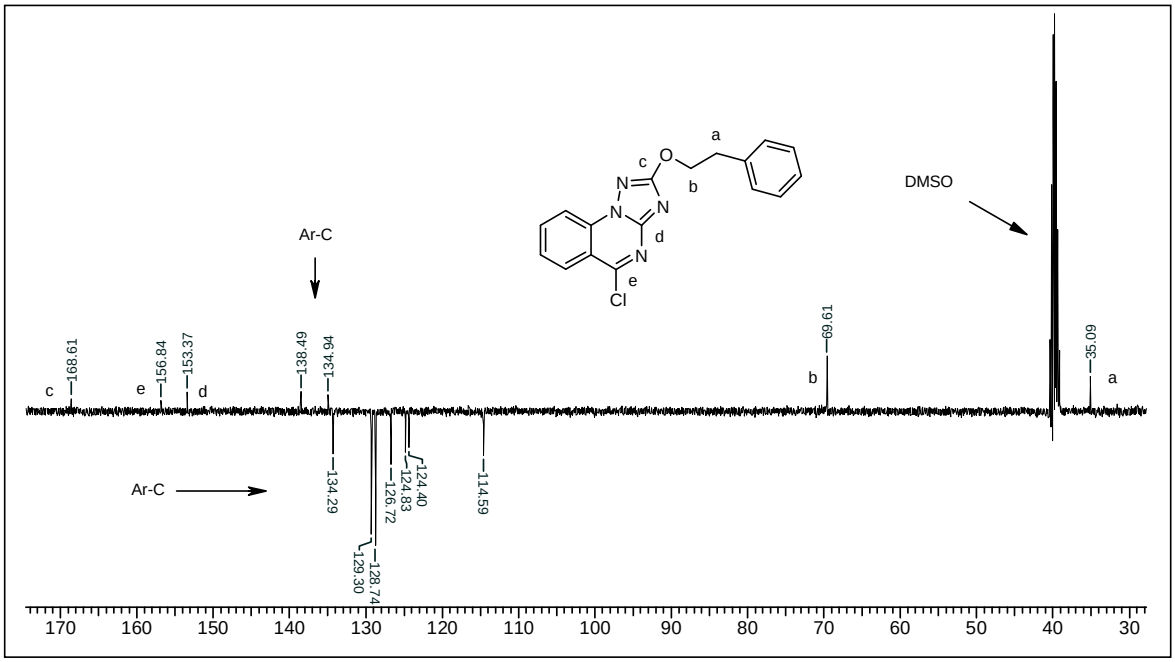


Fig. 21 *[13]C NMR Spectrum of 5-Chloro-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline* **(31f)**



2.2.4.1 Hydrazinolysis of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Hydrazine Hydrate

By hydrazinolysis of **31a,b,d,e,f,g** in boiling ethanol were formed the corresponding [1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazines **32** in good yields of 60-78% (Scheme 24). [124] Likewise, the appropriate thioxo derivatives **27** could be transformed into **32** as well in satisfactory yields of 61-67%.[130]

The IR spectra of the [1,2,4]triazoloquinazolin-5-yl-hydrazines **32a-f** are characterized by a (NH) absorption band at 3183-3291 cm^{-1} (Fig. 22). Representative ^{1}H NMR and ^{13}C NMR spectra are shown in Fig. 23 and 24.

Scheme 24 *Preparation of 2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazines* **(32a-f)**

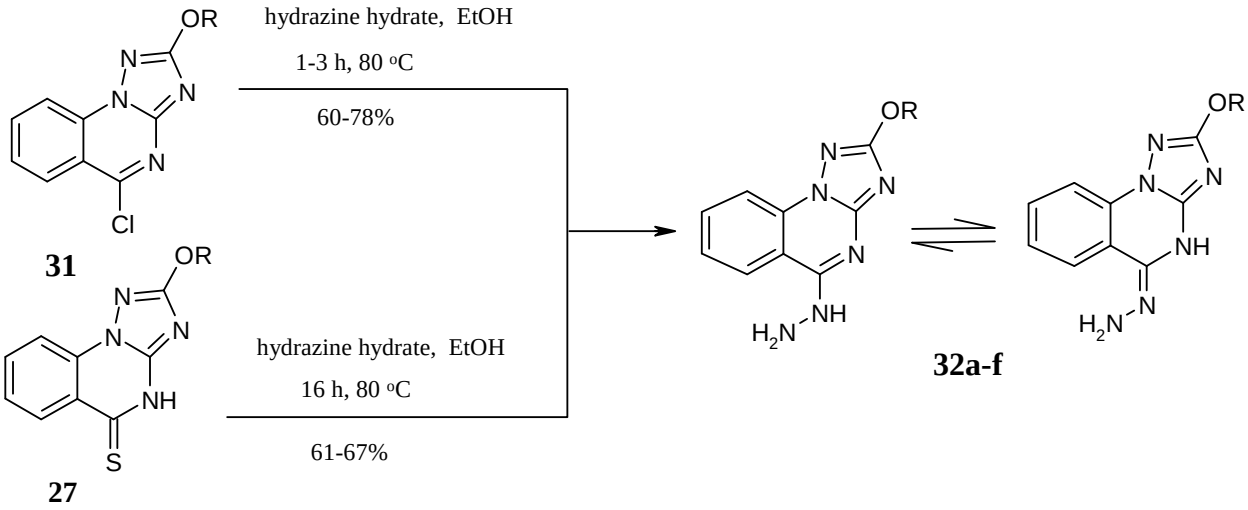


Table 8 *Prepared 2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazines* **(32a-f)**

32	R	Yield[%]
A	CH_3	60
B	CH_3CH_2-	69
C	CH_2=$CHCH_2$-	71
D	$CH_3CH_2CH_2CH_2CH_2$-	62
E	$C_6H_5CH_2$-	78
F	$C_6H_5CH_2CH_2$-	72

Fig. 22 *IR Spectrum of 2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine* **(32e)**

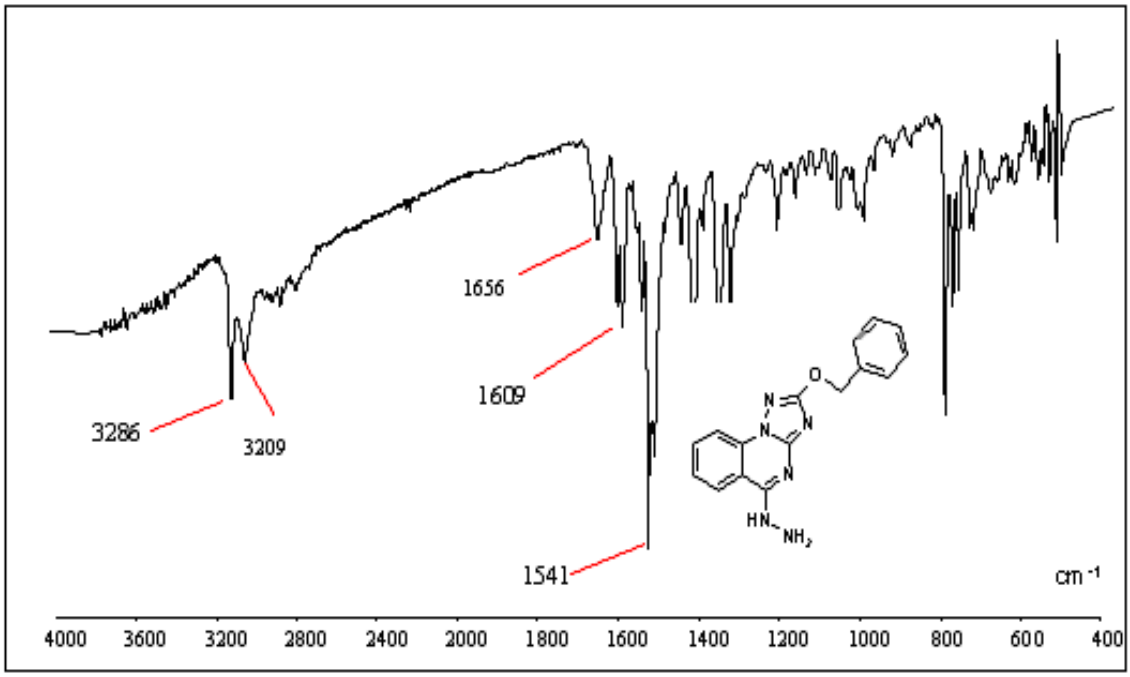


Fig. 23 *[1]H NMR Spectrum of 2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine* **(32e)**

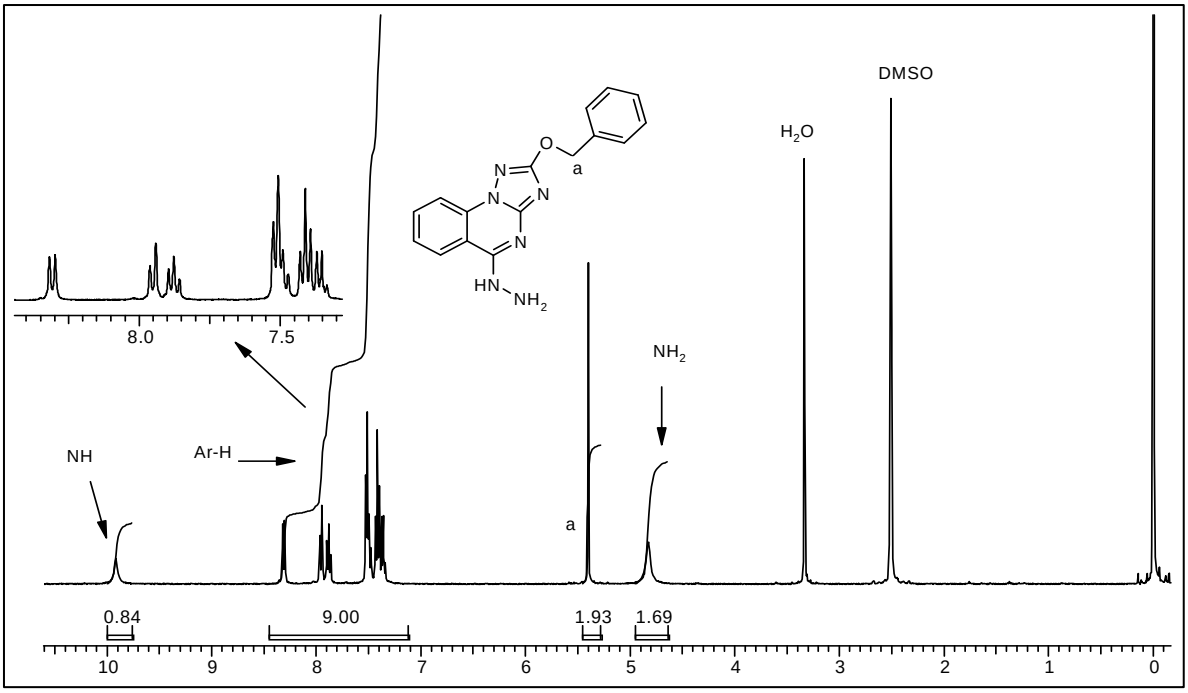
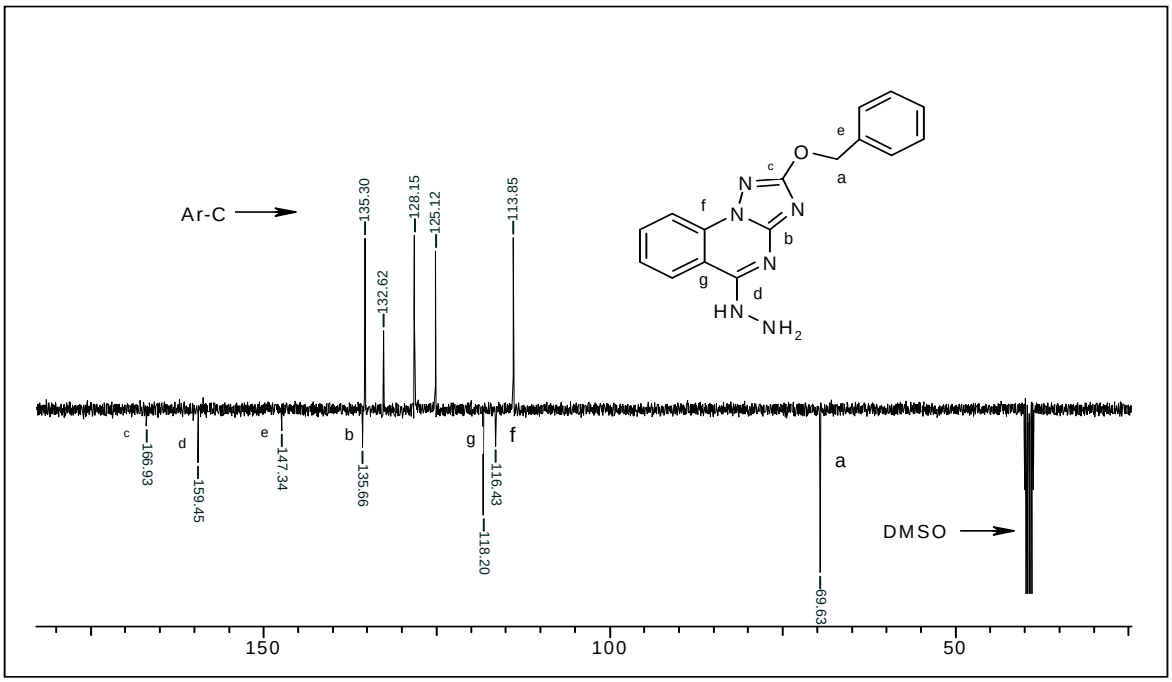


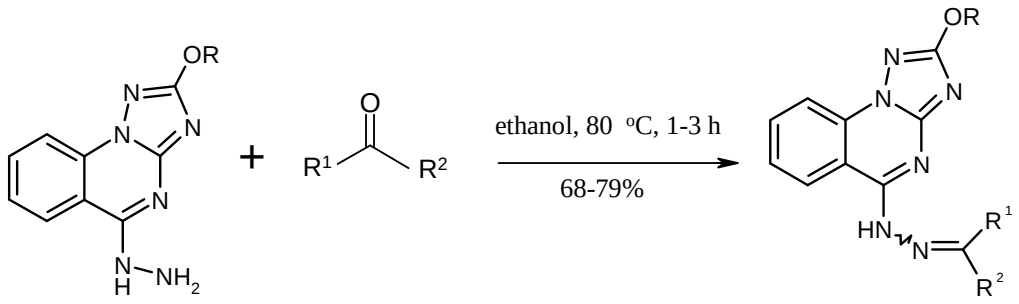
Fig. 24 *[13]C NMR Spectrum of 2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine* **(32e)**



2.2.4.1.1 Reaction of [1,2,4]Triazoloquinazolin-5-yl-hydrazines (32) with Aldehydes and Ketones

When equimolar amounts of compounds **32a,e,f** were reacted with benzaldehyde, acetone or acetophenone **(33)** in boiling ethanol for 1-3 h, the expected hydrazones **(34)** resulted in good yields of 68-79% [131] (Scheme 25). The synthesized **34a-d** were characterized by ^{1}H NMR and ^{13}C NMR spectra (Fig. 25, 26) and microanalysis.

Scheme 25 *Preparation of N-Aryl(alkylaryl)idene-N'-(2-alkoxy(aralkoxy)-[1,2,4]triazolo-[1,5-a]quinazolin-5-yl-hydrazines* **(34a-d)**



32a,e,f **33** **34a-d**

Table 9 *Prepared N-Aryl(alkylaryl)idene-N'-(2-alkoxy(aralkoxy)-[1,2,4]triazolo-[1,5-a]quinazolin-5-yl-hydrazines* **(34a-d)**

34	R	R^1	R^2	Yield[%]
a	CH_3	CH_3	CH_3	70
b	$C_6H_5CH_2$-	CH_3	CH_3	73
c	$C_6H_5CH_2CH_2$-	H	C_6H_5	79
d	$C_6H_5CH_2CH_2$-	CH_3	C_6H_5	68

Fig. 25 *^{1}H NMR Spectrum of N-Isopropylidene-N'-(2-benzyloxy-[1,2,4]triazolo[1,5-a]-quinazolin-5-yl-hydrazine* **(34b)**

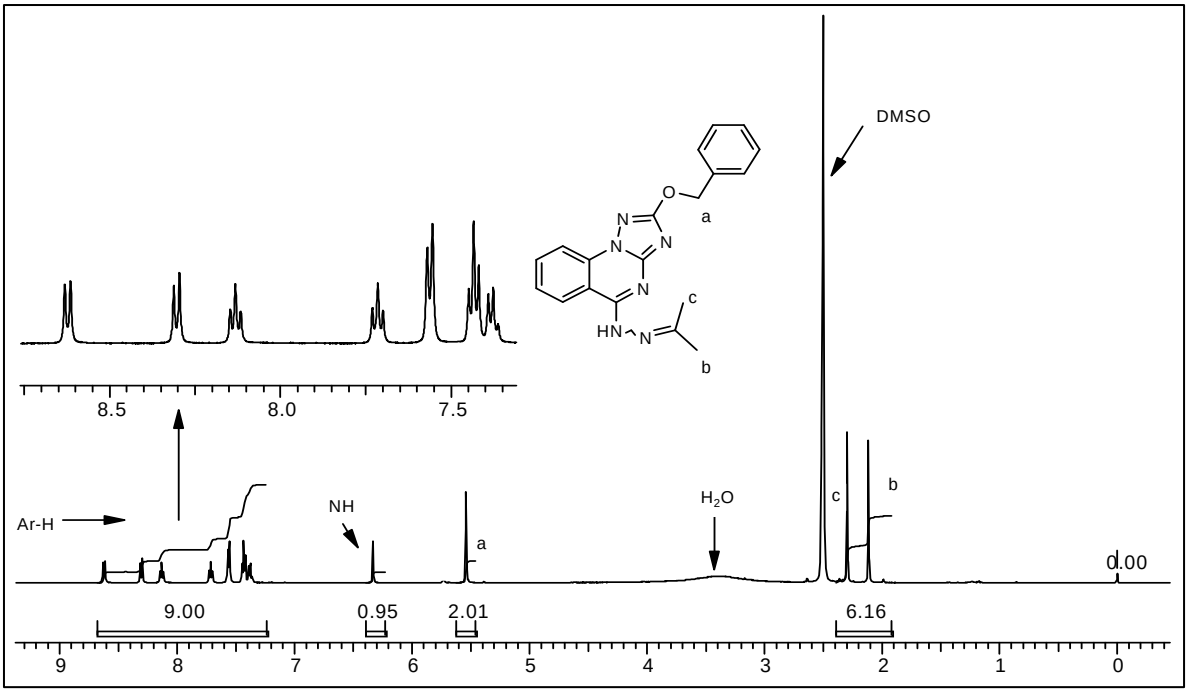
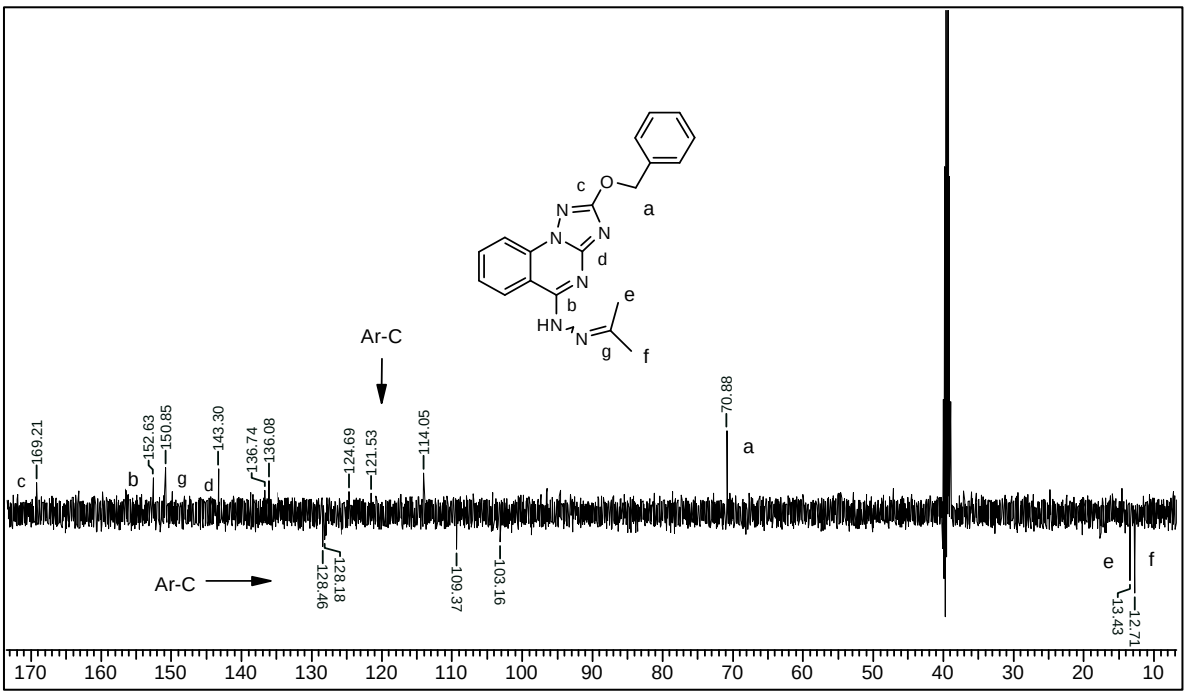


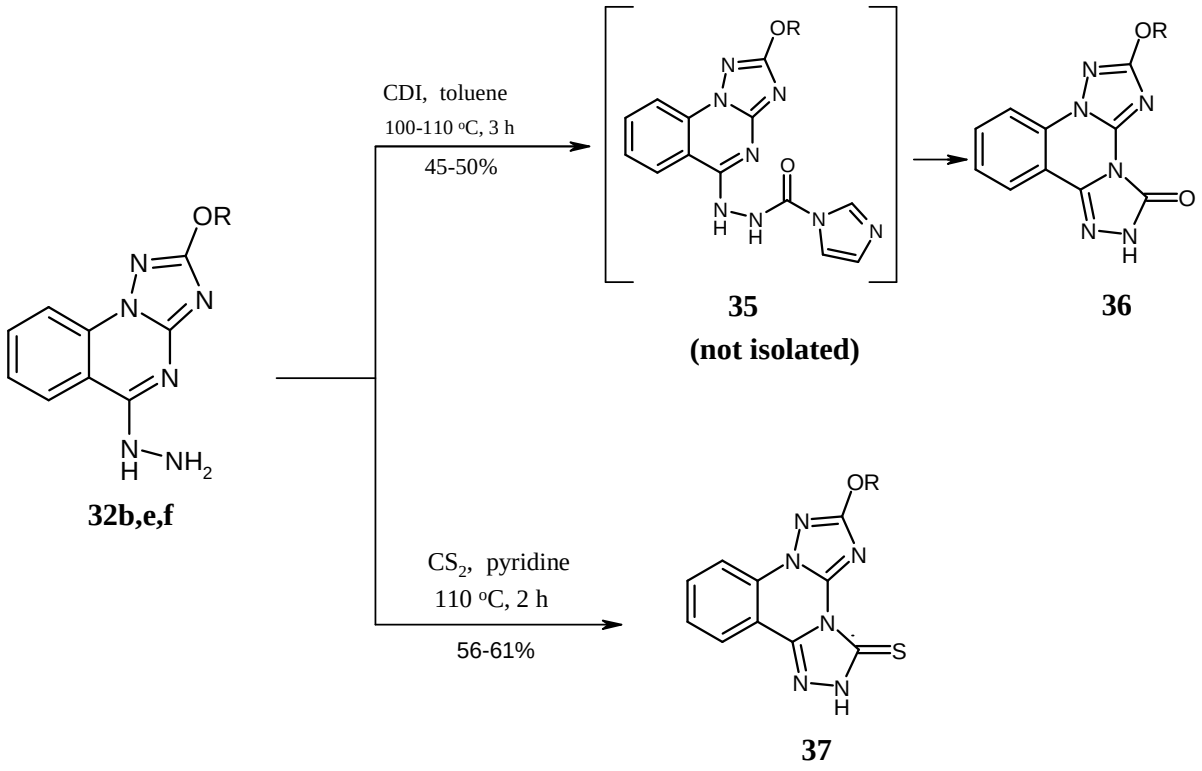
Fig. 26 *^{13}C NMR Spectrum of N-Isopropylidene-N'-(2-benzyloxy-[1,2,4]triazolo[1,5-a]-quinazolin-5-yl-hydrazine* **(34b)**



2.2.4.1.2 Reaction of [1,2,4]Triazoloquinazolin-5-yl-hydrazines (32) with 1,1′-Carbonyldiimidazole and Carbon Disulfide

Reaction of **32b,e** with 1,1′-carbonyldiimidazole in a molar ratio of 1:1.2 in boiling absolute toluene for 3 h provided the until hitherto unknown bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-ones (**36a,b)** in 45-50% yield. [132] Similarly, the corresponding thioxo derivatives **37a,b** could be obtained in 56-61 % yield from the reaction of **32e,f** with carbon disulfide in a molar ratio of 1:10 in boiling pyridine for 2 h [133] (Scheme 26).

Scheme 26 *Preparation of 2-Alkoxy(aralkoxy)-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-ones(thiones)* **(36, 37)**



The IR spectra of **36a,b** display strong (C=O) absorption bands at 1705 and 1709 cm^{-1} (Fig. 27), and the ^{13}C NMR spectra of **37a,b** are characterized by a (C=S) resonance at 185.00 and 185.7 ppm (Fig. 28).

Table 10 *Prepared 2-Alkoxy(aralkoxy)-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-ones(thiones)* **(36, 37)**

Entry	R	Yield[%]
36a	CH_3CH_2-	45
36b	$C_6H_5CH_2$-	50
37a	$C_6H_5CH_2$-	61
37b	$C_6H_5CH_2CH_2$-	56

Fig 27 *IR Spectrum of 2-Ethoxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-one* **(36a)**

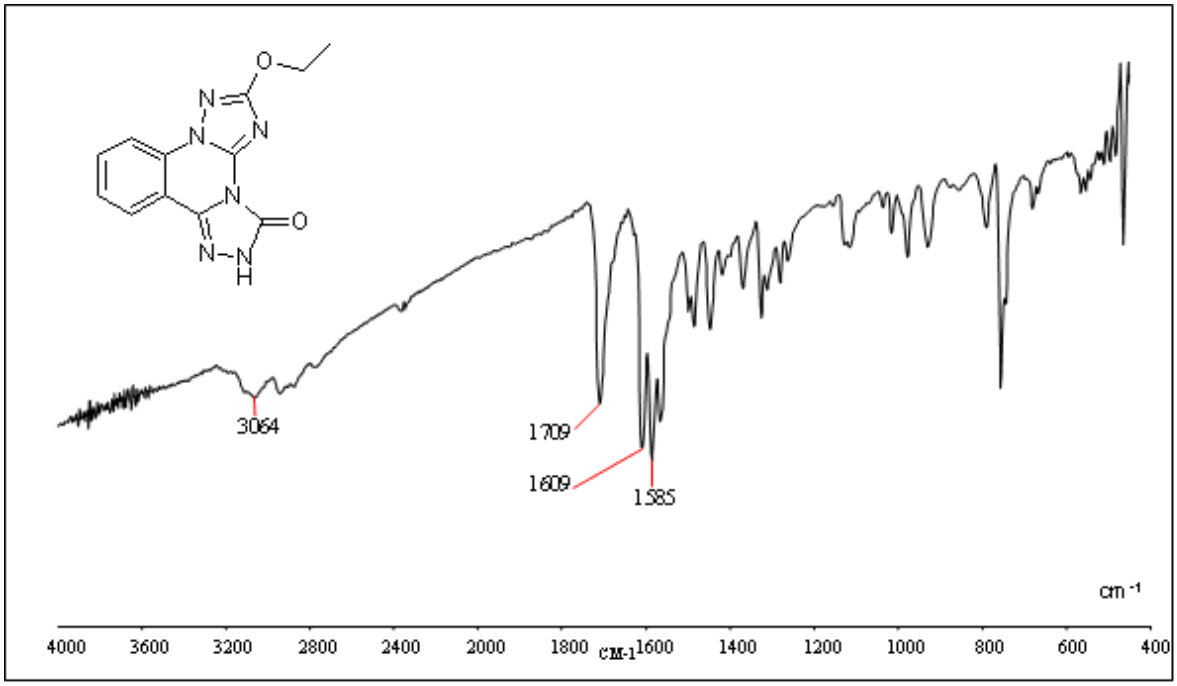
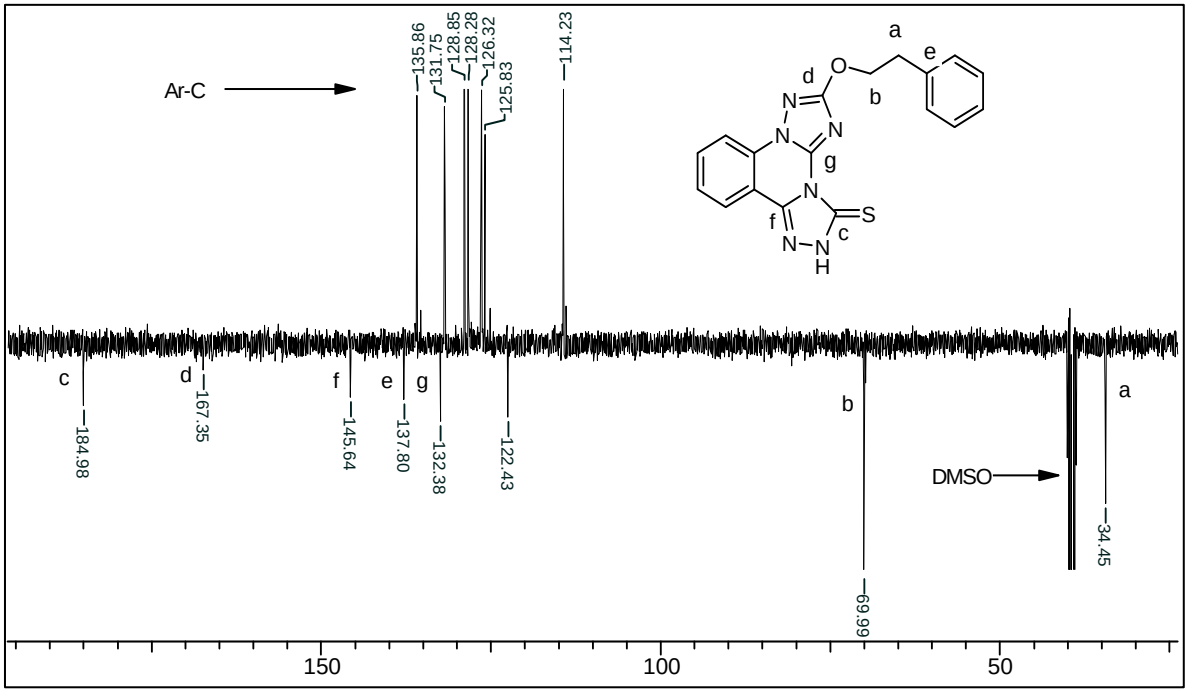


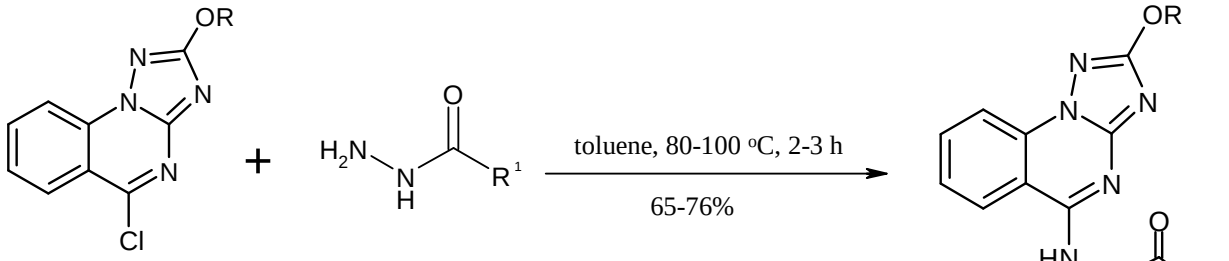
Fig. 28 *^{13}C NMR Spectrum of 2-Phenethyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-thione* **(37b)**



2.2.4.2 Reaction of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Hydrazides

Replacement of the chlorine in compounds **31** by different hydrazides **(38a-d)** occurred smoothly in boiling toluene to produce the [1,2,4]triazoloquinazolin-5-yl-carbohydrazides **(39a-f)** in good yields of 65-76% (Scheme 27) [134], which as themselves deserve interest as bioactive compounds and furthermore should open access to a number of triazolo-anellated compounds such as bis-[1,2,4]triazoloquinazolines.

Scheme 27 *Preparation of N-(2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-carbohydrazides* **(39a-f)**



31a,b,e **38a-d** **39a-f**

The IR spectra of **39a-f** are characterized by a strong-(C=O) absorption band at 1660-1670 and a weak (NH) band at 3189-3210 cm^{-1}, respectively (Fig. 29). Representative ^{1}H NMR and ^{13}C NMR spectra are shown in Fig. 30 and 31.

Table 11 *Prepared N-(2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-carbohydrazides* **(39a-f)**

39	R	R^1	Yield[%]
a	CH_3	CH_3	67
b	CH_3	C_6H_5	71
c	CH_3	3-pyridyl	65
d	CH_3CH_2-	C_6H_5	68
e	CH_3CH_2-	3-pyridyl	70
f	$C_6H_5CH_2$-	CH_3	76

Fig. 29 *IR Spectrum of N-(2-Methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-acetohydrazide* **(39a)**

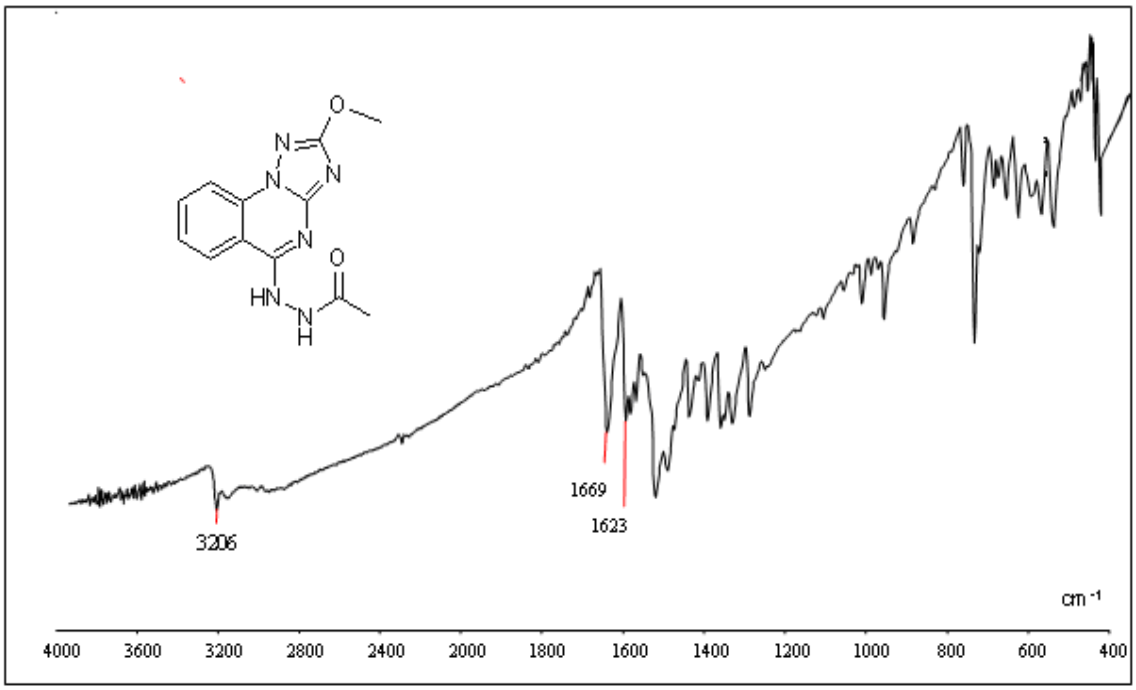


Fig. 30 *^{1}H NMR Spectrum of N-(2-Ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-benzohydrazide* **(39d)**

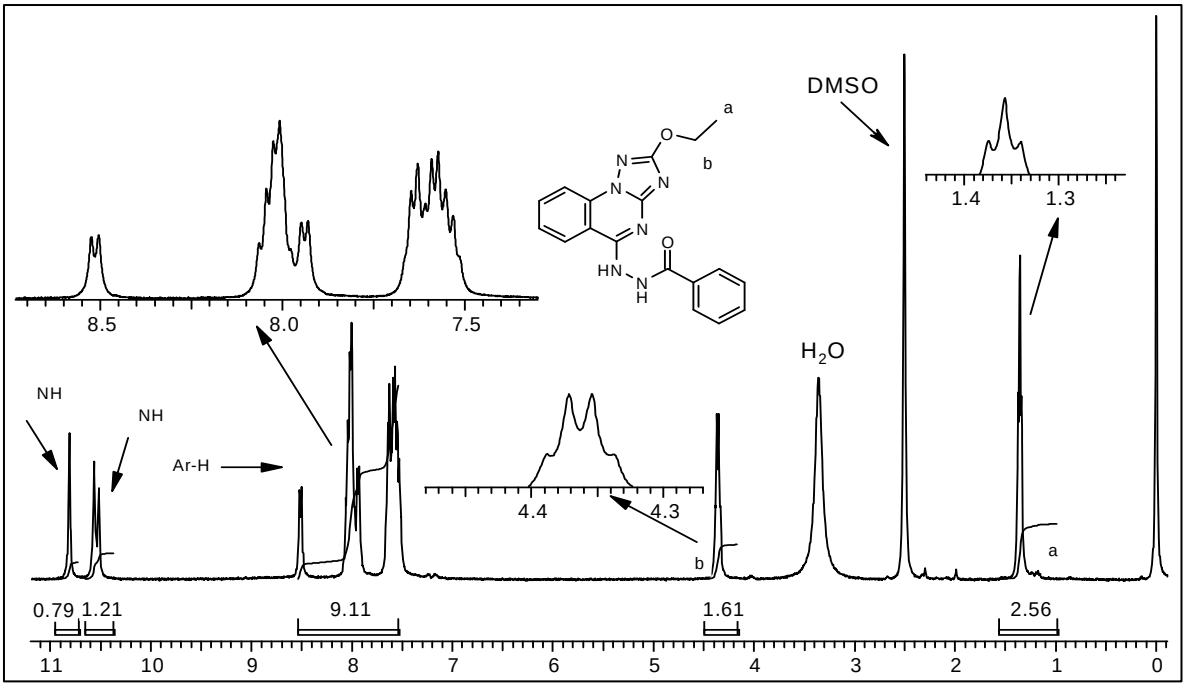
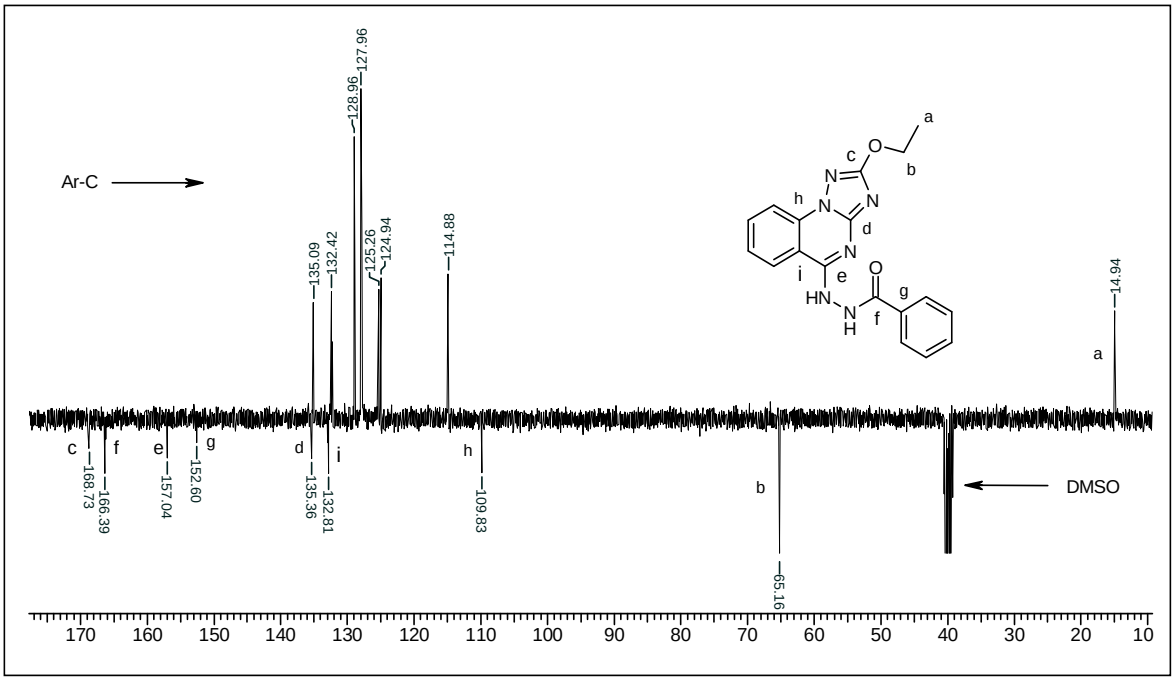


Fig. 31 *^{13}C NMR Spectrum of N-(2-Ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-benzohydrazide* **(39d)**

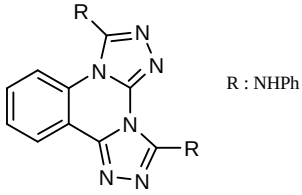


2.2.4.3 Synthesis of Bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolines (41)

After having successfully elaborated the synthesis of the hydrazides **39a-f,** my interest arose wether these compounds could be cyclo-condensed to the novel bis-[1,2,4]triazoloquinazolines of type **41**. Actually, when **31a,b,f** were treated with acylhydrazines **38** in a molar ratio of 1:2 in absolute toluene, the primarily formed acylamidrazones **40** underwent smoothly a base-catalyzed cyclization to provide the corresponding bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolines **41** [m] [134] (Scheme 28). This approach proved to be successful for the preparation of **41a-c** [n] but failed in the case of **41d-f**.

Therefore, the amidrazones **39b,c,d** were treated with phosphorous oxychloride at refluxing temperature for 2 h to furnish the respective intermediates **42d-f**, which upon subsequent neutralization with saturated potassium carbonate solution or aqueous ammonia delivered the targeted **41d-f**. [137]

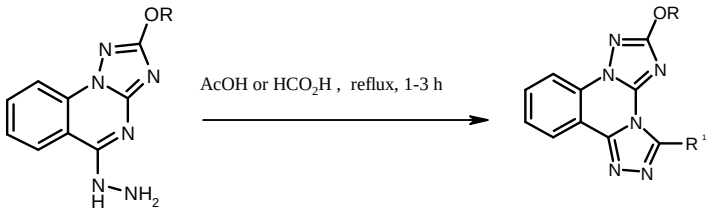
[m] The Bis-[1,2,4]triazolo[4,3-a:4`,3`-c]quinazoline of type **XXXII** has been reported to exhibit antitoxoplasmosis activity**.** [135]



XXXII

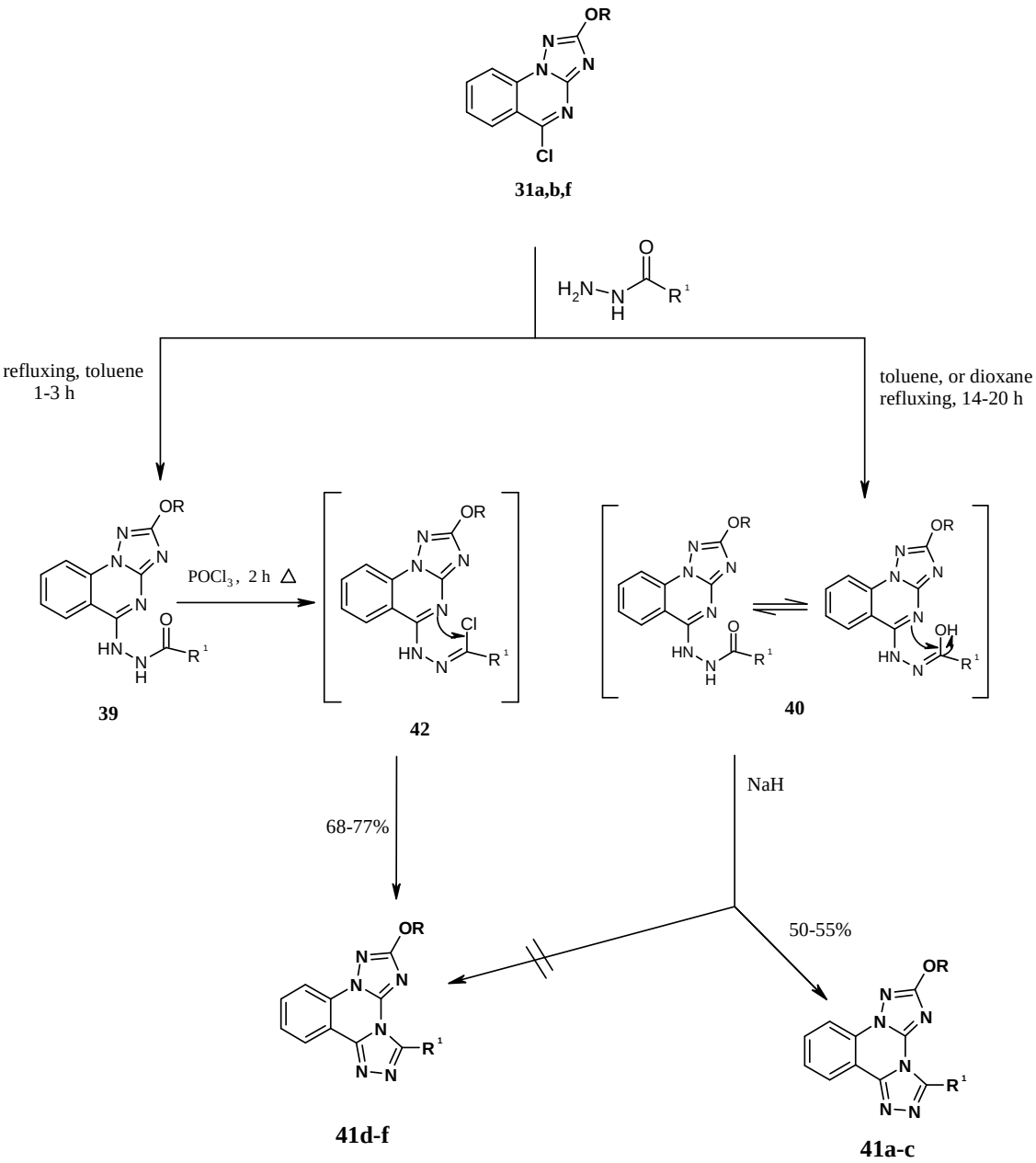
[n] Compounds **41a-c** could also be obtained by reaction of **32b,f** with formic and acetic acid [136] (Scheme 29).

Scheme 29 *Reaction of* **32b,f** *with formic and acetic acid*



32 b, f **41a-c**

Scheme 28 *Preparation of 2-Alkoxy(aralkoxy)-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolines* **(41a-f)**



The completion of the internal cyclization was monitored by IR spectroscopy: disappearence of the (C=O) and (NH) absorption bands at 1650-1670, 3173-3194 cm^{-1} signaled complete conversion of **40** or **42** to **41**.

The tetracyclic compounds **41** were obtained as solid materials and their structure was confirmed by IR, ^{1}H NMR and ^{13}C NMR spectra (Fig. 32-34) and microanalysis. In addition, the structure of compound **41b** has been unambiguously proven by X-ray crystallography (Fig. 35).

Table 12 *Prepared 2-Alkoxy(aralkoxy)-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolines* **(41a-f)**

41	R	R^1	Yield[%]
a	CH_3CH_2-	H	50
b	CH_3CH_2-	CH_3	55
c	$C_6H_5CH_2CH_2$-	H	51
d	CH_3CH_2-	C_6H_5	68
e	CH_3	C_6H_5	75
f	CH_3	3-pyridyl	77

Fig. 32 *IR Spectrum of 2-Ethoxy-3-methyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline* **(41b)**

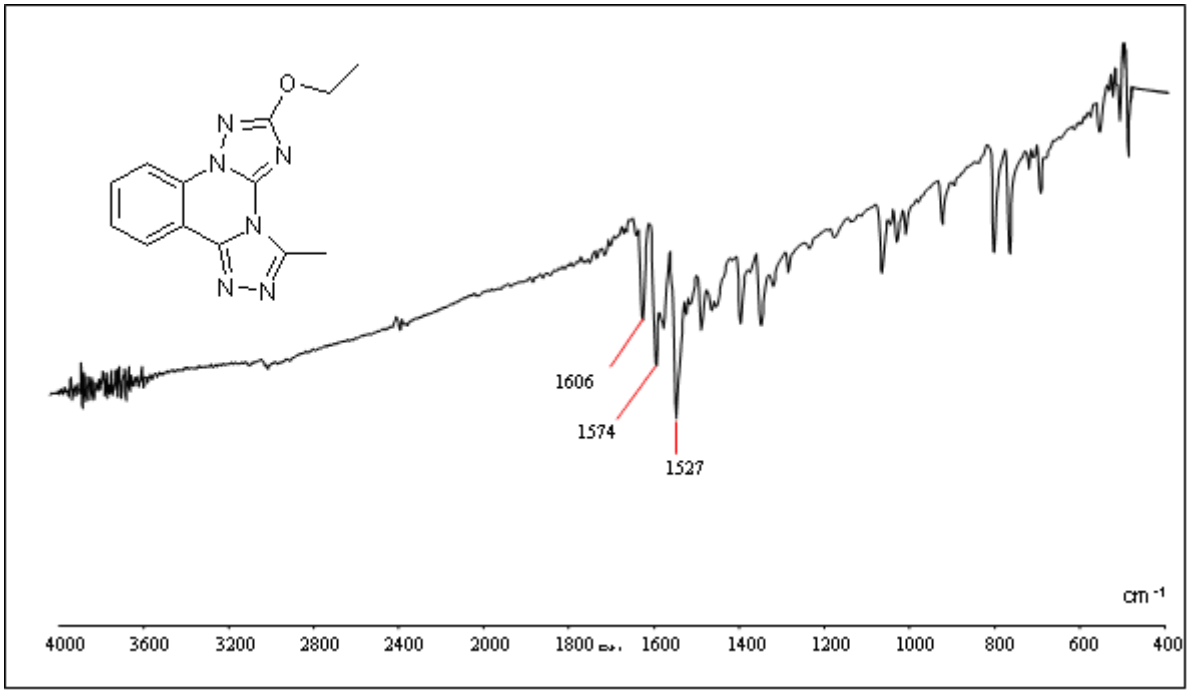


Fig.33 *^{1}H NMR Spectrum of 2-Phenethyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline* **(41c)**

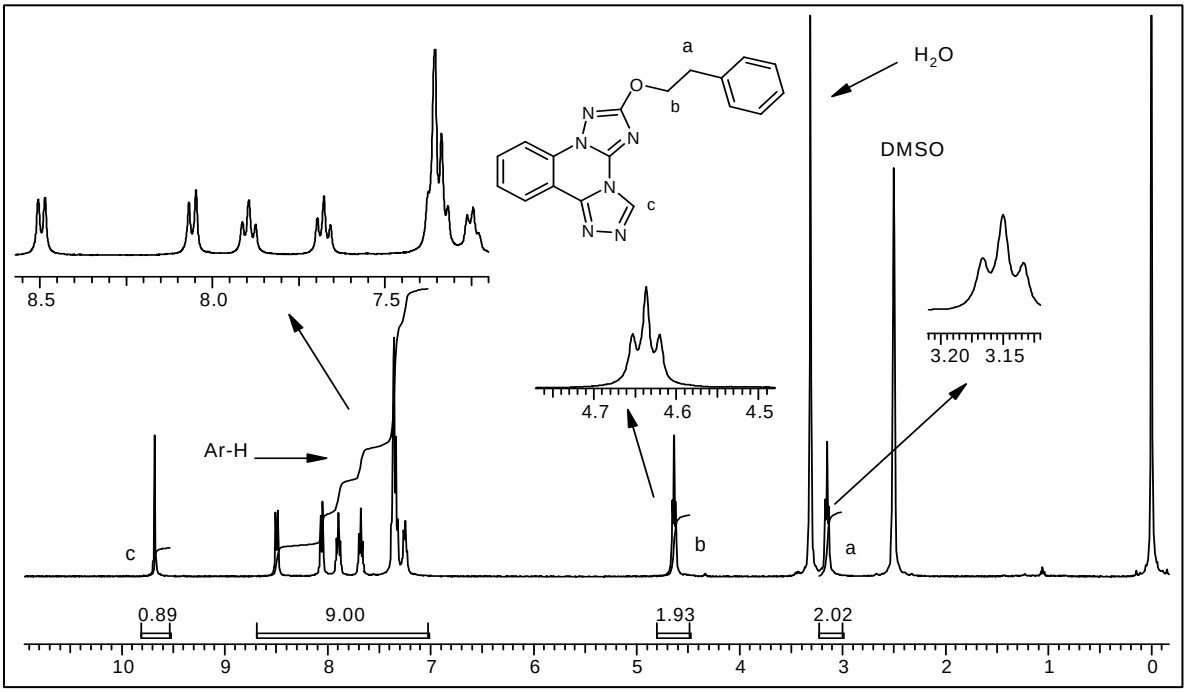


Fig. 34 *^{13}C NMR Spectrum of 2-Phenethyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline* **(41c)**

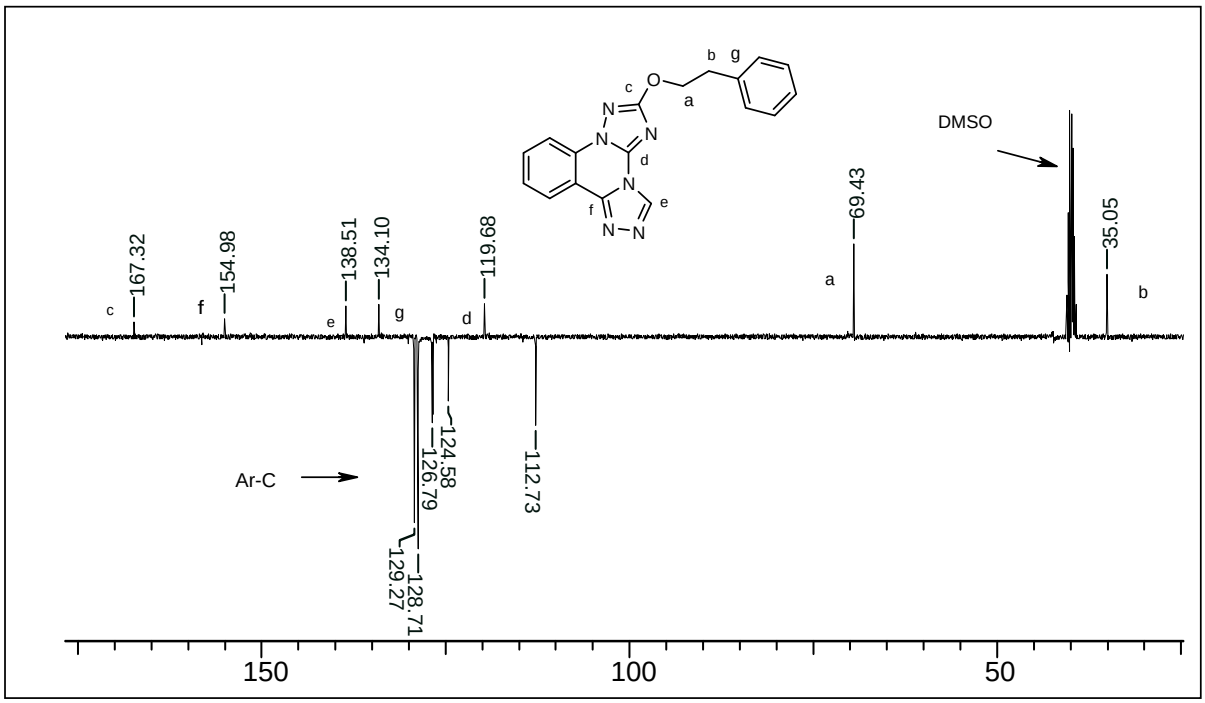
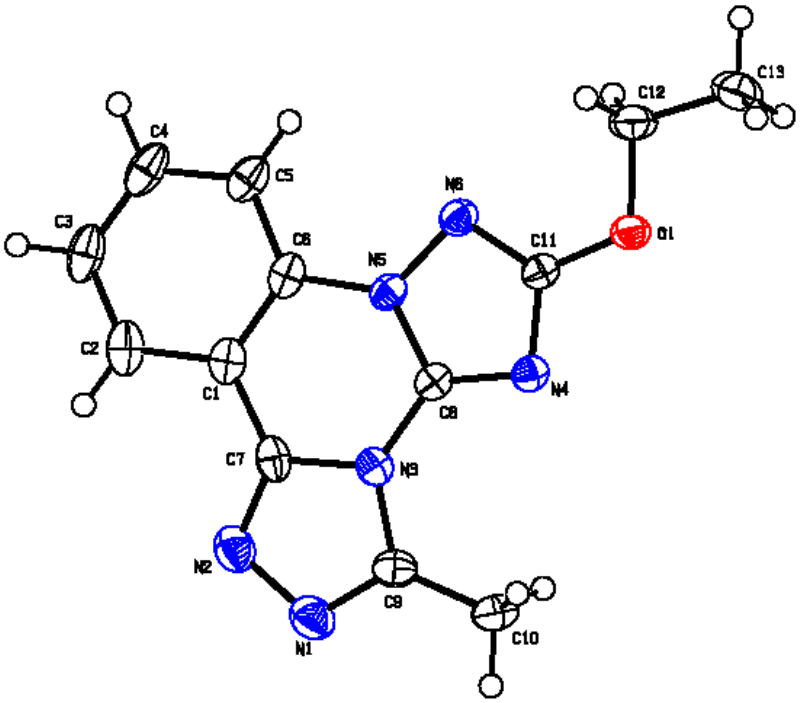
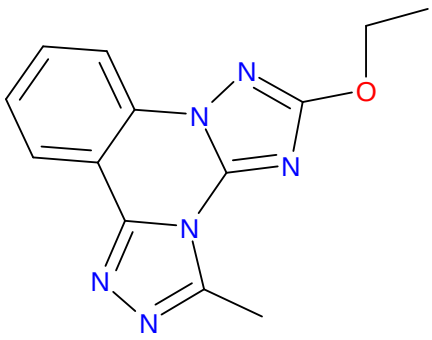


Fig. 35 *Molecular structure of 2-Ethoxy-3-methyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline* **(41b)** (diamond-visual crystal structure)



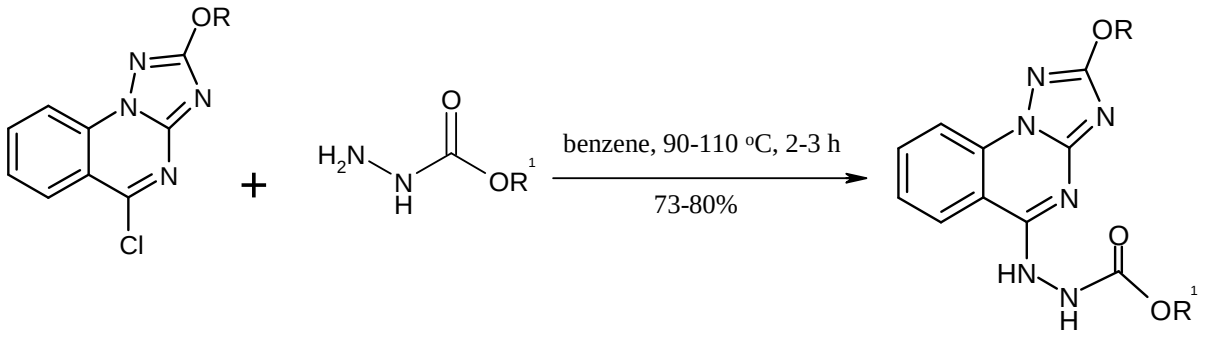


41b

2.2.4.4 Reaction of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Carbazates

Analogously to the reaction with hydrazides, the corresponding reaction of compounds **31** with carbazates (**43a,b**) according to literature [134] produced smoothly [1,2,4]triazoloquinazolin-5-yl-hydrazine-carboxylic acid esters of type **44** in 73-80 % yield as colorless solids (Scheme 30)**.**

Scheme 30 *Preparation of N-(2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazinecarboxylates* **(44a-d)**



31a,b **43** **44a-d**

The IR spectra of **44a-d** display a strong (C=O) absorption band at 1706-1718 and a weak (NH) absorption band at 3198-3261 cm^{-1}, respectively (Fig. 36), and compounds **44a-d** were further characterized by ^{1}H NMR, ^{13}C NMR spectra (Fig. 37, 38) and microanalysis.

Table 13 *Prepared N-(2-(Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylates* **(44a-d)**

44	R	R^1	Yield[%]
a	CH_3	CH_3CH_2-	73
b	CH_3	$C_6H_5CH_2$-	75
c	CH_3CH_2-	CH_3CH_2-	74
d	CH_3CH_2-	$C_6H_5CH_2$-	80

Fig. 36 *IR Spectrum of Benzyl N-(2-ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate* **(44d)**

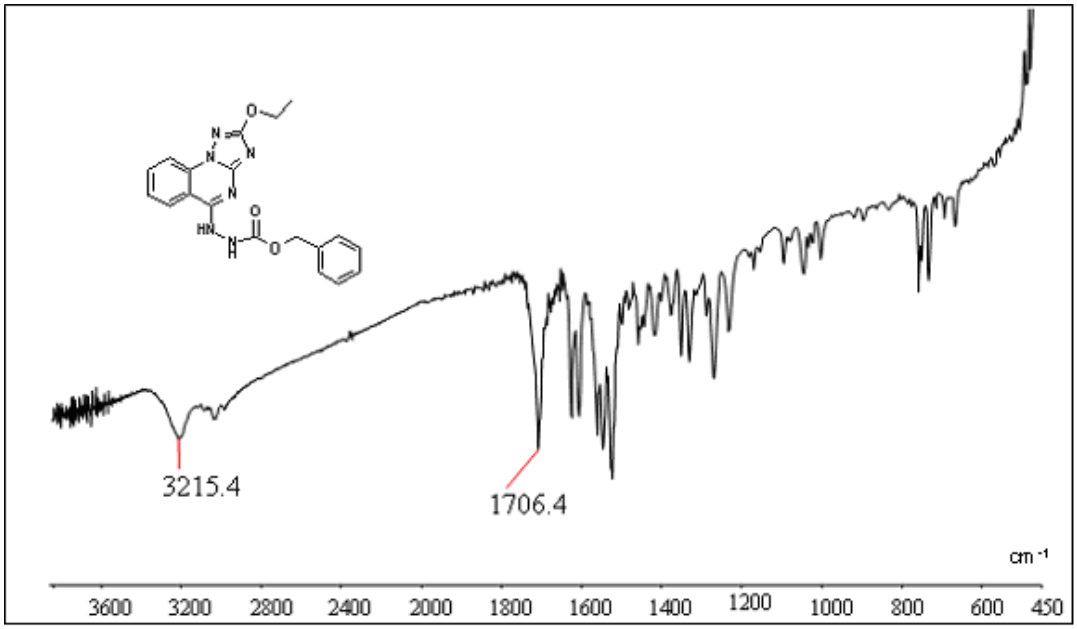


Fig. 37 *^{1}H NMR Spectrum of Benzyl N-(2-ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazinecarboxylate* **(44d)**

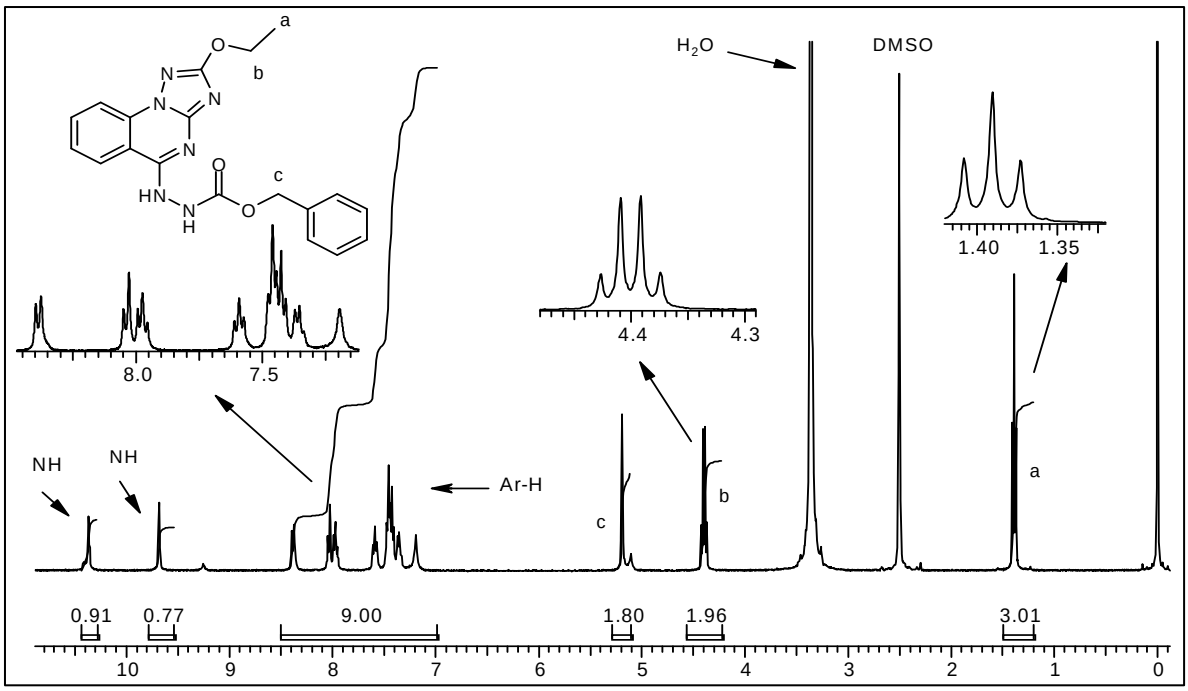
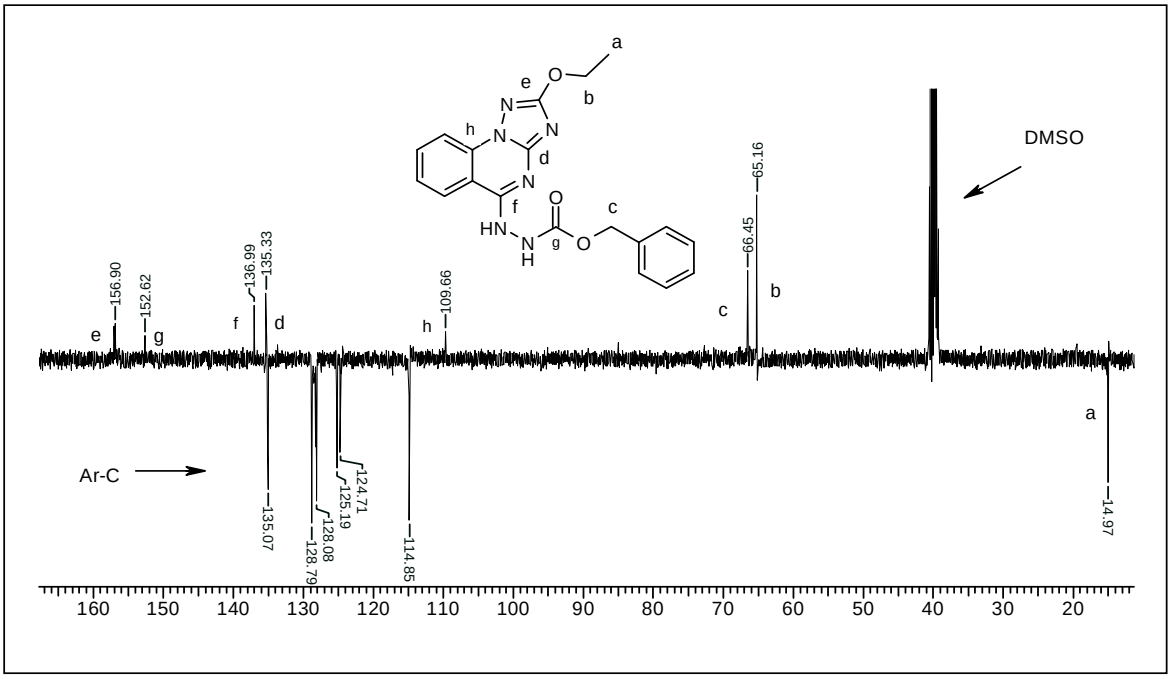


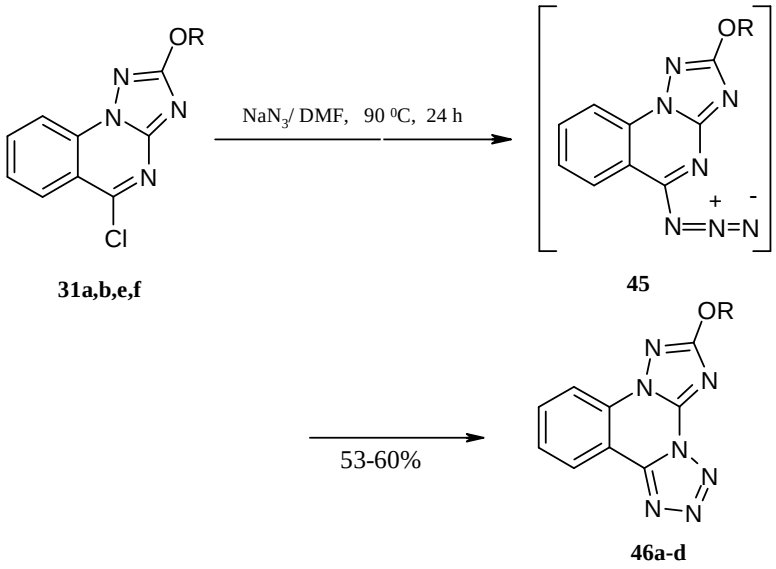
Fig. 38 *^{13}C NMR Spectrum of Benzyl N-(2-ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazinecarboxylate* **(44d)**



2.2.4.5 Reaction of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Sodium Azide

When 5-chloro-[1,2,4]triazoloquinazolines **31a,b,e,f** were reacted with sodium azide in a molar ratio of 1:1.2 in absolute dimethyl formamide for 24 h at 90 °C, the aimed 2-alkoxy(aralkoxy)-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazolines **46 a-d** were formed via the (not isolated) intermediates **45** as colorless solids in 51-60% yield [138] (Scheme 31). The novel tetrazolo-[1,2,4]triazoloquinazolines **46**[o] have been characterized by ^{1}H NMR, ^{13}C NMR spectra (Fig. 39, 40) and microanalysis.

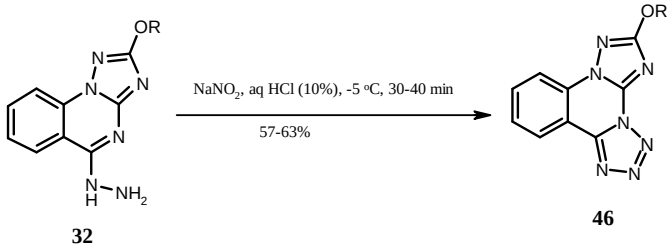
Scheme 31 *Preparation of 2-Alkoxy(aralkoxy)-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]-quinazolines* **(46a-d)**



31a,b,e,f **45** **46a-d**

[o] Transformation of **32** with nitrous acid at -5 °C for 30-40 min afforded the tetrazole products **46** in 57-63% yield [124] (Scheme 32).

Scheme 32 *Transformation of **32** to **46** by Nitrous Acid*



32 **46**

Table 14 *Prepared 2-Alkoxy(aralkoxy)-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazolines* **(46a-d)**

46	R	Yield[%]
A	CH_3	54
B	CH_3CH_2-	53
C	$C_6H_5CH_2$-	51
D	$C_6H_5CH_2CH_2$-	60

Fig. 39 *^{1}H NMR Spectrum of 2-Ethoxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline* **(46b)**

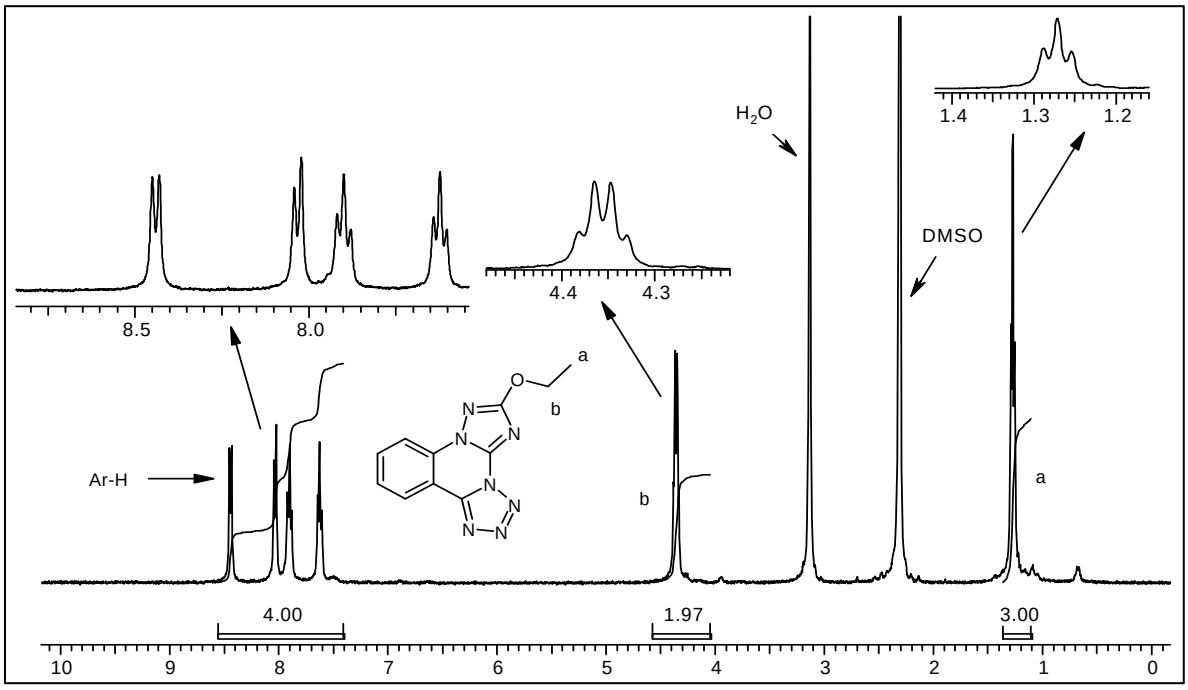
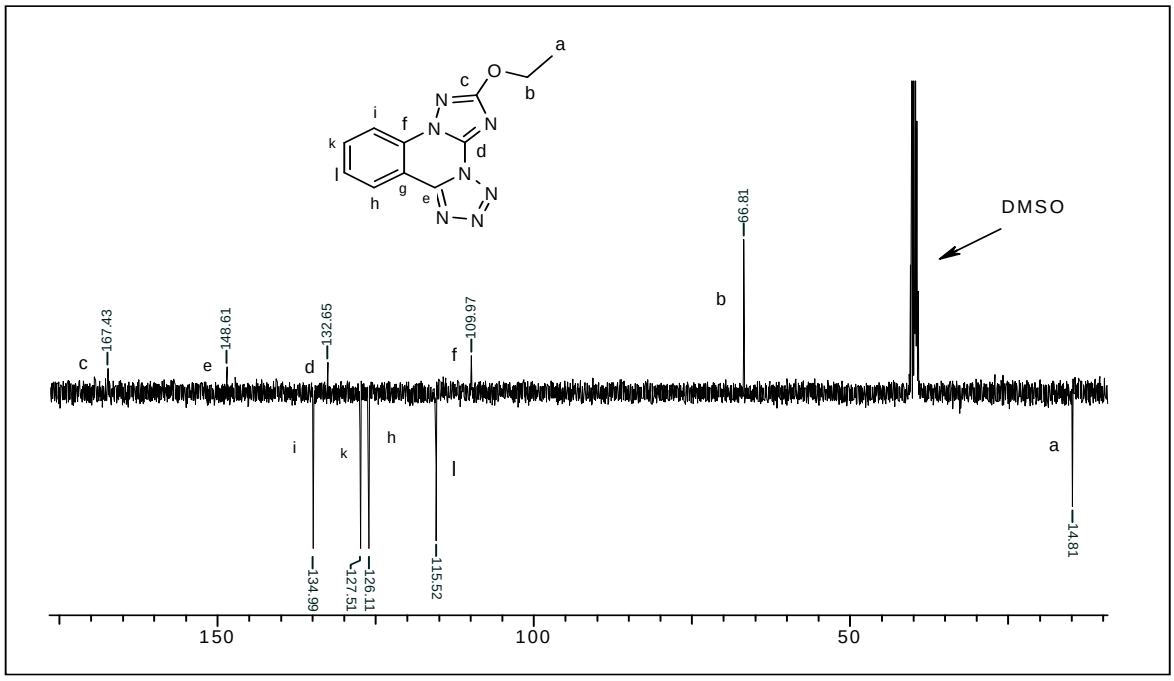


Fig. 40 *^{13}C NMR Spectrum of 2-Ethoxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline* **(46b)**

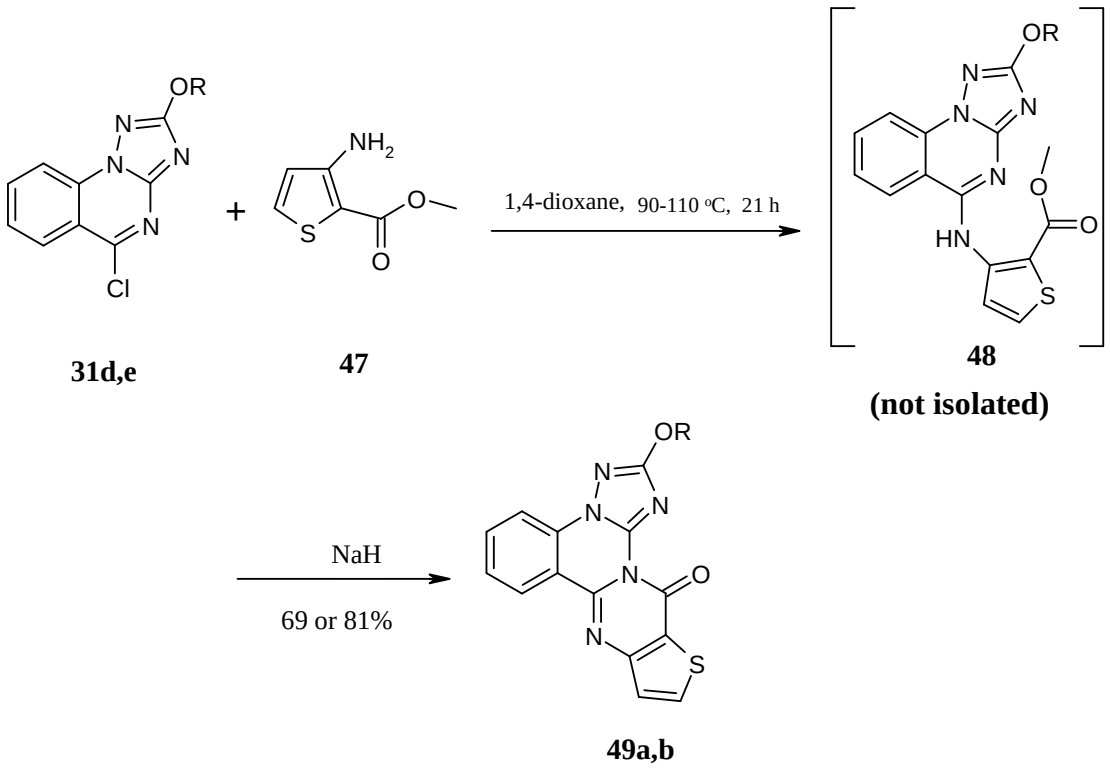


2.2.4.6 Reaction of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Methyl 3-Amino-thiophene-2-carboxylate

The beforementioned facile nucleophilic displacement of the chlorine atom in **31** prompted me to investigate the reaction of **31** with methyl 3-amino-thiophene-2-carboxylate (**47**) which theoretically should provide access to the novel pentacyclic compounds of type **49**. In fact, when **31d,e** were reacted with **47** in absolute dioxane in a molar ratio of 1:1.6, followed by addition of sodium hydride, the targeted **49a,b** could be isolated from the reaction mixture in 69 and 81% yield (Scheme 33).[134]

The IR spectra of compounds **49** are characterized by a (C=O) stretching at 1670 or 1667 cm^{-1} (Fig. 41).

Scheme 33 *Preparation of 3H-Thieno-[3,2-d]pyrimidin-4-one-[4,3-c][1,2,4]triazolo[1,5-a]quinazolines* **(49a,b)**

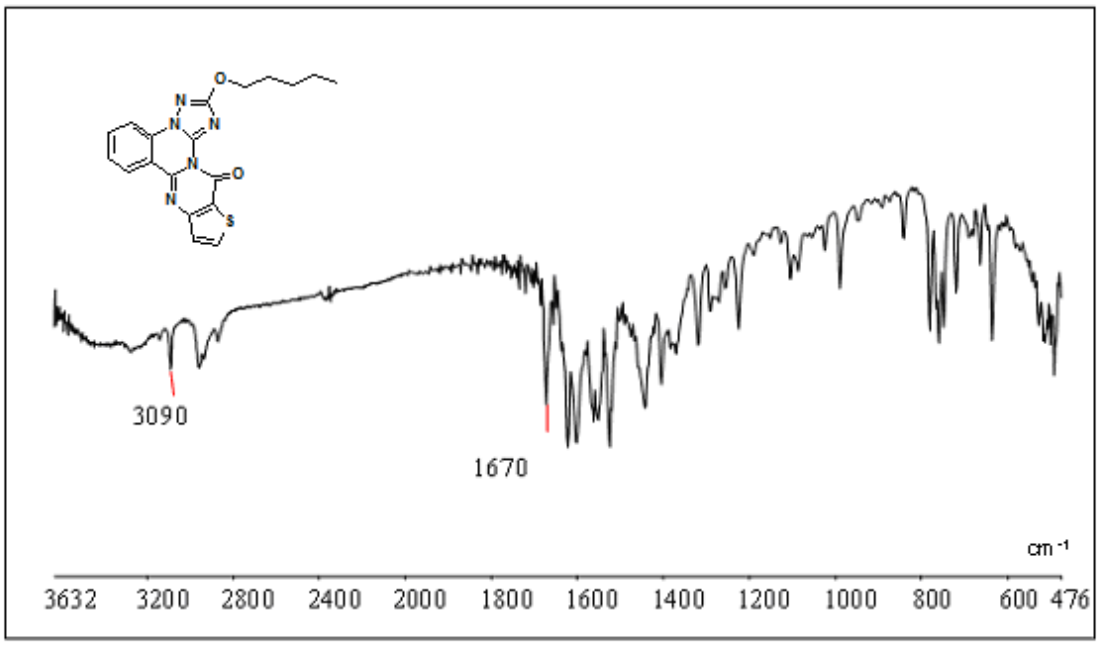


31d,e **47** **48** **(not isolated)** **49a,b**

Table 15 *Prepared 3H-Thieno-[3,2-d]pyrimidin-4-one-[4,3-c][1,2,4]triazolo[1,5-a]-quinazolines* **(49)**

49	R	Yield [%]
A	$CH_3CH_2CH_2CH_2CH_2$-	81
B	$C_6H_5CH_2$-	69

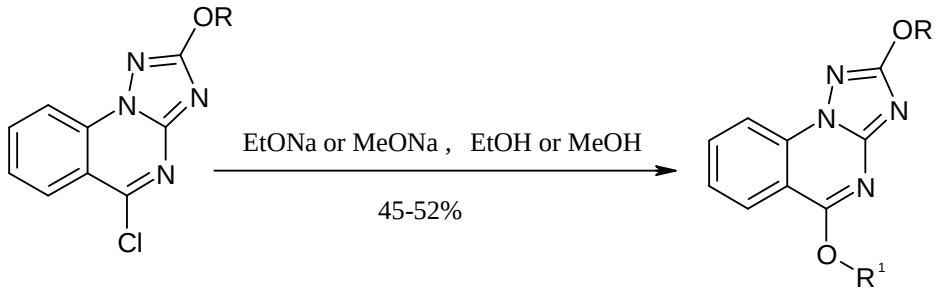
Fig. 41 *IR Spectrum of 2-Pentyloxy-(3H-thieno-[3,2-d]pyrimidin-4-one-[4,3-c][1,2,4]-triazolo[1,5-a]quinazoline* **(49a)**



2.2.4.7 Reaction of 5-Chloro-[1,2,4]triazoloquinazolines (31) with Sodium Alkoxides

When **31b,e,f** were reacted at ambient temperature with sodium alkoxides in the corresponding alcohol as solvent, the novel 2,5-dialkoxy-[1,2,4]triazoloquinazolines (**50a-d)** could be obtained in 45-52% yield [139] (Scheme 34).

Scheme 34 *Preparation of 2,5-Dialkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolines* **(50a-d)**



31b,e,f **50a-d**

The structure of **50a-d,** which are colorless and stable solids, follows unambiguously from their IR, ^{1}H NMR, ^{13}C NMR spectra (Fig. 42-44) and microanalysis.

Table 16 *Prepared 2,5-Dialkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolines* **(50a-d)**

50	R	R^1	Yield[%]
A	CH_3CH_2-	CH_3	45
B	$C_6H_5CH_2$-	CH_3	50
C	$C_6H_5CH_2$-	CH_3CH_2-	51
D	$C_6H_5CH_2CH_2$-	CH_3CH_2-	52

Fig. 42 *IR Spectrum of 2-Benzyloxy-5-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(50c)**

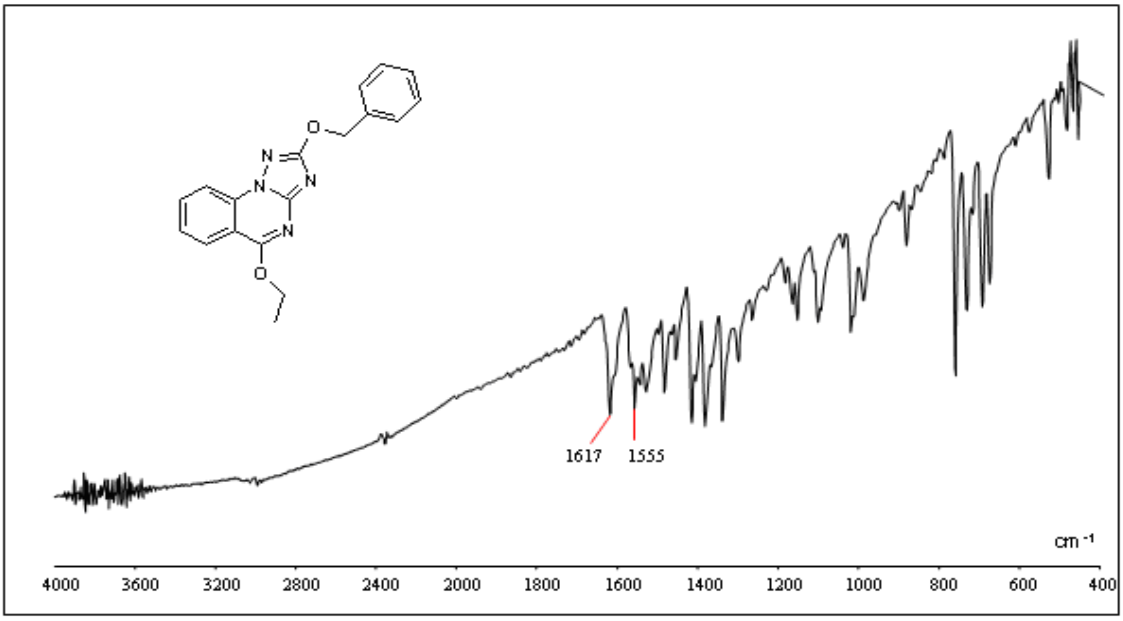


Fig. 43 *^{1}H NMR Spectrum of 2-Benzyloxy-5-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(50c)**

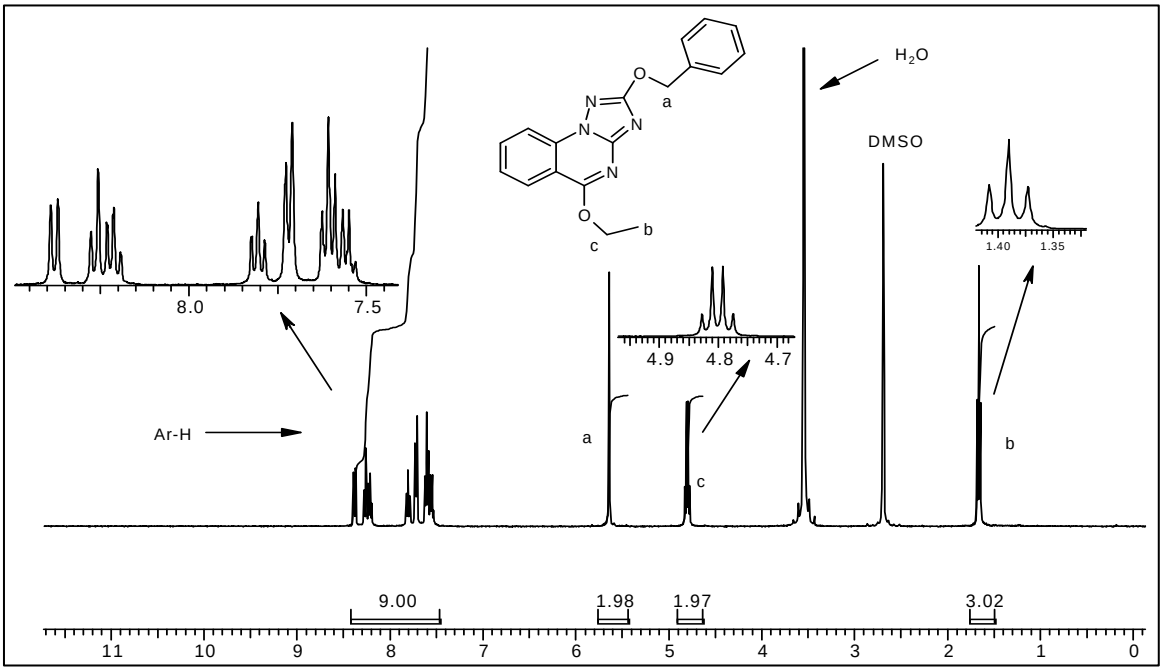
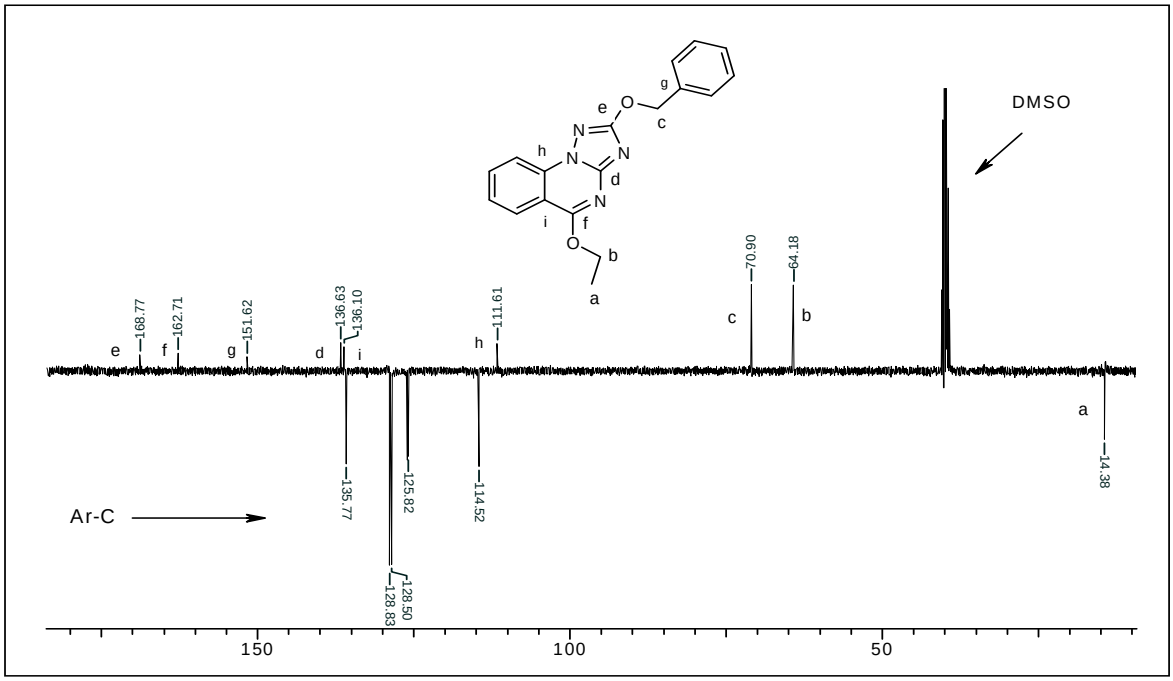


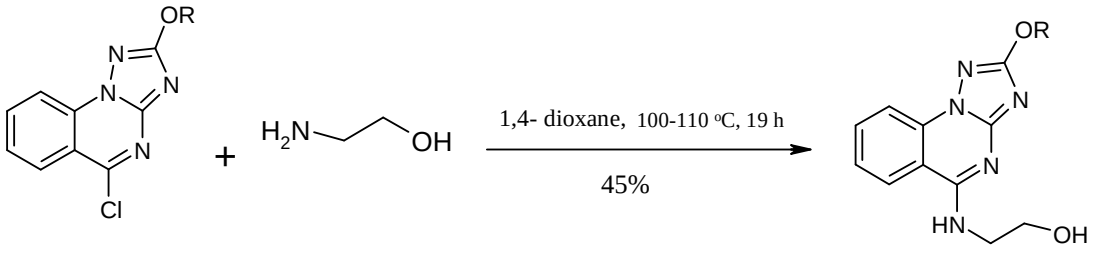
Fig. 44 *^{13}C NMR Spectrum of 2-Benzyloxy-5-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline* **(50c)**



2.2.4.8 Reaction of 5-Chloro-[1,2,4]triazoloquinazoline (31) with Ethanol-amine

Refluxing a mixture of compound **31f** with 2-amino-ethanol (**51**) in absolute dioxane provided the [1,2,4]triazolo[1,5-a]quinazolin-5-ylamino)-ethanol **52** as a colorless solid in 45% yield [140] which was characterized by microanalysis, IR, ^{1}H NMR, and ^{13}C NMR spectra (Scheme 35).

Scheme 35 *Preparation of 2-(2-Phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-ylamino)-ethanol* **(52)**



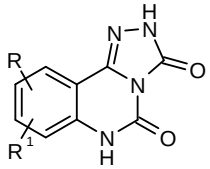
31f **51** **52**

2.2.5 Hydrogenolysis of 2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-one (6f) to 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione (53)

The benzyl group has found common use in organic chemistry as a suitable protecting group that can be removed under neutral conditions by hydrogenolysis.[141] Accordingly, catalytic hydrogenation of the 2-benzyloxy-[1,2,4]triazoloquinazolin-5-one **6f** should deliver the corresponding [1,2,4]triazoloquinazolin-2,5-dione **53** suited with a semicyclic semicarbazide functionality.[p] In fact, hydrogenolysis of **6f** [q] on Pd/C in tetrahydrofuran cleanly afforded 1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione (**53)** as a colorless solid in excellent yield of 95% (Scheme 37).

The structure of compound **53** follows unambiguously from microanalysis, IR, ^{1}H NMR and ^{13}C NMR spectra (Fig. 45-47) .

[p] Triazoloquinazolines containing dicarbonyl functionalities **XXXIII** are receiving growing interest due to their remarkable biological activities such as treatment and prevention of ischemia and hemorrhagia.[142]

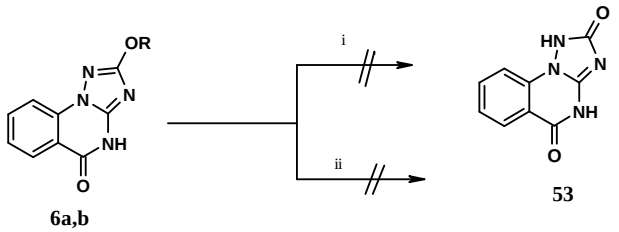


R: H, alkyl, aryl, alkoxy
R^1: alkyl, halogen, cyano, amine, nitro

XXXIII

[q] Attempts, to remove the alkoxy groups of **6a,b** by means of BBr_3 or trifluoroacetic acid in dichloromethane to deliver the corresponding [1,2,4]triazoloquinazolin-2,5-dione **53** failed (Scheme 36).

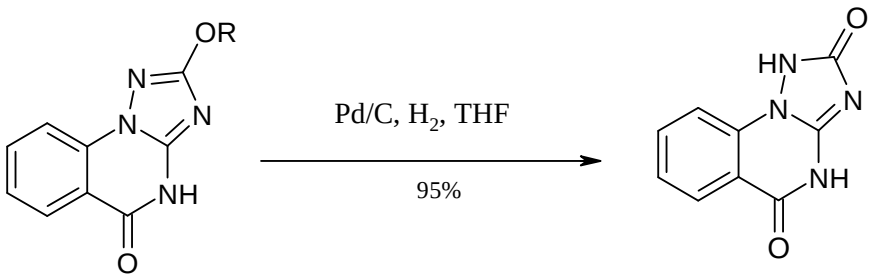
Scheme 36 *Failed deprotection of* **6a,b**



6a,b **53**

i: CF_3COOH, DCM ii: BBr_3, DCM

Scheme 37 *Preparation of 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(53)**



6f **53**

Fig. 45 *IR Spectrum of 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(53)**

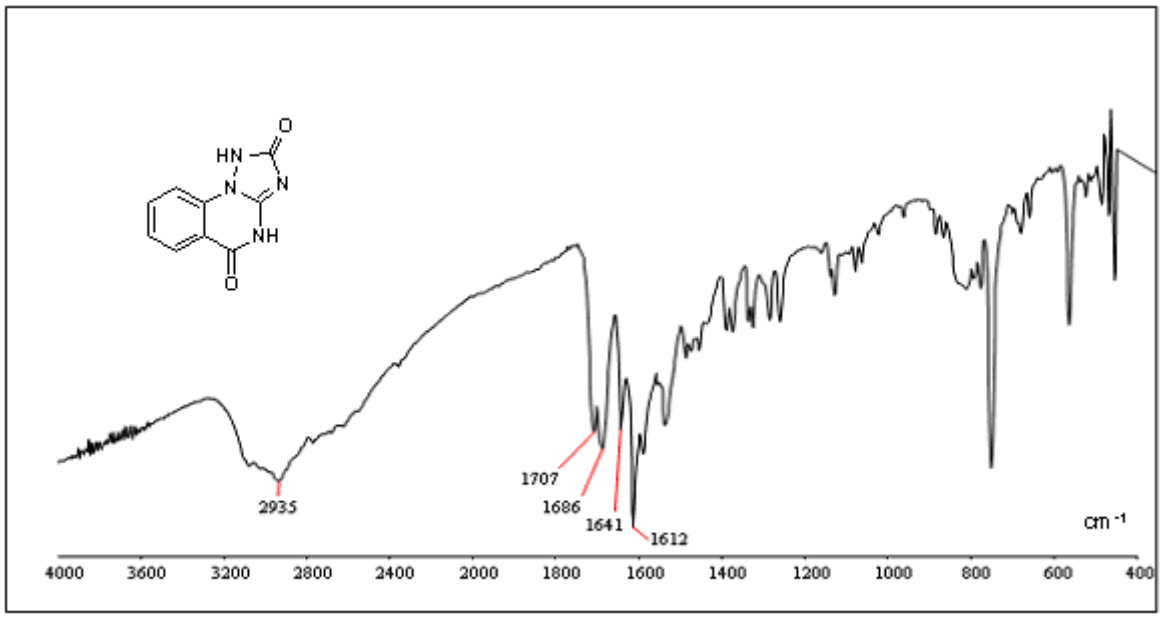


Fig. 46 *[1]H NMR Spectrum of 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(53)**

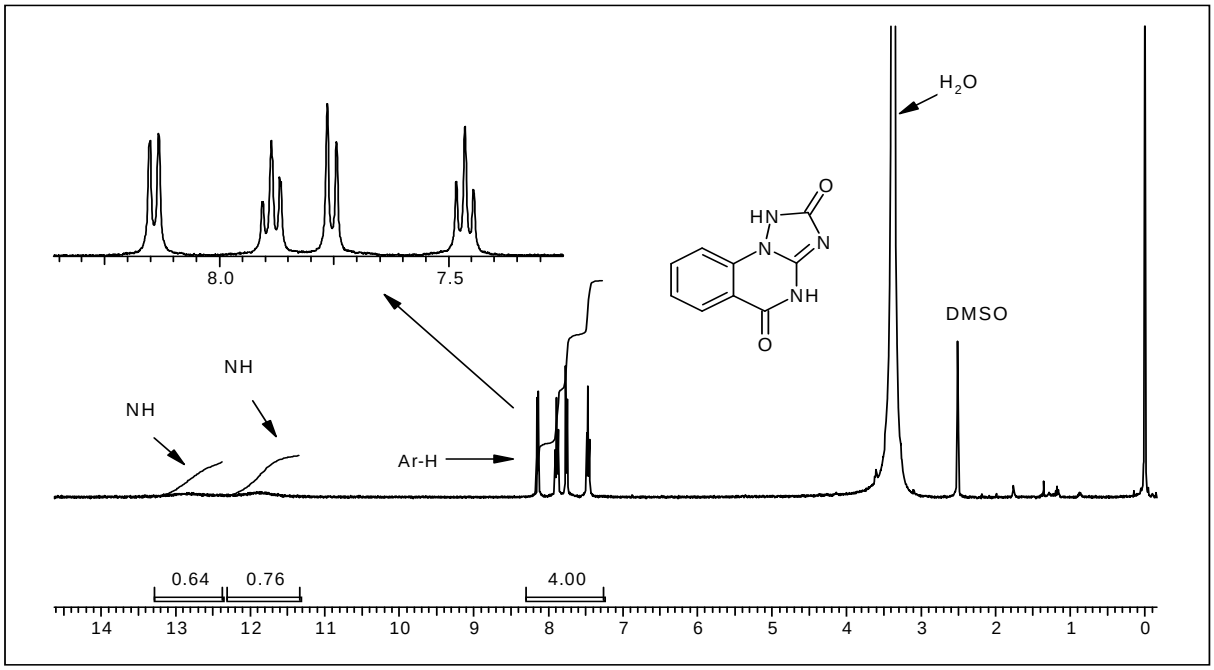
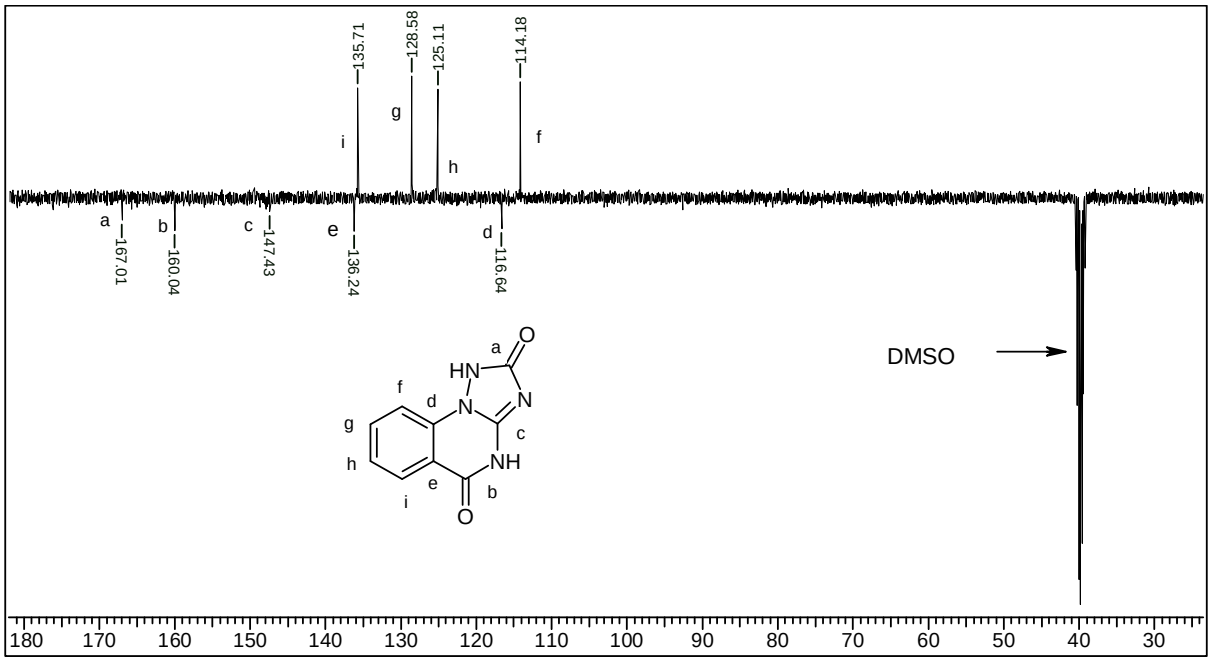


Fig. 47 *[13]C NMR Spectrum of 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(53)**



2.2.5.1 Alkylation of [1,2,4]Triazolo[1,5-a]quinazolin-2,5-dione (53) with Benzyl Bromide

When **53** was treated with benzyl bromide (**54)** in a molar ratio of 1:3 in absolute dimethyl formamide, the dibenzylated product **55** was formed in 79% yield (Scheme 38). The structure of **55** was confirmed by micronanalysis, and IR, ^{1}H NMR, ^{13}C NMR spectra (Fig. 48-50). The IR spectrum of compound **55** is characterized by a weak (C=O) absorption band at 1670 cm^{-1}.

Scheme 38 *Preparation of O,N-Dibenzyl-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(55)**

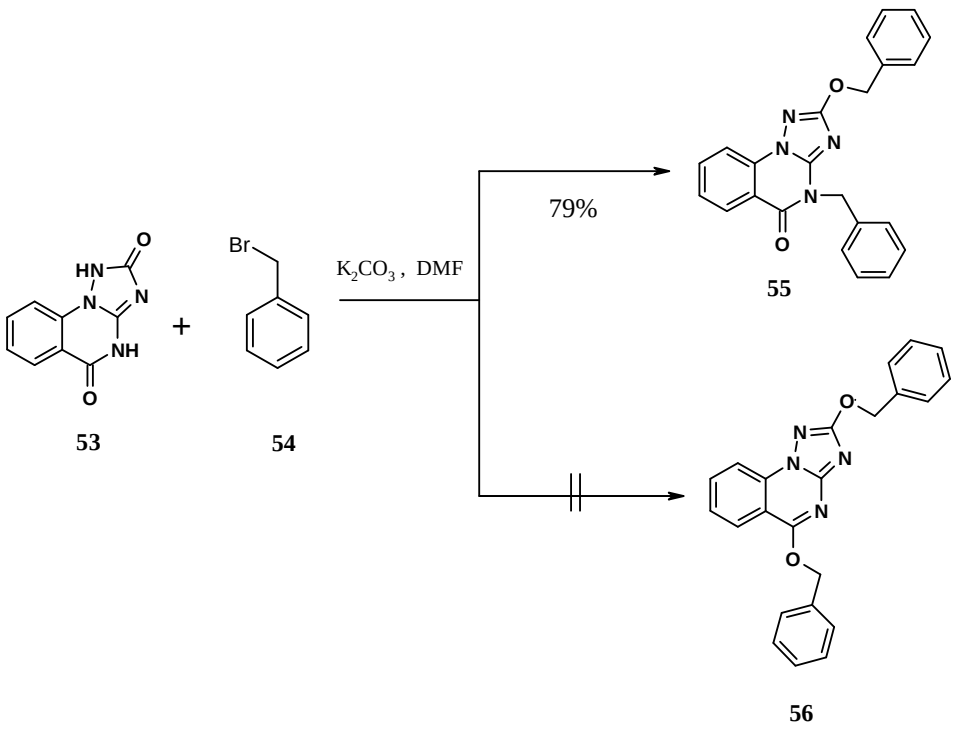


Fig. 48 *IR Spectrum of 2-Benzyloxy-4-benzyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(55)**

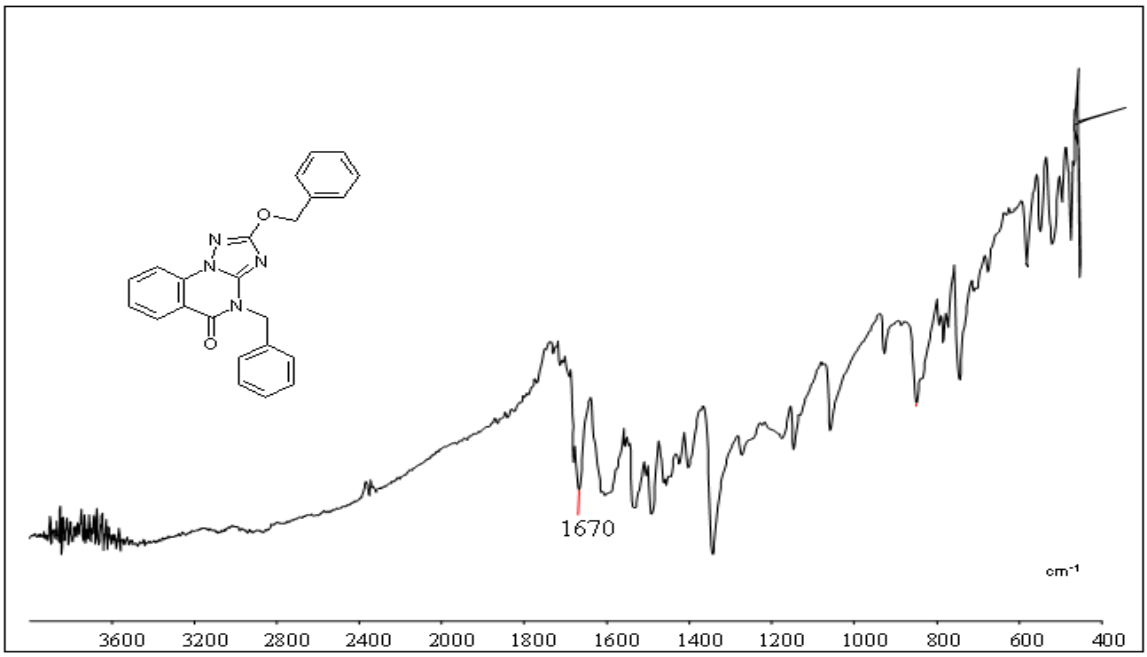


Fig. 49 *^{1}H NMR Spectrum of 2-Benzyloxy-4-benzyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(55)**

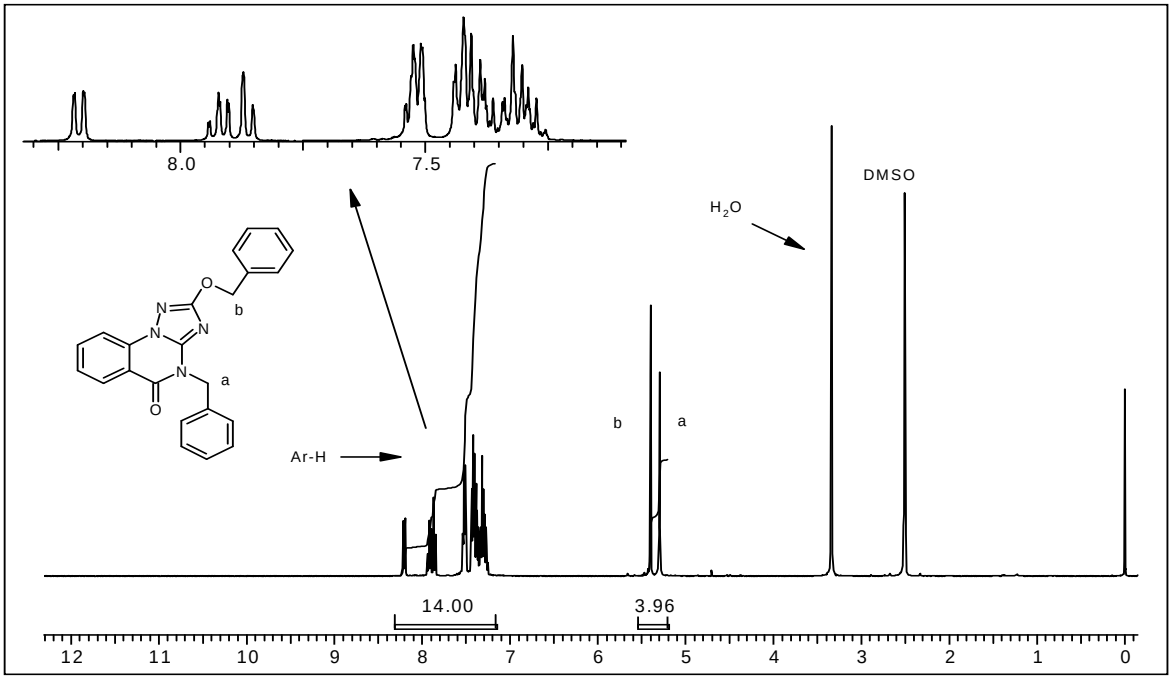
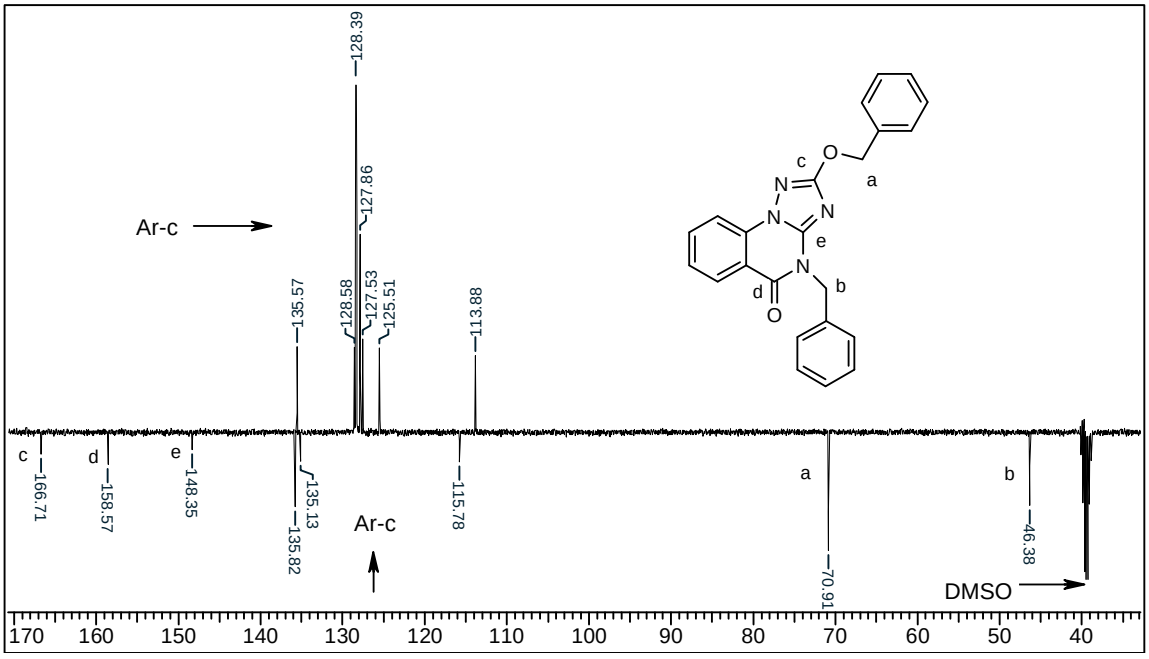


Fig. 50 *^{13}C NMR Spectrum of 2-Benzyloxy-4-benzyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(55)**



2.2.6 Nitration of 2-Allyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-one (6e) to 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione (58)

The nitro group represents an important pharmacophore in various pharmaceuticals [143-145], and serves as a valuable precursor for further chemical transformations in organic synthesis. [146] Hence, it became of interest to investigate the nitration of the novel tricyclic compounds **6**. For this purpose, **6e** was treated with potassium nitrate in concentrated sulfuric acid at 0 ^{o}C, followed by stirring at room temperature for 17 h according to literature. [147] However, not the expected 2-allyloxy-8-nitro-[1,2,4]triazolo[1,5-a]quinazolin-5-one **57** was obtained but instead 8-nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione (**58)** was formed in 54% yield, the structure of which has been established by micronanalysis, IR, ^{13}C NMR and ^{1}H NMR spectra (Fig. 51-53). The IR spectrum of compound **58** is characterized by two weak (C=O) absorption bands at 1696 and 1718 cm^{-1}.

Scheme 39 *Nitration of 2-Allyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-one* **(6e)**

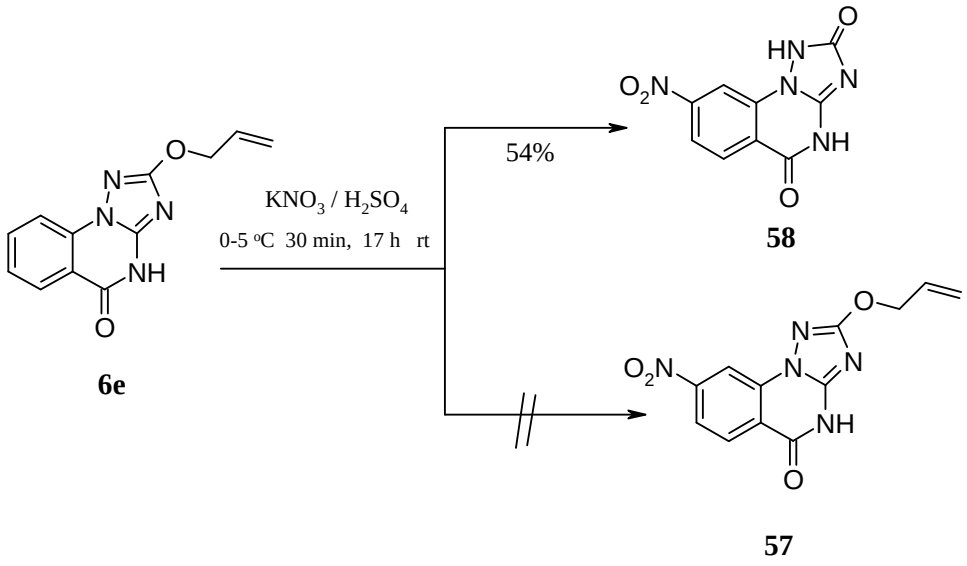


Fig. 51 *IR Spectrum of 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(58)**

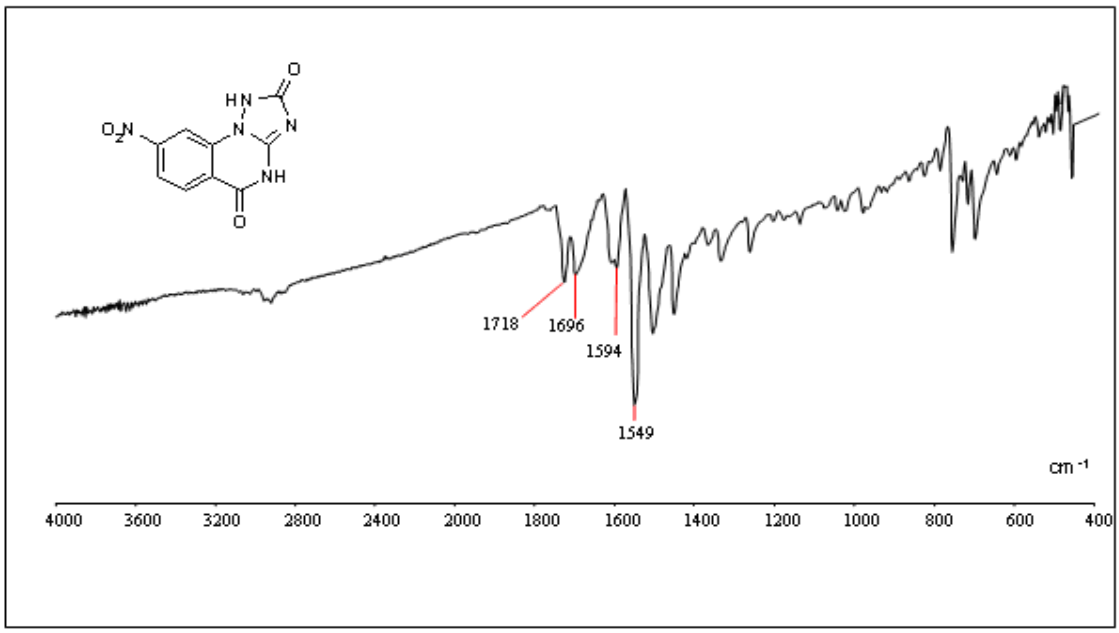


Fig. 52 *^{1}H NMR Spectrum of 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* **(58)**

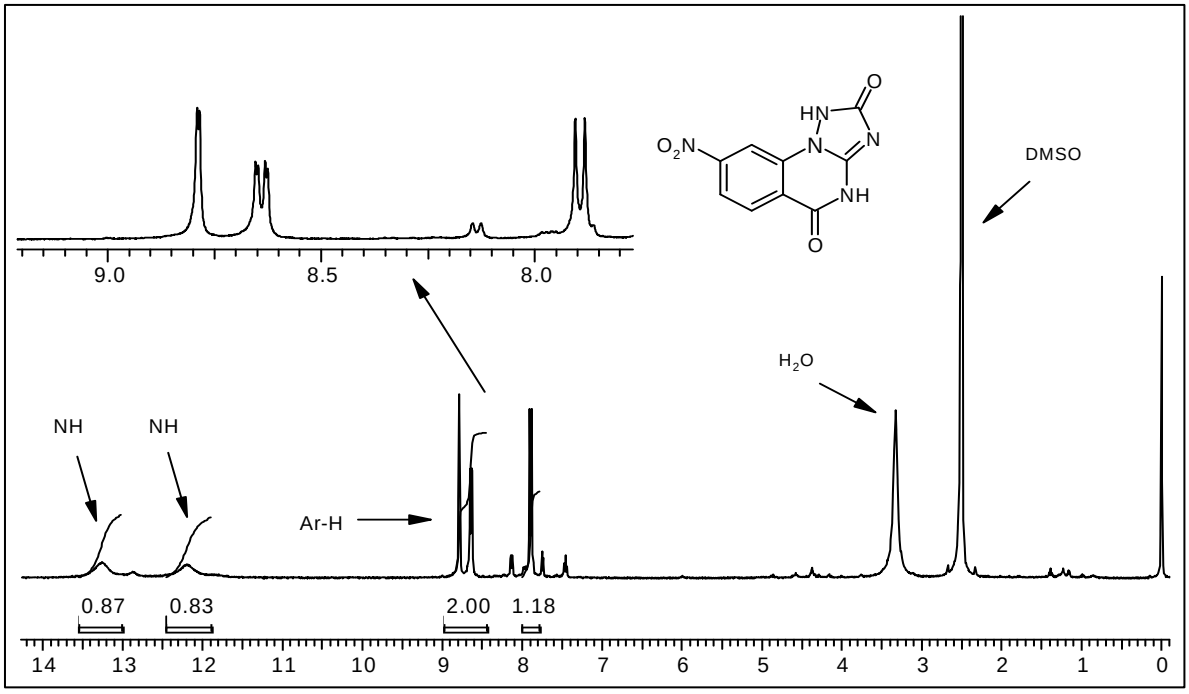
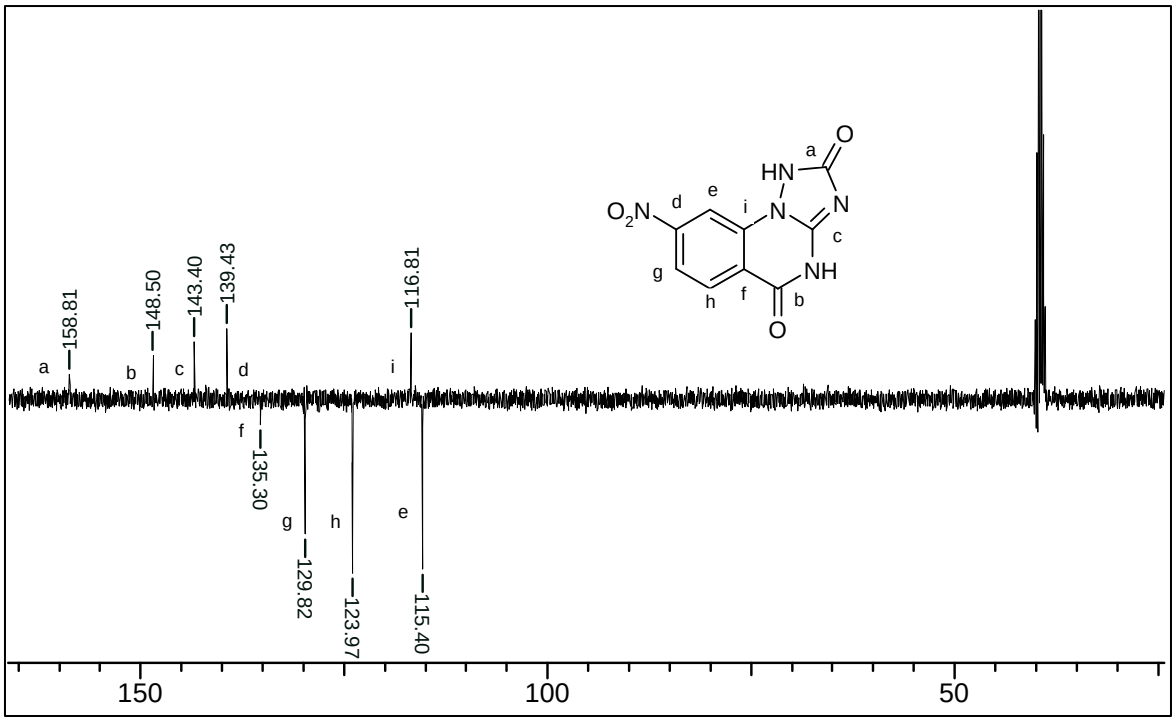


Fig. 53 *^{13}C NMR Spectrum of 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione* ***(58)***



3 Experimental

Melting points

Melting points (uncorrected) were determined on a Mettler FP 62

IR Spectra

Shimadzu FT-IR 8300
Measured as KBr-pressling or as film on NaCl plate

^{1}H NMR Spectra

Bruker AMX 400 (400 MHz)
Chemical shift δ measured in ppm
Internal standard: Trimethylsilane (TMS)
DMSO-d_6, D_2O, and $CDCl_3$ as solvents
Number of protons determined by integration
Abbreviation of signal multiplicity;
s = singlet, d = duplet, t = triplet, q = quartet, m = multiplet
Coupling constant *J* measured in Hz

^{13}C NMR Spectra

Bruker AMX 400 (101 MHz)
Chemical shift δ measured in ppm
Internal standard: Trimethylsilane (TMS)
DMSO-d_6, D_2O, and $CDCl_3$ as solvents

Mass Spectra

HRFAB-Mass spectra**:** Mass spectrometer VG 70- 250S
ESI- Mass spectra: Varian MS 1200L

Elemental analysis

Heraeus CHN-O-Rapid

Thin layer chromatography

DC-Mikrokarten polygram SIL G/$UV_{254,}$ from the Macherey-Nagel Firm, Duren Thickness: 0.25 m

Column chromatography

Kieselgel ICN Silica 100-200, aktiv 60 Å

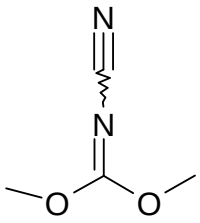
Drying agent for organic phases

Dry magnesium sulfate

General procedure for the preparation of Dialkyl *N*-Cyanoimidocarbonates (2a-g)

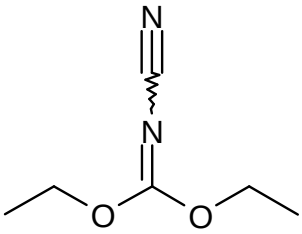
Under ice cooling, cyanogen bromide (10 mmol) was added dropwise to a stirred mixture of sodium hydroxide (20 mmol), alcohol (20 mmol) in MTBE (10 mL) over 1.5 h. After the addition was complete, the mixture was stirred at 0-5 ^{o}C for an additional 2 h, at the end of the holding period, the reaction mixture was filtered and the salt was washed with MTBE (5 mL). The filtrates were collected and added to a stirred mixture of sodium carbonate (10 mmol), triethylamine (0.2 mmol) and few drops of water in MTBE (5 mL). The flask contents were cooled at 0 ^{o}C, cyanogen bromide (10 mmol) was added dropwise over 1 h while maintaining the reaction mixture at 0-5 ^{o}C. After the addition was complete, the mixture was stirred for 1 h at 5-10 ^{o}C and then warmed to room temperature for 30 min. The reaction mixture was filtered, and the solvent was removed under reduced pressure to give the desired dialkyl *N*-cyanoimidocarbonates.

Dimethyl *N*-Cyanoimidocarbonate **(2a)**



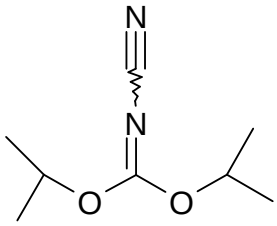
Yield: 50% (1.14 g), yellow oil; IR (film): 2205 (C≡N), 1614 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.32 (s, 6H); ^{13}C NMR (DMSO-d_6): δ(ppm): 9.05, 13.27, 113.23, 164.35; $C_4H_6N_2O_2$ [114.10]; MS (EI): 114.

Diethyl *N*-Cyanoimidocarbonate **(2b)**



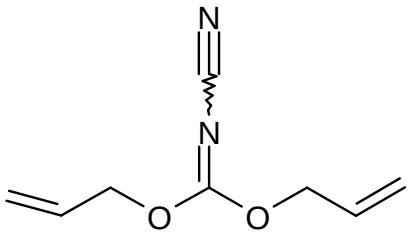
Yield: 53% (1.5 g), yellow oil; IR (film): 2219 (C≡N), 1614 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.34 (t, J = 7.07 Hz, 6H), 4.38 (q, J = 14.13 Hz, 4H); ^{13}C NMR (DMSO-d_6): δ (ppm): 14.16, 14.42, 59.50, 70.32, 113.47, 163.55; $C_6H_{10}N_2O_2$ [142.16]; MS (EI): 142.

Diisopropyl *N*-Cyanoimidocarbonate **(2c)**



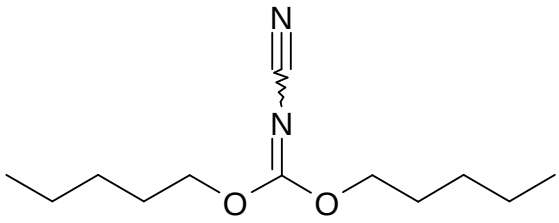
Yield: 40% (1.21 g), colorless oil; IR (film): 2205 (C≡N), 1612 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.47 (d, J = 7.35 Hz, 12H), 4.95-5.02 (m, 2H); ^{13}C NMR (DMSO-d_6): δ(ppm): 9.05, 22.05, 22.17, 22.22, 22.43, 46.35, 114.03, 162.60; $C_8H_{14}N_2O_2$ [170.21]; MS (EI): 170.

Diallyl *N*-Cyanoimidocarbonate **(2d)**



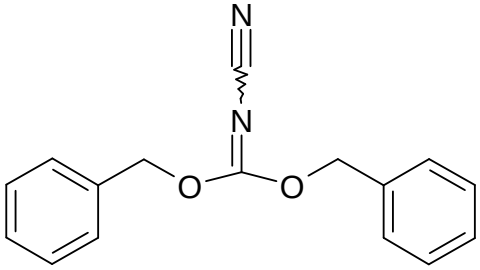
Yield: 48% (1.6 g), colorless oil; IR (film): 2210 (C≡N), 1611 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.92 (d, J = 5.68 Hz, 4H), 5.32-5.45 (m, 4H), 6.05-6.13 (m, 2H); ^{13}C NMR (DMSO-d_6): δ (ppm): 58.89, 69.60, 113.82, 116.40, 115.65, 118.12, 119.43, 165.44; $C_8H_{10}N_2O_2$ [166.18]; MS (EI): 166.

Dipentyl *N*-Cyanoimidocarbonate **(2e)**



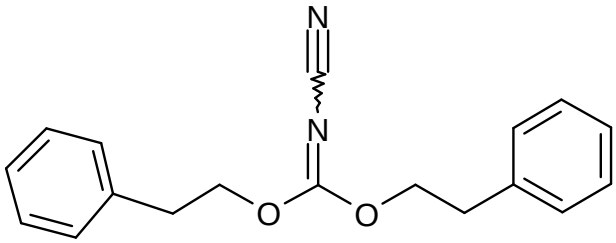
Yield: 50% (2.26 g), colorless oil; IR (film): 2205 (C≡N), 1614 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.95 (t, J = 7.40 Hz, 6H), 1.38-1.45 (m, 8H), 1.71-1.75 (m, 4H), 4.35 (t, J = 7.6 Hz, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 4.25, 21.90, 22.20, 22.51, 32.48, 34.02, 62.65, 65.34, 76.22, 76.81, 113.24, 163.29; $C_{12}H_{22}N_2O_2$ [226.32]; MS (EI): 226.

Dibenzyl *N*-Cyanoimidocarbonate **(2f)**



Yield: 55% (2.92 g), yellow oil; IR (film): 2205 (C≡N), 1614 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.60 (s, 4H), 7.21-7.83 (m, 10H); ^{13}C NMR (DMSO-d_6): δ(ppm): 65.75, 67.40, 114.34, 116.83, 127.72, 128.06, 128.24, 128.37, 128.67, 128.85, 129.28, 129.90, 141.32, 167.43; $C_{16}H_{14}N_2O_2$ [266.30]; MS (EI): 266.

Diphenethyl *N*-Cyanoimidocarbonate **(2g)**

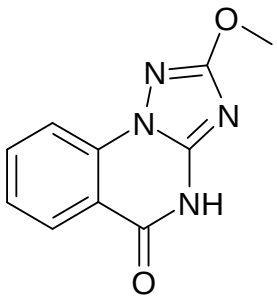


Yield: 52% (3.06 g), yellow oil, IR (film): 2205 (C≡N), 1610 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.82 (t, J = 7.30 Hz, 4H), 3.96 (t, J = 7.41 Hz, 4H), 7.19-7.50 (m, 10H); ^{13}C NMR (DMSO-d_6): δ(ppm): 39.20, 43.23, 63.68, 68.28, 114.23, 125.12, 125.76, 127.12, 127.45, 128.12, 128.34, 128.86, 129.32, 129.67, 142.23, 163.23; $C_{18}H_{18}N_2O_2$ [294.36]; MS (EI): 294.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-ones (6a-g)

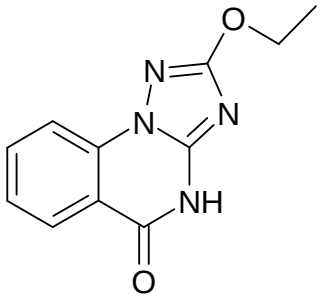
10 mmol of 2-hydrazinobenzoic acid was added portionwise to a stirred solution of **2a-g** (10 mmol) in ethanol (20 mL) at 0 ^{o}C. Afterwards triethylamine (30 mmol) was added dropwise over a period of 30 min. After the addition was complete, the reaction mixture was left to stirr overnight at room temperature. Acidification of the mixture was performed by conc. HCl under ice cooling followed by refluxing for 1-3 h. After cooling, the mixture was poured into ice/water, the resulting solid was filtered, washed with water and dried. Recrystallization from tetrahydrofuran gave analytically pure colored **6a-g**.

2-Methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6a)**



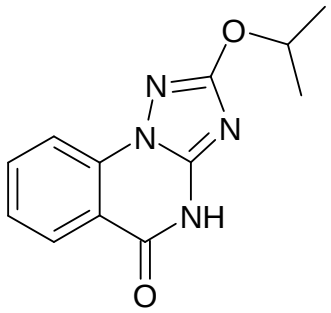
Yield: 60% (1.29 g), yellow solid; Mp.: 228 ^{o}C; IR (KBr): 1685 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.99 (s, 3H), 7.48-8.15 (m, 4H), 13.15 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 57.16, 114.25, 116.83, 125.50, 128.58, 135.72, 136.12, 147.87, 159.93, 168.26; $C_{10}H_8N_4O_2$ [216.20]: calcd.: C 55.56, H 3.73, N 25.91; Found: C 55.38, H 3.83, N 25.99; MS (EI): 216.

2-Ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6b)**



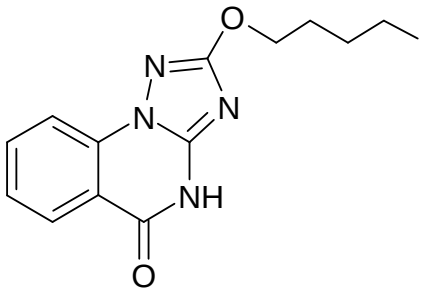
Yield: 60% (1.38 g), yellow solid; Mp.: 244 ^{o}C; IR (KBr): 1689 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.38 (t, J = 7.07 Hz, 3H), 4.35 (q, J = 14.13 Hz, 2H), 7.47-8.16 (m, 4H), 13.01 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.86, 65.64, 114.26, 116.79, 125.50, 128.59, 135.75, 136.12, 147.74, 159.92, 167.56; $C_{11}H_{10}N_4O_2$ [230.23]: calcd.: C 57.39, H 4.38, N 24.34; Found: C 57.18, H 4.49, N 24.40; MS (EI): 230.

2-Isopropoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6c)**



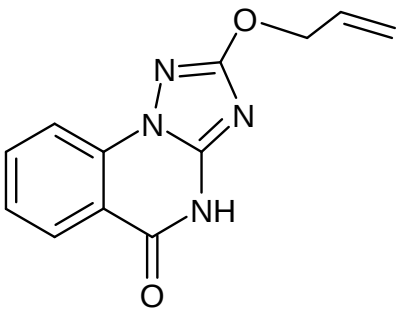
Yield: 40% (0.976 g), pale brown solid; Mp.: 221 ^{o}C; IR (KBr): 1691 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.37 (d, J = 7.35 Hz, 6H), 4.95-5.02 (m, 1H), 6.96-8.16 (m, 4H), 11.34 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 22.16, 73.10, 114.25, 116.83, 125.46, 128.61, 135.73, 136.64, 147.60, 158.85, 167.47; $C_{12}H_{12}N_4O_2$ [244.26]: calcd.: C 59.01, H 4.95, N 22.94; Found: C 59.37, H 4.88, N 22.55; MS (EI): 244.

2-Pentyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6d)**



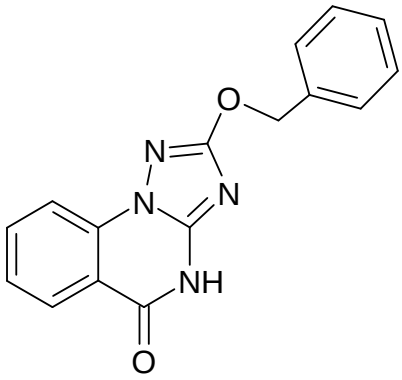
Yield: 50% (1.36 g), yellow solid; Mp.: 234 ^{o}C; IR (KBr): 1692 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.91 (t, J = 7.41 Hz, 3H), 1.33-1.42 (m, 4H), 1.73-1.79 (m, 2H), 4.30 (t, J = 7.60 Hz, 2H), 7.45-8.16 (m, 4H), 12.98 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.27, 22.14, 27.63, 28.47, 69.74, 114.21, 116.80, 125.45, 128.6, 135.72, 136.11, 147.74, 159.91, 167.70; $C_{14}H_{16}N_4O_2$ [272.31]: calcd.: C 61.75, H 5.92, N 20.57; Found: C 61.68, H 6.02, N 20.52; MS (EI): 272.

2-Allyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6e)**



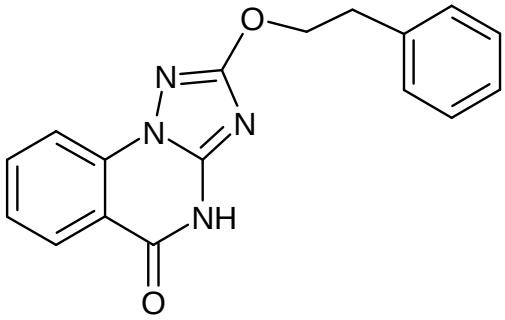
Yield: 55% (1.33 g), yellow solid; Mp.: 215 ^{o}C; IR (KBr): 1696 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.86 (d, J = 5.68 Hz, 2H), 5.42-5.65 (m, 2H), 6.05-6.15 (m, 1H), 7.48-8.17 (m, 4H), 13.01 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.60, 113.82, 116.44, 118.25, 125.16, 128.13, 134.11, 135.30, 135.62, 147.30, 159.45, 166.92; $C_{12}H_{10}N_4O_2$ [242.24]: calcd.: C 59.50, H 4.16, N 23.13; Found: C 59.20, H 4.42, N 22.85; MS (EI): 242.

2-Benzyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6f)**



Yield: 58% (1.69 g), white solid; Mp.: 258 ^{o}C; IR (KBr): 1701 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.39 (s, 2H), 7.37-8.16 (m, 9H), 13.04 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 71.18, 114.34, 116.81, 125.53, 127.74, 128.03, 128.85, 135.75, 136.11, 136.77, 147.11, 160.40, 167.17; $C_{16}H_{12}N_4O_2$ [292.30]: calcd.: C 65.75, H 4.14, N 19.17; Found: C 65.39, H 4.04 , N 19.06; MS (EI): 292.

2-Phenethyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(6g)**

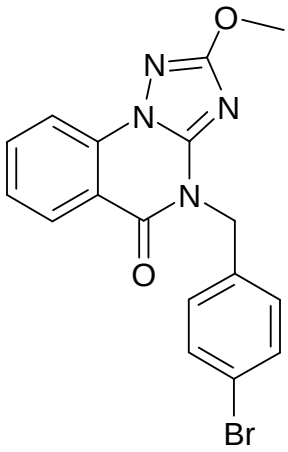


Yield: 56% (1.71 g), white solid; Mp.: 227 ^{o}C; IR (KBr): 1705 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.20 (t, J = 7.50 Hz, 2H), 4.50 (t, J = 7.51 Hz, 2H), 7.20-8.19 (m, 9H), 13.75 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.94, 70.23, 116.81, 114.32, 126.80, 125.51, 128.59, 128.74, 129.37, 136.14, 138.33, 147.72, 159.91, 167.57; $C_{17}H_{14}N_4O_2$ [306.33]: calcd.: C 66.66, H 4.61, N 18.29; Found: C 66.32, H 4.94, N 18.33; MS (EI): 306.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-4-alkyl(aralkyl)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-ones (12a-r)

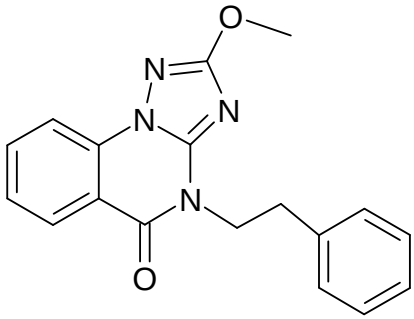
To a solution of **6a,b,d** (1 mmol) in DMF (5 mL) was added potassium carbonate (1.2 mmol) portionwise over a period of 10 min at room temperature. After stirring for 20 min, the appropriate alkyl halide (1.5 mmol) was added dropwise and the reaction mixture was stirred for 18 h at room temperature. The mixture was poured into ice/water, the precipitate was filtered off, washed with water and dried. Analytically pure products were obtained after recrystallization from tetrahydrofuran.

4-(4-Bromobenzyl)-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12a)**



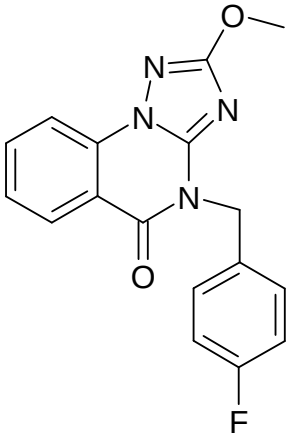
Yield: 83% (0.319 g), yellow solid; Mp.: 194 ^{o}C; IR (KBr): 1676 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.12 (s, 3H), 5.37 (s, 2H), 7.50-8.33 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 46.21, 57.23, 114.28, 116.13, 118.45, 121.03, 125.88, 128.96, 130.50, 131.68, 135.65, 136.02, 148.80, 159.02, 167.84; $C_{17}H_{13}BrN_4O_2$ [385.22]: calcd.: C 53.01, H 3.40, N 14.54; Found: C 52.78, H 3.47, N 14.43; MS (EI): 385.

2-Methoxy-4-phenethyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12b)**



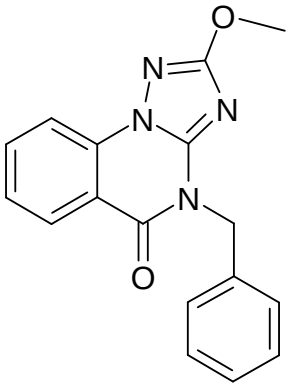
Yield: 85% (0.272 g), white solid; Mp.: 155 ^{o}C; IR (KBr): 1675 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.04 (t, J = 7.54 Hz, 2H), 4.02 (s, 3H), 4.31 (t, J = 7.51 Hz, 2H), 7.22-8.20 (m, 9H), ^{13}C NMR (DMSO-d_6): δ(ppm): 33.08, 44.66, 57.21, 114.18, 116.11, 125.82, 126.88, 128.87, 135.42, 135.84, 138.39, 148.59, 158.76, 167.97; $C_{18}H_{16}N_4O_2$ [320.35]: calcd.: C 67.49, H 5.03, N 17.49; Found: C 67.49, H 5.15, N 17.18; MS (EI): 320.

4-(4-Fluorobenzyl)-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12c)**



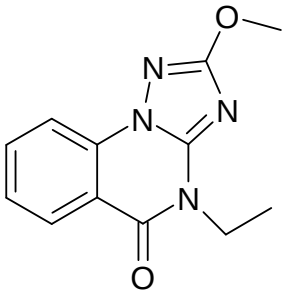
Yield: 83% (0.268 g), white solid; Mp.: 125 ^{o}C; IR (KBr): 1673 (C=O) cm^{-1}, ^{1}H NMR (DMSO-d_6): δ(ppm): 4.12 (s, 3H), 5.37 (s, 2H), 7.50-8.33 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 46.21, 57.23, 114.28, 116.13, 118.45, 121.03, 126.88, 127.96, 131.50, 132.68, 135.65, 136.02, 148.80, 158.64, 167.84; $C_{17}H_{13}FN_4O_2$ [324.32]: calcd.: C 62.96, H 4.04, N 17.28; Found: C 62.59, H 4.24, N 17.02; MS (EI): 324.

4-Benzyl-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12d)**



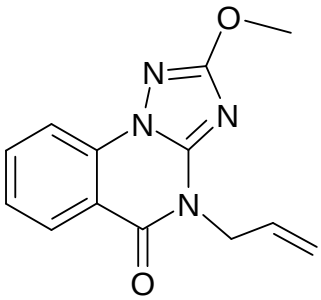
Yield: 82% (0.250 g), yellow solid; Mp.: 134 ^{o}C; IR (KBr): 1678 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.13 (s, 3H), 5.34 (s, 2H), 7.50-8.30 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 46.75, 57.21, 114.24, 116.86, 117.79, 125.80, 128.89, 129.11, 131.66, 132.45, 135.86, 135.52, 148.85, 158.96, 167.86; $C_{17}H_{14}N_4O_2$ [306.33]: calcd.: C 66.66, H 4.61, N 18.29; Found: C 66.46, H 4.69, N 17.93; MS (EI): 306.

4-Ethyl-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (**12e)**



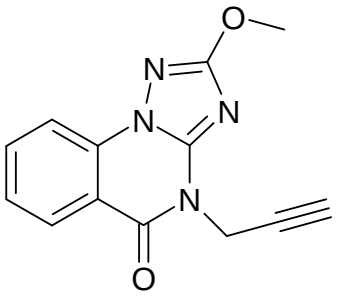
Yield: 62% (0.151 g), white solid; Mp.: 135 ^{o}C; IR (KBr): 1672 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.37 (t, J = 7.04 Hz, 3H), 4.24 (q, J = 14.31 Hz, 2H), 4.11 (s, 3H), 7.58-8.29 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.81, 52.34, 57.18, 114.13, 116.22, 125.71, 128.79, 135.20, 135.42, 148.49, 158.64, 167.99; $C_{12}H_{12}N_4O_2$ [244.26]: calcd.: C 59.01, H 4.95, N 22.94; Found: C 58.79, H 5.04, N 22.58; MS (EI): 244.

4-Allyl-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12f)**



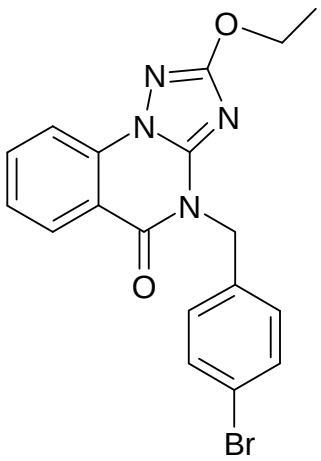
Yield: 82% (0.209 g), yellow solid; Mp.: 132 ^{o}C; IR (KBr): 1680 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.13 (s, 3H), 4.83 (d, J = 4.60 Hz, 2H), 5.30-5.42 (m, 2H), 6.04-6.30 (m, 1H), 7.46-8.31 (m, 4H), ^{13}C NMR (DMSO-d_6): δ(ppm): 45.53, 57.14, 114.47, 116.10, 117.18, 125.83, 128.82, 131.66, 135.42, 135.86, 148.79, 157.81, 168.43; $C_{13}H_{12}N_4O_2$ [256.27]: calcd.: C 60.93, H 4.72, N 21.86; Found: C 60.79, H 5.01, N 21.76; MS (EI): 256.

2-Methoxy-4-prop-2-ynyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12g)**



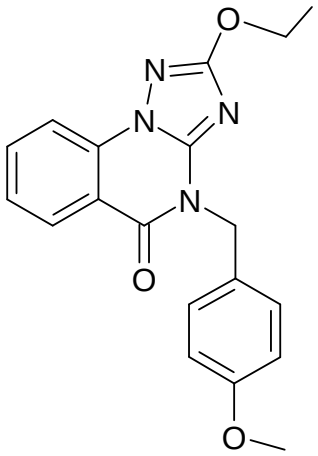
Yield: 84% (0.213 g), white solid; Mp.: 170 ^{o}C; IR (KBr): 1683 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.31 (s, 1H), 4.03 (s, 3H), 4.86 (s, 2H), 7.64-8.31 (m, 4H), ^{13}C NMR (DMSO-d_6): δ(ppm): 33.26, 57.91, 74.96, 75.23, 114.31, 115.84, 126.17, 128.93, 135.12, 136.21, 148.48, 157.57, 168.16; $C_{13}H_{10}N_4O_2$ [254.25]: calcd.: C 61.41, H 3.96, N 22.04; Found: C 61.15, H 3.99, N 21.74; MS (EI): 254.

4-(4-Bromobenzyl)-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12h)**



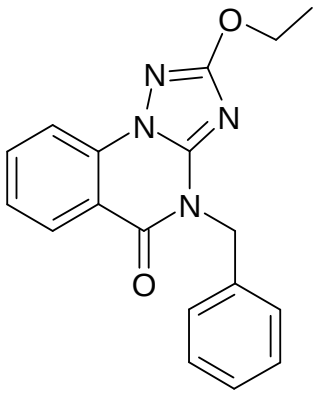
Yield: 85% (0.339 g), white solid; Mp.: 145 ^{o}C; IR (KBr): 1679 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.48 (t, J = 7.01 Hz, 3H), 4.46 (q, J = 14.07 Hz, 2H), 5.35 (s, 2H), 7.94-8.31 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 15.16, 46.77, 66.48, 114.70, 116.30, 118.86, 122.45, 125.83, 129.68, 131.61, 132.11, 134.96, 135.71, 148.53, 159.55, 173.39; $C_{18}H_{15}BrN_4O_2$ [399.25]: calcd.: C 54.15, H 3.79, N 14.03; Found: C 53.86, H 3.78, N 13.75; MS (EI): 399.

2-Ethoxy-4-(4-methoxybenzyl)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12i)**



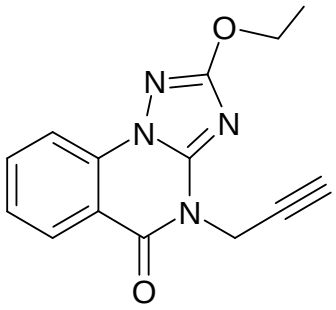
Yield: 71% (0.248 g), white solid; Mp.: 173 ^{o}C; IR (KBr): 1671 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.38 (t, J = 7.11 Hz, 3H), 3.71 (s, 3H), 4.38 (q, J = 14.22 Hz, 2H), 5.22 (s, 2H), 6.88-8.21 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.84, 46.29, 55.43, 65.87, 114.11, 116.17, 125.80, 128.24, 128.93, 130.24, 131.23, 132.30, 135.95, 148.67, 159.15, 167.15; $C_{19}H_{18}N_4O_3$ [350.38]: calcd.: C 65.13, H 5.18, N 15.99; Found: C 64.94, H 5.28, N 15.78; MS (EI): 350.

4-Benzyl-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12j)**



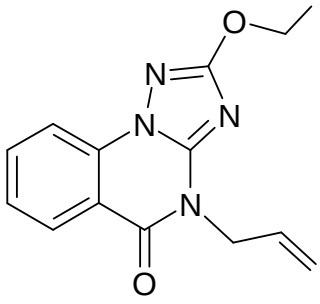
Yield: 81% (0.259 g), white solid; Mp.: 138 ^{o}C; IR (KBr): 1675 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.41 (t, J = 7.07 Hz, 3H), 4.41 (q, J = 14.01 Hz, 2H), 5.30 (s, 2H), 7.30-8.21 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 64.70, 71.16, 114.33, 116.87, 125.59, 125.97, 126.50, 127.03, 127.70, 128.03, 128.71, 128.85, 129.24, 135.52, 136.19, 136.77, 147.18, 155.21, 167.18; $C_{18}H_{16}N_4O_2$ [320.35]: calcd.: C 67.49, H 5.03, N 17.49; Found: C 67.59, H 4.92, N 17.44; MS (EI): 320.

2-Ethoxy-4-prop-2-ynyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12k)**



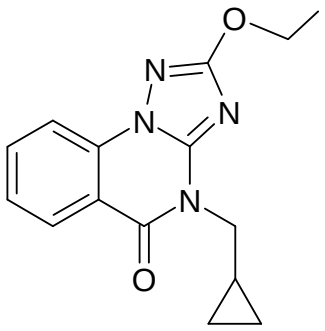
Yield: 87% (0.233 g), white solid; Mp.: 147 ^{o}C; IR (KBr): 1685 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.64 (t, J = 7.26 Hz, 3H), 3.58 (s, 1H), 4.64 (q, J = 14.32 Hz, 2H), 5.10 (s, 2H), 7.77-8.48 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.18, 32.99, 65.77, 74.88, 78.13, 122.45, 125.83, 129.68, 131.61, 148.46, 163.58, 167.53; $C_{14}H_{12}N_4O_2$ [268.28]: calcd.: C 62.68, H 4.51, N 20.88; Found: C 62.45, H 4.75, N 21.08; MS (EI): 268.

4-Allyl-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12l)**



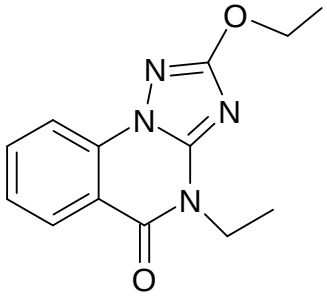
Yield: 83% (0.224 g), yellow solid; Mp.: 106 ^{o}C; IR (KBr): 1671 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.33 (t, J = 7.01 Hz, 3H), 4.32 (q, J = 14.37 Hz, 2H), 4.63 (d, J = 4.66 Hz, 2H), 5.14-5.28 (m, 2H), 5.85-5.95 (m, 1H), 7.43-8.13 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.60, 45.51, 65.77, 114.18, 116.05, 117.85, 125.74, 128.87, 131.60, 135.13, 135.50, 148.40, 158.60, 167.23; $C_{14}H_{14}N_4O_2$ [270.29]: calcd.: C 62.21, H 5.22, N 20.73; Found: C 61.98, H 5.40, N 20.83; MS (EI): 270.

4-Cyclopropylmethyl-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12m)**



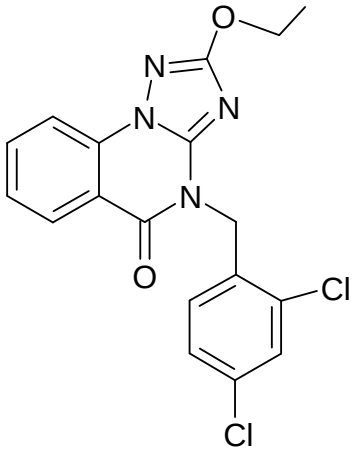
Yield: 70% (0.198 g), white solid; Mp.: 116 ^{o}C; IR (KBr): 1677 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.63-0.69 (m, 5H), 1.56 (t, J = 7.12 Hz, 3H), 4.17 (s, 2H), 4.47 (q, J = 14.34 Hz, 2H), 7.68-8.38 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 3.93, 9.81, 14.85, 48.37, 65.80, 114.17, 116.23, 125.85, 128.93, 135.43, 135.97, 148.78, 158.94, 167.20; $C_{15}H_{16}N_4O_2$ [284.32]: calcd.: C 63.37, H 5.67, N 19.71; Found: C 63.55, H 5.74, N 19.50; MS (EI): 284.

2-Ethoxy-4-ethyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12n)**



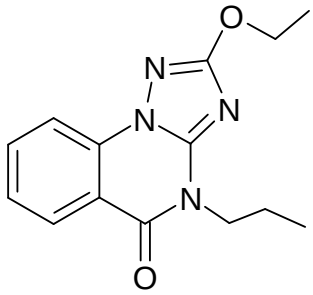
Yield: 65% (0.167 g), white solid; Mp.: 137 ^{o}C; IR (KBr): 1672 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.53 (t, J = 7.01 Hz, 3H), 1.63 (t, J = 7.04 Hz, 3H), 4.37 (q, J = 14.02 Hz, 2H), 4.61 (q, J = 14.05 Hz, 2H), 7.71-8.64 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.18, 14.83, 35.12, 52.71, 65.77, 113.12, 114.40, 125.31, 128.12, 142.20, 148.43, 159.65, 164.78; $C_{13}H_{14}N_4O_2$ [258.28]: calcd.: C 60.46, H 5.46, N 21.69; Found: C 60.13, H 5.65, N 21.70; MS (EI): 258.

4-(2,4-Dichlorobenzyl)-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12o)**



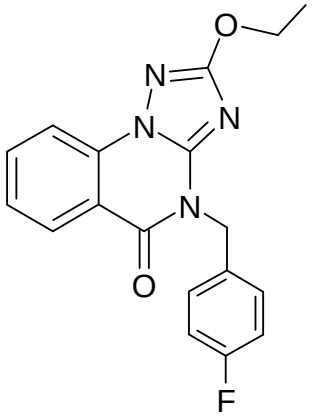
Yield: 73% (0.283 g), white solid; Mp.: 203 ^{o}C; IR (KBr): 1676 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.63 (t, *J* =7.02 Hz, 3H), 4.61 (q, *J* = 14.02 Hz, 2H), 5.31 (s, 2H), 7.31-8.19 (m, 7H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.73, 44.96, 65.80, 114.34, 116.1, 125.81, 127.83, 129.01, 129.70, 131.62, 132.40, 133.15, 135.83, 136.17, 148.63, 159.27, 167.19; $C_{18}H_{14}Cl_2N_4O_2$ [389.24]: calcd.: C 55.54, H 3.63, N 14.39; Found: C 55.17, H 3.75, N 14.37; MS (EI): 389.

2-Ethoxy-4-propyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12p)**



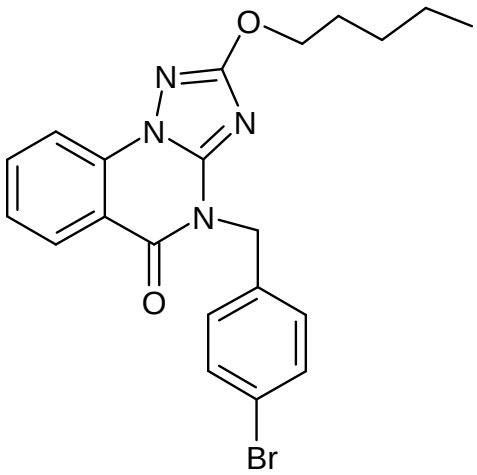
Yield: 66% (0.179 g), white solid; Mp.: 103 ^{o}C; IR (KBr): 1678 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.87 (t, *J* = 7.01 Hz, 3H), 1.32-1.47 (m, 2H), 1.73 (t, *J* =7.11 Hz, 2H), 1.93 (t, *J* =7.07 Hz, 3H), 4.37 (q, *J* =14.7 Hz, 2H), 7.49-8.20 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.35, 21.66, 28.17, 65.30, 113.69, 115.69, 125.25, 128.40, 135.27, 134.99, 148.16, 158.42, 166.81; $C_{14}H_{16}N_4O_2$ [272.31]: calcd.: C 61.75, H 5.92, N 20.57; Found: C 61.95, H 5.58, N 20.49; MS (EI): 272.

2-Ethoxy-4-(4-fluorobenzyl)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(12q)**



Yield: 81% (0.273 g), white solid; Mp.: 137 ^{o}C; IR (KBr): 1678 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.38 (t, J = 7.13 Hz, 3H), 4.39 (q, J = 14.18 Hz, 2H), 5.27 (s, 2H), 7.13-8.22 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.73, 40.25, 65.86, 114.20, 115.18, 116.11, 118.45, 121.60, 125.81, 128.90, 130.43, 131.50, 135.62, 148.84, 159.18, 167.83; $C_{18}H_{15}FN_4O_2$ [338.34]: calcd.: C 63.90, H 4.47, N 16.56; Found: C 63.79, H 4.57, N 16.43; MS (EI): 338.

4-(4-Bromobenzyl)-2-pentyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (**12r**)

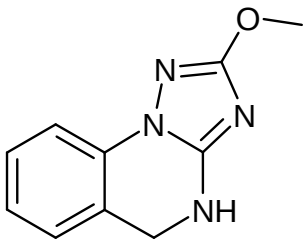


Yield: 77% (0.339 g), brown solid; Mp.: 202 ^{o}C; IR (KBr): 1677 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.94 (t, J = 7.6 Hz, 3H), 1.36-1.43 (m, 4H), 1.70-1.78 (m, 2H), 4.28 (t, J = 7.4 Hz, 2H), 5.37 (s, 2H), 7.45-8.16 (m, 8H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.24, 22.81, 28.37, 29.09, 32.79, 46.76, 66.58, 114.71, 122.72, 125.82, 129.67, 132.11, 134.97, 135.76, 136.03, 148.99, 159.54, 167.73; $C_{21}H_{21}BrN_4O_2$ [441.33]: calcd.: C 57.15, H 4.80, N 12.69; Found: C 57.48, H 5.02, N 12.42; MS (EI): 441.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-4,5-dihydro-[1,2,4]triazolo[1,5-a]quinazolines (16a-f)

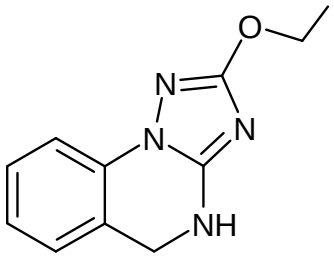
A solution of **6 (**1 mmol**)** in dry THF (5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (3 mmol) in dry THF (10 mL). After stirring at room temperature for 3 h, water (0.4 mL) was added carefully and the mixture was stirred for an additional 30 min. The reaction mixture was filtered and the solvent removed under reduced pressure, the residue was dissolved in THF and passed through a short column chromatography, the solvent was removed under reduced pressure, and the obtained solid was recrystallized from ethyl acetate /n-hexane

4,5-Dihydro-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(16a)**



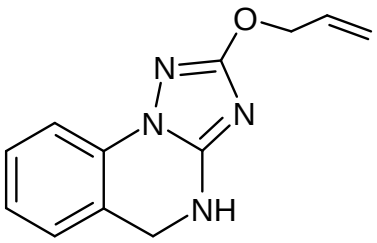
Yield: 60% (0.121 g), white solid; Mp.: 133 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 3.90 (s, 3H), 4.20 (s, 2H), 7.28-7.82 (m, 4H), 7.95 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.35, 112.72, 114.83, 119.64, 124.50, 126.23, 130.75, 134.16, 155.18, 165.29; $C_{10}H_{10}N_4O$ [202.22]: calcd.: C 59.40, H 4.98, N 27.71; Found: C 59.15, H 5.18, N 27.38; MS (EI): 202

4,5-Dihydro-2-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline **(16b)**



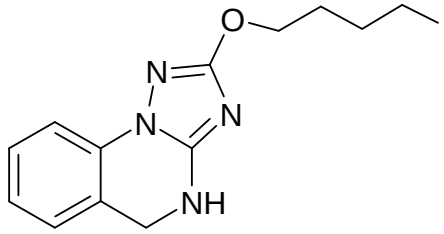
Yield: 61% (0.131 g), white solid; Mp.: 142 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 1.31 (t, J = 7.21 Hz, 3H), 4.24 (q, J = 14.40 Hz, 2H), 4.49 (s, 2H), 7.08-7.33 (m, 4H), 7.76 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.94, 42.38, 64.71, 112.71, 119.70, 124.52, 126.79, 128.79, 134.14, 154.99, 167.37; $C_{11}H_{12}N_4O$ [216.24]: calcd.: C 61.10, H 5.59, N 25.91; Found: C 60.86, H 5.57, N 25.63; MS (EI): 216.

2-Allyloxy-4,5-dihydro-[1,2,4]triazolo[1,5-a]quinazoline **(16c)**



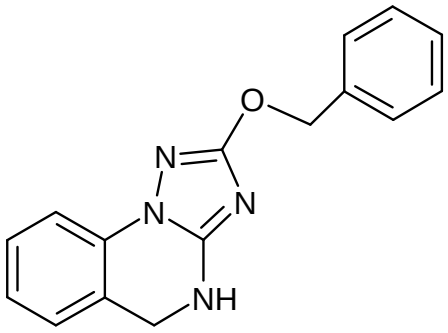
Yield: 55% (0.125 g), white solid; Mp.: 105 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 4.76 (d, J = 6.76 Hz, 2H), 4.92 (s, 2H), 5.32-5.43 (m, 2H), 6.09-6.16 (m, 1H), 7.48-8.10 (m, 4H), 8.25 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.63, 113.87, 116.45, 118.20, 119.24, 125.33, 128.12, 134.57, 135.20, 135.52, 159.37, 166.70; $C_{12}H_{12}N_4O$ [228.26]: calcd.: C 63.15, H 5.30, N 24.55; Found: C 63.43, H 5.23, N 24.42; MS (EI): 228.

4,5-Dihydro-2-pentyloxy-[1,2,4]triazolo[1,5-a]quinazoline **(16d)**



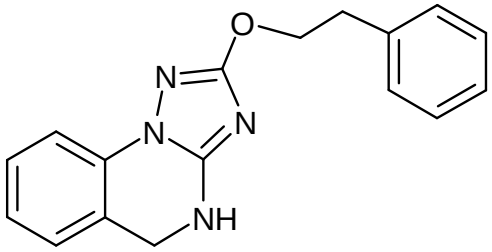
Yield: 45% (0.116 g), white solid; Mp.: 174 ^{o}C (EtOAc-hexane);.^{1}H NMR (DMSO-d_6): δ(ppm): 0.95 (t, J = 7.62 Hz, 3H), 1.37-1.48 (m, 4H), 1.63-1.69 (m, 2H), 4.43 (t, J = 7.61 Hz, 2H), 5.45 (s, 2H), 7.15-8.06 (m, 4H), 8.35 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.17, 22.64, 27.33, 28.57, 68.54, 114.41, 117.80, 125.35, 128.23, 135.42, 136.71, 143.24, 157.11, 162.70; $C_{14}H_{18}N_4O$ [258.33]: calcd.: C 65.09, H 7.02, N 21.69; Found: C 65.48, H 6.82, N 21.42; MS (EI): 258.

2-Benzyloxy-4,5-dihydro-[1,2,4]triazolo[1,5-a]quinazoline **(16e)**



Yield: 70% (0.194 g), white solid; Mp.: 158 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 4.50 (s, 2H), 5.26 (s, 2H), 7.11-7.46 (m, 9H), 7.81 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.94, 112.27, 119.23, 124.10, 126.30, 127.02, 127.95, 128.27, 128.95, 133.67, 136.40, 154.55, 166.87; $C_{16}H_{14}N_4O$ [278.32]: calcd.: C 69.05, H 5.07, N 20.13; Found: C 69.35, H 5.10, N 19.83; MS (EI): 278.

4,5-Dihydro-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline **(16f)**

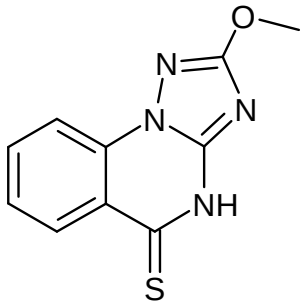


Yield: 64% (0.186 g), white solid; Mp.: 119 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 3.04 (t, J = 7.40 Hz, 2H), 4.39 (t, J = 7.51 Hz, 2H), 4.48 (s, 2H), 7.10-7.32 (m, 9H), 7.77 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.90, 68.95, 113.33, 119.27, 126.80, 128.51, 129.37, 135.74, 136.11, 138.33, 154.90, 166.85; $C_{17}H_{16}N_4O$ [292.34]: calcd.: C 69.85, H 5.52, N 19.16; Found: C 69.51, H 5.56, N 18.93; MS (EI): 292

General procedure for the preparation of 2-Alkoxy(aralkoxy)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thiones (27a-e)

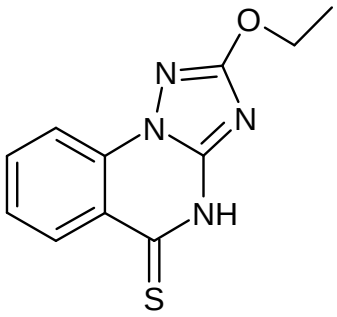
Compound **6** (1 mmol) was refluxed with phosphorous pentasulfide (1 mmol) in absolute pyridine (5 mL) for 2 h. Afterwards the reaction mixture was cooled and poured into ice/water, the yellow precipitate was separated by filtration and washed thoroughly with water. Recrystallization from aq. DMF furnished analytically pure **27a-e.**

2-Methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione **(27a)**



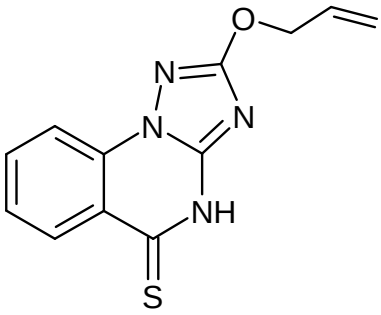
Yield: 85% (0.197 g), yellow solid; Mp.: 230 ^{o}C; IR (KBr): 1250 (C=S) cm^{-1} ; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.02 (s, 3H), 7.52-7.96 (m, 4H), 14.72 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.84, 114.21, 122.43, 125.83, 131.77, 132.41, 135.88, 149.59, 162.78, 185.01; $C_{10}H_8N_4OS$ [232.27]: calcd.: C 51.71, H 3.47, N 24.12, S 13.80; Found: C 51.99, H 3.22, N 24.52, S 13.65; MS (EI): 232.

2-Ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione **(27b)**



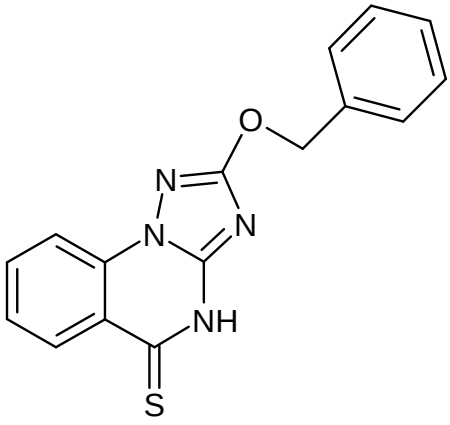
Yield: 92% (0.226 g), yellow solid; Mp.: 226 ^{o}C; IR (KBr): 1248 (C=S) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.39 (t, J = 7.28 Hz, 3H), 4.40 (q, J = 14.20 Hz, 2H), 7.51-8.62 (m, 4H), 14.70 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.39, 65.46, 114.20, 122.90, 125.79, 131.39, 132.39, 145.63, 162.12, 184.94; $C_{11}H_{10}N_4OS$ [246.29]: calcd.: C 53.64, H 4.09, N 22.75, S 13.02; Found: C 53.42, H 3.87, N 22.32, S 13.17; MS (EI): 246.

2-Allyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione **(27c)**



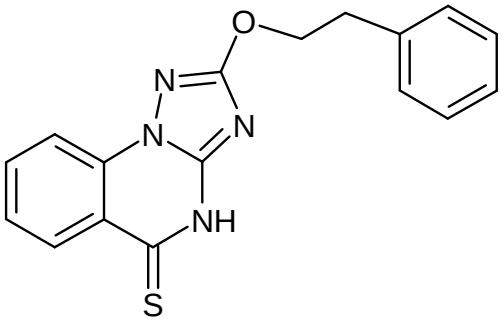
Yield: 95% (0.245 g), yellow solid; Mp.: 190 ^{o}C; IR (KBr): 1244 (C=S) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.85-4.89 (m, 2H), 5.31-5.46 (m, 2H), 6.08-6.15 (m, 1H), 7.48-8.62 (m, 4H), 14.72 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.92, 114.27, 118.39, 122.53, 125.92, 128.21, 131.83, 132.42, 135.92, 145.75, 167.31, 185.08; $C_{12}H_{10}N_4OS$ [258.30]: calcd.: C 55.80, H 3.90, N 21.69, S 12.41; Found: C 55.65, H 3.97, N 21.73, S 12.18; MS (EI): 258.

2-Benzyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione **(27d)**



Yield: 97% (0.298 g), yellow solid; Mp.: 210 ^{o}C; IR (KBr): 1253 (C=S) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.42 (s, 2H), 7.37-8.62 (m, 9H), 14.74 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 70.60, 114.24, 122.40, 125.37, 128.06, 128.10, 128.90, 131.72, 132.33, 135.38, 145.90, 167.34, 185.62; $C_{16}H_{12}N_4OS$ [308.36]: calcd.: C 62.32, H 3.92, N 18.17, S 10.40; Found: C 61.96, H 4.05, N 17.87, S 10.06; MS (EI): 308.

2-Phenethyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione **(27e)**

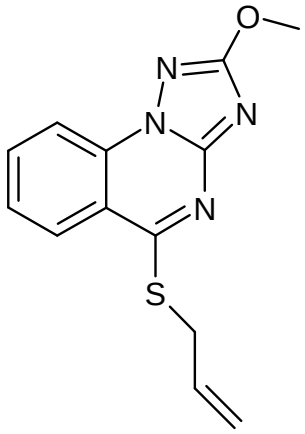


Yield: 89% (0.286 g), yellow solid; Mp.: 221 ^{o}C; IR (KBr): 1257 (C=S) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.11 (t, J = 6.35 Hz, 2H), 4.55 (t, J = 6.63 Hz, 2H), 7.24-8.61 (m, 9H), 14.70 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.45, 69.72, 114.23, 122.42, 125.00, 125.82, 126.30, 128.28, 128.85, 131.76, 135.83, 137.80, 145.63, 165.20, 184.91; $C_{17}H_{14}N_4OS$ [322.39]: calcd.: C 63.34, H 4.38, N 17.38, S 9.95; Found: C 62.95, H 4.65, N 17.02, S 10.03; MS (EI): 322.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-5-alkyl(aralkyl)sulfanyl-[1,2,4]triazolo[1,5-a]quinazolines (29a-e)

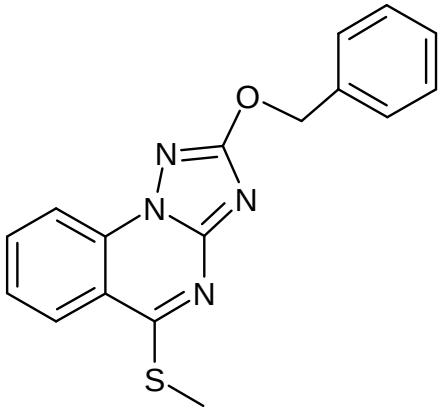
Compound **27a,d** (1 mmol) was dissolved in 0.5 M sodium hydroxide solution (10 mL), alkyl halide (1.5 mmol) was added dropwise over a period 2 min, the mixture was left to stirr for 5-20 min at room temperature, and the obtained solid was separated by filtration, washed thoroughly with water and dried. Recrystallization of the crude products from ethanol afforded **29a-e** as colored pure solids.

5-Allylsulfanyl-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(29a)**



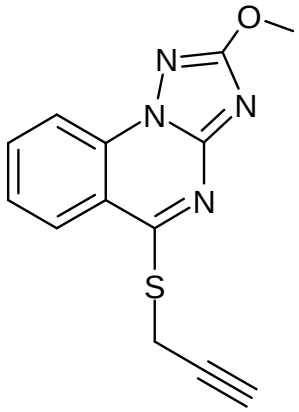
Yield: 70% (0.190 g), white solid; Mp.: 123 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.07 (s, 3H), 4.09 (d, J = 10.12 Hz, 2H), 5.22-5.50 (m, 2H) 5.99-6.09 (m, 1H), 7.63-8.22 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 32.03, 56.67, 114.81, 116.99, 118.94, 125.54, 132.59, 133.54, 135.57, 165.88, 169.24; $C_{13}H_{12}N_4OS$ [272.33]: calcd.: C 57.34, H 4.44, N 20.57, S 11.77; Found: C 57.70, H 4.32, N 20.53, S 11.48; MS (EI): 272.

2-Benzyloxy-5-methylsulfanyl-[1,2,4]triazolo[1,5-a]quinazoline **(29b)**



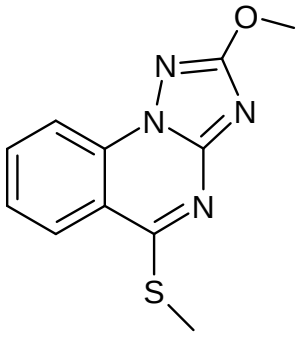
Yield: 73% (0.235 g), yellow solid; Mp.: 185 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.45 (s, 3H), 5.34 (s, 2H), 7.20-8.86 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.69, 69.78, 113.19, 114.79, 123.25, 125.45, 125.78, 127.78, 128.26, 131.87, 132.14, 135.45, 136.69, 152.67, 168.11; $C_{17}H_{14}N_4OS$ [322.39]: calcd.: C 63.34, H 4.38, N 17.38, S 9.95; Found: C 63.02, H 4.32, N 17.24, S 10.01; MS (EI): 322.

2-Methoxy-5-prop-2-ynylsulfanyl-[1,2,4]triazolo[1,5-a]quinazoline **(29c)**



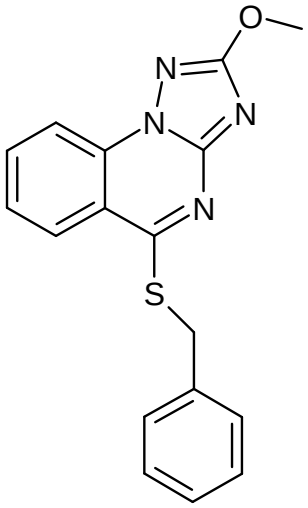
Yield: 61% (0.164 g), pale brown solid; Mp.: 190 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.23 (s, 1H), 4.20 (s, 3H), 4.45 (s, 2H), 7.60-8.34 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 18.45, 57.11, 79.57, 80.74, 115.23, 117.04, 125.64, 125.79, 126.28, 133.91, 136.16, 151.02, 165.08, 169.60; $C_{13}H_{10}N_4OS$ [270.31]: calcd.: C 57.76, H 3.73, N 20.73, S 11.86; Found: C 57.61, H 3.90, N 21.08, S 11.55; MS (EI): 270.

2-Methoxy-5-methylsulfanyl-[1,2,4]triazolo[1,5-a]quinazoline **(29d)**



Yield: 60% (0.147 g), yellow solid; Mp.: 146 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.73 (s, 3H), 4.07 (s, 3H), 7.66-8.22 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 31.45, 56.64, 114.21, 122.27, 125.32, 131.81, 132.52, 135.88, 140.47, 159.22, 166.20; $C_{11}H_{10}N_4OS$ [246.29]: calcd.: C 53.64, H 4.09, N 22.75, S 13.02; Found: C 53.91, H 3.86, N 22.45, S 12.81; MS (EI): 246.

5-Benzylsulfanyl-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(29e)**

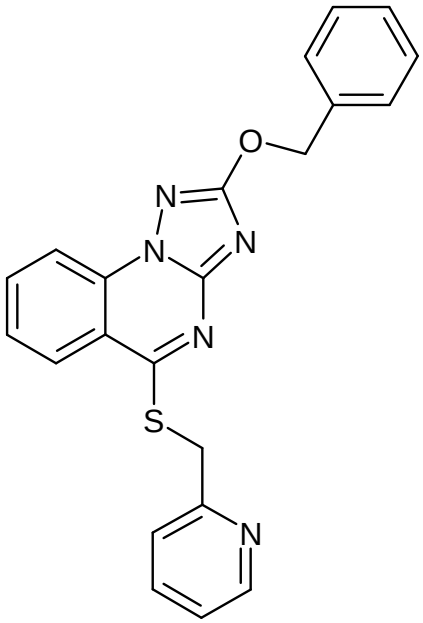


Yield: 58% (0.186 g), yellow solid; Mp.: 118 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.08 (s, 3H), 4.67 (s, 2H), 7.21-8.20 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 33.85, 57.09, 115.16, 117.14, 125.72, 125.89, 126.15, 126.70, 128.70, 128.86, 129.84, 136.71, 150.15, 163.12, 166.41; $C_{17}H_{14}N_4OS$ [322.39]: calcd.: C 63.34, H 4.38, N 17.38, S 9.95; Found C 63.20, H 4.27, N 17.25, S 9.63; MS (EI): 322

Procedure for the preparation of 2-Benzyloxy-5-(pyridin-2-methylsulfanyl)-[1,2,4]triazolo[1,5-a]quinazoline (29f)

To a mixture of **27d** (1 mmol) and 2-(chloromethyl)pyridine (1.5 mmol) in methanol (10 mL), 28% methanolic solution of sodium methoxide (2 mL) was added and the reaction mixture was left to stirr at room temperature for 7 h. Afterwards the mixture was poured into water and exctracted with $CHCl_3$. The $CHCl_3$ layer was washed with an aq. sodium carbonate solution, dried over $MgSO_4$, the solvent was evaporated and the residue recrystallized from ethyl acetate/n-hexane to afford **29f** as yellow pure solid.

2-Benzyloxy-5-(pyridin-2-methylsulfanyl)-[1,2,4]triazolo[1,5-a]quinazoline **(29f)**

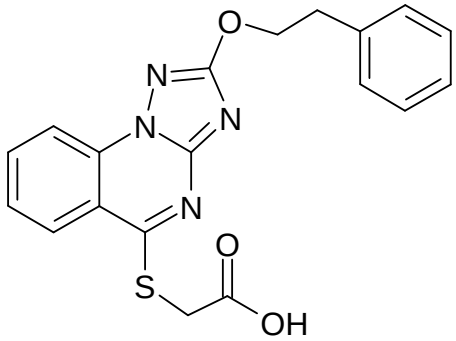


Yield: 45% (0.179 g), yellow solid; Mp.: 183 ^{o}C (EtOAc-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 3.87 (s, 2H), 5.48 (s, 2H), 7.36-8.28 (m, 13H); ^{13}C NMR (DMSO-d_6): δ(ppm): 66.12, 70.99, 115.68, 117.69, 123.15, 124.04, 125.17, 126.03, 126.14, 126.90, 128.56, 128.83, 135.52, 136.63, 140.17, 152.13, 162.37; $C_{22}H_{17}N_5OS$ [399.48]: calcd.: C 66.15, H 4.29, N 17.53, S 8.03; Found: C 66.54, H 4.02, N 17.32, S 8.14; MS (EI): 399.

Procedure for the preparation of 2-Phenethyloxy-[1,2,4]triazolo[1,5-a]-quinazolin-5-ylsulfanyl-acetic acid (29g)

Compound **27e (**1 mmol) was dissolved in 0.5 M ethanolic solution of sodium hydroxide (10 mL), bromoacetic acid (1 mmol) was added, and the mixture was refluxed for 3 h. Afterwards, the mixture was cooled and neutralized with aq. HCl (20%). The obtained solid was separated by filtration, washed with water, dried and recrystallized from ethanol.

2-Phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-ylsulfanyl-acetic acid (**29g)**



Yield: 56% (0.212 g), yellow solid; Mp.: 159 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.13 (t, J = 6.92 Hz, 2H), 4.16 (s, 2H), 4.20 (s, 1H), 4.59 (t, J = 6.95 Hz, 2H), 7.23-8.20 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.55, 55.03, 69.55, 111.04, 114.09, 125.35, 125.51, 126.29, 128.28, 128.86, 129.67, 135.30, 135.60, 137.90, 145.56, 157.22, 168.34; $C_{19}H_{16}N_4O_3S$ [380.43]: calcd.: C 59.99, H 4.24, N 14.73, S 8.43; Found: C 60.35, H 4.50, N 15.01, S 8.17; MS (EI): 380.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-5-chloro-[1,2,4]triazolo[1,5-a]quinazolines (31a-f)

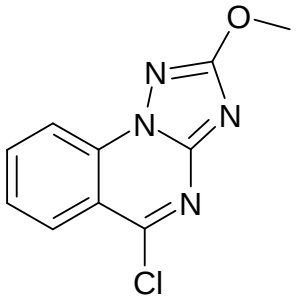
Method-A

Compound **6** (2 mmol) was refluxed with oxalyl chloride (6 mmol) in 1,1,2-trichloroethane (12 mL) for 19 h at 105 ^{o}C. The solution was cooled and methanol (0.2 mL) was added dropwise. The obtained solid was filtered, washed with n-hexane, dried and recrystallized from THF-hexane.

Method-B

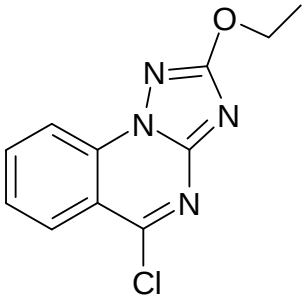
Compound **6** (1 mmol) was refluxed with Phosphorous oxychloride (1 mL) in benzene (7 mL) for 2 h. The solvent was evaporated and the residue was treated with saturated solution of potassium carbonate. The solid was filtered, washed thoroughly with water, dried and recrystallized from THF-hexane.

5-Chloro-2-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(31a)**



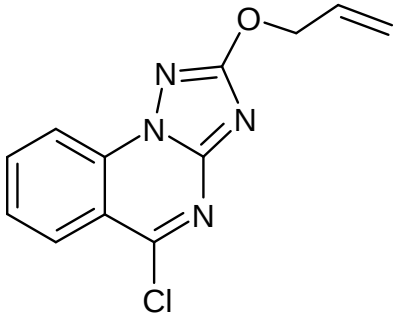
Yield**:** 80% (0.187 g), white solid; Mp.: 148 ^{o}C (THF-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 3.99 (s, 3H), 7.48-8.15 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 57.16, 114.20, 116.83, 125.51, 128.57, 135.74, 136.19, 141.11, 159.90, 168.26; $C_{10}H_7ClN_4O$ [234.65]: calcd.: C 51.19, H 3.01, N 23.88; Found: C 51.12, H 3.18, N 23.98; MS (EI): 234.

5-Chloro-2-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline **(31b)**



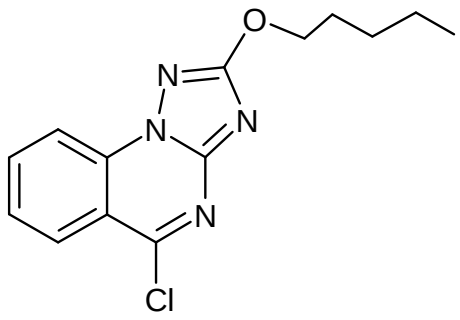
Yield: 89% (0.220 g), white solid; Mp.: 134 ^{o}C (THF-hexane);. ^{1}H NMR (DMSO-d_6): δ(ppm): 1.37 (t, J = 7.07 Hz, 3H), 4.34 (q, J = 14.13 Hz, 2H), 7.49-8.15 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.83, 65.67, 114.17, 116.75, 125.52, 128.80, 135.18, 136.13, 142.20, 159.92, 167.38; $C_{11}H_9ClN_4O$ [248.67]: calcd.: C 53.13, H 3.65, N 22.53; Found: C 53.33, H 3.98, N 22.33; MS (EI): 248.

2-Allyloxy-5-chloro-[1,2,4]triazolo[1,5-a]quinazoline **(31c)**



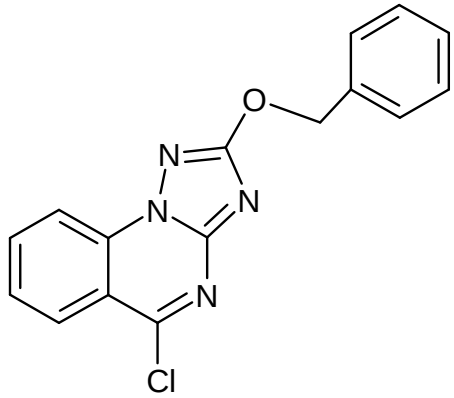
Yield: 87% (0.226 g), yellow solid; Mp.: 115^{o}C (THF-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 4.86 (d, J = 6.53 Hz, 2H), 5.42-5.65 (m, 2H), 6.15-6.20 (m, 1H), 7.48-8.04 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 70.32, 115.17, 117.44, 118.80, 127.13, 128.17, 134.10, 135.30, 135.62, 137.19, 159.11, 167.90; $C_{12}H_9ClN_4O$ [260.68]: calcd.: C 55.29, H 3.48, N 21.49; Found: C 54.94, H 3.67, N 21.09; MS (EI): 260.

5-Chloro-2-pentyloxy-[1,2,4]triazolo[1,5-a]quinazoline **(31d)**



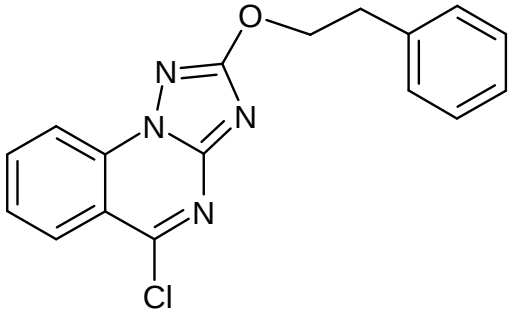
Yield: 81% (0.234 g), pale brown solid; Mp.: 110 ^{o}C (THF-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 0.96 (t, J = 7.45 Hz, 3H), 1.37-1.47 (m, 4H), 1.83-1.89 (m, 2H), 4.43 (t, J = 7.60 Hz, 2H), 7.45-8.16 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 13.75, 21.70, 27.35, 28.16, 69.52, 114.70, 116.81, 126.54, 127.95, 135.57, 136.63, 155.33, 166.57; $C_{14}H_{15}ClN_4O$ [290.75]: calcd.: C 57.83, H 5.20, N 19.27; Found: C 57.93, H 5.29, N 18.98; MS (EI): 290.

2-Benzyloxy-5-chloro-[1,2,4]triazolo[1,5-a]quinazoline **(31e)**



Yield: 90% (0.279 g), white solid; Mp.: 130 ^{o}C (THF-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 5.79 (s, 2H), 7.37-8.45 (m, 9H), ^{13}C NMR (DMSO-d_6): δ(ppm): 71.34, 115.20, 117.42, 125.50, 126.71, 127.14, 128.07, 128.70, 132.41, 135.90, 136.11, 136.77, 155.93, 165.25; $C_{16}H_{11}ClN_4O$ [310.75]: calcd.: C 61.84, H 3.57, N 18.03; Found: C 61.80, H 3.82, N 17.88; MS (EI): 310.

5-Chloro-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline **(31f)**



Yield: 91% (0.294 g), white solid; Mp.: 140 ^{o}C (THF-hexane); ^{1}H NMR (DMSO-d_6): δ(ppm): 3.15 (t, J = 7.50 Hz, 2H), 4.65 (t, J = 7.51 Hz, 2H), 7.22-8.37 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 35.09, 69.61, 114.59, 124.40, 124.83, 126.72, 128.74, 129.30, 134.29, 134.94, 138.49, 153.37, 156.84, 168.61; $C_{17}H_{13}ClN_4O$ [324.77]: calcd.: C 62.87, H 4.03, N 17.25; Found: C 62.57, H 4.22, N 17.15; MS (EI): 324.

General procedure for the preparation of 2-Alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazines (32a-f)

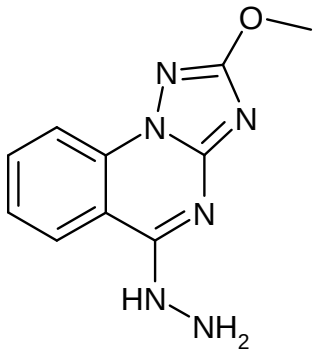
Method A

Compound **31** (1 mmol) was heated under reflux with hydrazine hydrate (5 mmol) in ethanol (8 mL) for 3 h. After cooling, the precipitate was filtered off and washed with water. Recrystallization from ethanol afforded **32a-f** as colored pure solids

Method B

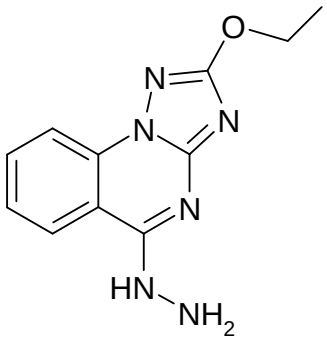
Compound **27** (1 mmol) was refluxed with hydrazine hydrate (0.5 mL) in ethanol (10 mL) for 16 h. After cooling, the precipitate was filtered off, washed with water, and recrystallized from ethanol.

2-Methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32a)**



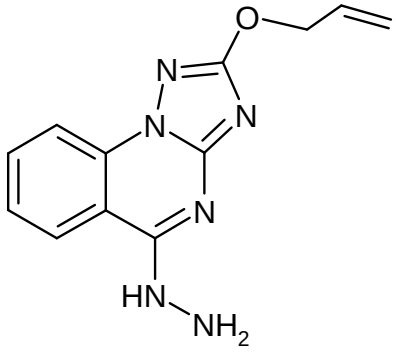
Yield: 60% (0.138 g), white solid; Mp.: 235 ^{o}C; IR (KBr): 3205, 3250 (NH) cm^{-1};^{1}H NMR (DMSO-d_6): δ(ppm): 3.98 (s, 3H), 4.94 (s, 2H), 7.47-8.30 (m, 4H), 9.37 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.48, 114.48, 124.40, 124.77, 125.40, 127.35, 134.24, 134.98, 153.51, 169.23; $C_{10}H_{10}N_6O$ [230.23]: calcd.: C 52.17, H 4.38, N 36.50; Found: C 52.46, H 4.25, N 36.15; MS (EI): 230.

2-Ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32b)**



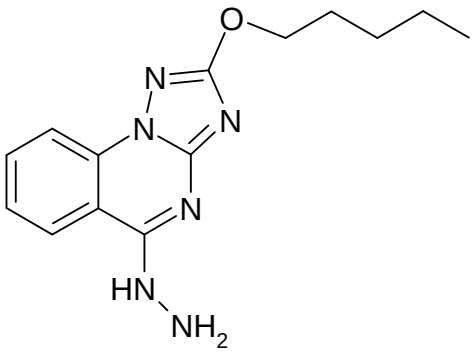
Yield: 69% (0.168 g), white solid; Mp.: 218 ^{o}C; IR (KBr): 3189, 3231 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.30 (t, J = 7.07 Hz, 3H), 4,37 (q, J = 14.13 Hz, 2H), 4.65 (s, 2H), 7.49-8.15 (m, 4H), 9.42 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.73, 65.61, 114.12, 116.45, 125.62, 128.43, 135.13, 136.29, 142.38, 159.82, 167.92; $C_{11}H_{12}N_6O$ [244.26]: calcd.: C 54.09, H 4.95, N 34.41; Found: C 54.37, H 5.12, N 34.27; MS (EI): 244.

2-Allyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32c)**



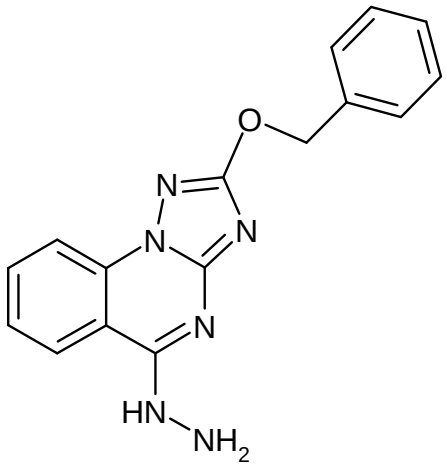
Yield: 71% (0.181 g), yellow solid; Mp.: 223 ^{o}C; IR (KBr): 3210, 3267 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.81 (s, 2H), 4.85 (d, J = 5.30 Hz, 2H), 5.29-5.43 (m, 2H), 6.06-6.12 (m, 1H) 7.47-8.30 (m, 4H), 9.90 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.53, 70.55, 113.12, 114.59, 118.32, 124.41, 133.52, 134.26, 134.95, 150.72, 161.12, 168.50; $C_{12}H_{12}N_6O$ [256.27]: calcd.: C 56.24, H 4.72, N 32.79; Found: C 56.60, H 4.54, N 32.93; MS (EI): 256.

2-Pentyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32d)**



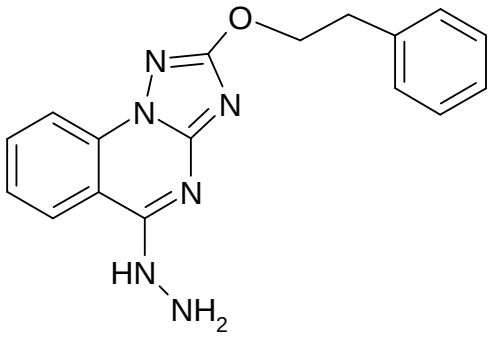
Yield: 62% (0.177 g), white solid; Mp.: 200 ^{o}C; IR (KBr): 3183, 3256 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.94 (t, J = 7.40 Hz, 3H), 1.34-1.44 (m, 4H), 1.71-1.77 (m, 2H), 4.35 (t, J = 7.60 Hz, 2H), 4.93 (s, 2H), 7.55-8.17 (m, 4H), 9.98 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.23, 22.18, 27.89, 28.63, 69.05, 114.2, 124.41, 124.55, 124.70, 134.20, 134.99, 147.72, 153.90, 167.74; $C_{14}H_{18}N_6O$ [286.34]: calcd.: C 58.73, H 6.34, N 29.35; Found: C 59.21, H 6.02, N 29.28; MS (EI): 286.

2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32e)**



Yield: 78% (0.238 g), white solid; Mp.: 215 ^{o}C; IR (KBr): 3209, 3286 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.82 (s, 2H), 5.40 (s, 2H), 7.33-8.32 (m, 9H), 9.91 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 69.63, 113.85, 116.43, 118.20, 125.12, 128.15, 132.62, 135.30, 135.66, 147.34, 159.45, 166.93; $C_{16}H_{14}N_6O$ [306.33]: calcd.: C 62.74, H 4.61, N 27.43; Found: C 62.54, H 4.43, N 27.24; MS (EI): 306.

2-Phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine **(32f)**

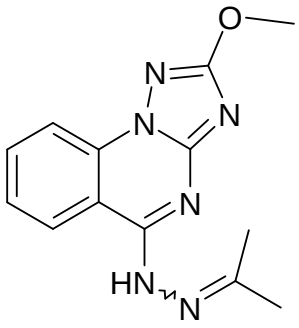


Yield: 72% (0.230 g), yellow solid; Mp.: 190 ^{o}C; IR (KBr): 3217, 3280 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.40 (t, J = 7.70 Hz, 2H), 4.62 (t, J = 7.45 Hz, 2H), 4.95 (s, 2H), 7.20-8.24 (m, 9H), 9.94 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.66, 69.13, 109.89, 114.12, 125.51, 126.8, 128.59, 128.74, 133.76, 134.75, 136.15, 138.30, 152.94, 156.35, 168.18; $C_{17}H_{16}N_6O$ [320.36]: calcd.: C 63.74, H 5.03, N 26.23; Found: C 63.47, H 4.94, N 26.43; MS (EI): 320.

General procedure for the preparation of Compounds 34a-e

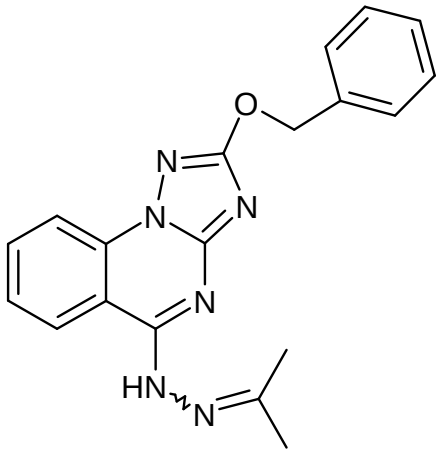
A mixture of **32a,e,f (**1 mmol**)** and aldehyde or ketone (1 mmol) was refluxed in ethanol (10 mL) for 3 h. The solvent was removed under reduced pressure, and the resulting solids were recrystallized from ethanol.

N-Isopropylidene-*N'*-(2-methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine **(34a)**



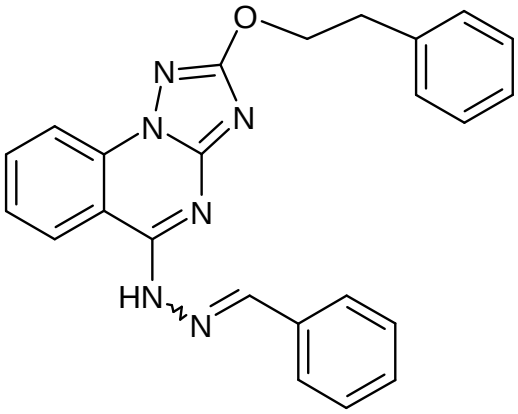
Yield: 70 % (0.189 g), yellow solid; Mp.: 189 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.21 (s, 3H), 2.63 (s, 3H), 2.85 (s, 3H), 7.37-8.54 (m, 4H), 10.45 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 13.80, 18.67, 25.27, 115.08, 124.90, 125.75, 126.06, 134.24, 134.96, 163.37, 164.54; $C_{13}H_{14}N_6O$ [270.30]: calcd.: C 57.77, H 5.22, N 31.09; Found: C 57.52, H 4.94, N 31.42; MS (EI): 270.

N-(2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-*N'*-isopropylidene-hydrazine **(34b)**



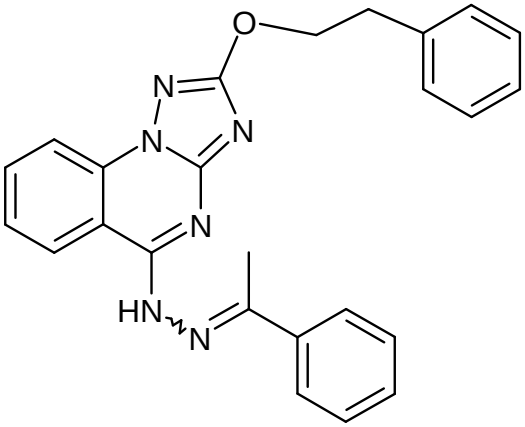
Yield: 73% (0.252 g), yellow solid; Mp.: 198 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.12 (s, 3H), 2.30 (s, 3H), 5.54 (s, 2H), 6.34 (s, 1H), 7.37-8.63 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.71, 13.43, 70.88, 103.16, 109.37, 114.05, 121.53, 124.69, 128.18, 128.46, 136.08, 136.74, 143.30, 150.85, 152.63, 169.21; $C_{19}H_{18}N_6O$ [346.39]: calcd.: C 65.88, H 5.24, N 24.26; Found: C 65.73, H 4.98, N 24.31; MS (EI): 346.

N-Benzylidene-*N*'-(2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine **(34c)**



Yield: 79% (0.322 g), yellow solid; Mp.: 218 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.12 (t, J = 7.34 Hz, 2H), 3.33 (s, 1H), 4.57 (t, J = 7.23 Hz, 2H), 7.25-8.55 (m, 14H), 11.83 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 35.11, 69.79, 110.23, 114.12, 115.37, 124.65, 126.43, 127.54, 128.61, 129.20, 130.11, 131.58, 132.27, 135.78, 139.52, 141.32, 154.20, 168.97; $C_{24}H_{20}N_6O$ [408.47]: calcd.: C 70.57, H 4.94, N 20.57; Found: C 70.23, H 5.14, N 20.21; MS (EI): 408.

N-(2-Phenethyloxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-*N*'-(1-phenyl-ethylidene)-hydrazine **(34d)**

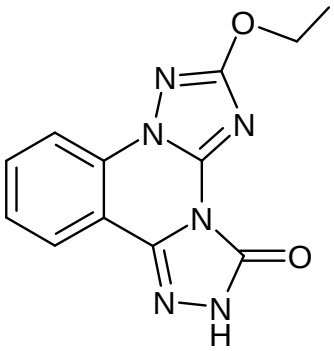


Yield: 68% (0.286 g), yellow solid; Mp.: 203 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.87 (s, 3H), 3.43 (t, J = 7.74 Hz, 2H), 4.77 (t, J = 7.83 Hz, 2H), 7.25-8.55 (m, 14H), 9.91 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.65, 35.10, 69.79, 110.73, 114.62, 116.73, 124.65, 125.33, 126.23, 128.11, 129.20, 131.11, 131.58, 132.27, 135.78, 139.52, 141.32, 145.34, 152.20, 161.57; $C_{25}H_{22}N_6O$ [422.49]: calcd.: C 71.07, H 5.25, N 19.89; Found: C 70.81, H 5.01, N 20.28; MS (EI): 422.

General procedure for the preparation of compounds 36a,b

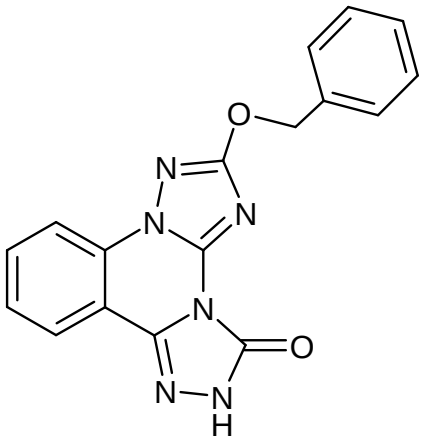
A mixture of **32b,e** (0.5 mmol) and 1,1`-carbonyldiimidazole (0.6 mmol) was refluxed in absolute toluene (7 mL) for 3 h. The solvent was removed under reduced pressure and the residue was treated with $CHCl_3$. The resulting solid was separated by filtration and recrystallized from ethanol.

2-Ethoxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-one **(36a)**



Yield: 45% (0.61 g), white solid; Mp.: 211 ^{o}C; IR (KBr): 1709 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.47 (t, J = 7.24 Hz, 3H), 4.14 (q, J = 13.77 Hz, 2H), 7.31-7.92 (m, 4H), 12.24 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 13.73, 66.15, 114.63, 116.43, 125.12, 127.64, 135.66, 136.76, 147.73, 157.43, 168.37; $C_{12}H_{10}N_6O_2$ [270.25]: calcd.: C 53.33, H 3.73, N 31.10; Found: C 53.78, H 4.02, N 30.89; MS (EI): 270.

2-Benzyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-one **(36b)**

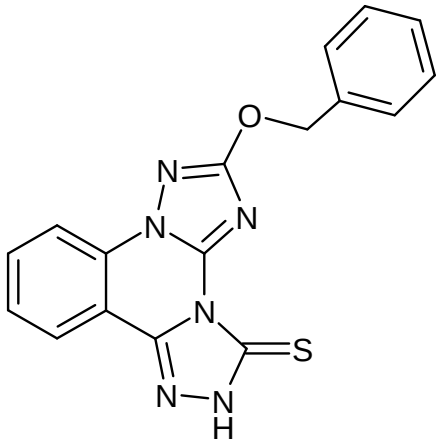


Yield: 50% (0.83 g), yellow solid; Mp.: 206 ^{o}C; IR (KBr): 1705 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.41 (s, 2H), 7.28-8.22 (m, 9H), 12.87 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 70.53, 110.38, 114.59, 120.67, 124.87, 128.48, 133.33, 134.30, 134.89, 136.89, 147.67, 153.38, 156.80, 168.62; $C_{17}H_{12}N_6O_2$ [332.32]: calcd.: C 61.44, H 3.64, N 25.29; Found; C 61.78, H 3.40, N 25.42; MS (EI): 332.

General procedure for the preparation of compounds 37a,b

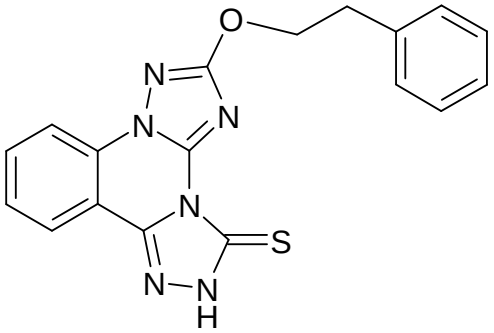
A mixture of **32e,f** (0.5 mmol) and CS_2 (2.5 mmol) in pyridine (5 mL) was refluxed for 2 h. After cooling, the mixture was poured into ice/water, the yellow precipitate was filtered off, washed with water and recrystallized from methanol.

2-Benzyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-thione **(37a)**



Yield: 61% (0.106 g), yellow solid; Mp.: 230 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.48 (s, 2H), 7.38-822 (m, 9H), 14.60 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 71.52, 112.05, 115.19, 124.16, 125.63, 126.87, 128.74, 128.83, 133.33, 134.42, 136.15, 142.06, 157.12, 163.17, 185.67; $C_{17}H_{12}N_6OS$ [348.39]: calcd.: C 58.61, H 3.47, N 24.12, S 9.20; Found; C 58.37, H 3.42, N 24.43, S 8.93; MS (EI): 348.

2-Phenethyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-thione **(37b)**

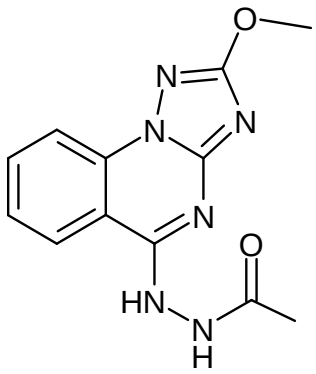


Yield: 56% (0.102 g), yellow solid; Mp.: 195 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.25 (t, J = 7.82 Hz, 2H), 4.76 (t, J = 7.65 Hz, 2H), 7.10-8.45 (m, 9H), 14.54 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.45, 69.99, 114.23, 122.43, 125.83, 126.32, 128.28, 128.85, 131.75, 132.38, 135.86, 137.80, 145.64, 167.35, 184.98; $C_{18}H_{14}N_6OS$ [362.42]: calcd.: C 59.66, H 3.89, N 23.19, S 8.85; Found: C 60.04, H 3.95, N 23.02, S 8.53; MS (EI): 362.

General procedure for the preparation of compounds 39a-h

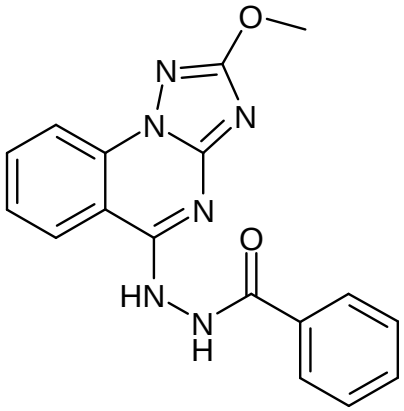
A mixture of **31a,b,e (**1 mmol) and the corresponding carbohydrazide (2.2 mmol) was refluxed in toluene (10 mL) for 2.5 h. After cooling, the solid was collected by filtration. Analytically pure products **39a-f** were obtained by recrystallization from methanol.

N-(2-Methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-acetohydrazide **(39a)**



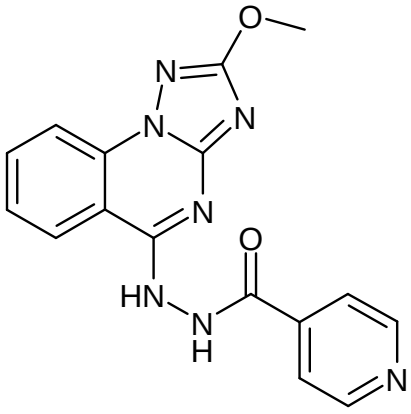
Yield: 67% (0.182 g), white solid; Mp.: 210 ^{o}C; IR (KBr): 1669 (C=O), 3206 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.02 (s, 3H), 4.00 (s, 3H), 7.58-8.42 (m, 4H), 10.17 (s, 1H), 10.31 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.07, 61.22, 109.71, 114.80, 124.06, 125.14, 134.98, 135.34, 152.81, 156.69, 166.23, 169.46; $C_{12}H_{12}N_6O_2$ [272.27]: calcd.: C 52.94, H 4.44, N 30.87; Found; C 52.51, H 4.31, N 30.69; MS (EI): 272.

N-(2-Methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-benzohydrazide **(39b)**



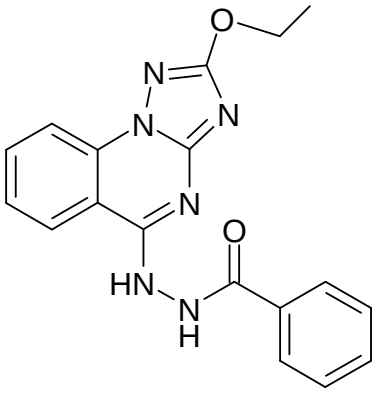
Yield: 71% (0.237 g), white solid; Mp.: 180 ^{o}C; IR (KBr): 1665 (C=O), 3193 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.98 (s, 3H), 7.53-8.51 (m, 9H), 10.52 (s, 1H), 10.81 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.67, 109.83, 114.88, 124.93, 125.29, 127.81, 127.99, 128.87, 129.07, 132.21, 132.81, 133.04, 135.09, 157.07, 169.44; $C_{17}H_{14}N_6O_2$ [334.34]: calcd.: C 61.07, H 4.22, N 25.14 ; Found: C 61.35, H 4.34, N 24.90; MS (EI): 334.

N-(2-Methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-isonicotinichydrazide **(39c)**



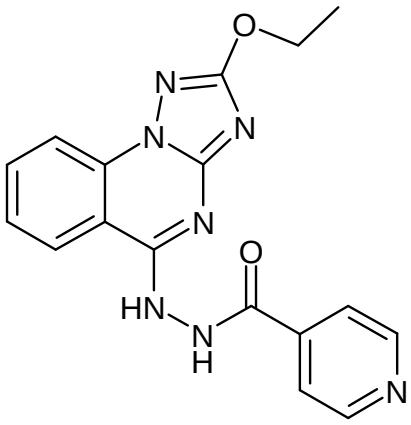
Yield: 65% (0.217 g), white solid; Mp.: 150 ^{o}C; IR (KBr): 1668 (C=O), 3210 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.98 (s, 3H), 7.65-8.50 (m, 8H), 10.66 (s, 1H), 11.14 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 65.69, 109.73, 114.94, 121.73, 124.88, 125.36, 128.45, 133.20, 135.21, 139.74, 150.94, 152.66, 155.50, 164.82; $C_{16}H_{13}N_7O_2$ [335.33]: calcd.: C 57.31, H 3.91, N 29.24; Found: C 57.67, H 3.73, N 28.93; MS (EI): 335.

N-(2-Ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-benzohydrazide (**39d)**



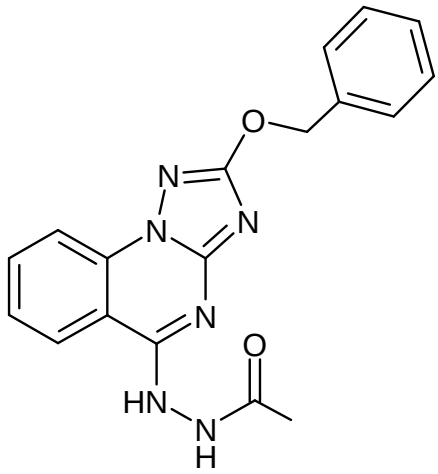
Yield: 68% (0.236 g), white solid; Mp.: 164 ^{o}C; IR (KBr): 1660 (C=O), 3189 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.36 (t, J = 7.20 Hz, 3H), 4.35 (q, J = 13.99 Hz, 2H), 7.53-8.51 (m, 9H), 10.57 (s, 1H), 10.81 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.94, 65.16, 109.83, 114.88, 124.94, 125.26, 127.96, 128.96, 132.42, 132.81, 135.09, 135.36, 152.60, 157.04, 166.39, 168.73; $C_{18}H_{16}N_6O_2$ [348.37]: calcd.: C 62.06, H 4.63, N 24.12; Found: C 62.30, H 4.52, N 23.95, MS (EI): 348.

N-(2-Ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-isonicotinichydrazide **(39e)**



Yield: 70% (0.244 g), white solid; Mp.: 173 ^{o}C; IR (KBr): 1664 (C=O), 3206 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.35 (t, J = 7.50 Hz, 3H), 4.38 (q, J = 14.04 Hz, 2H), 7.51-8.48 (m, 8H), 10.42 (s, 1H), 10.91 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.46, 64.80, 109.30, 114.45, 122.18, 122.70, 124.92, 134.79, 147.91, 148.92, 156.25, 163.54, 168.03; $C_{17}H_{15}N_7O_2$ [349.35]: calcd.: C 58.45, H 4.33, N 28.07; Found: C 58.61, H 4.22, N 28.35; MS (EI): 349.

N-(2-Benzyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-acetohydrazide **(39f)**

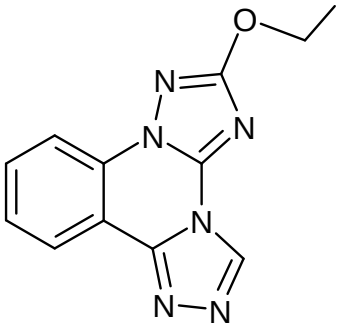


Yield: 76% (0.264 g), yellow solid; Mp.: 192 ^{o}C; IR (KBr): 1670 (C=O), 3197 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 2.27 (s, 3H), 5.66 (s, 2H), 7.59-8.76 (m, 9H), 10.48 (s, 1H), 10.59 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.09, 71.67, 114.88, 115.24, 124.78, 125.21, 127.67, 128.46, 128.80, 131.16, 135.60, 136.06, 137.08, 156.68, 168.72, 169.22; $C_{18}H_{16}N_6O_2$ [348.37]: calcd.: C 62.06, H 4.63, N 24.12; Found: C 62.44, H 4.51, N 24.21; MS (EI): 348.

General procedure for the preparation of compounds 41a-c

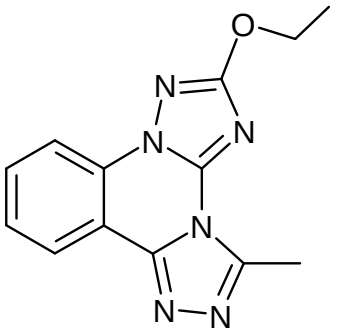
A mixture of **31b,f** (1 mmol) and formohydrazide or acetohydrazide (2.2 mmol) was refluxed in absolute toluene (15 mL) in the presence of sodium hydride (0.8 mmol) for 14-20 h. The solvent was removed under reduced pressure, and the residue was recrystallized from methanol.

2-Ethoxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41a)**



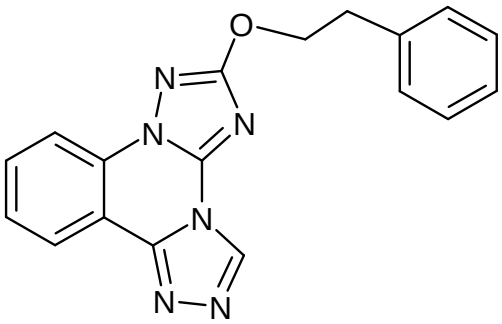
Yield: 50% (0.127 g), yellow solid; Mp.: 195 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.48 (t, J = 7.75 Hz, 3H), 4.48 (q, J = 14.12 Hz, 2H), 7.65-8.30 (m, 4H), 9.90 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.84, 66.37, 111.71, 115.18, 123.57, 124.77, 126.99, 134.34, 137.50, 142.17, 152.17, 164.25; $C_{12}H_{10}N_6O$ [254.25]: calcd.: C 56.69, H 3.96, N 33.05; Found: C 57.11, H 4.17, N 33.30; MS (EI): 254.

2-Ethoxy-3-methyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41b)**



Yield: 55% (0.147 g), yellow solid; Mp.: 205 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.43 (t, J = 7.49 Hz, 3H), 2.89 (s, 3H), 4.46 (q, J = 14.97 Hz, 2H), 7.62-8.42 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 12.10, 14.70, 66.29, 111.99, 115.16, 124.38, 126.94, 131.07, 132.61, 146.83, 151.12, 162.17; $C_{13}H_{12}N_6O$ [268.28]: calcd.: C 58.20, H 4.51, N 31.33; Found: C 58.87, H 4.40, N 31.49; MS (EI): 268.

2-Phenethyloxy-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41c)**

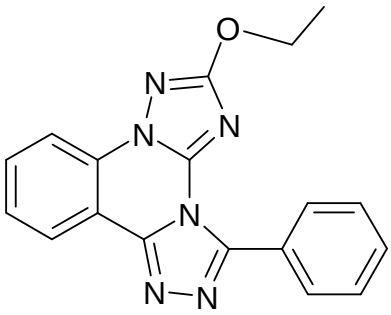


Yield: 51% (0.168 g), yellow solid; Mp.: 228 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.15 (t, J = 7.23 Hz, 2H), 4.64 (t, J = 7.13 Hz, 2H), 7.25-8.50 (m, 9H), 9.68 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 35.05, 69.43, 112.73, 119.68, 124.58, 126.79, 128.71, 129.27, 134.10, 138.51, 154.98, 167.32; $C_{18}H_{14}N_6O$ [330.35]: calcd.: C 65.45, H 4.27, N 25.44; Found: C 65.96, H 3.98, N 25.25; MS (EI): 330.

General procedure for the preparation of compounds 41d-f

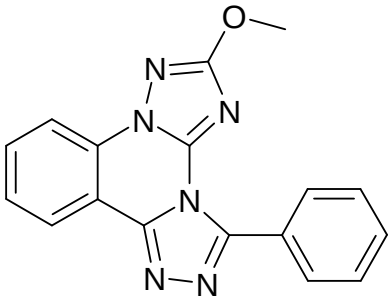
A mixture of **39b,c,d** (0.5 mmol) and $POCl_3$ (5 mL) was refluxed at 100 ^{o}C for 2 h. After cooling, the excess of $POCl_3$ was removed under reduced pressure and the residue was treated with saturated solution of NH_4OH or K_2CO_3 under ice cooling. The resulting solids were collected by filtration and recrystallized from methanol to afford **41d-f** as colored pure products

2-Ethoxy-3-phenyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41d)**



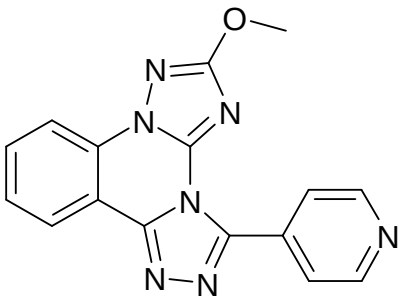
Yield: 68% (0.224 g), yellow solid; Mp.: 225 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.68 (t, J = 7.85 Hz, 3H), 4.58 (q, J =13.98 Hz, 2H), 7.65-8.81 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.73, 66.21, 111.71, 114.88, 115.18, 124.89, 125.24, 126.99, 127.04, 130.59, 132.22, 134.34, 137.50, 142.17, 152.17, 164.25; $C_{18}H_{14}N_6O$ [330.35]: calcd.: C 65.45, H 4.27, N 25.44; Found: C 65.98, H 3.98, N 25.37; MS (EI): 330.

2-Methoxy-3-phenyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41e)**



Yield: 75% (0.237 g), white solid; Mp.:198 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.02 (s, 3H), 7.62-8.76 (m, 9H), ^{13}C NMR (DMSO-d_6): δ(ppm): 57.46, 111.94, 115.17, 124.56, 126.12, 127.09, 128.35, 129.80, 130.59, 130.89, 131.09, 141.82, 147.67, 149.47, 167.34; $C_{17}H_{12}N_6O$ [316.32]: calcd.: C 64.55, H 3.82, N 26.57; Found: C 65.08, H 3.67, N 26.41; MS (EI): 316.

2-Methoxy-3-pyridyl-bis-[1,2,4]triazolo[1,5-a:4,3-c]quinazoline **(41f)**

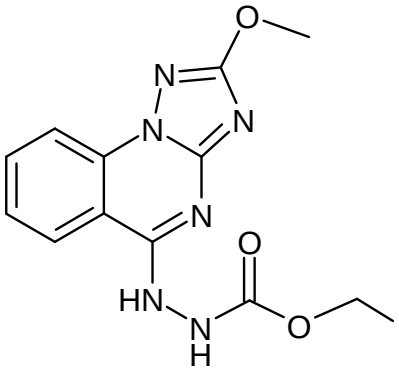


Yield: 77% (0.244 g), white solid; Mp.: 210 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.12 (s, 3H), 7.75-8.89 (m, 8H), ^{13}C NMR (DMSO-d_6): δ(ppm): 57.39, 111.24, 115.23, 124.39, 124.75, 127.29, 129.80, 130.59, 133.35, 142.52, 145.67, 150.03, 161.24; $C_{16}H_{11}N_7O$ [317.31]: calcd.: C 60.56, H 3.49, N 30.90; Found: C 61.10, H 3.52, N 31.27; MS (EI): 317.

General procedure for the preparation of compounds 44a-d

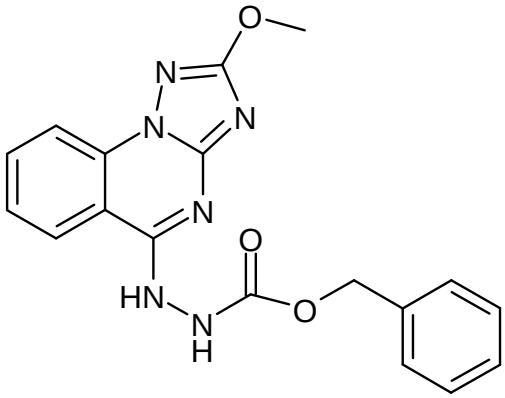
A mixture of **31a,b (**1 mmol) and benzyl carbazate or ethyl carbazate (2.2 mmol) was refluxed in benzene (10 mL) for 2.5 h. The solvent was removed under reduced pressure, the resulting solid was filtered off and recrystallized from methanol.

Ethyl-*N*-(2-methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate **(44a)**



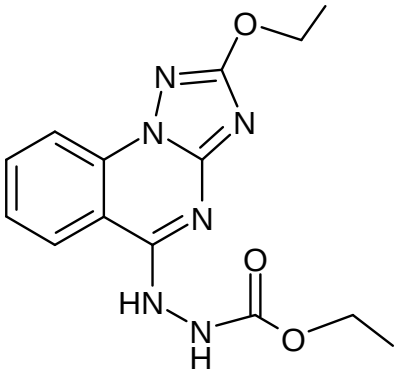
Yield: 73% (0.220 g), white solid; Mp.: 130 ^{o}C; IR (KBr): 1707 (C=O), 3198 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.23 (t, J = 7.91 Hz, 3H), 4.00 (q, J = 10.12 Hz, 2H), 4.10 (s, 3H), 7.59-8.27 (m, 4H), 9.50 (s, 1H), 10.34 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.92, 57.33, 61.15, 109.71, 114.83, 124.75, 125.21, 127.07, 134.70, 135.06, 137.15, 156.69, 169.23; $C_{13}H_{14}N_6O_3$ [302.29]: calcd.: C 51.65, H 4.67, N 27.80; Found: C 51.93, H 4.55, N 27.64; MS (EI): 302.

Benzyl-*N*-(2-methoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate **(44b)**



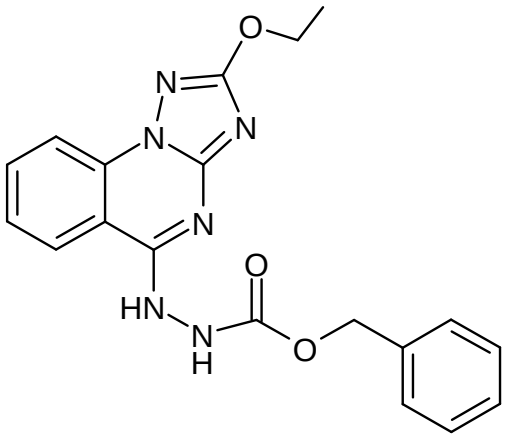
Yield: 75% (0.273 g), white solid; Mp.: 200 ^{o}C; IR (KBr): 1718 (C=O), 3215 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.01 (s, 3H), 5.15 (s, 2H), 7.20-8.41 (m, 9H), 9.68 (s, 1H), 10.40 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.69, 66.98, 109.67, 114.85, 124.75, 125.25, 126.25, 128.54, 128.81, 135.11, 135.33, 136.98, 152.74, 157.10, 168.42; $C_{18}H_{16}N_6O_3$ [364.37]: calcd.: C 59.34, H 4.43, N 23.06; Found: C 59.16, H 4.33, N 22.85; MS (EI): 364.

Ethyl-*N*-(2-ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate **(44c)**



Yield: 74% (0.233 g), white solid; Mp.: 167 ^{o}C; IR (KBr): 1710 (C=O), 3261 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.30 (t, J = 7.75 Hz, 3H), 1.73 (t, J = 7.89 Hz, 3H), 4.20 (q, J = 14.04 Hz, 2H), 4.65 (q, J = 14.06 Hz, 2H), 7.50-8.40 (m, 4H), 9.89 (s, 1H), 10.54 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.70, 14.96, 61.15, 65.12, 114.84, 124.71, 125.18, 127.24, 128.11, 129.34, 131.87, 135.05, 151.12, 167.32; $C_{14}H_{16}N_6O_3$ [316.32]: calcd.: C 53.16, H 5.10, N 26.57; Found: C 53.56, H 4.96, N 26.41; MS (EI): 316.

Benzyl-*N*-(2-ethoxy-[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate **(44d)**



Yield: 80% (0.302 g), white solid; Mp.: 122 ^{o}C; IR (KBr):1706 (C=O), 3215 (NH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.39 (t, J = 7.30 Hz, 3H), 4.40 (q, J = 14.20 Hz, 2H), 5.20 (s, 2H), 7.19-8.39 (m, 9H), 9.69 (s, 1H), 10.37 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.97, 65.16, 66.45, 109.66, 114.85, 124.71, 125.19, 128.08, 128.79, 135.07, 135.33, 136.99, 152.62, 156.90; $C_{19}H_{18}N_6O_3$ [378.39]: calcd.: C 60.31, H 4.79, N 22.21; Found: C 60.04, H 4.90, N 22.21; MS (EI): 378.

General procedure for the preparation of compounds 46a-d

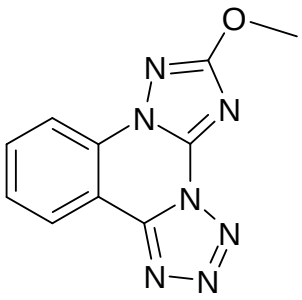
Method-A

A mixture of **31a,b,e,f** (1 mmol) and NaN_3 (1.2 mmol) in absolute DMF (5 mL) was heated at 90 ^oC in a nitrogen atmosphere for 24 h. After cooling, the reaction mixture was poured into water and saturated with brine solution. The resulting solid was filtered off, dried and recrystallized from methanol.

Method-B

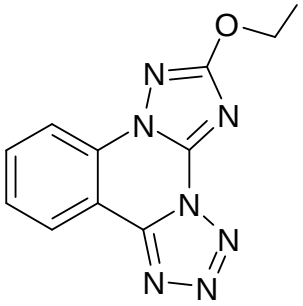
To a stirred solution of sodium nitrite (1.2 mmol) in water (5 mL) was added dropwise at -5 ^oC a mixture of **32a,b,e,f** (0.8 mmol) in 10% of hydrochloric acid (1.6 mL). After stirring for 30 min, the precipitate was collected by filtration, washed thoroughly with water, dried and recrystallized from methanol

2-Methoxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline **(46a)**



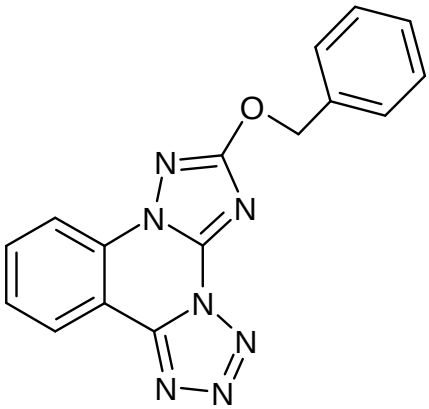
Yield**:** 54% (0.130 g), white solid; Mp.: 178 ^oC; ^1H NMR (DMSO-d_6): δ(ppm): 3.99 (s, 3H), 7.18-7.95 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 56.36, 114.67, 116.23, 125.81, 128.27, 134.74, 136.49, 145.01, 157.32, 167.54; $C_{10}H_7N_7O$ [241.21]: calcd.: C 49.79, H 2.93, N 40.65; Found: C 50.12, H 3.18, N 40.42; MS (EI): 241.

2-Ethoxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline **(46b)**



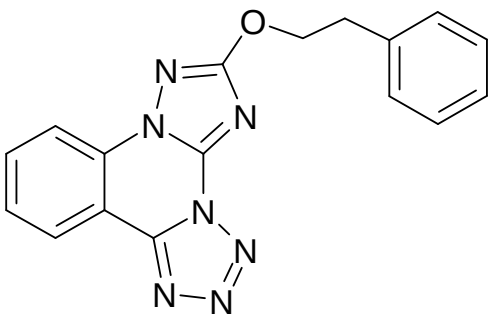
Yield: 53% (0.135 g), white solid; Mp.: 160 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.38 (t, J = 7.54 Hz, 3H), 4.46 (q, J = 13.98 Hz, 2H), 7.51-8.53 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.81, 66.81, 109.97, 115.52, 126.11, 127.51, 132.65, 134.99, 148.61, 167.43; $C_{11}H_9N_7O$ [255.24]: calcd.: C 51.76, H 3.55, N 38.41; Found: C 52.10, H 3.51 , N 38.56; MS (EI): 255.

2-Benzyloxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline (**46c)**



Yield: 51% (0.161 g), white solid; M.p.: 180 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.75 (s, 2H), 7.37-8.35 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 71.57, 109.58, 115.08, 125.5, 127.72, 128.23, 128.75, 130.36, 134.21, 134.53, 135.47, 148.17, 160.43, 167.16; $C_{16}H_{11}N_7O$ [317.31]: calcd.: C 60.56, H 3.49, N 30.90; Found: C 60.96, H 3.64 , N 30.98; MS (EI): 317.

2-Phenethyloxy-tetrazolo-[4,3-c][1,2,4]triazolo[1,5-a]quinazoline **(46d)**



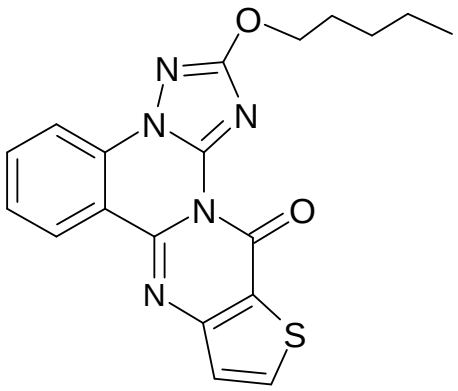
Yield: 60% (0.198 g), white solid; Mp.: 173 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.22 (t, J = 7.50 Hz, 2H), 4.79 (t, J = 7.51 Hz, 2H), 7.23-8.67 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 34.83, 71.21, 115.57, 124.39, 126.10, 126.87, 127.56, 128.80, 129.35, 130.23, 134.99, 138.27, 142.32, 156.34, 167.54; $C_{17}H_{13}N_7O$ [331.34]: calcd.: C 61.63, H 3.95, N 29.59; Found: C 61.88, H 3.73, N 29.68; MS (EI): 331.

General procedure for the preparation of compounds 49a,b[r]

A mixture of **31d,e (**1 mmol) and 3-amino-thiophene-2-methylcarboxylic acid ester (2.2 mmol) in absolute dioxane (10 mL) was refluxed in the presence of NaH (0.4 mmol) for 21 h. The solvent was removed under reduced pressure and the residue was treated with water and methanol. The resulting solid was filtered off and dried.

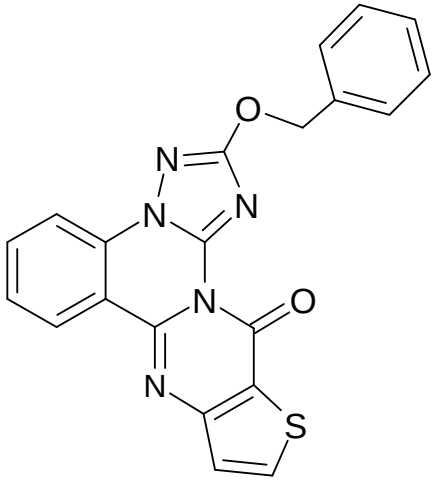
[r] Due to the difficult solubility of **49** in organic solvents, i can not get pure sample for the elemental analysis.

2-Pentyloxy-(3H-thieno-[3,2-d]pyrimidin-4-one-[4,3-c][1,2,4]triazolo[1,5-a]-quinazoline **(49a)**



Yield: 81% (0.307 g), yellow solid; Mp.; 240 ^{o}C; IR (KBr) 1670 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 0.68 (t, J = 7.40 Hz, 3H), 1.14-1.18 (m, 4H), 1.50-1.65 (m, 2H), 4.02 (t, J = 7.60 Hz, 2H), 6.18-8.05 (m, 6H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.63, 22.18, 27.69, 28.63, 69.35, 114.82, 124.71, 124.25, 124.80, 134.50, 134.19, 147.72, 153.60, 167.84; $C_{19}H_{17}N_5O_2S$ [379.44]: MS (EI): 379.

2-Benzyloxy-(3H-thieno-[3,2-d]pyrimidin-4-one-[4,3-c][1,2,4]triazolo[1,5-a]-quinazoline **(49b)**

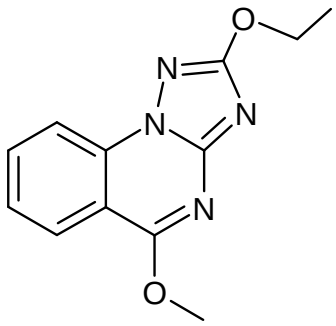


Yield: 69% (0.274 g), yellow solid; Mp.; 207 ^{o}C; IR (KBr) 1667 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ(ppm): 5.32 (s, 2H), 6.48-8.05 (m, 11H); ^{13}C NMR (DMSO-d_6): δ(ppm): 73.57, 109.08, 116.08, 124.25, 127.02, 128.13, 128.75, 131.36, 131.93, 133.23, 134.21, 134.53, 135.47, 148.17, 160.43, 167.16; $C_{21}H_{13}N_5O_2S$ [399.43]: MS (EI): 399.

General procedure for the preparation of 2,5-Dialkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolines (50a-d)

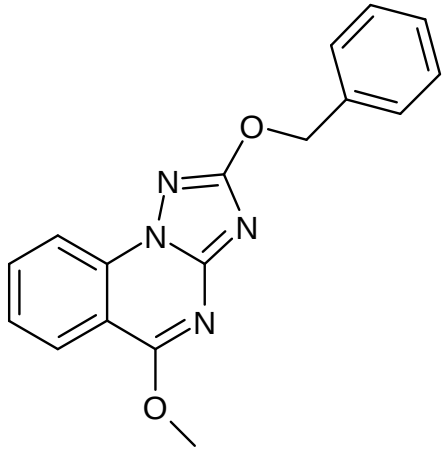
A freshly prepared sodium alkoxide solution from sodium (150 mg) and the corresponding absolute alcohol (35 mL) was reacted with **31b,e,f** (1 mmol) by stirring at room temperature for 30 min. Afterwards the product was collected by filtration, air dried, and recrystallized from ethanol.

2-Ethoxy-5-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(50a)**



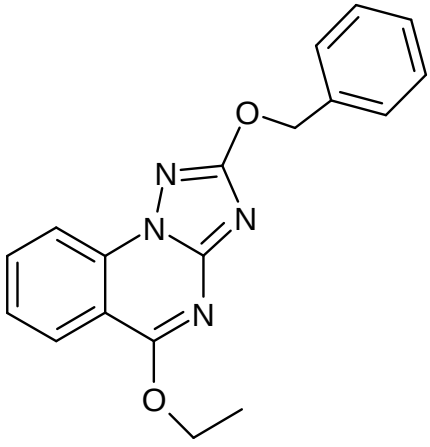
Yield: 45% (0.109 g), white solid; Mp.: 138 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.52 (t, J = 7.87 Hz, 3H), 4.28 (s, 3H), 4.51 (q, J = 13.57 Hz, 2H), 7.72-8.32 (m, 4H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.93, 55.48, 65.43, 111.47, 114.51, 125.77, 125.98, 128.86, 135.76, 136.06, 151.56, 163.14; $C_{12}H_{12}N_4O_2$ [244.26]: calcd.: C 59.01, H 4.95, N 22.94; Found: C 58.71, H 5.04, N 22.60; MS (EI): 244.

2-Benzyloxy-5-methoxy-[1,2,4]triazolo[1,5-a]quinazoline **(50b)**



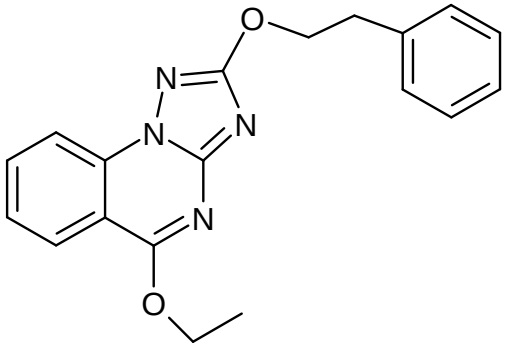
Yield: 50% (0.153 g), white solid; Mp.: 145 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 4.17 (s, 3H), 4.46 (s, 2H), 7.35-8.22 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 55.52, 70.93, 114.56, 125.88, 126.01, 128.52, 128.58, 135.28, 136.07, 136.62, 150.52, 163.24; $C_{17}H_{14}N_4O_2$ [306.33]: calcd.: C 66.66, H 4.61, N 18.29; Found: C 66.42, H 4.37, N 18.40; MS (EI): 306.

2-Benzyloxy-5-ethoxy-[1,2,4]triazolo[1,5-a]quinazoline (**50c)**



Yield: 51% (0.163 g), white solid; Mp.: 130 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.66 (t, J = 7.73 Hz, 3H), 4.79 (q, J = 13.97 Hz, 2H), 5.64 (s, 2H), 7.53-8.39 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.38, 64.18, 70.90, 111.61, 114.52, 125.82, 128.50, 128.83, 135.77, 136.10, 136.63, 151.62, 162.71, 168.77; $C_{18}H_{16}N_4O_2$ [320.35]: calcd.: C 67.49, H 5.03, N 17.49; Found: C 67.74, H 4.86, N 17.14; MS (EI): 320.

5-Ethoxy-2-phenethyloxy-[1,2,4]triazolo[1,5-a]quinazoline **(50d)**

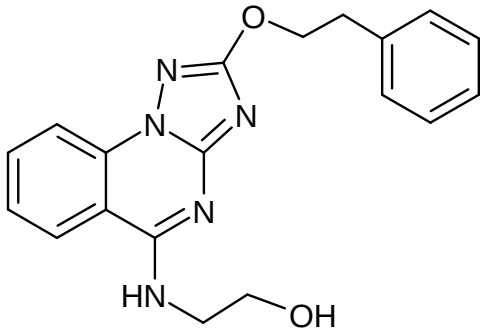


Yield: 52% (0.173 g), white solid; Mp.: 133 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 1.45 (t, J = 7.82 Hz, 3H), 3.24 (t, J = 8.11 Hz, 2H), 4.76 (q, J = 14.12 Hz, 2H), 4.79 (t, J = 7.97 Hz, 2H), 7.10-8.22 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 14.38, 35.03, 64.15, 70.00, 111.55, 114.52, 125.74, 125.97, 126.75, 128.75, 129.32, 133.67, 135.71, 136.09, 151.58, 162.65, 168.77; $C_{19}H_{18}N_4O_2$ [334.38]: calcd.: C 68.25, H 5.43, N 16.76; Found: C 68.47, H 5.37, N 16.83; MS (EI): 334.

Procedure for the preparation of 2-(2-Phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-ylamino)-ethanol (52)

A mixture of **31f** (1 mmol) and of 2-amino-ethanol (5 mmol) was heated under reflux in absolute dioxane (7 mL) for 19 h. Evaporation of the solvent gave an oil which solidified upon treatment with water and the solid was recrystallized from ethanol.

2-(2-Phenethyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-ylamino)-ethanol **(52)**

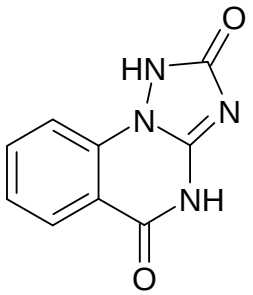


Yield: 45% (0.157 g), white solid; Mp.: 173 ^{o}C; ^{1}H NMR (DMSO-d_6): δ(ppm): 3.54 (t, J = 7.45 Hz, 4H), 3.62 (t, J = 7.87 Hz, 4H), 4.92 (s, 1H), 5.54 (s, 1H), 7.10-8.89 (m, 9H); ^{13}C NMR (DMSO-d_6): δ(ppm): 44.09, 59.21, 70.50, 111.37, 114.61, 124.73, 125.15, 128.40, 128.77, 134.35, 135.25, 136.94, 153.28, 156.86, 168.67; $C_{19}H_{19}N_5O_2$ [349.40]: calcd.: C 65.32, H 5.48, N 20.04; Found: C 65.72, H 5.39, N 19.89; MS (EI): 349

Procedure for the preparation of 1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione (53)

A mixture of **6f** (1 mmol) and Pd-C 10% (120 mg) as a catalyst was hydrogenated in THF (75 mL) for 2 h. The suspension was filtered off and the solvent evaporated. The resulting solid was suspended in ethyl acetate (2 mL) and filtered again to afford analytically pure **53**.

1,2,4,5-Tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione **(53)**

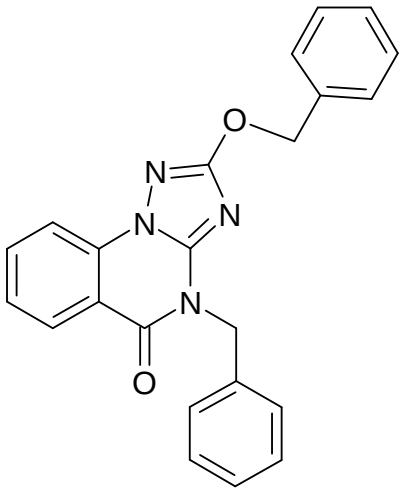


Yield: 95% (0.191 g), white solid; Mp.: 177 ^{o}C; IR (KBr): 1707, 1686 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ(ppm): 7.45-8.15 (m, 4H), 11.84 (s, 1H), 12.98 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 114.18, 116.64, 125.11, 128.58, 135.71, 136.24, 147.43, 160.04, 167.01; $C_9H_6N_4O_2$ [202.17]: calcd.: C 53.47, H 2.99, N 27.71; Found: C 53.67, H 3.02, N 27.52; MS (EI): 202.

Procedure for the preparation of *O*, *N*-Dibenzyl-[1,2,4]triazolo[1,5-a]quinazolin-5-one (55)

To a solution of **53** (1 mmol) in DMF (5 mL) was added potassium carbonate (1.6 mmol) portionwise over a period of 10 min at room temperature. After stirring for 20 min, benzyl bromide (3 mmol) was added and the reaction mixture was stirred for 18 h at room temperature. The mixture was then poured into ice/water, and the precipitate was filtered off, washed with water, dried and recrystallized from THF.

2-Benzyloxy-4-benzyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one **(55)**

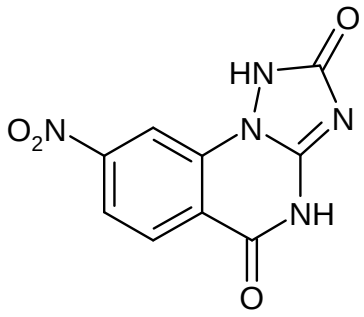


Yield: 79% (0.301 g), white solid; Mp.: 189 ^{o}C; IR (KBr): 1670 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ(ppm): 5.30 (s, 2H), 5.40 (s, 2H), 7.27-8.28 (m, 14H); ^{13}C NMR (DMSO-d_6): δ(ppm): 46.38, 70.91, 113.88, 115.78, 125.51, 127.53, 127.86, 128.39, 128.58, 135.13, 135.57, 135.82, 148.35, 158.57, 166.71; $C_{23}H_{18}N_4O_2$ [382.43]: calcd.: C 72.24, H 4.74, N 14.65; Found: C 72.54, H 4.69, N 14.42; MS (EI): 382.

Procedure for the preparation of 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo-[1,5-a]quinazolin-2,5-dione (58)

Compound **6e** (1 mmol) was dissolved in conc. H_2SO_4 (3.5 mL) and cooled at 0 ^oC. Afterwards KNO_3 (0.95 mmol) was added in three portions over 10 min. The reaction mixture was warmed to room temperature and left to stirr for 17 h. The mixture was poured into ice and stirred for 15 min, the yellow precipitate was collected by filtration, washed with water, dried and recrystallized from acetone/hexane

8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]quinazolin-2,5-dione **(58)**



Yield: 54% (0.133 g), yellow solid; Mp.: 173 ^oC (Acetone-hexane); IR (KBr): 1718, 1696 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6): δ(ppm): 7.88-8.79 (m, 3H), 12.23 (s, 1H) 13.27 (s, 1H); ^{13}C NMR (DMSO-d_6): δ(ppm): 115.40, 116.81, 123.97, 129.82, 135.30, 139.43, 143.40, 148.50, 158.81; $C_9H_5N_5O_4$ [247.17]: calcd.: C 43.73, H 2.04, N 28.33; Found: C 43.35, H 2.37, N 28.75; MS (EI): 247.

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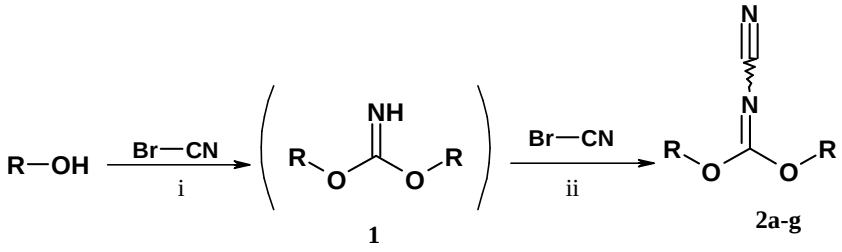
5 Summary

The current study focuses on the synthesis of the novel 2-alkoxy(aralkoxy)-[1,2,4]triazolo[1,5-a]quinazolin-5-ones **6** and their substituted/anellated heterocyclic derivatives.

First, the preparation of several dialkyl *N*-cyanoimidocarbonates (**2)** from equimolar amounts of cyanogen bromide and the corresponding alcohol according to a slightly modified literature procedure is described (Scheme I).

Scheme I

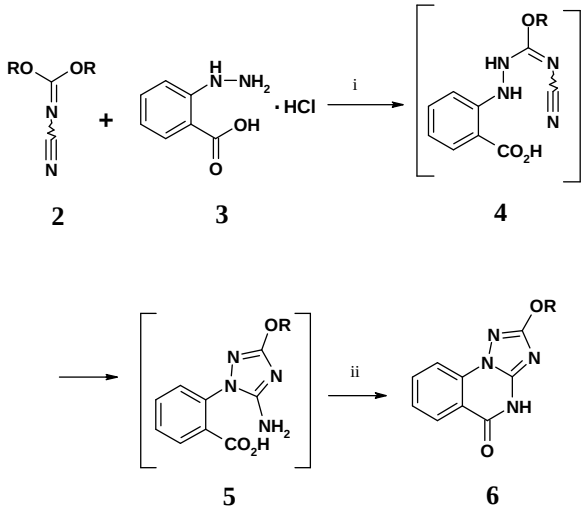


1 **2a-g**

i: NaOH, TMBE ii: Na_2CO_3, Et_3N

The dialkyl *N*-cyanoimidocarbonates **2** were then reacted with 2-hydrazinobenzoic acid **3** in ethanol in the presence of triethylamine to afford the targeted tricyclic heterocycles **6** via the intermediates **5** (Scheme II).

Scheme II



2 **3** **4** **5** **6**

i : Et_3N, EtOH ii : conc. HCl, 80 °C

Treatment of **6** with different alkyl halides at room temperature in the presence of potassium carbonate afforded cleanly and exclusively *N*-alkylated products **12**, whereas the corresponding dihydro-triazoloquinazolines **16** were obtained as pure compounds from the reduction of the lactam **6** by lithium aluminum hydride in tetrahydrofuran.

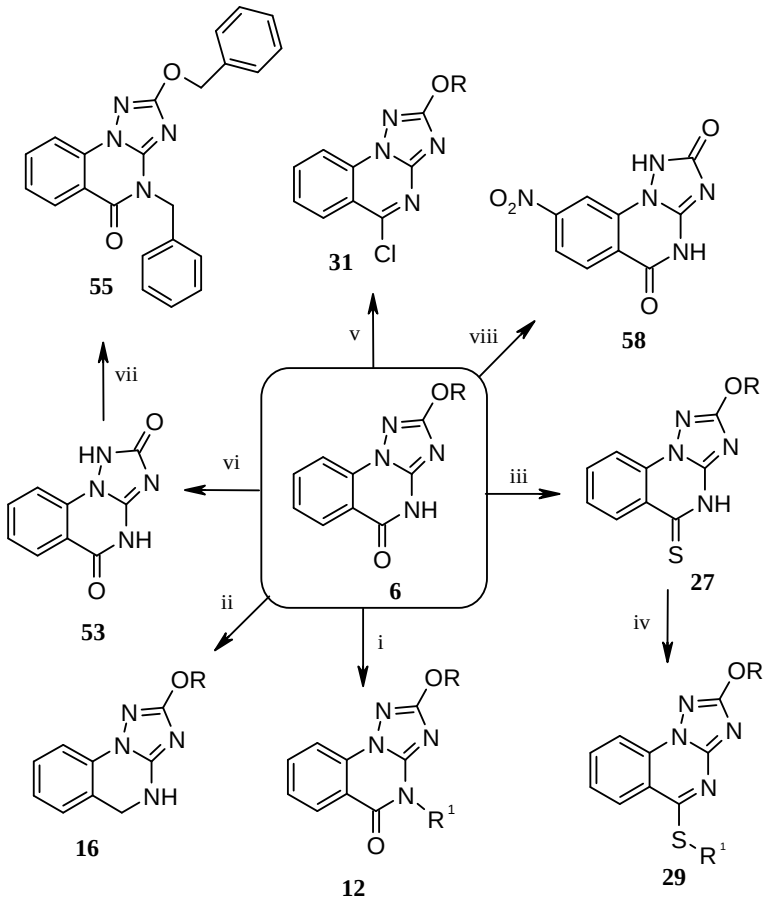
Reaction of **6** with phosphorous pentasulfide in refluxing pyridine afforded the [1,2,4]triazoloquinazolin-5-thiones **27** in excellent yields which were subsequently transformed into the thioethers **29** with alkyl halides in the presence of sodium hydroxide.

Furthermore, chlorination of **6** with oxalyl chloride in trichloroethane or with phosphorous oxychloride in benzene opened access to the novel compounds of type **31**.

Catalytic hydrogenation of **6f** on Pd/C in tetrahydrofuran provided the corresponding **53** which subsequently underwent alkylation with benzyl bromide in the presence of potassium carbonate to produce the dibenzylated product **55**.

In addition, nitration of 2-allyloxy-[1,2,4]triazolo[1,5-a]quinazolin-5-one (**6e**) with potassium nitrate in concentrated sulfuric acid furnished cleanly the targeted **58** (Scheme III).

Scheme III



i : alkyl halides, DMF ii : $LiAlH_4$, THF iii : P_2S_5, pyridine iv : alkyl halides, NaOH
v : $POCl_3$, benzene or $C_2O_2Cl_2$, trichloroethane vi : Pd/C -H_2, THF
vii : benzyl bromide, DMF viii : KNO_3, conc. H_2SO_4

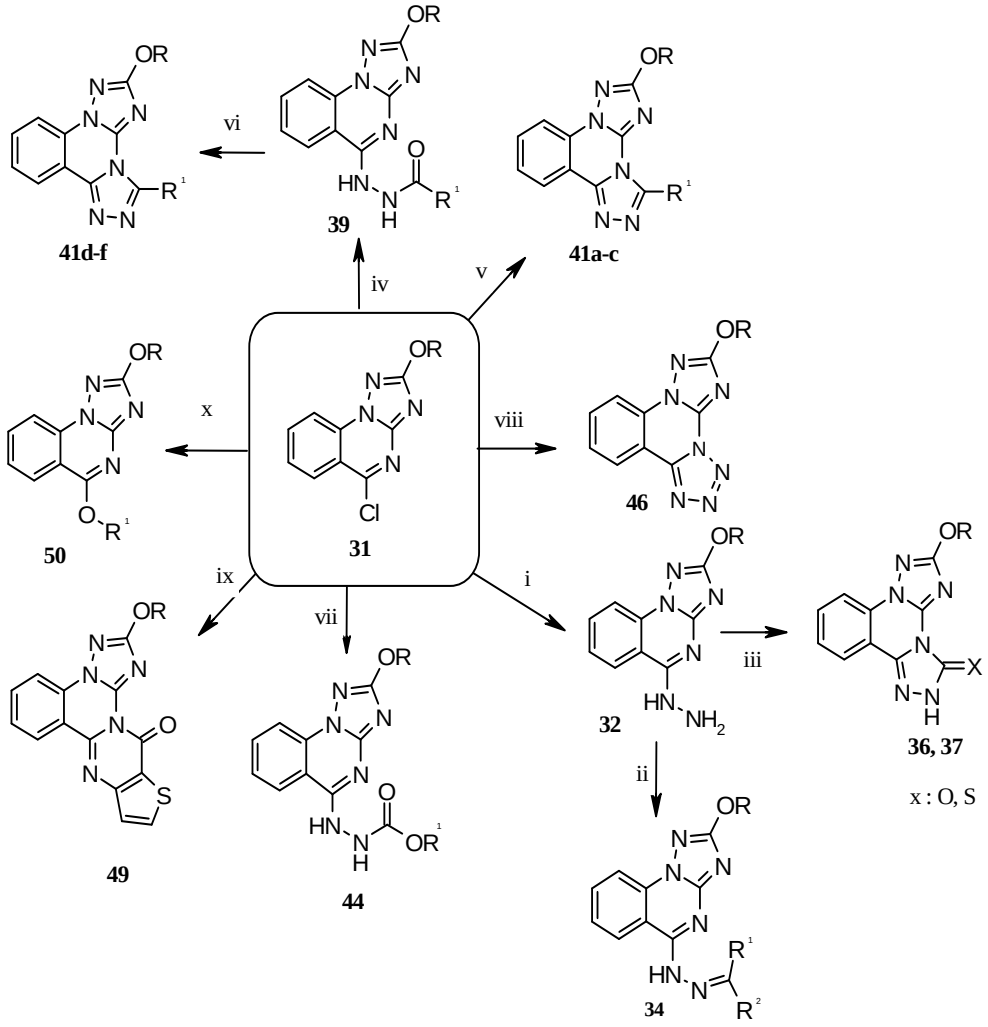
Replacement of the chlorine atom in **31** by different nucleophiles provided access to a variety of derivatives. For example, hydrazinolysis of **31** produced the hydrazine derivatives **32** which upon treatment with an aldehyde or ketone delivered the corresponding hydrazones **34**.

From the reaction of **31** with different hydrazides in refluxing toluene, the amidrazones **39** were obtained in good yields.

Similarly, compounds of type **44** were obtained from treatment of **31** with the respective carbazates in refluxing toluene. Tetracyclic systems of type **36, 37** were prepared by reaction of **32** with 1,1′-carbonyldiimidazole or carbon disulfide in toluene or pyridine, respectively. Condensation of **31** with acylhydrazines in the presence of sodium hydride produced smoothly the targeted **41a-c,** whereas the novel condensed heterocycles of type **41d-f** resulted from **39** by treatment with phosphorous oxychloride.

Furthermore, reaction of **31** with sodium azide in dimethyl formamide afforded the tetracyclic copmpounds of type **46,** whereas the corresponding reaction of **31** with thiophene-3-amino-methylcarboxylate produced the novel pentacyclic compound **49.** Finally, reaction of **31** with sodium alkoxides furnished 2,5-dialkoxy-[1,2,4]triazoloquinazolines (**50)** (Scheme IV).

Scheme IV

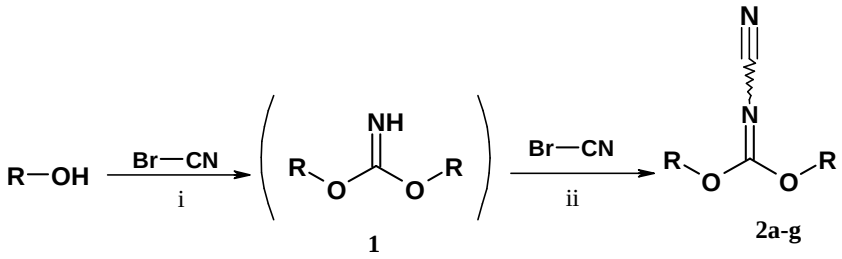


i : hydrazine hydrate, EtOH ii : aldehyde or ketone, EtOH
iii : CDI, toluene or CS_2 , pyridine iv : hydrazides, toluene
v : acylhydrazines, toluene, NaH vi : $POCl_3$ vii : carbazates, toluene
viii : NaN_3, DMF ix : methlyl-3-amino-thiophene carboxylate, dioxane
x : MeONa or EtONa, EtOH/MeOH

6 Zusammenfassung

Die vorliegende Arbeit beschäftigt sich mit der Synthese von neuartigen 2-Alkoxy(Aralkoxy)-[1,2,4]triazolochinazolin-5-onen (**6**) und mit deren substituierten/anellierten Derivaten. Im ersten Teil der Arbeit wurden verschiedene Dialkyl-*N*-cyanoimidocarbonate (**2**) durch die Umsetzung äquimolarer Mengen Bromcyans mit den entsprechenden Alkoholen nach einer leicht modifizierten Literaturvorschrift hergestellt (Schema I).

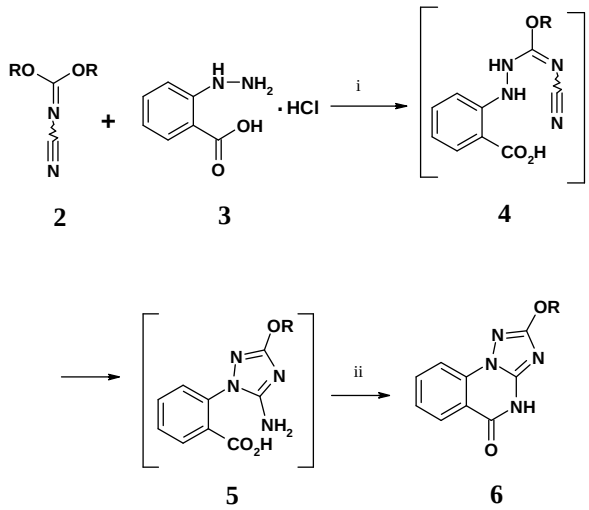
Schema I



i: NaOH, TMBE ii: Na_2CO_3, Et_3N

Durch Umsetzung der Dialkyl-*N*-cyanoimidocarbonate **2** mit 2-Hydrazinobenzoesäure **3** in Ethanol konnten die [1,2,4]Triazolochinazolin-5-one **6** gewonnen werden (Schema II).

Schema II



i : Et_3N, EtOH ii : konz. HCl, 80 °C

Die Alkylierung von **6** bei Raumtemperatur erbrachte die entsprechenden 4-Alkyl(Aralkyl)-[1,2,4]triazolochinazolin-5-one **12**. Durch Reduction der Lactamgruppe von **6** mit Lithiumaluminiumhydrid in Tetrahydrofuran waren die Dihydro-triazolochinazoline **16** zugänglich.

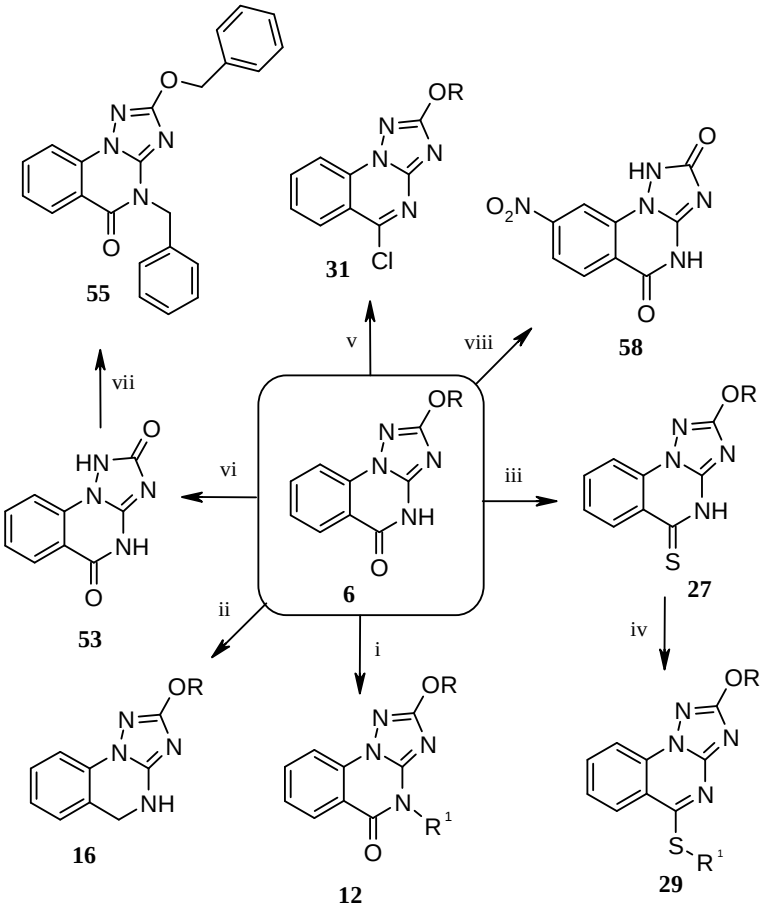
Die Reaktion von **6** mit Phosphorpentasulfid in Pyridin unter Rückfluss erbrachte die [1,2,4]Triazolochinazolin-5-thione **27**, welche mit Alkylhalogeniden in Anwesenheit von Natriumhydroxid die Thioether **29** erbrachten.

Darüber hinaus konnten die neuartigen Verbindungen vom Typ **31** durch Chlorierung von **6** mit Oxalylchlorid in Trichloroethan oder mit Phosphoroxychlorid in Benzol erhalten werden.

Die katalytische Hydrierung von **6f** über Pd/C in Tetrahydrofuran führte zu den [1,2,4]Triazolochinazolin-2,5-dionen **53,** deren Umsetzung mit Benzylbromid in Anwesenheit von Kaliumcarbonat die Verbindungen vom Typ **55** lieferte.

Aus der Nitrierung von 2-Allyloxy-[1,2,4]triazolochinazolin-5-one (**6e)** mit Kaliumnitrat in konzentrierter Schwefelsäure ging das 8-Nitro-1,2,4,5-tetrahydro-[1,2,4]triazolo[1,5-a]chinazolin-2,5-dion **58** hervor. (Schema III).

Schema III



i : Alkylhalogenid, DMF ii : $LiAlH_4$, THF iii : P_2S_5, Pyridin iv : Alkylhalogenid, NaOH
v : $POCl_3$, Benzol oder $C_2O_2Cl_2$, Trichloroethan vi : Pd/C -H_2, THF
vii : Benzylbromid, DMF viii : KNO_3, konz. H_2SO_4

Die Hydrazinolyse von **31** in siedenden Ethanol erbrachte die neuartigen Heterocyclen vom Typ **32**, die durch die Umsetzung mit Aldehyden bzw. Ketonen die Hydrazonoabkömmlinge vom Typ **34** lieferten.

Die Amidrazone vom Typ **39** waren aus **31** durch Umsetzung mit verschiedenen Hydraziden erhältlich.

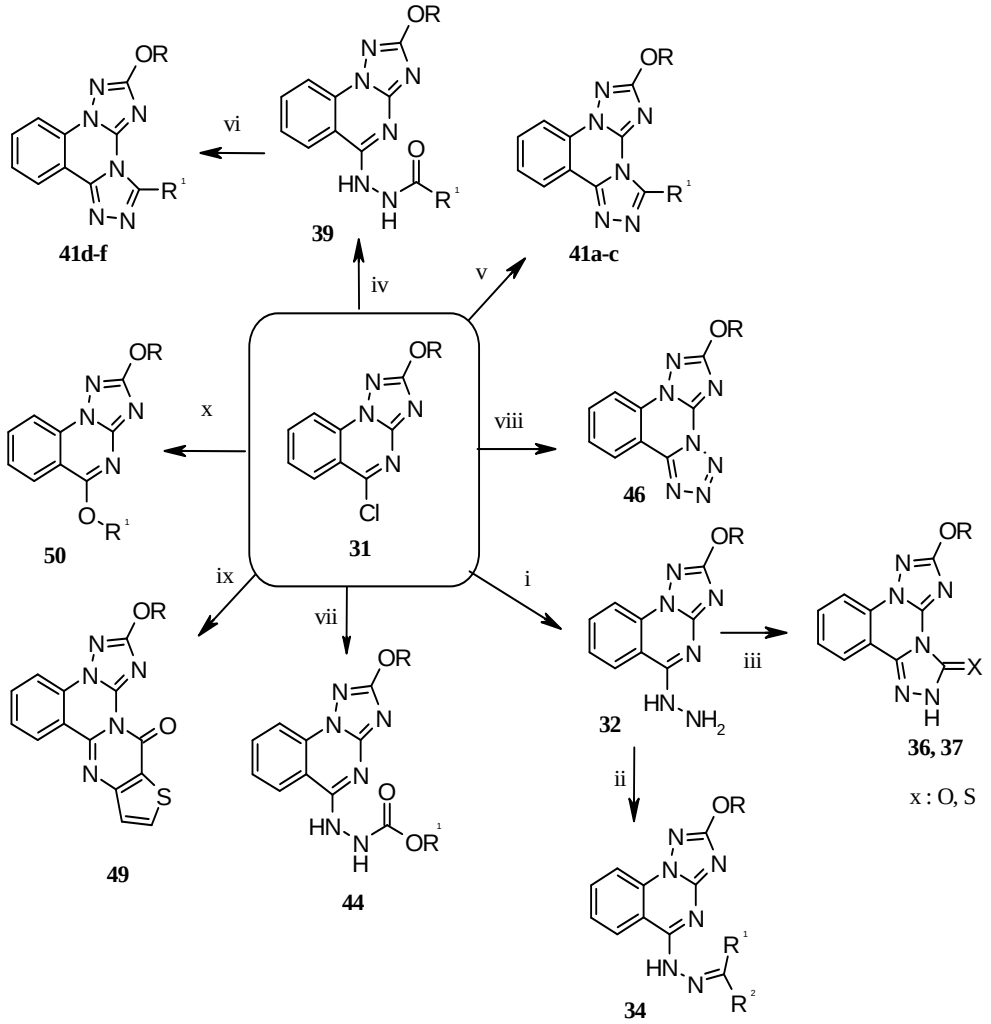
In analoger Weise konnten die Verbindungen vom Typ **44** aus Umsetzung **31** durch Carbazatolyse erhältlich.

Die tetracyclischen Verbindungen vom Typ **36** bzw. **37** wurden durch die Reaktion von **32** mit 1,1′-Carbonyldiimidazol bzw. Kohlenstoffdisulfid gewonnen.

Die Kondensation von **31** mit Acylhydrazinen in Anwesenheit von Natriumhydrid führte zu den Bis-[1,2,4]triazolo[1,5-a:4,3-c]chinazolinen **41a-c**, während die gewünschten Heterocyclen vom Typ **41d-f** durch Umsetzung von **39** mit Phosphoroxychlorid erhalten wurden.

Mit Natriumazid reagierte **31** zu den entsprechenden tetracyklischen Verbindungen vom Typ **46**, mit Thiophen-3-amino-methylcarboxylat reagierte **31** zu den pentacyklischen Verbindungen **49** und mit Natriumalkoxiden bildete **31** die 2,5-Dialkoxy-[1,2,4]triazolochinazoline **50** aus (Schema IV).

Schema IV



i : Hydrazinhydrat, EtOH ii : Aldehyd oder Keton, EtOH
iii : CDI, Toluen oder CS_2 , Pyridin iv : Hydrazid, Toluen
v : Acylhydrazin, Toluen, NaH vi : $POCl_3$ vii : Carbazat, Toluen
viii : NaN_3, DMF ix : Methlyl-3-amino-thiophen carboxylat, Dioxan
x : MeONa oder EtONa, EtOH/MeOH

Hazard information

Concerning the toxicological characteristics of the compounds synthesized within the scope of this thesis, no informations are available. Hence, hazardous properties cannot be excluded. Therefore the chemicals should be regarded as hazardous substances and treated with appropriate caution.

Toxicological properties of the solvents and chemicals employed within the course of this project are summarized in the tables below.

Solvents	**Category of Danger**	**Safety Phrases**
Acetone	F, Xi	S 9-16-26
Benzene	F, T	S 35-45
Chloroform	Xn	S 36/37
Dichloromethane	Xn	S 23.2-24/25-36/37
Diethyl ether	F^+, Xn	S 9-16-29-33
Ethanol	F	S 7-16
Ethyl acetate	F, Xn	S 16-26-33
n-Hexane	F, Xn, N	S 9-16-29-33-36/37-61-62
Methanol	F, T	S 7-16-36/37-45
Pyridine	F, Xn	S 26-28.1
Tetrahydrofuran	F, Xn	S 16-29-33
N,*N*-Dimethylformamide	T	S 53.1-45
Toluene	Xn, F	S 16-25-29-33

Chemicals	Category of Danger	Safety Phrases
Acetophenone	Xn	S 26
Benzaldehyde	Xn	S 24
Benzyl bromide	Xi	S 39
Bromoacetic acid	T, C, N	S 26-36/37/39-45-61
2-Hydrazinobenzoic acid hydrochloride	Xi	S 26-36
Cyanogen bromide	T^+ N	S 28.1-36/37/39-45-60-61
Sodium carbonate	Xi	S 22-26
Lithium aluminum hydride	F	S 7/8-24/25-43
Phosphorous oxychloride	T^+ C	S 7/8-26-36/37/39-45
Phosphorous pentasulfide	F , N, Xn	S 61
Carbon disulfide	F , T	S 16-33-36/37-45
Sodium hydride	F, Xi	S 24/25-26-43.11-7/8
Sodium hydroxide	C	S 26-37/39-45
Sodium azide	F^+ N	S 28-45-60-61
1,1′-Carbonyldiimidazole	Xn	S 26-36/37/39-45
Methyl iodide	T	S 61
Potassium nitrate	O	S 17-24/25
Hydrazine hydrate	T, N	S 53-45-60-61
Hydrochloric acid	C	S 26-36/37/39-45
Oxalyl chloride	T, F , C	S 26-36/37/39-43.4-45
Triethylamine	C, F	S 3-16-26-29-36/37-45
Potassium carbonate	Xn	S 26-36
Benzyl carbazate	Xi	S 26-36
Ethyl carbazate	T	S 22-36/37-45
Sodium nitrite	N, O, T	S 45-61

Curriculum vitae

Name	Rashad Al-salahi
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