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Intramolecular [2 + 2] Cycloaddition of Ketenimines with Imines. Synthesis and Chemical Behaviour of Azeto[2,1-*b*]quinazolines

Mateo Alajarín*, Pedro Molina, Angel Vidal and Fulgencio Tovar

Departamento de Química Orgánica, Facultad de Química, Universidad de Murcia.
Campus de Espinardo, E-30071 Murcia, Spain

Abstract: Azeto[2,1-*b*]quinazolines **5** have been prepared by the novel intramolecular [2 + 2] cycloaddition reaction of ketenimines with imines. The applicability and limitations of the synthetic methodology, and explorations on the reactivity of compounds **5** are discussed.

INTRODUCTION

One of the most important endeavours in synthetic organic chemistry is the construction of carbon skeletons *via* the formation of carbon-carbon bonds. Cycloaddition reactions are of widespread application and value to achieve this goal, and are among the most widely-used synthetic strategies.[1] [2 + 2] Cycloadditions of heterocumulenes[2] are of growing interest since they provide a general route to four-membered rings and constitute a testing ground for theoretical arguments of chemical reactivity. Ketenes are specially prone to [2 + 2] cycloadditions and their reaction with imines, known as the Staudinger reaction, has been extensively explored and is now recognized as one of the most convenient approaches to β-lactams.[3] As a alternative to free ketenes, keteniminium salts have given excellent results in cycloaddition reactions with imines.[4] By contrary, [2 + 2] cycloadditions of ketenimines with imines to provide azetidin-2-imines are scarce[5]; it has been pointed out that such reactions are only amenable intermolecularly if the electrophilic character of the ketenimine is enhanced by electron-withdrawing substituents on the nitrogen atom, such as tosyl[6] or cyano.[7]

In a preliminary communication[8] we recently reported that entropically-assisted intramolecular [2 + 2] cycloadditions of ketenimines with imines successfully led to fused azetidine-2-imines overcoming the above mentioned electronic constraints. We here describe the results obtained on the investigation of the scope and applicability of such processes with regards to the chemical nature of the imino and ketenimine functions and the length of the tether linking the reactive groupings, as well as initial explorations on the chemical behaviour of the reaction products, the previously unknown cyclic amidines azeto[2,1-*b*]quinazolines, and related compounds. The many biological roles of cyclic amidines have long attracted interest[9] and justify recent synthetic efforts which focus on their preparation.[10] We hope that the combination of the cyclic amidine character with the four-membered azetidine ring, both present in azeto[2,1-*b*]quinazolines, would supply relevant biological activities to these compounds.

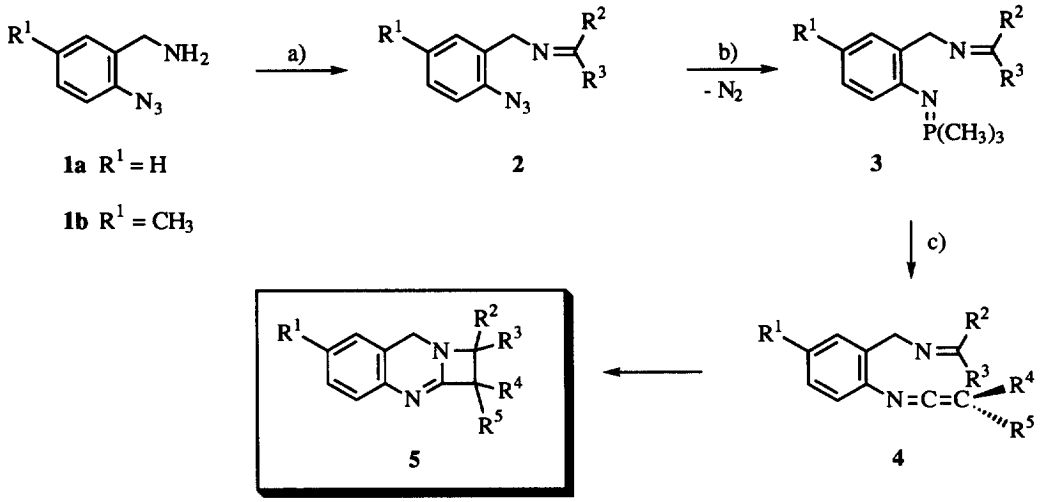
RESULTS AND DISCUSSION

2-Azidobenzylamines **1a,b** were easily prepared by simple chemistry starting from the commercially available 2-aminobenzyl alcohols and have been previously reported.[11] Their reactions with aldehydes or ketones under standard conditions (see Scheme 1 and Table) gave rise to the corresponding aldimines and ketimines **2** in nearly quantitative yield, which were generally used as crude products in the next step due to the partial hydrolytic cleavage of the imino bond experienced by some of them during purification attempts by crystallization or column chromatography. In all the cases ^{1}H- and ^{13}C-NMR data of imines **2** showed only one set of signals which were assigned as corresponding to the *E* isomers, fact that could be ascertained for some examples.[12] Treatment of crude imines **2** with one equivalent of a 1 M toluene solution of trimethylphosphane was followed by the evolution of dinitrogen, indicative of the conversion of the azide function into the corresponding trimethylphosphazene **3**.[13,14] The transformation **2** → **3** was completed in less than 1 h, as followed by IR (dissapearance of the azide vibration near 2100 cm^{-1}) and ^{31}P-NMR.[15] The isolation and purification of **3** were prevented by the extreme hydrolytic sensitivity of the phosphazene group. When these compounds were treated in the same reaction flask with a disubstituted ketene at room temperature the pale-yellow reaction mixture inmediatly turned orange and then slowly faded in less than 1 h to a colourless solution. IR spectra of the orange reaction mixtures showed strong absorptions around 2000 cm^{-1} attributable to the C=C=N grouping of ketenimines **4** which resulted from an aza-Wittig reaction[16] of the phosphazene with the ketene. Transient ketenimines **4** were converted in solution at room temperature, through a formal [2 + 2] cycloaddition between the imino C=N and cumulated C=C bonds, into the corresponding azeto[2,1-*b*]quinazolines **5** which were isolated in moderate to good yields from the final reaction mixture after column chromatography (Scheme 1 and Table).

Table. Azeto[2,1-*b*]quinazolines **5** Prepared.

Compd.	Method[a]	R^1	R^2	R^3	R^4	R^5	Yield (%)[b]
5a	B	H	H	$CH(CH_3)_2$	C_6H_5	C_6H_5	36
5b	A	H	H	*E*-CH=CH-C_6H_5	C_6H_5	C_6H_5	72
5c	A	H	H	3-Furyl	C_6H_5	C_6H_5	50
5d	A	H	H	4-CH_3O-C_6H_4	C_6H_5	C_6H_5	63
5e	A	H	H	4-O_2N-C_6H_4	C_6H_5	C_6H_5	81
5f	A	H	CH_3	4-O_2N-C_6H_4	C_6H_5	C_6H_5	46
5g	A	CH_3	H	4-CH_3O-C_6H_4	C_6H_5	C_6H_5	91
5h	A	CH_3	H	4-O_2N-C_6H_4	C_6H_5	C_6H_5	88
5i	C	H	C_6H_5	C_6H_5	C_6H_5	C_6H_5	60
5j	C	H	C_6H_5	C_6H_5	C_6H_5	CH_3	75

[a] For an explanation of methods A, B and C see Scheme 1. [b] Global yield for the conversion **1** → **5**.



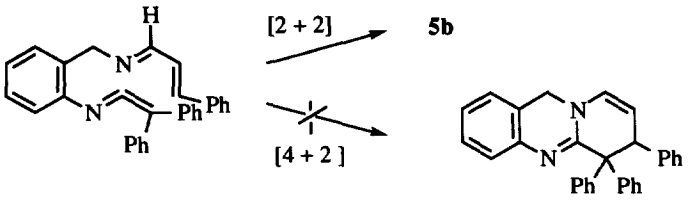
Reagents and conditions: a) Method A: R^2COR^3, Et_2O, anh. $MgSO_4$, r.t., 12 h; Method B: R^2COR^3, basic Al_2O_3, r.t., 12 h; Method C: $Ph_2C{=}NH$, 50°C, 6 h; b) $P(CH_3)_3$, toluene, r.t., 30 min; c) $R^4R^5C{=}C{=}O$, toluene, r.t., 1 h.

Scheme 1

Spectroscopic characterization of compounds **5** relies on their IR absorptions at 1664-1677 cm^{-1} corresponding to the C=N vibration as well on the appearance of their ^1H- and ^{13}C-NMR spectra: the methylene protons resonate at 4.42-4.67 ppm, either as a broad singlet or as an AB-type double doublet (with the exception of the non-stereogenic **5i**, sharp singlet); the quaternary amidine carbon atom appeared in the range 163.95-165.99 ppm, the methylene carbon at 40.80-47.73 ppm, and the two new sp^3 carbons C-1 and C-2 at 66.74-77.22 and 66.45-72.61 ppm respectively; additionally, the two phenyl rings over the same carbon atom (C1 or C2) were revealed as diastereotopic by the ^{13}C-NMR spectra, again with the exception of **5i**.

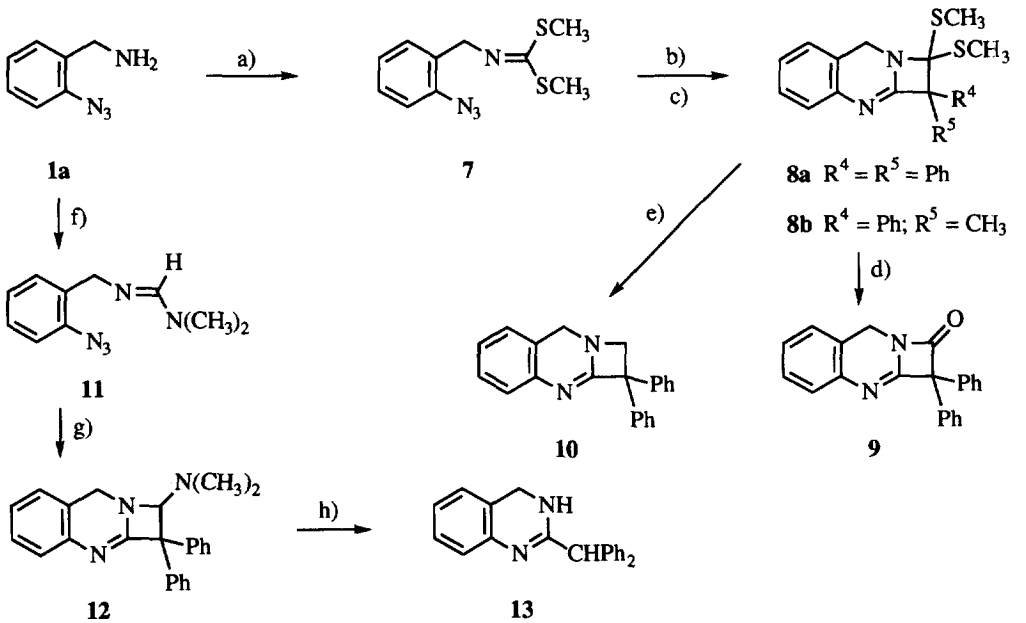
The Imino Function

Concerning the applicability of the synthetic sequence leading to **5** with regards to the imino function, a variety of aldimines and ketimines derived from 2-azidobenzylamines **1** and aliphatic, aromatic, heteroaromatic, and α,β-unsaturated aldehydes, acetophenones and benzophenone have given satisfactory results. The lowest yield was found for the imine derived from isobutyraldehyde probably due to the instability of the enolizable aldimine and the occurrence of competitive deprotonation by the strongly basic phosphazene function, which paralleled a similar effect observed in the related imine-ketene [2 + 2] cycloadditions.[17] Also is worth noting the case of the α,β-unsaturated aldimine derived from cinnamaldehyde, leading exclusively to **5b**, as determined by high field ^1H-NMR analysis of the crude reaction mixture where the [4 + 2] cycloaddition product **6** could not be detected (Scheme 2), whereas both types of cycloadducts have been found experimentally in some examples of the Staudinger reaction.[18]



Scheme 2 **6**

Iminodithiocarbonates have been widely used as the imine component in the Staudinger reaction to result in an orthoester functionality on the C-4 carbon atom of the β-lactam ring,[19] which could be further elaborated either by desulfurization,[19c,f] iminodithiocarbonates as formaldehyde imine equivalents, or by unmasking the oxo functionality on C-4 to yield azetidine-2,4-diones (malonimides).[19d,e] In our hands iminodithiocarbonates were also suitable imine partners in the intramolecular [2 + 2] cycloaddition imine-ketenimine. Thus 2-azidobenzylamine **1a** was converted into the iminodithiocarbonate dimethyl ester **7** by the action of CS_2/CH_3I[20] in 80% yield. When this compound was sequentially treated with trimethylphosphane and diphenyl or phenyl methyl ketenes the corresponding 1,1-bis(methylthio) azeto[2,1-*b*]-quinazolines **8** were formed in acceptable yields (40-70%) (Scheme 3).



Reagents and conditions: a) CS_2, CH_3I, NaOH 20%, DMF, 0°C, 15 min; b) $P(CH_3)_3$, toluene, r.t, 30 min; c) $R^4R^5C{=}C{=}O$, toluene, r.t., 1 h; d) $HgCl_2$, $CaCO_3$, 100°C, 5 h or NBS, CH_3CN, - 5°C, 30 min; e) Raney-Ni, ethyl acetate, r. t., 24 h; f) DMFDMA, toluene, reflux, 6 h; g) $P(CH_3)_3$, toluene, r. t., 1 h, then $Ph_2C{=}C{=}O$, r.t., 1 h; h) silica gel, ethyl acetate.

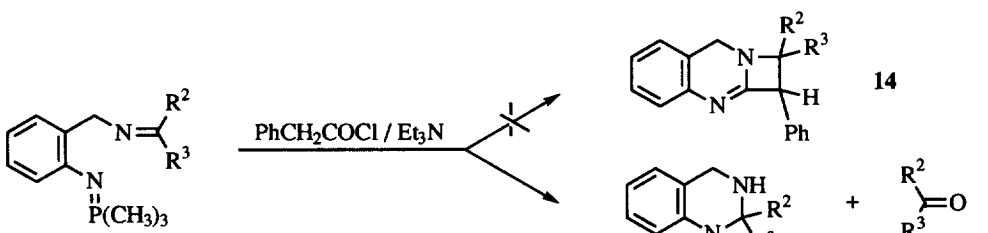
Scheme 3

Unmasking of the keto function in C-1 of compound **8a** was readily achieved by mercury (II) promoted hydrolysis[21] as well as by the action of *N*-bromosuccinimide in acetonitrile[22] thus affording the 1-oxo derivative **9** in 35% and 80% yield respectively. Compound **9** may be structurally regarded as a new fused tricyclic β-lactam of the type benz-1-azacephem. Fused bi- and tricyclic β-lactams are currently attracting synthetic and medicinal interest,[23] and the azacephem synthesis seems to be a relatively unexplored area.[24] On the other hand, we also tried to desulfurize the C-1 carbon atom of azeto[2,1-*b*]quinazolines **8** by the action of Raney-Ni[19c] and nickel boride[19f] with limited success. Only from the reaction of **8a** with Raney-Ni we could isolate the 1-unsubstituted azeto[2,1-*b*]quinazoline **10** albeit in low yield.

The C=N bond of a formamidine functionality also participated efficiently on the current [2 + 2] intramolecular cycloaddition. When crude formamidine **11**, obtained from amine **1a** and dimethylformamide dimethylacetal[25] (DMFDMA), was sequentially treated with trimethylphosphane and diphenylketene gave rise to 1-dimethylamino-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline **12** in 38% global yield (three steps). Compound **12** was difficult to obtain in pure state, as crystallization or column chromatography converted it into 2-diphenylmethyl-3,4-dihydroquinazoline **13**.

The Ketenimine Component

A major limitation of the synthetic sequence depicted in Scheme 1 leading to **5** was found in the step **3** → **4**: the only ketenes that could be used successfully were those enough stable to be isolated as manageable compounds in the usual working conditions, prepared in circumstances where they can be directly characterized by spectroscopic means. These conditions are fullfilled by the examples of diphenyl and phenyl methyl ketene used in this work as partners of the phosphazene imines **3** in the aza-Wittig reaction. Many other ketenes have been obtained previously as reactive intermediates involved in chemical reactions.[26a] Arylaldoketenes ArCH=C=O are particularly reactive species and have been generated as unobserved intermediates by dehydrohalogenation of the acyl chlorides with Et_3N.[26b] When we tried the preparation of 2-phenyl azeto[2,1-*b*]quinazolines **14** by reaction of some phosphazene imines with phenylketene, generated *in situ* from phenylacetyl chloride and Et_3N, under a variety of experimental conditions (temperatures of 25, 0, -20 and -78°C; normal and inverted addition procedures; dry toluene, CH_2Cl_2 and THF as solvents; from one to ten equivalents of base; inert atmosphere), the expected cycloaddition products **14** could not be either isolated or detected. Instead of the only species clearly identifed after the usual work-up of the final reaction mixtures were the tetrahydroquinazolines **15** and the corresponding aldehyde or ketone (Scheme 4).



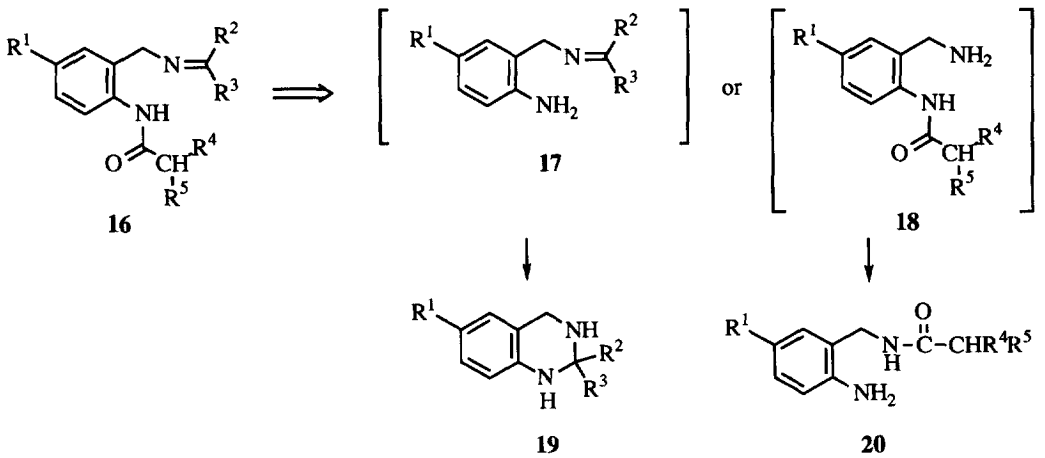
R^2 = H; R^3 = 4-CH_3O-C_6H_4

R^2 = H; R^3 = 4-O_2N-C_6H_4

Scheme 4

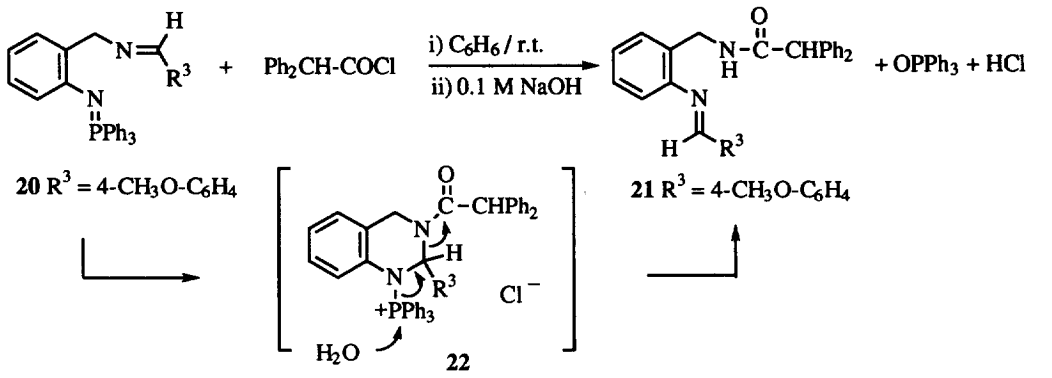
The 2-substituted 1,2,3,4-tetrahydroquinazolines **15** are well-known species, which have been prepared in advance by treatment of 2-aminobenzylamine with carbonyl compounds.[27] Thus the formation of **15** and $R_2R_3C{=}O$ in the above reactions can be understood as due to the hydrolysis of the phosphazene function and the imino bond respectively during the work-up of the mixture containing either the unreacted starting phosphazene imines or their hydrochlorides. Similar results were obtained by using phosphazene base P_4-*t*-Bu instead of triethylamine, and a 1:2 molar ratio acyl chloride: phosphazene imine.

Other approaches were then explored for the preparation of the ketenimine function avoiding the employ of ketenes as reagents. The dehydration of *N*-monosubstituted carboxamides with at least one hydrogen atom on the α carbon to the carbonyl group is a useful method for the synthesis of ketenimines.[28] For our purpose an easy access to the imine carboxamides **16** as inmediate precursors of the intermediates **4** needed to be attained, and that proved to be a difficult task. Suitable forerunner **17** actually did not exist but converted[27] into the cyclic ring-chain tautomer **15**, whereas the availability of the anilide **18** was precluded by its expected[29] intramolecular transamidation to **19** (Scheme 5).



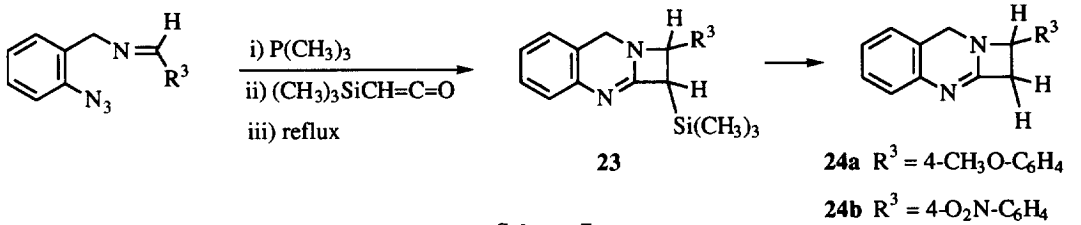
Scheme 5

The two above transformations, along with the stronger nucleophilic character of the benzylic nitrogen over the aryl one, prevented all the efforts we made to reach **16**, some of them leading to rather surprising results. For instance, it is known[30] that phosphazenes react with acyl halides to give *N*-acylaminophosphonium salts or imidoyl halides, which could be readily hydrolysed to the corresponding carboxamides; when the triphenylphosphazene imine **20** was reacted with diphenylacetyl chloride in dry benzene in an attempt to acylate the aryl nitrogen, an insoluble and very hygroscopic compound gradually came out from the reaction mixture, which when treated with 0.1 M aqueous NaOH transformed into a crystalline solid identified as the iminocarboxamide **21** (Scheme 6). This result can be rationalized through the ocurrence of an intermediate phosphonium chloride such as **22** in which the imino carbon atom becomes simultaneously linked to both nitrogen atoms.



Scheme 6

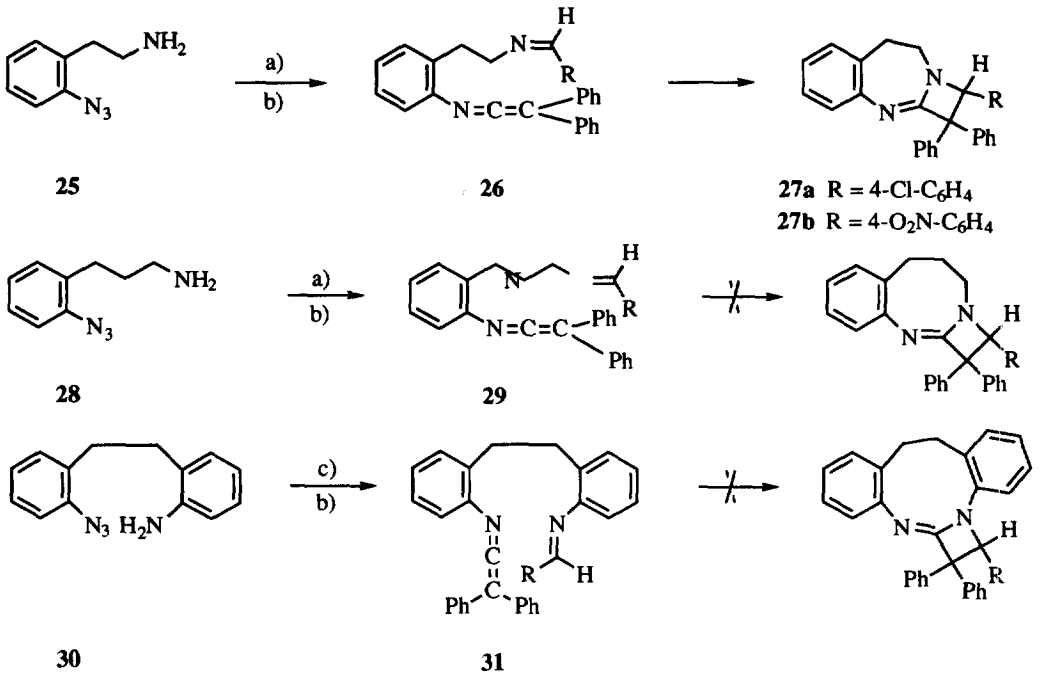
Then we turned our attention to other stable ketenes capable of reacting with phosphazenes in an aza-Wittig fashion. Silylketenes are well-known stable ketenes of increasing employ in synthetic chemistry.[26c] Trimethylsilylketene proved to be reactive toward the *in situ* generated trimethylphosphazenes **3** giving rise to the 2-trimethylsilyl azeto[2,1-*b*]quinazolines **23** that were not isolated as such but experienced protonolysis of the carbon-silicon bond during the chromatographic purification (SiO_2 gel column) to give the 2-unsubstituted derivatives **24** (Scheme 7).



Scheme 7

The Tether Length

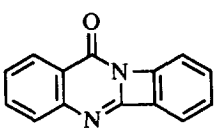
The success of an intramolecular cycloaddition is critically dependent on the relative rates of the cycloaddition and unproductive decomposition reactions. The length and nature of the chain linking the reactive functions, usually known as the tether, influences $\Delta S^{\neq}$ for intramolecular cycloaddition reactions without affecting the rate of the decomposition processes. Thus it was expected that increasing the length and flexibility of the tether between the imine and ketenimine functionalities would difficult the occurrence of the intramolecular [2+2] cycloaddition. In fact we have experienced that increasing by one methylene unit the aliphatic chain of intermediates **4**, that is the case of compound **26**, still allowed to reach the corresponding cycloaddition product **27**, although requiring longer reaction times (overnight, room temperature) than the conversion **4** → **5**. However a further lengthening of the tether in **26** either by one methylene unit, compound **29**, or by two aromatic carbon atoms, compound **31**, clearly prevented the intramolecular [2 + 2] cycloaddition, as these two imino-ketenimines remained unchanged in toluene solution under heating at reflux for several hours, and only led to decomposition under more drastic conditions (Scheme 8).



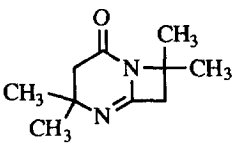
Scheme 8

Reactivity of Azeto[2,1-b]quinazolines

To the best of our knowledge derivatives of the fused heterocyclic system azeto[2,1-*b*]quinazoline were not previously known, but some closely related structures, such as the benzo and debenzo analogs **32** and **33** respectively, have been reported in the literature and synthesized by methods[31,32] not related to the one described in the present work.



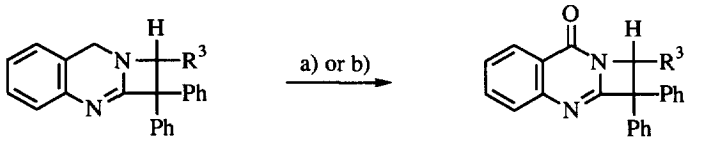
32



33

The presence of an oxo functionality in α position to the bridgehead nitrogen in the above two related structures **32** and **33** seems to forecast the reactivity of the azeto[2,1-*b*]quinazolines **5**. Compounds **5d** and **5e** spontaneously oxidized in chloroform or dichloromethane solution to the corresponding azeto[2,1-*b*]-quinazolin-9-ones **34** in variable extensions, and these processes were accelerated by the sunlight. Actually we

were aware of the cited oxidations during the work-up and chromatographic purification of the reaction mixtures leading to **5**, and this fact occasionally rendered difficult the isolation of pure **5** (Scheme 9). The spontaneous oxidation observed is not unprecedented: it has been reported that the alkaloid vasicine, a pyrrolo[2,1-*b*]quinazoline derivative, gradually converted to vasicinone (its quinazolin-4-one analog) by autooxidation during partition chromatography experiments or in chloroform solution[33]; other dihydroquinazolines have been reported to experience similar oxidations.[34] Complete conversions of **5d,e** to **34** have been also achieved by conventional oxidants, e.g. activated MnO_2, in short reaction times.



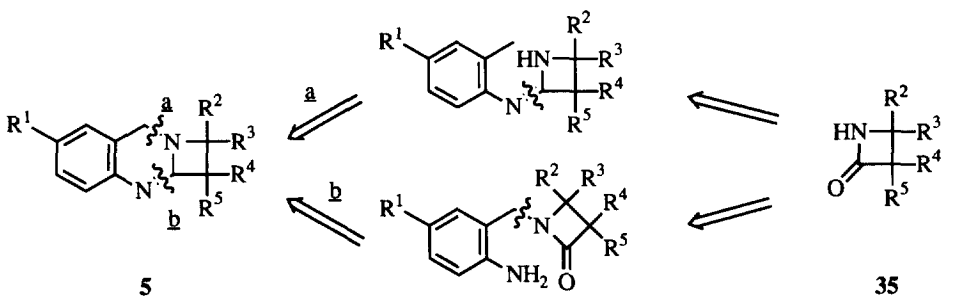
5d,e **34a** R = 4-CH_3O-C_6H_4

34b R = 4-O_2N-C_6H_4

Reagents and conditions: a) air / sunlight, $CHCl_3$; b) activated MnO_2, CH_2Cl_2, r. t., 4 h

Scheme 9

We considered that a suitable fragmentation sequence of azeto[2,1-*b*]quinazolines **5** resulting into the β-lactam ring **35** could be an interesting extension of the present work and consequently we devoted some efforts to this aim. We reasoned that the above objective, requiring the cleavage of the C-N single and double bonds, paths a and b respectively in Scheme 10, under conditions that preserve the four-membered ring would not be an easy task but some attempts directed either to the reductive fission of the benzylic C-N bond (path a) or the hydrolytic cleavage of the C=N bond (path b) were undertaken without apparent success. Thus the employ of reagents habitually employed to achieve the hydrogenolysis of benzylic C-N bonds, such as molecular H_2 or formic acid in the presence of several Pd-based catalysts,[35] left the starting compounds **5** unchanged, whereas its treatment with metals (Na, Li) in liquid ammonia[36] gave rise to complex mixtures in which any product derived from the expected reductive fission of bond a could be detected by ^{1}H-NMR analysis of the crude.

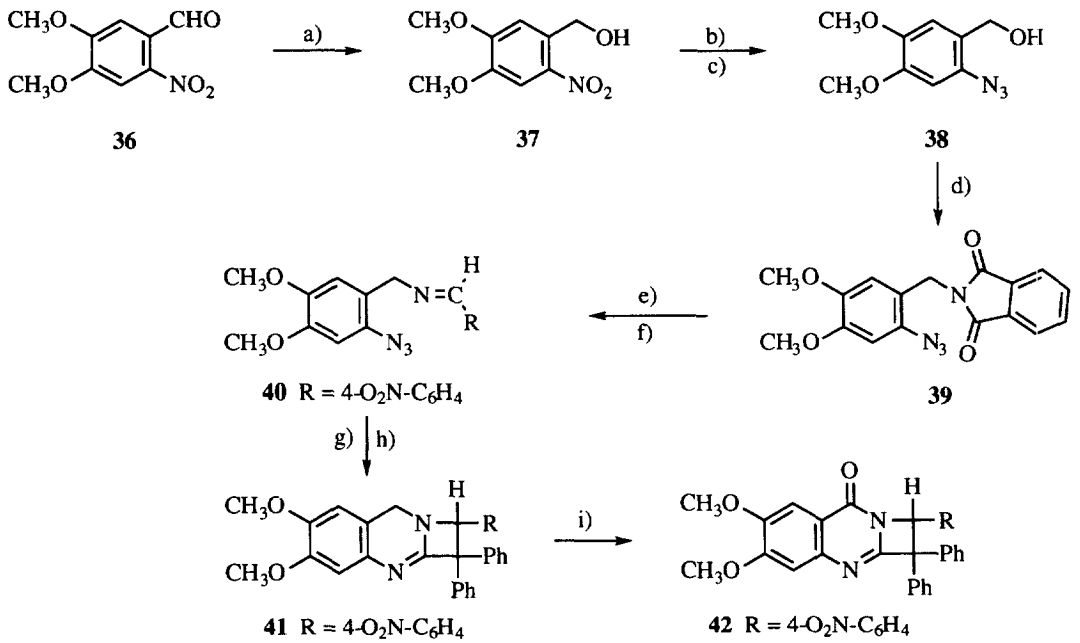


5 **35**

Scheme 10

Oxidative methods have also been used for the deprotection of the amino group in benzylamine derivatives as an alternative to reductive fission. When representative examples of **5** were treated with CAN[37] or $K_2S_2O_8$[38] under the usual conditions the reactions halted at the corresponding benzylic oxidation product **34**.

The *p*-methoxybenzyl group is one of the most widely used *N*-protecting groups in β-lactam chemistry[3] given its easy removal under oxidative conditions without affecting the four-membered ring. With this in mind we synthesized an azeto[2,1-*b*]quinazoline bearing a methoxy group in the *para* position relative to the benzylic C-N bond, compound **41**, starting from the commercially available 4,5-dimethoxy-2-nitrobenzaldehyde **36** and following the synthetic sequence depicted in Scheme 11.

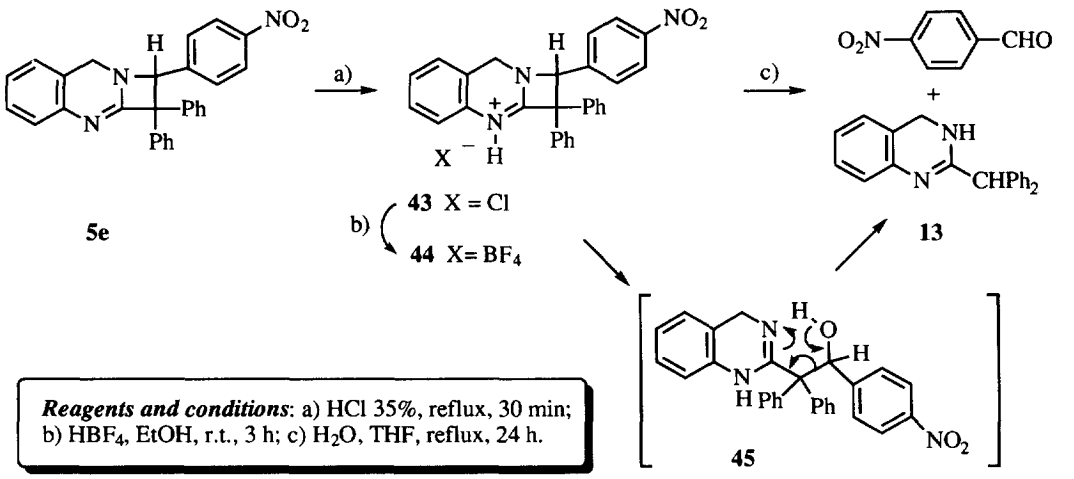


Reagents and conditions: a) $NaBH_4$, THF, 0°C, 6 h; b) H_2, Pd/C, EtOH, r.t., 6 h; c) $NaNO_2$, H_2SO_4 10%, 0°C, 30 min followed by addition of NaN_3, r.t., 6 h; d) Phtalimide, EtOOC-N=N-COOEt, PPh_3, THF, r.t., 24 h; e) N_2H_4, EtOH, reflux, 3 h; f) 4-O_2N-C_6H_4-CHO, Et_2O, anh. $MgSO_4$, r.t., 12 h; g) $P(CH_3)_3$, toluene, r.t., 30 min; h) Ph_2C=C=O, toluene, r.t., 1 h; i) $K_2S_2O_8$, Na_2HPO_4, CH_3CN/H_2O, reflux, 24 h.

Scheme 11

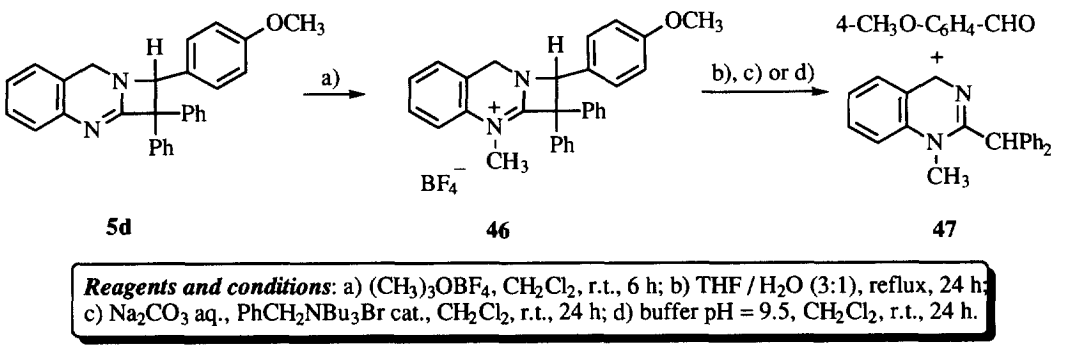
When compound **41** was subjected to the action of $K_2S_2O_8$ or excess of CAN the only reaction product that could be isolated and identified in both cases was the azeto[2,1-*b*]quinazolin-9-one **42**, a result which demonstrated that the fast oxidation of the benzylic methylene group of compounds **5** to its oxo derivatives precluded the cleavage of the single C-N bond under oxidative conditions. Probably this oxidation is driven by the heteroaromatic nature of the quinazolone fragment in compounds **34** and **42**.

As far as the hydrolytic attempts to fragment compounds **5** via C=N bond cleavage (path b in Scheme 10) are concerned, heating for 15 min a suspension of **5d** in concentrated HCl gave rise to the unstable hydrochloride **43**, which was converted to the tetrafluoroborate **44** by anion exchange and identified as such. Basic treatments of **44** only led to deprotonation and the neutral **5d** was recovered. When a THF/H_2O (3:1) solution of **44** was heated at reflux temperature for 24 h and then neutralized by addition of NH_4OH the isolated products were *p*-anisaldehyde and the 3,4-dihydroquinazoline **13**. A reasonable mechanism to explain the formation of both compounds is presented in Scheme 12: nucleophilic attack of the water molecule to the C1 atom with simultaneous cleavage of the C1-N bond would lead to the non-isolated intermediate **45** which then underwent fragmentation of the C-C bond of the side-chain as indicated to give the final products.



Scheme 12

Azeto[2,1-*b*]quinazoline **5d** was easily methylated by the action of trimethyloxonium tetrafluoroborate to yield **46** as crystalline solid (Scheme 13). Different hydrolytic treatments of **46** under neutral or basic conditions led to the formation of *p*-anisaldehyde and the 1,4-dihydroquinazoline **47**, probably by a mechanism similar to the one above.



Scheme 13

Considering the results obtained in the hydrolytic treatments of species **44** and **46** we may conclude than the C1 atom is more electrophilic than the amidinium carbon atom C3 when exposed to water or the hydroxide anion, and this fact is responsible of their cleavage through the C1-N bond and consequently precluded both the preservation of the four-membered ring and the desired breaking of the C3-N double bond, making impracticable the strategy designed as path b in Scheme 10.

SUMMARY

In summary, the intramolecular [2 + 2] cycloaddition of ketenimines to imines here described resulted in the synthesis of representative samples of the new heterocyclic system azeto[2,1-*b*]quinazoline. The applicability and limitations of the method have been discussed, as well explorations on the chemical behaviour of the reaction products. Current research in our laboratory is showing that good levels of diastereoselection are obtained in similar intramolecular [2 + 2] cycloadditions involving imino-ketenimines derived either from ketenes with enantiotopic faces or from imines possesing stereogenic carbon atoms close to the imine function, and these results will be reported in the near future.

EXPERIMENTAL

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as nujol emulsions or films on a Nicolet Impact 400 spectrophotometer. NMR spectra were recorded on a Bruker AC-200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Carlo Erba EA-1108 instrument.

Compounds 2-azidobenzylamine **(1a)**,[11a] 2-azido-5-methylbenzylamine **(1b)**,[11b] 2-azidophenethylamine **(25)**,[11b] 3-(2-azidophenyl)propylamine **(28)**[11b] and 2-(2-azidophenethyl)aniline **(30)**[39] were prepared following previously reported procedures.

N-(2-Azidobenzyl)imines **2** were obtained from the corresponding 2-azidobenzylamine **1** by standard procedures: Method A,[40] Method B[41] or Method C[42] (see Scheme 1 and Table).

General Procedure for the Preparation of Azeto[2,1-*b*]quinazolines 5

To a solution of the corresponding *N*-(2-azidobenzyl)imine **2** (3 mmol) in dry toluene (15 mL) trimethylphosphane (3 mmol) was added and the reaction mixture was stirred at room temperature until the evolution of nitrogen ceased (15-30 min). Then the appropriate ketene (diphenylketene or methyl phenyl ketene) (3 mmol) was added, and the reaction mixture was stirred at room temperature until the ketenimine band around 2000 cm^{-1} was not observed by IR (1-12 h). The solvent was removed under reduced pressure and the resulting material was chromatographed on a silica gel column, using hexanes / ethyl acetate (4:1, v/v) as eluent.

2,2-Diphenyl-1-isopropyl-1,2-dihydroazeto[2,1-*b*]quinazoline (5a): yield 36%; m.p. 153-154°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 0.79 (d, 3H, *J* = 6.5 Hz), 0.98 (d, 3H, *J* = 6.5 Hz), 1.57-1.73 (m, 1H), 4.00 (d, 1H, *J* = 9.9 Hz), 4.48 (d, 1H, *J* = 12.4 Hz), 4.60 (d, 1H, *J* = 12.4 Hz), 6.85 (d, 1H, *J* =

7.9 Hz), 6.94-6.97 (m, 1H), 7.16-7.39 (m, 8H), 7.39 (t, 2H, *J* = 7.8 Hz), 7.68 (d, 2H, *J* = 7.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 19.41, 19.97, 29.83, 47.73, 66.45 (s), 77.22, 121.49 (s), 124.28, 125.29, 126.60, 127.14, 127.17, 127.93, 128.30, 128.37, 128.79, 129.00, 139.07 (s), 140.42 (s), 142.99 (s), 165.99 (s); IR (Nujol) 1669, 1601, 1221, 1146, 753, 702 cm^{-1}; mass spectrum m/z (%): 352 (M^+, 49), 165 (100); Anal. Calcd. for $C_{25}H_{24}N_2$: C, 81.19; H, 6.86; N, 7.95. Found: C, 81.32; H, 6.78; N, 7.81.

2,2-Diphenyl-1-(*E*-2-phenylethenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5b): yield 72%; ^{1}H-NMR ($CDCl_3$) δ 4.46 (d, 1H, *J* = 12.6 Hz), 4.54 (d, 1H, *J* = 12.6 Hz), 4.99 (d, 1H, *J* = 8.9 Hz), 5.75 (dd, 1H, *J* = 8.9, 15.8 Hz), 6.98-7.66 (m, 20H); ^{13}C-NMR ($CDCl_3$) δ 44.21, 68.36 (s), 73.22, 121.13 (s), 124.54, 125.55, 125.78, 126.71, 127.02, 127.26, 127.36, 127.69, 128.32, 128.49, 128.54, 128.62, 128.66, 129.10, 131.26, 135.15, 135.98, 138.17 (s), 141.11 (s), 142.93 (s), 152.76, 164.97 (s); IR (Nujol) 1669, 1645, 1597, 1148, 969, 753, 700 cm^{-1}; mass spectrum m/z (%): 412 (M^+, 6), 115 (100); Anal. Calcd. for $C_{30}H_{24}N_2$: C, 87.34; H, 5.86; N, 6.79. Found: C, 87.21; H, 5.93; N, 6.67.

2,2-Diphenyl-1-(3-furyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5c): yield 50%; m.p. 190-192°C (colour-less prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.47 (s, 2H), 5.42 (s, 1H), 5.87 (s, 1H), 6.87 (d, 1H, *J* = 6.8 Hz), 7.01 (t, 1H, *J* = 7.5 Hz), 7.12-7.97 (m, 12H), 7.65 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 44.26, 66.74, 68.95 (s), 109.37, 121.19 (s), 121.31 (s), 124.51, 125.67, 126.98, 127.00, 127.28, 127.62, 127.97, 128.23, 128.52, 128.56, 138.78 (s), 141.15 (s), 141.21, 142.99 (s), 143.33, 165.01 (s); IR (Nujol) 1664, 1593, 1328, 1156, 1137, 1013, 751, 704 cm^{-1}; mass spectrum m/z (%): 376 (M^+, 100), 165 (45); Anal. Calcd. for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.35; N, 7.44. Found: C, 82.78; H, 5.42; N, 7.35.

2,2-Diphenyl-1-(4-methoxyphenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5d): yield 63%; m.p. 144-145°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.71 (s, 3H), 4.49 (s, 2H), 5.45 (s, 1H), 6.70 (d, 2H, *J* = 8.7 Hz), 6.86 (d, 1H, *J* = 7.2 Hz), 6.97-7.40 (m, 13H), 7.70 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 44.31, 55.16, 70.04 (s), 73.99, 113.62, 121.21 (s), 124.40, 125.69, 126.57, 127.02, 127.15, 127.69, 127.76, 128.35, 128.50, 128.54, 128.95, 137.96 (s), 141.67 (s), 143.24 (s), 159.53 (s), 165.25 (s), one quaternary carbon was not observed; IR (Nujol) 1668, 1598, 1512, 1246, 1173, 1025, 771, 725, 700 cm^{-1}; mass spectrum m/z (%): 416 (M^+, 76), 165 (100); Anal. Calcd. for $C_{29}H_{24}N_2O$: C, 83.62; H, 5.81; N, 6.72. Found: C, 83.47; H, 5.90; N, 6.64.

2,2-Diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5e): yield 81%; m.p. 159-160°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.49 (d, 1H, *J* = 12.4 Hz), 4.56 (d, 1H, *J* = 12.4 Hz), 5.61 (s, 1H), 6.92 (d, 1H, *J* = 7.5 Hz), 7.00-7.09 (m, 6H), 7.24-7.44 (m, 7H), 7.72 (d, 2H, *J* = 8.7 Hz), 8.03 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 44.92, 71.09 (s), 72.79, 120.97 (s), 123.39, 124.97, 125.92, 127.03, 127.24, 127.63, 127.81, 128.12, 128.34, 128.76, 137.17 (s), 140.47 (s), 142.51 (s), 143.06 (s), 147.55 (s), 164.56 (s), two methine carbons were not observed; IR (Nujol) 1677, 1599, 1523, 1345, 1219, 1134, 1032, 854, 764, 700 cm^{-1}; mass spectrum m/z (%): 431 (M^+, 22), 165 (62), 89 (100); Anal. Calcd. for $C_{28}H_{21}N_3O_2$: C, 77.94; H, 4.90; N, 9.74. Found: C, 77.82; H, 4.97; N, 9.65.

2,2-Diphenyl-1-methyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5f): yield 46%; m.p. 174-175°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 1.72 (s, 3H), 4.44 (d, 1H, *J* = 12.7 Hz), 4.67 (d, 1H, *J* = 12.7 Hz), 6.93-7.44 (m, 14H), 7.91 (d, 2H, *J* = 8.7 Hz), 8.02 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 22.78, 40.80, 72.61 (s), 75.23 (s), 120.58 (s), 123.21, 124.83, 125.83, 126.85, 127.17, 127.39,

127.73, 127.75, 128.15, 128.35, 128.42, 128.77, 137.71 (s), 138.20 (s), 142.80 (s), 146.84 (s), 148.02 (s), 163.95 (s); IR (Nujol) 1669, 1599, 1510, 1348, 1213, 1167, 859, 776, 762, 710 cm^{-1}; mass spectrum m/z (%): 445 (M^+, 65), 165 (100); Anal. Calcd. for $C_{29}H_{23}N_3O_2$: C, 78.18; H, 5.20; N, 9.43. Found: C, 78.08; H, 5.10; N, 9.55.

2,2-Diphenyl-1-(4-methoxyphenyl)-6-methyl-1,2-dihydroazeto[2,1-*b*]quinazoline (5g): yield 91%; m.p. 166-167°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 2.26 (s, 3H), 3.68 (s, 3H), 4.42 (s, 2H), 5.43 (s, 1H), 6.66-6.71 (m, 3H), 6.94-7.38 (m, 12H), 7.69 (d, 2H, *J* = 8.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 20.96, 44.46, 55.28, 70.14 (s), 73.99, 125.41, 126.50, 127.07, 127.23 (s), 127.57, 127.69, 128.33, 128.48, 128.88, 128.99, 131.88, 134.00 (s), 138.02 (s), 140.57 (s), 141.68 (s), 159.45 (s), 164.61 (s), one quaternary carbon and one methine carbon were not observed; IR (Nujol) 1671, 1613, 1513, 1295, 1250, 1172, 1139, 1112, 1029, 884, 835, 703 cm^{-1}; mass spectrum m/z (%): 430 (M^+, 18), 218 (100); Anal. Calcd. for $C_{30}H_{26}N_2O$: C, 83.69; H, 6.08; N, 6.51. Found: C, 83.55; H, 6.17; N, 6.42.

2,2-Diphenyl-6-methyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (5h): yield 88%; m.p. 154-155°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 2.29 (s, 3H), 4.42 (d, 1H, *J* = 12.4 Hz), 4.51 (d, 1H, *J* = 12.4 Hz), 5.59 (s, 1H), 6.73 (s, 1H), 6.96-7.07 (m, 6H), 7.20 (d, 1H, *J* = 8.1 Hz), 7.28-7.44 (m, 5H), 7.70 (d, 2H, *J* = 8.5 Hz), 8.00 (d, 2H, *J* = 8.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 20.94, 44.99, 71.09 (s), 72.72, 120.81 (s), 123.40, 125.73, 127.24, 127.62, 127.68, 127.88, 128.13, 128.20, 128.38, 128.78, 129.33, 134.72 (s), 137.38 (s), 140.06 (s), 140.63 (s), 143.27 (s), 147.56 (s), 163.98 (s); IR (Nujol) 1674, 1600, 1517, 1345, 1212, 1136, 854, 825, 774, 744 cm^{-1}; mass spectrum m/z (%): 445 (M^+, 30), 165 (100); Anal. Calcd. for $C_{29}H_{23}N_3O_2$: C, 78.18; H, 5.20; N, 9.43. Found: C, 78.01; H, 5.29; N, 9.34.

1,1,2,2-Tetraphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (5i): yield 65%; m.p. 213-214°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.64 (s, 2H), 7.02-7.31 (m, 24H); ^{13}C-NMR ($CDCl_3$) δ 43.53, 75.06 (s), 84.23 (s), 121.13 (s), 124.57, 125.93, 126.63, 127.15, 127.24, 127.56, 128.61, 129.49, 129.69, 138.05 (s), 138.57 (s), 142.99 (s), 165.71 (s), one methine carbon was not observed; IR (Nujol) 1671, 1605, 1575, 1446, 1393, 1186, 1115, 1080, 760, 699 cm^{-1}; mass spectrum m/z (%): 462 (M^+, 20), 165 (33), 77 (100); Anal. Calcd. for $C_{34}H_{26}N_2$: C, 88.21; H, 5.63; N, 6.05. Found: C, 88.00; H, 5.70; N, 5.91.

2-Methyl-1,1,2-triphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (5j): yield 75%; m.p. 257-259°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 1.45 (s, 3H), 4.39 (d, 1H, *J* = 13.1 Hz), 4.55 (d, 1H, *J* = 13.1 Hz), 6.86 (d, 1H, *J* = 7.5 Hz), 6.99-7.27 (m, 10H), 7.42-7.43 (m, 1H), 7.52-7.57 (m, 7H); ^{13}C-NMR ($CDCl_3$) δ 28.12, 42.92, 66.07 (s), 81.23 (s), 121.29 (s), 124.45, 125.53, 126.43, 127.26, 127.46, 127.51, 127.61, 127.70, 128.02, 128.16, 128.48, 128.63, 130.04, 136.61 (s), 138.77 (s), 141.04 (s), 142.98 (s), 166.93 (s); IR (Nujol) 1665, 1599, 1569, 1327, 1243, 776, 716, 697 cm^{-1}; mass spectrum m/z (%): 400 (M^+, 87), 165 (62), 77 (100); Anal. Calcd. for $C_{29}H_{24}N_2$: C, 86.95; H, 6.06; N, 6.99. Found: C, 86.76; H, 6.12; N, 7.10.

General Procedure for the Preparation of Azeto[2,1-*b*]quinazolines 8

To a well-stirred solution of 2-azidobenzylamine **(1a)** (0.74 g, 5 mmol) in DMF (5 mL), in a ice/water bath, aqueous NaOH 20M (0.27 mL), carbon disulfide (0.54 mL), aqueous NaOH 20M (0.27 mL), and methyl iodide (1.42 g, 5.5 mmol) were sequentially added. Stirring is continued for 10 min and the mixture is poured in water (25 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with

water (50 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the resulting oil was chromatographed on a silica gel column using hexanes / ethyl acetate (4:1, v/v) as eluent to give **dimethyl *N*-(2-azidobenzyl)dithiocarbonimidate (7)**: yield 80%, oil; ^{1}H-NMR ($CDCl_3$) δ 2.41 (s, 3H), 2.54 (s, 3H), 4.50 (s, 2H), 7.11 (td, 2H, *J* = 1.2, 7.5 Hz), 7.24 (td, 1H, *J* = 1.5, 7.8 Hz), 7.53 (dd, 1H, *J* = 0.9, 7.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.62, 14.66, 51.28, 117.63, 124.60, 127.63, 128.81, 131.44 (s), 137.13 (s), 159.54 (s); IR (Neat) 2129, 1573, 1489, 1455, 1294, 1033, 916, 755 cm^{-1}; mass spectrum m/z (%): 252 (M^+, 6), 132 (76), 104 (100); Anal. Calcd. for $C_{10}H_{12}N_4S_2$: C, 47.56; H, 4.78; N, 22.24. Found: C, 47.43; H, 4.80; N, 22.05.

Compounds **8** were prepared from **7** using the procedure described above for the preparation of azeto[2,1-*b*]quinazolines **5**.

1,1-Bis(methylthio)-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (8a): yield 70%; m.p. 143°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 1.78 (s, 6H), 4.67 (s, 2H), 6.95 (d, 1H, *J* = 7.0 Hz), 7.07 (td, 1H, *J* = 1.9, 6.7 Hz), 7.21-7.37 (m, 8H), 7.87-7.91 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ 14.88, 42.05, 74.46 (s), 90.42 (s), 120.37 (s), 125.08, 126.34, 127.38, 127.60, 127.95, 128.49, 128.76, 137.79 (s), 142.42 (s), 160.76 (s); IR (Nujol) 1669, 1595, 1454, 1407, 1313, 1118, 903, 715, 769 cm^{-1}; mass spectrum m/z (%): 402 (M^+, 30), 387 (100); Anal. Calcd. for $C_{24}H_{22}N_2S_2$: C, 71.59; H, 5.52; N, 6.96. Found: C, 71.45; H, 5.65; N, 6.90.

1,1-Bis(methylthio)-2-methyl-2-phenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (8b): yield 40%; m.p. 195-196°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 1.77 (s, 3H), 1.94 (s, 3H), 2.33 (s, 3H), 4.61 (s, 2H), 6.92 (d, 1H, *J* = 7.3 Hz), 7.00-7.08 (m, 1H), 7.18-7.37 (m, 5H), 7.54-7.57 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 14.79, 15.23, 23.05, 42.14, 67.67 (s), 90.45 (s), 121.02 (s), 124.90, 125.77, 127.27, 127.53, 127.66, 128.11, 128.72, 136.68 (s), 142.29 (s), 162.72 (s); IR (Nujol) 1673, 1597, 1485, 1121, 910, 774, 703 cm^{-1}; mass spectrum m/z (%): 340 (M^+, 10), 325 (100); Anal. Calcd. for $C_{19}H_{20}N_2S_2$: C, 67.01; H, 5.93; N, 8.22. Found: C, 66.89; H, 6.00; N, 8.11.

2,2-Diphenylazeto[2,1-*b*]quinazolin-1-one (9)

Method A: To a suspension of 1,1-bis(methylthio)-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline **(8a)** (0.2 g, 0.5 mmol) in ethylenglycol (10 mL) and water (1.5 mL), $HgCl_2$ (0.29 g, 1 mmol) and $CaCO_3$ (0.094 g, 0.55 mmol) were added. The mixture was heated at 90°C for 30 min and then the temperature was rised up to 110°C and stirring continued for 2 h. After cooling at room temperature brine (20 mL) was added and the mixture extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the resulting solid was chromatographed on a silica gel column using hexanes / ethyl acetate (4:1, v/v) as eluent to give **9**: yield 35%; m.p. 232-235°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.83 (s, 2H), 6.95 (d, 1H, *J* = 7.5 Hz), 7.13 (t, 1H, *J* = 6.2 Hz), 7.23-7.41 (m, 8H), 7.63 (dd, 4H, *J* = 1.9, 7.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 41.30, 119.64 (s), 126.87, 127.39, 127.90, 128.17, 128.96, 129.13, 136.18 (s), 140.74 (s), 157.24 (s), 168.32 (s), one methine carbon and one quaternary carbon were not observed; IR (Nujol) 1817, 1678, 1600, 1407, 1342, 960, 779, 704 cm^{-1}; mass spectrum m/z (%): 324 (100), 295 (75), 165 (56); Anal. Calcd. for $C_{22}H_{16}N_2O$: C, 81.47; H, 4.98; N, 8.63. Found: C, 81.29; H, 4.90; N, 8.55.

Method B: A solution of 1,1-bis(methylthio)-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (**8a**) (0.2 g, 0.5 mmol) in CH_3CN (10 mL) was added dropwise, under nitrogen, to a cold solution (ice-salt bath) of *N*-bromosuccinimide (0.71 g, 4 mmol) in CH_3CN / H_2O (4:1, v/v; 30 mL). The yellow mixture was allowed to reach room temperature and stirred for 15 min. Then, saturated aqueous Na_2SO_3 was added until complete decoloration. The organic layer was separated and the aqueous one was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with saturated $NaHCO_3$, brine and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column using hexanes / ethyl acetate (4:1, v/v) as eluent to give **9** (yield 80%).

2,2-Diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (10)

To a solution of 1,1-bis(methylthio)-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (**8a**) (0.2 g, 0.5 mmol) in ethyl acetate (25 mL) Raney-Ni (4 g) was added. The mixture was stirred at room temperature, under hydrogen atmosphere, for 24 h. The solution was filtered over celite and the solvent was removed under reduced presure to give a solid residue which was chromatographed on a silica gel column using hexanes / ethyl acetate (4:1, v/v) as eluent to give **10:** yield 27%; m.p. 184-186°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.16 (s, 2H), 4.54 (s, 2H), 6.88 (d, 1H, *J* = 7.3 Hz), 6.93-7.01 (m, 1H), 7.16-7.30 (m, 8H), 7.46-7.52 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ 45.67, 62.43, 63.24 (s), 121.46 (s), 124.40, 125.65, 126.95, 127.33, 127.39, 128.50, 128.67, 140.92 (s), 142.95 (s), 166.55 (s); IR (Nujol) 1660, 1601, 1487, 1212, 1155, 950, 774, 717 cm^{-1}; mass spectrum m/z (%): 310 (M^+, 78), 309 (100), 204 (58), 165 (58); Anal. Calcd. for $C_{22}H_{18}N_2$: C, 85.06; H, 5.81; N, 9.03. Found: C, 84.93; H, 5.70; N, 8.90.

1-Dimethylamino-2,2-diphenyl-1,2-dihydroazeto[2,1-*b*]quinazoline (12) and 2-Diphenylmethyl-3,4-dihydroquinazoline (13)

A solution of 2-azidobenzylamine (**1a**) (0.44 g, 3 mmol) and DMFDMA (0.36 g, 3 mmol) in anhydrous toluene (15 mL) was heated at reflux temperature for 6 h. After cooling at room temperature the solvent was removed under reduced pressure to give **11** as an oil which was used in the following step without purification.

To a solution of **11** (3 mmol) in dry toluene (15 mL) trimethylphosphane (3 mmol) was added and the reaction mixture was stirred at room temperature until the evolution of nitrogen ceased (15-30 min). Then diphenylketene (3 mmol) was added, and the mixture was stirred at room temperature until the ketenimine vibration around 2000 cm^{-1} was not observed by IR. The solvent was removed under reduced pressure and the resulting material was treated with methylene chloride to afford a solid which could not be further purified due to its hydrolytic sensitivity but which was unambiguously identified by spectroscopic means as compound **12:** yield 38%; ^{1}H-NMR ($CDCl_3$) δ 2.22 (s, 6H), 4.52 (d, 1H, *J* = 12.76 Hz), 4.63 (d, 1H, *J* = 12.76 Hz), 4.99 (s, 1H), 6.86 (d, 1H, *J* = 7.5 Hz), 6.99 (td, 1H, *J* = 1.2, 7.5 Hz), 7.17-7.34 (m, 9H), 7.59-7.62 (m, 3H); ^{13}C-NMR ($CDCl_3$) δ 40.31, 46.64, 69.36 (s), 89.07, 120.87, 124.39, 125.75, 126.91, 126.96, 127.49, 128.20, 128.25, 128.48, 128.51, 138.39 (s), 141.99 (s), 143.54 (s), 163.28 (s); IR (Nujol) 1661, 1598, 1285, 1223, 1107, 1032, 769, 751, 711 cm^{-1}; mass spectrum m/z (%): 326 (15), 297 (100), 165 (66).

When compound **12** was chromatographed on a silica gel column using ethyl acetate as eluent converted into **13**: m.p. 129-130°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.66 (s, 2H), 6.02 (s, 1H), 6.86-

6.88 (m, 1H), 7.07-7.45 (m, 13H), the NH proton was not observed; ^{13}C-NMR ($CDCl_3$) δ 42.89, 53.21, 116.91 (s), 118.18, 126.15, 127.35, 128.26, 129.06, 129.43, 131.53 (s), 135.68 (s), 162.94 (s), a methine carbon was not observed; IR (Nujol) 3375, 1651, 1634, 1577, 1301, 1262, 1033, 765, 726, 700 cm^{-1}; mass spectrum m/z (%): 298 (M^+, 69), 297 (100), 165 (58); Anal. Calcd. for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08; N, 9.39. Found: C, 84.40; H, 6.00; N, 9.51.

***N*-{[2-(4-Methoxybenzylideneamino)methyl]phenyl}-*P*,*P*,*P*-triphenyl-λ^5-phosphazene (20)**

To a solution of triphenylphosphane (1.31 g, 5 mmol) in anhydrous Et_2O (20 mL) was added a solution of *N*-(2-azidobenzyl)imine **2d** (1.33 g, 5 mmol) in the same solvent (10 mL). The mixture was stirred at room temperature for 6 h. The precipitated solid was collected by filtration, air dried and recrystallized to give **20**: yield 55%; m.p. 101-103°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.79 (s, 3H), 5.14 (s, 2H), 6.48 (d, 1H, J = 7.6 Hz), 6.65 (t, 1H, J = 7.6 Hz), 6.80 (d, 1H, J = 7.6 Hz), 6.86 (d, 2H, J = 8.4 Hz), 7.18-7.22 (m, 1H), 7.36-7.87 (m, 17H), 8.27 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 55.21, 61.57, 113.66, 117.25, 120.75 (J_{CP} = 10.1Hz), 126.83, 128.44 (J_{CP} = 11.6 Hz), 128.83, 129.45, 129.76 (s), 131.41 (s, J_{CP} = 99.2 Hz), 131.62 (J_{CP} = 3.0 Hz), 132.45 (J_{CP} = 9.6 Hz), 133.32 (s, J_{CP} = 21.7 Hz), 148.97 (s), 160.67, 161.09 (s); ^{31}P-NMR ($CDCl_3$) δ 0.33; IR (Nujol) 1654, 1606, 1591, 1514, 1355, 1311, 1260, 1168, 1114, 1033, 840, 759, 720, 702 cm^{-1}; mass spectrum m/z (%): 500 (M^+, 31), 183 (100); Anal. Calcd. for $C_{33}H_{29}N_2OP$: C, 79.18; H, 5.83; N, 5.59. Found: C, 79.00; H, 5.69; N, 5.71.

***N*-[2-(4-Methoxybenzylideneamino)benzyl] Diphenylacetamide (21)**

To a solution of the triphenylphosphazene **20** (0.50 g, 1 mmol) in dry benzene (20 mL) was added diphenylacetyl chloride (0.23 g, 1 mmol). The mixture was stirred at room temperature for 24 h. The precipitated solid was isolated by filtration. This solid was dissolved in THF (20 mL) and NaOH 0.1 M was added (1 mL). The mixture was stirred at room temperature for 24 h. The THF was removed under reduced pressure and the residue was extracted with methylene chloride (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration, the solvent was removed and the residue was chromatographed on a silica gel column using diethyl ether / hexanes (7:3, v/v) as eluent to give **21**: yield 77%; m.p. 147-148°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.86 (s, 3H), 4.58 (d, 2H, J = 5.2 Hz), 4.89 (s, 1H), 6.60 (t, 1H, J = 5.2 Hz), 6.89-6.98 (m, 3H), 7.16-7.33 (m, 13H), 7.61 (d, 2H, J = 7.8 Hz), 8.22 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 41.38, 55.49, 59.27, 114.22, 117.61, 126.01, 127.03, 128.63, 128.75, 128.91, 129.00 (s), 129.44, 130.66, 132.11 (s), 139.62 (s), 150.41 (s), 159.19, 162.43 (s), 171.51 (s); IR (Nujol) 3280, 1654, 1605, 1552, 1511, 1260, 1161, 1029, 883, 829, 757, 732, 700 cm^{-1}; mass spectrum m/z (%):434 (M^+, 25), 223 (100); Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 80.16; H, 6.03; N, 6.44. Found: C, 80.01; H, 6.20; N, 6.25.

General Procedure for the Preparation of Azeto[2,1-*b*]quinazolines (24)

To a solution of the corresponding *N*-(2-azidobenzyl)imine **2** (3 mmol) in dry toluene (15 mL) trimethylphosphane (3 mmol) was added and the reaction mixture was stirred at room temperature until the evolution of nitrogen ceased (15-30 min). Then trimethylsilylethenone (0.34 g, 3 mmol) was added and the

reaction mixture was stirred at room temperature for 15 min and 2 h at reflux temperature. The solvent was removed under reduced pressure and the resulting material was chromatographed on a silica gel column, using hexanes / ethyl acetate (1:1; v/v) as eluent.

1-(4-Methoxyphenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (24a): yield 25%; m.p. 120-121°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.00 (dd, 1H, *J* = 3.1, 14.9 Hz), 3.54 (dd, 1H, *J* = 5.3, 14.9 Hz), 3.82 (s, 3H), 4.41 (s, 2H), 4.77 (dd, 1H, *J* = 3.1, 5.3 Hz), 6.84 (d, 1H, *J* = 7.5 Hz), 6.92 (d, 2H, *J* = 8.7 Hz), 6.98 (td, 1H, *J* = 1.2, 7.5 Hz), 7.08 (dd, 1H, *J* = 1.6, 7.8 Hz), 7.18 (td, 1H, *J* = 1.6, 7.2 Hz), 7.32 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 42.51, 44.25, 55.41, 61.32, 114.37, 121.04 (s), 124.25, 124.98, 127.11, 127.61, 128.53, 130.08 (s), 142.97 (s), 159.85 (s), 161.89 (s); IR (Nujol) 1682, 1597, 1516, 1251, 1152, 1033, 828, 780, 733, 727 cm^{-1}; mass spectrum m/z (%): 264 (M^+, 69), 263 (100), 233 (99); Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.59. Found: C, 77.10; H, 6.21; N, 10.45.

1-(4-Nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (24b): yield 35%; m.p. 156-157°C (colourless prisms from Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.04 (dd, 1H, *J* = 3.1, 14.9 Hz), 3.66 (dd, 1H, *J* = 5.6, 14.9 Hz), 4.44 (d, 1H, *J* = 12.4 Hz), 4.51 (d, 1H, *J* = 12.4 Hz), 4.90 (dd, 1H, *J* = 3.1, 5.6 Hz), 6.89 (d, 1H, *J* = 7.5 Hz), 7.04 (t, 1H, *J* = 7.5 Hz), 7.11 (d, 1H, *J* = 7.8 Hz), 7.22 (t, 1H, *J* = 7.8 Hz), 7.58 (d, 2H, *J* = 8.4 Hz), 8.26 (d, 2H, *J* = 8.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 42.54, 45.02, 65.87, 120.86 (s), 124.32, 124.82, 125.19, 127.00, 127.11, 128.79, 142.28 (s), 145.95 (s), 147.99 (s), 160.79 (s); IR (Nujol) 1686, 1597, 1512, 1346, 1307, 1155, 1059, 851, 796, 775, 744, 698 cm^{-1}; mass spectrum m/z (%): 279 (M^+, 100), 232 (79); Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.69; H, 4.76; N, 15.20.

General Procedure for the Preparation of 1,2,8,9-Tetrahydroazeto[2,1-*b*][1,3]benzodiazepines 27

Compounds **27** were prepared from the corresponding *N*-(2-azidophenethyl)imine, obtained by reaction of 2-azidophenethylamine **25** and the adequate aldehyde, using the procedure described for the preparation of azeto[2,1-*b*]quinazolines **5**.

1-(4-Chlorophenyl)-2,2-diphenyl-1,2,8,9-tetrahydroazeto[2,1-*b*][1,3]benzodiazepine (27a): yield 69%; m.p. 259-261°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.03-3.08 (m, 2H), 3.45-3.52 (m, 1H), 3.59-3.66 (m, 1H), 5.40 (s, 1H), 6.98-7.12 (m, 9H), 7.21-7.30 (m, 4H), 7.30-7.44 (m, 3H), 7.75 (d, 2H, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 36.13, 52.79, 66.92 (s), 73.11, 123.43, 126.66, 127.21, 127.68, 127.69, 127.80, 128.01, 128.39, 128.55, 128.82, 129.28, 130.21, 133.79 (s), 133.86 (s), 135.03 (s), 138.32 (s), 142.31 (s), 147.80 (s), 159.76 (s); mass spectrum m/z (%): 436 (M^+ + 2, 16) 434 (M^+, 48), 165 (60), 125 (100); Anal. Calcd. for $C_{29}H_{23}ClN_2$: C, 80.08; H, 5.33; N, 6.44. Found: C, 79.95; H, 5.41; N, 6.35.

2,2-Diphenyl-1-(4-nitrophenyl)-1,2,8,9-tetrahydroazeto[2,1-*b*][1,3]benzodiazepine (27b): yield 74%; m.p. 264-265°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.02-3.10 (m, 2H), 3.52 (dt, 1H, *J* = 4.1, 12.7 Hz), 3.64-3.76 (m, 1H), 5.53 (s, 1H), 6.97-7.40 (m, 14H), 7.77 (d, 2H, *J* = 8.7 Hz), 7.97 (d. 2H, *J* = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 35.94, 53.66, 67.44 (s), 72.58, 123.30, 123.64, 126.95, 127.43, 127.64, 127.72, 127.92, 128.01, 128.56, 128.63, 130.19, 133.77 (s), 137.90 (s), 141.61 (s), 144.37 (s), 147.34 (s), 147.53 (s), 159.25 (s), a methine carbon was not observed; IR (Nujol) 1671, 1595, 1518, 1343, 1130, 1111, 1036, 953, 866, 759, 745, 708 cm^{-1}; mass spectrum m/z (%): 445 (M^+, 17), 165 (70), 89 (100); Anal. Calcd. for $C_{29}H_{23}N_3O_2$: C, 78.18; H, 5.20; N, 9.43. Found: C, 78.01; H, 5.31; N, 9.49.

General Procedure for the Preparation of Azeto[2,1-*b*]quinazolin-8-ones 34

To a solution of the corresponding azeto[2,1-*b*]quinazoline **5** (0.5 mmol) in CH_2Cl_2 (10 mL) was added activated MnO_2 (4 g). The suspension was stirred at room temperature for 4 h. The MnO_2 was separated by filtration over celite and the solvent removed under reduced pressure to give a solid which was chromatographed on a silica gel column using hexanes / ethyl acetate (2:3, v/v).

2,2-Diphenyl-1-(4-methoxyphenyl)-1,2-dihydroazeto[2,1-*b*]quinazolin-8-one (34a): yield 77%; m.p. 200-201°C (colourless prisms from $CHCl_3$ / hexanes); ^{1}H-NMR ($CDCl_3$) δ 3.70 (s, 3H), 6.42 (s, 1H), 6.69 (d, 2H, *J* = 8.7 Hz), 6.98-7.19 (m, 8H), 7.30-7.53 (m, 4H), 7.72-7.83 (m, 2H), 7.88 (td, 1H, *J* = 1.5, 10.7 Hz), 8.32 (dd, 1H, *J* = 1.4, 8.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 55.30, 69.75 (s), 73.83, 113.92, 124.20 (s), 125.32 (s), 126.45, 126.85, 127.28, 127.39, 127.90, 127.95, 128.16, 128.22, 128.75, 129.02, 134.07, 136.67 (s), 140.81 (s), 150.56 (s), 158.65 (s), 159.78 (s), 161.13 (s); IR (Nujol) 1691, 1651, 1611 cm^{-1}; mass spectrum m/z (%): 430 (M^+, 62), 165 (100); Anal. Calcd. for $C_{29}H_{22}N_2O_2$: C, 80.91; H, 5.15; N, 6.50. Found: C, 80.78; H, 5.24; N, 6.61.

2,2-Diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazolin-8-one (34b): yield 75%; ^{1}H-NMR ($CDCl_3$) δ 6.58 (s, 1H), 7.01-7.07 (m, 5H), 7.28-7.39 (m, 3H), 7.44-7.54 (m, 3H), 7.76-7.84 (m, 3H), 7.90 (d, 1H, *J* = 8.1 Hz), 8.01 (d, 2H, *J* = 7.8 Hz), 8.31 (d, 1H, *J* = 8.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 70.53 (s), 72.24, 123.48, 123.86 (s), 126.77, 127.46, 127.86, 127.97, 128.03, 128.22, 128.27, 128.39, 129.11, 134.36, 136.03 (s), 139.43 (s), 140.61 (s), 147.64 (s), 150.35 (s), 158.45 (s), 160.33 (s); IR (Nujol) 1692, 1679, 1649, 1608, 1521, 1348, 1163, 1112, 1035, 895, 854, 775, 702 cm^{-1}; mass spectrum m/z (%): 445 (M^+, 86), 323 (100), 165 (76); Anal. Calcd. for $C_{28}H_{19}N_3O_3$: C, 75.49; H, 4.30; N, 9.43. Found: C, 75.60; H, 4.23; N, 9.32.

4,5-Dimethoxy-2-nitrobenzyl alcohol (37)

To an ice-cooled solution of 4,5-dimethoxy-2-nitrobenzaldehyde (**36**) (4.22 g, 20 mmol) in anhydrous THF (100 mL) $NaBH_4$ (0.75 g, 20 mmol) was added and the mixture was stirred at 0-5°C for 6 h. The reaction was quenched by addition of water (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 75 mL), and the combined organics were dried over anhydrous $MgSO_4$. After filtration, the solvent was removed to dryness to give a solid which was recrystallized from Et_2O to give **37**: yield 90%; m.p. 152-153°C (yellow prisms); ^{1}H-NMR ($CDCl_3$) δ 2.78 (t, 1H, *J* = 5.9 Hz), 3.96 (s, 3H), 4.01 (s, 3H), 4.97 (d, 2H, *J* = 5.9 Hz), 7.19 (s, 1H), 7.70 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 56.33, 56.41, 62.64, 108.06, 110.83, 132.32 (s), 139.61 (s), 147.87 (s), 153.84 (s); IR (Nujol) 3503, 1581, 1519, 1330, 1268, 1213, 1073, 982, 872, 796 cm^{-1}; mass spectrum m/z (%): 213 (M^+, 22), 136 (100); Anal. Calcd. for $C_9H_{11}NO_5$: C, 50.70; H, 5.20; N, 6.57. Found: C, 50.90; H, 5.11; N, 6.43.

2-Azido-4,5-dimethoxybenzyl alcohol (38)

4,5-Dimethoxy-2-nitrobenzyl alcohol (**37**) (3.20 g, 15 mmol) was dissolved in ethanol (75 mL) and Pd/C (0.30 g) was added. The mixture was stirred at room temperature under hydrogen atmosphere for 6 h. The catalyst was removed by filtration over celite. The solvent was removed under reduced pressure and the resulting oil was dissolved in H_2SO_4 10% aqueous solution (100 mL). After cooling at 0°C a solution of $NaNO_2$ (1.29 g, 18.75 mmol) in water (25 mL) was added dropwise, and stirring continued for 30 min. Then a solution of NaN_3 (1.22 g, 18.75 mmol) in water (25 mL) was added. After 6 h the mixture was extracted with

CH_2Cl_2 (3 x 75 mL), the organics were washed with water (100 mL) and brine (100 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was chromatographed on a silica gel column using ether / hexanes (4:1, v/v) to give **38**: yield 29%; m.p. 104-105°C (colourless prisms from Et_2O / hexanes); ^{1}H-NMR ($CDCl_3$) δ 2.23 (br s, 1H), 3.86 (s, 3H), 3.90 (s, 3H), 4.56 (s, 2H), 6.64 (s, 1H), 6.89 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 56.23, 56.24, 61.02, 101.96, 112.47, 124.02 (s), 129.66 (s), 146.44 (s), 149.46 (s); IR (Nujol) 3503, 2107, 1513, 1343, 1251, 1210, 1163, 1082, 992, 760, 720 cm^{-1}; mass spectrum m/z (%): 209 (M^+, 16), 166 (100); Anal. Calcd. for $C_9H_{11}N_3O_3$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.48; H, 5.19; N, 20.00.

***N*-(2-Azido-4,5-dimethoxybenzyl)phthalimide (39)**

To a solution of triphenylphosphane (1.97 g, 7.5 mmol) in 40 mL of dry THF at 0°C was added diethyl azodicarboxylate (1.30 g, 7.5 mmol). The mixture was stirred 30 min at that temperature, and then 2-azido-4,5-dimethoxybenzyl alcohol (**38**) (1.05 g, 5 mmol) and phtalimide (1.10 g, 7.5 mmol) were added. The reaction mixture was stirred at 0°C 1 h and at room temperature 24 h. The solvent was removed, and the residue was chromatographed [silica gel, ethyl acetate / hexanes (3:7, v/v)] to obtain **39**: yield 35%; m.p. 150-152°C (colourless prisms form $CHCl_3$ / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.82 (s, 3H), 3.89 (s, 3H), 4.79 (s, 2H), 6.63 (s, 1H), 6.91 (s, 1H), 7.70-7.74 (m, 2H), 7.83-7.87 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 36.85, 56.18, 56.35, 101.92, 113.49, 119.27 (s), 123.41, 130.33 (s), 132.10 (s), 134.07, 146.47 (s), 149.73 (s), 168.09 (s); IR (Nujol) 2108, 1774, 1715, 1521, 1254, 1220, 1114, 993, 947, 877, 847, 736, 723 cm^{-1}; mass spectrum m/z (%): 338 (M^+, 5), 310 (13), 104 (100); Anal. Calcd. for $C_{17}H_{14}N_4O_4$: C, 60.35; H, 4.17; N, 16.56. Found: C, 60.19; H, 4.07; N, 16.40.

5,6-Dimethoxy-2,2-diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (41)

N-(2-Azido-4,5-dimethoxybenzyl)phthalimide (**39**) (1.01 g, 3 mmol) was dissolved in 50 mL of EtOH, and 85% aqueous hydrazine (7.5 equiv) was added. The mixture was stirred at reflux temperature for 3 h. After cooling, the precipitate that formed was dissolved by adding 30 mL of 10% sodium hydroxide solution. The resulting solution was extracted with CH_2Cl_2 (2 x 30 mL), and the extracts were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the resulting oil (2-azido-4,5-dimethoxybenzyl amine) was used inmediately in the preparation of the corresponding *N*-(2-azido-4,5-dimethoxybenzyl)imine by reaction with 4-nitrobenzaldehyde (Method A, Scheme 1). Compound **41** was prepared from that imine using the procedure described for the preparation of azeto[2,1-*b*]quinazolines **5**.

41: yield 53%; m.p. 161-163°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.91 (s, 3H), 4.26 (d, 1H, J = 12.5 Hz), 4.63 (d, 1H, J = 12.5 Hz), 5.62 (s, 1H), 6.43 (s, 1H), 6.92 (s, 1H), 7.00-7.07 (m, 5H), 7.32-7.45 (m, 5H), 7.70 (d, 2H, J = 8.7 Hz), 8.03 (d, 2H, J = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 44.69, 55.99, 56.26, 71.06 (s), 72.63, 109.64, 109.92, 111.85 (s), 123.38, 127.23, 127.61, 127.79, 128.12, 128.14, 128.32, 128.77, 136.09 (s), 137.28 (s), 140.55 (s), 143.16 (s), 146.24 (s), 147.53 (s), 148.91 (s), 163.29 (s); IR (Nujol) 1682, 1617, 1509, 1346, 1212, 1103, 1006, 865, 703 cm^{-1}; mass spectrum m/z (%): 491 (M^+, 22), 279 (57), 167 (100); Anal. Calcd. for $C_{30}H_{25}N_3O_4$: C, 73.30; H, 5.13; N, 8.55. Found: C, 73.11; H, 5.02; N, 8.67.

5,6-Dimethoxy-2,2-diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazolin-8-one (42)

5,6-Dimethoxy-2,2-diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline **(41)** (0.24 g, 0.5 mmol), $K_2S_2O_8$ (0.54 g, 2 mmol) and Na_2HPO_4 (0.14 g, 1 mmol) were added to a mixture of CH_3CN (12 mL) and H_2O (8 mL) and refluxed for 24 h. After cooling at room temperature the CH_3CN was removed under reduced pressure and the aqueous phase was extracted with CH_2Cl_2 (2 x 15 mL). The organics were washed with water (25 mL), brine (25 mL) and dried over anhydrous $MgSO_4$. The solvent was removed to dryness and the residue chromatographed on a silica gel column using hexanes /ethyl acetate (1:1, v/v) as eluent to give **42**: yield 77%; m.p. 205-206°C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.00 (s, 3H), 4.06 (s, 3H), 6.58 (s, 1H), 7.03-7.05 (m, 5H), 7.27-7.49 (m, 6H), 7.65 (s, 1H), 7.75 (d, 2H, J = 8.7 Hz), 8.02 (d, 2H, J = 8.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 56.34, 56.36, 70.39 (s), 72.20, 105.92, 108.74, 116.92 (s), 123.45, 127.44, 127.81, 127.99, 128.19, 128.36, 129.09, 136.16 (s), 139.53 (s), 140.77 (s), 146.50 (s), 147.60 (s), 148.78 (s), 154.76 (s), 157.96 (s), 159.02 (s); IR (Nujol) 1684, 1646, 1611, 1526, 1352, 1279, 1227, 1127, 1014, 860, 775, 752, 702 cm^{-1}; mass spectrum m/z (%): 505 (M^+, 65), 383 (71), 165 (100). Anal. Calcd. for $C_{30}H_{23}N_3O_5$: C, 71.28; H, 4.58; N, 8.31. Found: C, 71.10; H, 4.44; N, 8.50.

2,2-Diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazolinium Tetrafluoroborate (44)

A suspension of 2,2-diphenyl-1-(4-nitrophenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline **(5e)** (0.43 g, 1 mmol) in HCl 35% (10 mL) was heated at reflux temperature for 30 min. After cooling at room temperature the precipitated solid was collected by filtration and air dried to give the hydrochloride **43**.

The salt **43** was dissolved in EtOH (15 mL) and aqueous HBF_4 50% was added (10% excess). The solution was stirred a room temperature for 3 h. The solvent was removed under reduced pressure, the residue was dissolved in CH_2Cl_2 (20 mL) and anhydrous $MgSO_4$ was added. The $MgSO_4$ was separated by filtration and the solvent removed to dryness to give a solid which was recrystallized to give **44**: yield 69%; m.p. 187-188 °C (colourless prisms from CH_2Cl_2 / Et_2O); ^{1}H-NMR (DMSO-d_6) δ 4.94 (s, 2H), 6.66 (s, 1H), 7.02-7.61 (m, 13H), 7.79 (d, 4H, J = 8.8 Hz), 8.06 (d, 2H, J = 8.6 Hz), the NH proton was not observed; ^{13}C-NMR (DMSO-d_6) δ 43.53, 69.88 (s), 74.95, 118.47, 118.73 (s), 123.20, 127.41, 127.92, 128.10, 128.31, 128.52, 128.84, 129.23, 129.26, 129.59, 131.10 (s), 134.08 (s), 136.67 (s), 138.91 (s), 147.56 (s), 164.44 (s); IR (Nujol) 3244, 1703, 1567, 1523, 1353, 1081, 999, 857, 772, 700 cm^{-1}; mass spectrum m/z (%): 432 (M^+ - BF_4, 9), 310 (100), 165 (32); Anal. Calcd. for $C_{28}H_{22}BF_4N_3O_2$: C, 64.76; H, 4.27; N, 8.09. Found: C, 64.90; H, 4.18; N, 7.98.

Hydrolysis of the Tetrafluoroborate (44)

A solution of the salt **44** (0.26 g, 0.5 mmol) in a mixture of THF / H_2O (15mL / 5mL) was refluxed for 24 h. The THF was removed and the aqueous phase extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were mixed and washed with water (15 mL) and brine (15 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column using initially hexanes / ethyl acetate (1:1, v/v) and then ethanol / concentrated ammoniun hydroxide (95:5, v/v) as eluent to give 2-diphenylmethyl-3,4-dihydroquinazoline **13** (yield 47%).

2,2-Diphenyl-1-(4-methoxyphenyl)-3-methyl-1,2-dihydroazeto[2,1-b]quinazolinium Tetrafluoroborate (46)

To a solution of 2,2-diphenyl-1-(4-methoxyphenyl)-1,2-dihydroazeto[2,1-*b*]quinazoline (**5d**) (0.42 g, 1 mmol) in dry CH_2Cl_2 (10 mL) was added $(CH_3O)_3BF_4$ (0.15 g, 1 mmol) and the mixture was stirred at room temperature for 6 h. The solvent was removed under reduced pressure and the residue was recrystallized to give the salt **46**: yield 68%; m.p. 174-176°C (colourless prisms from CH_2Cl_2/Et_2O); ^{1}H-NMR ($CDCl_3$) δ 3.22 (s, 3H), 3.68 (s, 3H), 4.75 (d, 1H, *J* = 15.7 Hz), 5.25 (d, 1H, *J* = 15.7 Hz), 6.25 (s, 1H), 6.60 (d, 2H, *J* = 8.7 Hz), 6.82-6.88 (m, 3H), 7.07-7.12 (m, 2H), 7.22-7.30 (m, 5H), 7.39-7.50 (m, 4H), 7.58-7.61 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 33.19, 43.02, 55.25, 70.28 (s), 79.79, 113.98, 115.89, 118.54 (s), 121.93 (s), 127.96, 128.38, 128.50, 128.66, 128.86, 128.98, 129.50, 129.71, 129.84, 129.92, 131.57 (s), 132.45 (s), 133.66 (s), 160.56 (s), 165.76 (s); IR (Nujol) 1702, 1609, 1579, 1515, 1303, 1254, 1179, 1142, 1056, 837, 761, 702 cm^{-1}; mass spectrum m/z (%): 431 (M^+ - BF_4, 66), 430 (93), 323 (100); Anal. Calcd. for $C_{30}H_{27}BF_4N_2O$: C, 69.51; H, 5.25; N, 5.40. Found: C, 69.40; H, 5.11; N, 5.57.

Hydrolysis of the Tetrafluoroborate 46

The hydrolytic treatment of the salt **46** under the same reaction conditions described for the salt **44** gave **1-methyl-2-diphenylmethyl-1,4-dihydroquinazoline (47)**: yield 59%; ^{1}H-NMR ($CDCl_3$) δ 3.15 (s, 3H), 4.47 (s, 2H), 5.31 (s, 1H), 6.70 (d, 1H, *J* = 8.4 Hz), 7.01-7.03 (m, 1H), 7.14-7.30 (m, 12H); ^{13}C-NMR ($CDCl_3$) δ 33.17, H, 49.14, 54.75, 110.86, 122.57 (s), 122.85, 125.59, 126.86, 127.24, 128.54, 129.31, 140.61 (s), 141.28 (s), 158.66 (s); IR (Nujol) 1633, 1599, 1525, 1494, 1447, 699 cm^{-1}.

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