The reaction of 2-(tetrazol-5-yl)alkyl ketones and of 2-(tetrazol-5-yl)alkanoic acid derivatives with lead tetraacetate. A novel method of preparation of alk-2-ynyl ketones and alk-2-ynoic acid derivatives †

József Fetter,*[a] Ildikó Nagy,[a] Le Thanh Giang,[a] Mária Kajtár-Peredy,[b] Antal Rockenbauer,[c] László Korecz[b] and Gábor Czira[d]

[a] *Department of Organic Chemistry, Budapest University of Technology and Economics,‡ H-1521 Budapest, Hungary*
[b] *Institute of Chemistry, Chemical Research Center, Hungarian Academy of Sciences, H-1525 Budapest, Hungary*
[c] *Department of Physics, Budapest University of Technology and Economics, H-1521 Budapest, Hungary*
[d] *Gedeon Richter Chemical Works, Ltd., H-1475 Budapest 10, Hungary*

The majority of tetrazolylacetyl derivatives **2** and **7**, when treated with lead tetraacetate in dry 1,4-dioxane at room or lower temperature, are oxidized with elimination of molecular nitrogen mainly to the corresponding alkynoyl derivatives **4** and **8**, respectively. Vinylidenes (**25**) have been shown to be the intermediates of the reaction. The reaction does not take place when either the tetrazolyl group is N-substituted or the carbon atom separating the tetrazolyl and the carbonyl groups is disubstituted or these two groups are separated by two carbon atoms as in compound **17**. The reaction offers a convenient method for the conversion of 2-cyanoacetyl derivatives into alk-2-ynoyl derivatives *via* intermediate tetrazolylacetyl derivatives. The 4-methoxyanilide **7o** reacts differently, affording the fused heterocyclic compounds **19o** and **20o**.

Introduction

Compounds of type **1** (*m* = 0, 1), when treated with lead tetra-acetate (LTA) in boiling 1,4-dioxane, afford fused quinoxaline and benzodiazepine derivatives **3** (*m* = 0, 1).[1,2] In continuation of these studies the reactions of compounds **2a** and **2b**, containing tetrazolylacetyl instead of the tetrazolylalkyl groups, with LTA were now studied. Since these compounds reacted differently to compounds **1**, *viz.* they afforded, by fragmentation of the tetrazolyl group, the propiolyl derivatives **4a** and **4b**, respectively, the study was extended to the simpler tetrazolylmethyl ketones **7a**–**7h** (containing no lactam rings) as well as to the tetrazolylacetic esters **7i** and **7j** and the related amides **7k**–**7p**.

Results

In contrast to the compounds **1**, both compounds **2** underwent fragmentation with loss of nitrogen, leading to the formation of ethynyl ketones **4a** and **4b**, respectively, when treated with LTA in anhydrous 1,4-dioxane at 0 °C or below. **4b** was itself readily isolated but **4a** could be isolated only in the form of its transformation product **5a** or, on treatment of the reaction mixture with diazomethane, in the form of compound **6a**. The cycloadduct **6b** of compound **4b** with diazomethane was similarly obtained.

The ¹H and ¹³C NMR spectra and the molecular composition (established by HRMS) of product **5a** showed it to be built up from one molecule of the starting **2a** and a fragment of
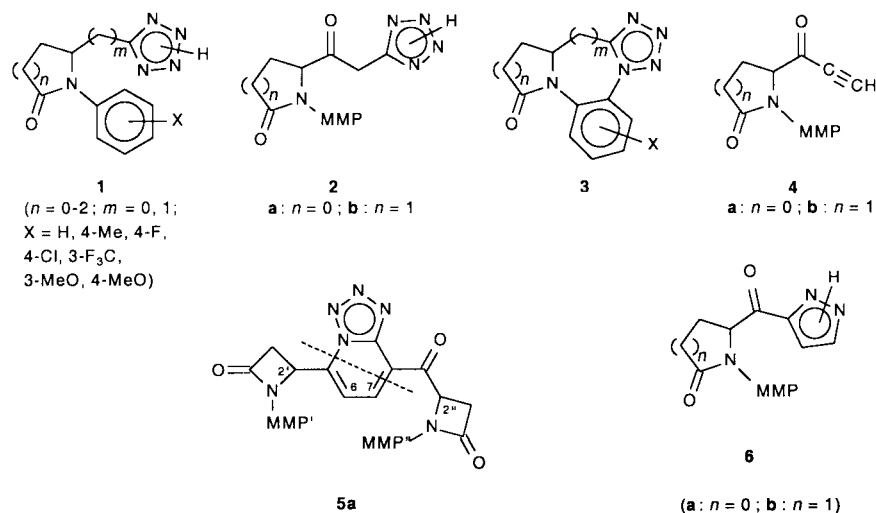
another. Due to the presence of two chiral centers (C2′ and C2″) compound **5a** proved to be a diastereoisomeric mixture. The long-range coupling between the 6-H and 2′-H protons (≈0.5 Hz) and the NOE effects§ resulting from selective saturation of the 6-H and 7-H resonances (see Experimental section) as well as the carbon–proton long-range correlations of C5, C8, C8a and the ketone carbonyl carbon (C5 with 7-H, 6-H, 2′-H and 3′-H₂; C8 with 6-H and 7-H; C8a with 7-H and 6-H; ketone carbonyl carbon with 7-H, 2″-H and 3″-H₂) clarified the manner of the connection of the two components of the molecule.

The formation of compounds **4a** and **4b** suggests that, in contrast to the compounds **1** which are attacked by LTA at the N-aryl substituent of the lactam ring, compounds **2a** and **2b** are attacked by the same oxidant at their tetrazolylacetyl moieties, and that the presence of the lactam ring is not a prerequisite of the novel oxidative fragmentation reaction. In order to test this hypothesis, the simpler tetrazolylmethyl ketones **7a**–**7h** (containing no lactam rings) were subjected to oxidation with LTA (see Table 1). While **7a** and **7b** afforded the expected products **8a** and **8b**, respectively, compound **7c** did not react and was not decomposed even at elevated temperatures. In addition to compound **8b** traces of compound **9b** as well as of two further compounds which, according to their IR and ¹H NMR spectra, appear to possess structures **10b** and **11b**, were obtained from compound **7b**, their yields increasing (with simultaneous significant decrease in the yield of compound **8b**) when the solvent 1,4-dioxane was replaced by acetic acid (see Table 1). The reaction of compound **7d** was totally different, acetoxy derivative **12d** and three dimeric compounds (**13d**–**15d**) being the products isolated.

---

† Electronic supplementary information (ESI) available: experimental data for compounds **2**, **7**, **17**, **30**, **35**–**38** and **40**–**42**. See http://www.rsc.org/suppdata/p1/b0/b005286h/
‡ Formerly Technical University Budapest.

§ NOEs are listed throughout this paper in the order of decreasing intensity.

1
($n = 0$-2; $m = 0$, 1;
X = H, 4-Me, 4-F,
4-Cl, 3-F$_3$C,
3-MeO, 4-MeO)

2
a : $n = 0$; **b** : $n = 1$

3

4
a : $n = 0$; **b** : $n = 1$

5a

6

(**a** : $n = 0$; **b** : $n = 1$)

MMP = 3-methoxyphenyl

The point of attachment of the substituent to the pyrazole ring follows from the value of the coupling constant between the pyrazole protons attached to carbon which shows them to be in adjacent positions relative to each other, *c.f.* ref. 3

Table 1 Reaction of compounds **2a**, **2b**, **7a**–**7p** and **17** with LTA in anhydrous 1,4-dioxane

Starting comp.	LTA (mol eq.)	Conditions	Products and yields[a]
2a	1.1	0 °C, 30 min	**5a** (12%) or **6a**[b] (41%)
2b	1.2	0 or −20 °C, 30 min	**4b** (48%) or **6b**[b] (50%)
7a	1.1	0 °C, 30 min	**8a** (53%)
7b	1.1	70–80 °C, 5 min	**8b** (42%), **9b**–**11b** (traces)
7b[c]	1.1	80 °C, 10 min	**8b** (19%), **9b** (6%), **10b** (10%)
7c	1.1	100 °C, 20 min	No reaction. 55% **7c** recovered
7d	1.1	25 °C, 30 min	**12d** (13.5%), **13d** (28%), **14d** (16%), **15d** (12%)
7e	1.1	10–15 °C, 20 min	**8e** (83%)
7f	1.1	6–8 °C, 20 min[d]	**8f** (56%)
7g	1.1	10–15 °C, 10 min	**8g** (45%) + **16g** (1.7%)
7h	1.1	10–15 °C, 20 min	**8h** (69%)
7i	1.5	100 °C, 30 min	**18i**[b] (7%)
7j	1.0	70 °C, 30 min	**8j** (55%)
7k	1.1	100 °C, 20 min	**8k** (18.5%)
7l	1.2	80 °C, 10 min	**8l** (51%)
7m	1.1	100 °C, 1 h	No reaction[e]
7n	1.1	100 °C, 2 h	**8n** (7%)
7o	3.1	100 °C, 3 h	**19o** (11%), **20o** (1.5%)
7p	1.3	100 °C, 1 h	**8p** (25%)
17	4.1	100 °C, 1 day	Considerable decomposition; 15% **17** recovered

[a] Non-optimized yields. In several cases complex reaction mixtures containing considerable amounts of tarry products were obtained. As a consequence, often considerable amounts of the products were lost during work-up and, possibly, often only part of the various products formed was isolated. [b] Cycloadducts of the original products **4a**, **4b** and **8i**, respectively, with diazomethane. [c] In acetic acid. [d] In THF. [e] 76% of the starting **7m** was recovered.

The structure of compound **13d** was determined by NMR spectroscopy. The δ_H- and δ_C-values of the methine group (7.19 and 73.1, respectively) reflect, in addition to the substituent effects of the carbonyl and tetrazolyl groups, the presence of an adjacent oxygen atom (connecting the two moieties of the *O,C*-dimer). The constitution of **13d** derived on this basis was corroborated by nuclear Overhauser enhancement (NOE) measurements which, in addition, permitted us to derive the *E* configuration for the olefinic bond.

The *C,C*-dimer **14d** was shown by its ^{1}H NMR spectrum to be a 2 : 1 mixture of two stereoisomers, *viz.* of the *meso* and racemic forms, but it is not known which is which. No attempts were made to establish whether the unsaturated dimer **15d** is the *E* or *Z* isomer.
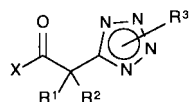
Ketones **7e**–**7h** reacted with LTA in a similar fashion to ketones **7a** and **7b** but, in the **g** series, a small amount of a further product, **16g**, was isolated.

The structure of compound **16g** was derived from its ^{1}H, ^{13}C and hetero-correlation NMR spectra, and is supported by its molecular composition determined by HRMS. The ^{1}H and [13]C

data of the compound defined its structural fragments while the connection of the fragments was established on the basis of 2D long-range hetero-correlation spectra. Thus, the olefinic proton correlations indicated the direct attachment of the benzoyl, 4-nitrophenyl and the substituted ethoxy groups to the olefinic carbon atoms. By the correlations of the methine proton with the second 4-nitrophenyl, the tetrazolyl and the acetoxy groups the substitution pattern of the methine carbon atom was defined. The structure and the substitution pattern of the central chain were established on the basis of the long-range correlations of the methylene groups with the other parts of the molecule. No NOE was observed between the methine and methylene groups, which suggested that the terminal methylene group of the central chain is linked to N2 of the tetrazole ring.

In addition, ketone **17** in which the carbonyl group and the tetrazole ring are separated by two methylene groups was also prepared, and was found to be decomposed by LTA slowly at 100 °C.
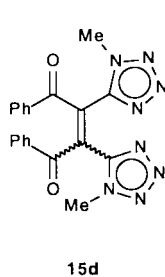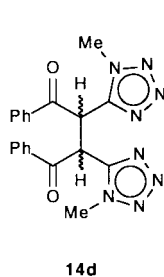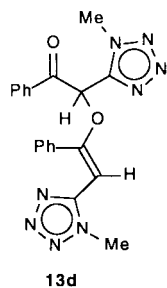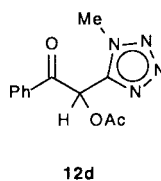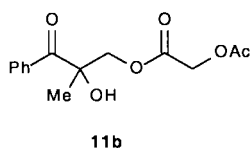
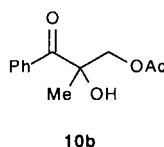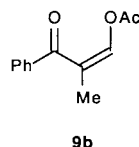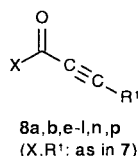A comparison of the behavior of compounds **7a**–**7h** and **17** toward LTA demonstrated that the necessary conditions for the

7

	X	R^1	R^2	R^3
a	Ph	H	H	H
b	Ph	Me	H	H
c	Ph	Me	Me	H
d	Ph	H	H	1-Me
e	Ph	Ph	H	H
f	Ph	PMP	H	H
g	Ph	4-NO$_2$-C$_6$H$_4$	H	H
h	(cyclohexyl)	H	H	H
i	EtO	H	H	H
j	BnO	H	H	H
k	Ph-NH	H	H	H
l	Ph/Me>N	H	H	H
m	Ph/Me>N	Me	H	H
n	MMP-NH	Me	H	H
o	PMP-NH	Me	H	H
p	(piperidinyl N)	H	H	H

PMP = 4-methoxyphenyl.

8a,b,e–l,n,p
(X,R^1: as in **7**)

9b

10b

11b

12d

13d

14d

15d

oxidative fragmentation reaction to take place are (*i*) the vicinal position of the carbonyl group and the tetrazole ring, (*ii*) the presence of one or two hydrogen atoms attached to the carbon atom separating the carbonyl group from the tetrazole ring and (*iii*) the absence of any N-substituent attached to the tetrazole ring.

The tetrazoleacetic acid esters **7i** and **7j** as well as the related amides **7k**, **7l** and **7n–7p** also underwent the oxidative fragmentation reaction when treated with LTA. Except for the case of compound **7i** where the product **8i** was isolated in the form of cycloadduct **18i** (obtained by treatment of the reaction mixture with diazomethane), the corresponding acetylene derivatives **8** were isolated. Amide **7m** did not react, and amide **7o** reacted

differently, the fused heterocyclic compounds **19o** and **20o** being the isolated products.

Discussion

Formation of the acetoxylated product **12d** (together with formation of the dimeric products **13d–15d**) on LTA treatment of compound **7d** is another example of the well known acetoxylation by LTA of saturated CH$_n$ groups activated by neighboring carbonyl groups, *viz.* mainly of ketones containing at least one α-hydrogen atom[4–7] and of the related reactions of phenols.[8] Triacetoxy-λ^4-plumbyl derivatives **21** formed by rate-determining enolization[5] of the ketone and reaction of the resulting enol (or of the phenol[8]) with LTA are the key intermediates of the reaction. The three electron-pair displacements indicated in formula **21** then lead to the acetoxylated product.[4a,8]

In the LTA oxidation of pentane-2,4-dione and ethyl acetoacetate (both containing doubly activated methylene groups) formation of dimers has been observed in addition to that of the acetoxylation products.[7] The formation of dimeric products **13d–15d** in addition to acetoxy derivative **12d** in the LTA oxidation of compound **7d** appears to be in agreement with this observation since the methylene group of the starting material **7d** is also doubly activated by the benzoyl and the electron-withdrawing aromatic tetrazol-5-yl group. Compound **13d** is the first *O,C*-dimer isolated from this type of LTA oxidation. Dimer **15d** is formed by dehydrogenation of part of the *C,C*-dimer **14d**.¶

In several cases formation of radicals accompanying the acetoxylation was observed but these radicals were shown not to be involved in the acetoxylation reaction.[10] We also have observed formation of radical **22d** during oxidation of compound **7d** (*cf.* below).

Ketones **2a**, **2b**, **7a**, **7b** and **7e–7h** containing *N*-unsubstituted tetrazol-5-yl groups are not acetoxylated by LTA but, instead, their tetrazole rings undergo fragmentation with elimination of nitrogen to afford ultimately ynones of type **8**. The precursors of the ynones are the vinylidenes [(2-oxoalkylidene)carbenes] **25** which afford the final products by 1,2-migration of either the benzoyl or the R^1 group (Scheme 1). The intermediacy of the vinylidenes is established beyond doubt by the isolation of the insertion product **9b** (formed with acetic acid, the co-product of the oxidation) and the hydration product **10b** of the latter. **9b** is necessarily formed by reaction of acetic acid with an intermediate in which the connectivity of the carbon skeleton of the starting **7b** is retained unchanged, obviously by insertion of vinylidene **25** (R = Ph, R^1 = Me) into the carboxyl group of acetic acid. The sharp increase in the yields of compounds **9b** and **10b**, together with the decrease in the yield of compound **8b**, when the solvent 1,4-dioxane was replaced by acetic acid is also significant in this connection.

Further support for the intermediacy of the vinylidenes **25** is furnished by the formation of compound **16g**. Although the mechanism of the reaction leading to this compound is not known, it seems highly probable that the key step is formation of an oxonium-ylide by reaction of vinylidene **25g** with the solvent 1,4-dioxane; the ylide is subsequently attacked by a tetrazole N-atom.

The obvious precursors of the vinylidenes **25** are the tetraazafulvenes **24** which, however, could neither be isolated nor detected. Related tetraazafulvenes **27** were assumed as the intermediates of the pyrolysis of several 5-substituted tetrazoles **26**, containing anionic leaving groups in position 1 of the 5-substituent, leading to acetylenes **28**[11] (Scheme 2), but were also not detected.

The tetraazafulvene intermediates **24** may be formed from the starting compounds **2** and **7** *via* the triacetoxy-λ^4-plumbyl

¶ For dehydrogenations with LTA, see ref. 9.
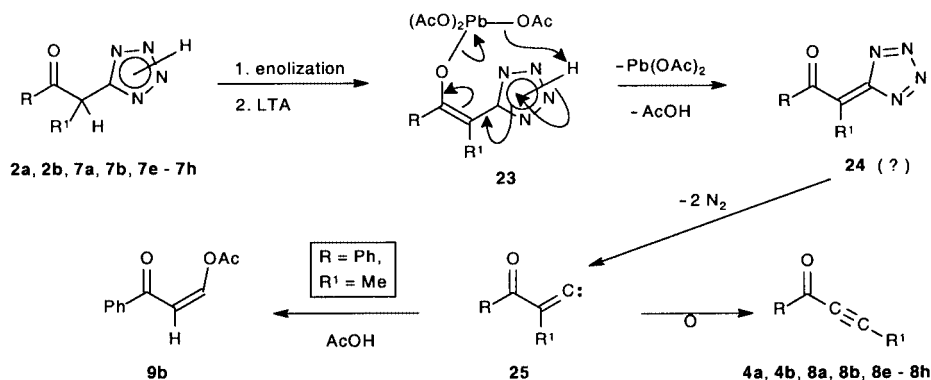
Scheme 1 Suggested mechanism for the reactions of compounds **2a**, **2b**, **7a**, **7b** and **7e–7h** with LTA.

16g

17

18l

19o : R = H
20o : R = OAc
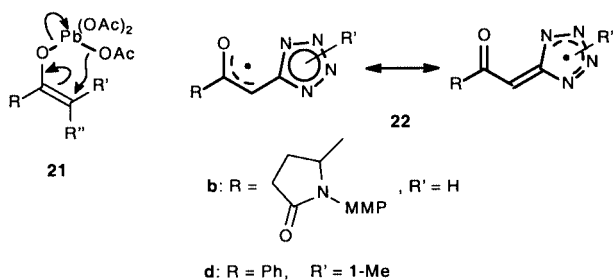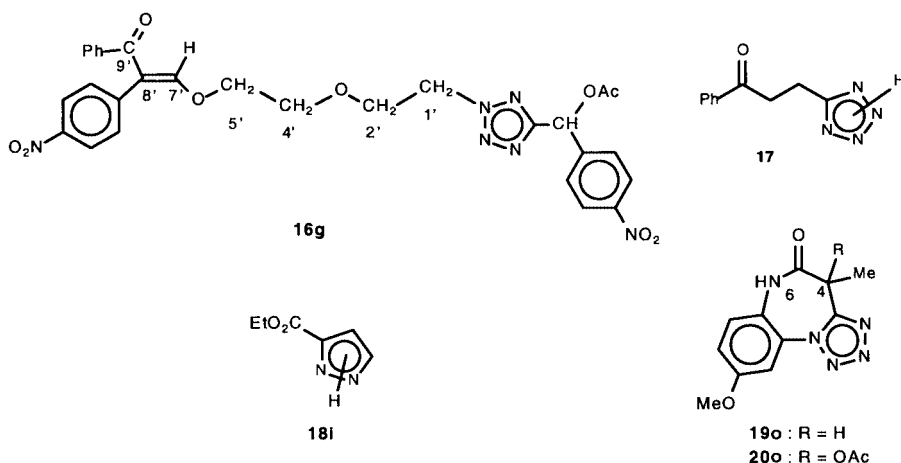
derivatives **23** (analogous to and similarly formed as the compounds **21**) as a result of the five electron-pair displacements indicated.‖

The necessary conditions stated above for the oxidative transformations discussed to take place are consistent with the mechanism shown in Scheme 1.

An alternative mode of transformation of the triacetoxy-λ^4-plumbyl derivatives **23** into the tetraazafulvenes **24** and thence into acetylenes **4** and **8** could in principle take place *via* electron-pair displacements similar to those shown for **21** and leading to the formation of acetoxy derivative **29**, followed by elimination of acetic acid. On the basis of the observations that the related compound **30** is stable to sodium acetate (2 mol equivalents) in boiling acetic acid at least for 2 h and is transformed into the acetylene **8a** (34%) only by sodium methoxide (1 mol equivalent) on boiling for 4 h in methanol, this pathway appears to be unlikely.

Similarly to the LTA oxidation of compound **7d**, formation of a radical **22b** accompanying the oxidation of compound **2b** was observed. None of the two enoxyl radicals **22** was stable enough for ESR detection but both could be trapped by *N*-(*tert*-butyl)-α-phenylnitrone, and the resulting secondary radicals

31b and **31d** were detected by ESR. The ESR spectra of both secondary radicals exhibited similar six-line patterns (**31b**: $g = 2.0059$, $a_N = 13.52$ G, $a_H = 1.99$ G; **31d**: $g = 2.0065$, $a_N = 13.19$ G, $a_H = 1.61$ G). The small nitrogen splittings for both secondary radicals are in accordance with the 'alkoxy' character **31** of the radicals, rather than with the isomeric structures **32**.[12]

The mechanisms of the LTA oxidation of tetrazolylacetic esters **7i** and **7j** as well as of 2-(tetrazol-5-yl)alkanamides **7k**, **7l**, **7n** and **7p** are thought to be analogous to those of ketones **2a**, **2b**, **7a**, **7b** and **7e–7h**. This implies that compounds **7i–7l**, **7n** and **7p** should be able to enolize to a significant extent, while simple esters and amides, as shown by their insensitivity to LTA, are not. This difference is due to the presence of the tetrazolyl groups and, as a result, of doubly activated aliphatic CH$_2$ or CH groups in compounds **7i–7l**, **7n** and **7p**. The insensitivity of compound **7m** towards LTA appears also to be consistent with the enolization mechanism. The extra *C*-methyl group in compound **7m** should reduce the propensity to enolization ** (*cf.* the influence of simple alkyl groups on keto–enol equilibria[13]).

From *N*-PMP amide **7o** products of a different type (**19o** and **20o**) were obtained. The central diazepine ring of these compounds is similar to those of compounds **3**. This suggests similar modes of formation for these compounds (Scheme 3), in particular that the site of attack of LTA is, in contrast to the case of all other compounds **7** studied, not the enolized COCHR group but, instead, the N-aryl substituent. That among all substrates containing N-aryl substituents (**2a**, **2b**, **7k–7o**) this mode of reaction has been observed only with compound **7o** appears to be reasonable since the *N*-PMP group is one of the most easily oxidizable N-aryl groups. However, due to the low yields of compounds **19o** and **20o**, the possibility

---

‖ We are grateful to a referee for suggesting this mechanism for the formation of the tetraazafulvene intermediates **24**.

** On the other hand, introduction of a (substituted) phenyl group (as in ketones **7e–7g**) at the saturated carbon atom adjacent to the carbonyl group does not prevent the oxidative fragmentation reaction. This, again, appears to be consistent with the enolization mechanism.
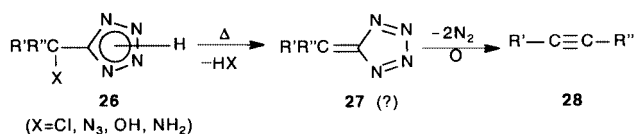
Scheme 2 Pyrolysis of some 5-substituted tetrazoles **26**.[11]

may not be ruled out at present that part of compound **7o** is attacked by LTA competitively also at the enolized COCHMe group, affording therefore products (lost during work-up of the reaction mixture) analogous to those resulting from compounds **7k**, **7l** and **7n**. Two alternative mechanisms are shown for the reaction **7o** ⟶ **19o** + **20o** in Scheme 3,†† the two mechanisms differing in the timing of the second one-electron oxidation and the closure of the third ring.

Starting compounds

Compounds **2a**, **2b** and, except for compounds **7d**,[14] **7i**,[15] **7j**[16] and **7k**,[17] all compounds **7** as well as compounds **17** and **30** were new.

The synthesis of compounds **2a** and **2b** is summarized in Scheme 4. Except for the known compound **7d** and compound **30**, all other ketonic compounds were obtained by cycloaddition of the corresponding cyano ketones **42a–c**, **42e–h** and **43** with aluminium triazide[18] as shown, together with the syntheses of compounds **7d** and **30** (that of the former being different from the reported[14] synthesis) as well as of the intermediates **42** in Scheme 5.

The known anilide **7k**[17] was synthesized by a new method, *viz.* by anilinolysis of compound **7i**. Reaction of the latter with *N*-methylaniline similarly afforded compound **7l**. Compounds **7m–7o** were obtained by reaction of 2-cyanopropionic acid, after activation of its carboxy group, with *N*-methylaniline, *m*- and *p*-anisidine, respectively, and cycloaddition of the resulting cyano anilides **42m–o** (X, R[1] and R[2] as in the corresponding compounds **7**). Piperidine derivative **7p** was obtained by cycloaddition of the known cyano amide **42p**[22] with aluminium triazide.

For details concerning the methods of preparation, yields, mps and spectra of the starting compounds and their intermediates, see the Electronic supplementary information.

Experimental

General

All reactions were monitored by TLC (DC-Alufolien 60 F$_{254}$, Merck) and allowed to go to completion. Separations of product mixtures by flash column chromatography (CC) were carried out using Kieselgel G (Merck) as the adsorbent unless otherwise stated (pressure differences between the two ends of the columns 10–25 kPa). For preparative TLC (PLC)

†† The timing of the acetoxylation step is not known. However, since the only compound **7** which underwent acetoxylation with LTA was compound **7d** containing an *N*-substituted tetrazole ring, acetoxylation in the case under discussion may be assumed to take place *after* closure of the new ring, probably at the stage of **19o**.
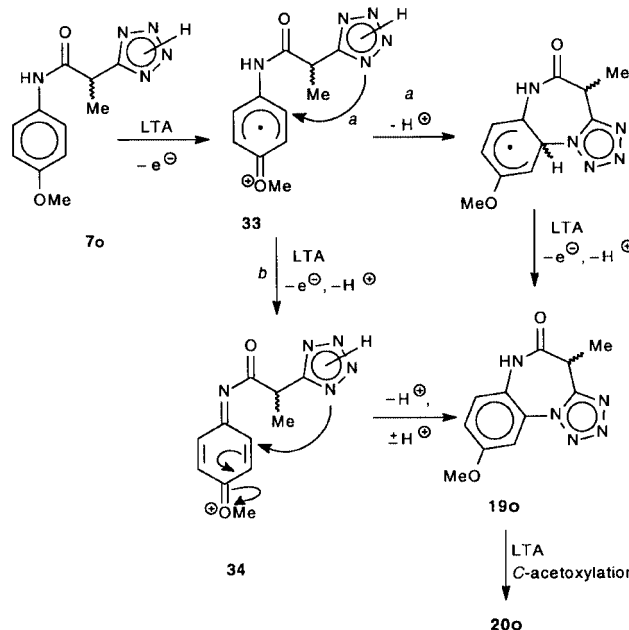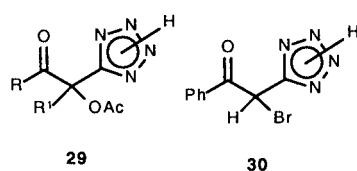

Scheme 3 Suggested alternative mechanisms for the formation of compounds **19o** and **20o**.

separations 20×20 cm glass plates coated with Kieselgel PF$_{254 + 366}$ (Merck; thickness of adsorbent layer 2.0 mm) were used (home-made ones, except where otherwise noted). The solvents are given in parentheses. Dichloromethane is abbreviated as DCM. The purity of the products was checked, in combination with IR spectroscopy, by TLC on DC-Alufolien 60 F$_{254}$ (Merck); the individual compounds were detected by UV irradiation or by using iodine or 5% ethanolic molybdophosphoric acid as the reagent. MgSO$_4$ was used as the drying agent. Evaporations to dryness as well as the removal of volatile components of reaction mixtures by distillation were carried out at reduced pressure (≈ 2.5 kPa, unless otherwise stated).

All new crystalline compounds described in the present paper were colorless. Mps were determined on a Kofler hot-stage mp apparatus and are uncorrected. IR spectra were recorded on a Specord-75 (Zeiss, Jena) spectrometer. ^{1}H and ^{13}C NMR spectra were obtained with Varian VRX-400 and Unity INOVA-400 spectrometers, using tetramethylsilane as the internal reference. *J*-Values are given in Hz. The ESR spectra were taken at room temperature (291 K) on an upgraded JEOL JES-FE3X spectrometer with 100 kHz field modulation, using a manganese(II)-doped MgO powder for the calibration of *g*-measurements. A Lake Shore Model 647 Magnet Power Supply and a Stanford Model SR830 DSP Lock-in Amplifier were applied. The field was measured by a temperature-stabilized Hall probe with an accuracy of 10^{-5} T. The spectrometer was controlled by a Pentium 100 computer. Exact molecular mass determinations were made at 70 eV with a Finnigan-MAT 95 SQ instrument of reversed geometry equipped with a direct-inlet system using PFK (perfluorokerosene) as the reference.

29   **30**

31   **32**

b: R =   , R' = H

d: R = Ph,   R' = 1-Me
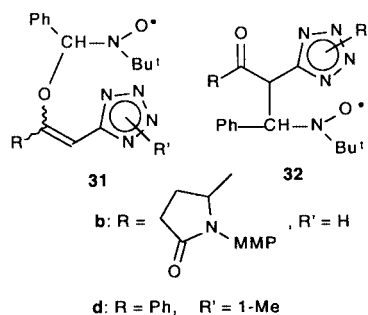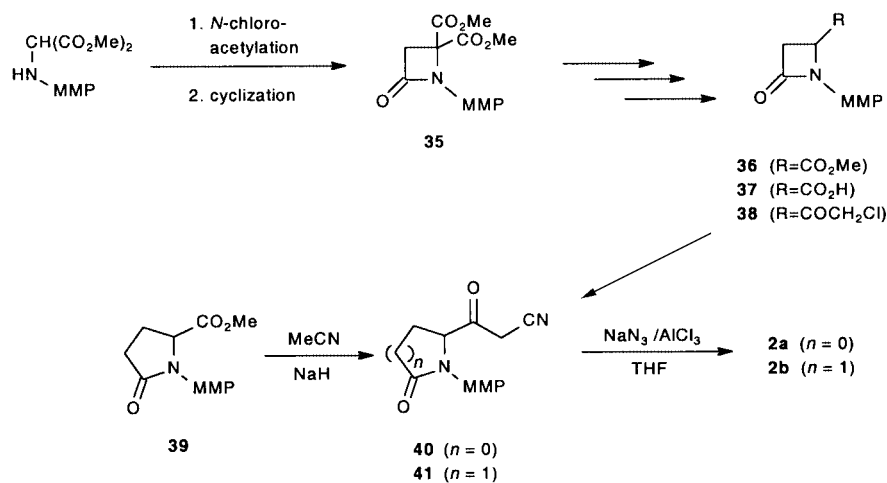
Scheme 4 Synthesis of compounds **2a** and **2b**. MMP means 3-methoxyphenyl. All chiral compounds shown are racemic.
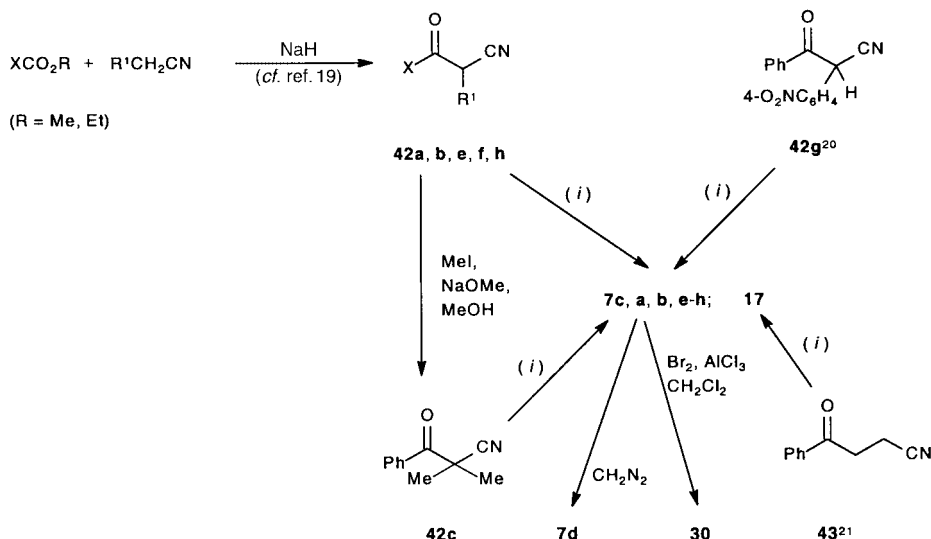
Scheme 5 Synthesis of compounds **7a–h**, **17** and **30**. X, R¹ and R² in all compounds shown are as in the corresponding compounds **7**. All chiral compounds shown are racemic. *Reagents*: (i) NaN₃, AlCl₃, THF.

LTA oxidation of compounds 2a, 2b, 7a–7p and 17

General method. LTA (1.1 mmol) was added to a suspension of a title compound (1 mmol) in dry 1,4-dioxane (15 cm³) at room temperature. The mixtures were stirred for 15 min, and the progress of the reactions was monitored by TLC. If no reaction took place at room temperature, the mixture was gradually heated (if necessary, to its bp), in order to initiate the reaction. The mixtures were heated and stirred until the evolution of nitrogen ceased and the reactions were shown by TLC to be complete. Work-up of the reaction mixtures was carried out by one of methods A–C described below.

Method A. Kieselgel 60 G (Merck) was added to the mixture [or, if a precipitate of Pb^II acetate was formed during the reaction, to its filtrate combined with the EtOAc washings]. The mixture was then evaporated to dryness. The residue was worked up by flash CC.

Method B. The reaction mixture was filtered through a Kieselgel 60 G column (10 g) and the products were eluted either with EtOAc, a 7 : 2 DCM–EtOAc mixture or DCM. The eluate was evaporated to dryness. The residue was taken up in DCM (30–50 cm³) and washed with 3% aq. NaHCO₃. The organic layer was dried and evaporated to dryness. The residue was taken up in DCM and worked up (B1) by PLC or (B2) by CC (DCM–hexane 1 : 2, followed by DCM–hexane 1 : 1 and DCM–MeOH, 10 : 0.5).

Method C. The reaction mixture was cooled to 0 °C. Methanolic NaOMe (2.2 mmol) was added, and the precipitate was

filtered off and washed with EtOAc. The combined filtrate and washings were cooled to −5 to 0 °C. Ethereal diazomethane (1.5 mmol) was slowly added and the mixture was stirred for 30 min with the temperature being kept at 0 °C throughout. At this point the cycloaddition was shown by TLC to be complete. The excess of diazomethane was destroyed by adding acetic acid and the mixture was evaporated to dryness.

The yields of the products obtained and the reaction conditions are compiled in Table 1 (see above); mps, HRMS and spectral data are listed below with the individual compounds.

5-[1-(3-Methoxyphenyl)-4-oxoazetidin-2-yl]-8-[1-(3-methoxyphenyl)-4-oxoazetidin-2-ylcarbonyl]tetrazolo[1,5-*a*]pyridine 5a. A 1 : 1 mixture of two diastereoisomers; work-up: Method B1 (solvent used for TLC DCM–acetone, 10 : 0.5), mp 155 °C; HRMS (FAB), Found: (M + H)⁺, 499.1747. $C_{26}H_{23}N_6O_5$ requires m/z, 499.1730; ν_{max}/cm⁻¹ (KBr) 1760 (CO), 1750 (CO), 1680 (CO); δ_H‡‡ (CDCl₃) 3.01 (1H, dd, J 15.0, 3.0, 3″-H^A), 3.16 + 3.17 (together 1H, 2 dd, J 15.4, 2.7, 3′-H^A), 3.776 + 3.781 (together 3H, 2 s, MeO, MMP″), 3.795 + 3.799 (together 3H, 2 s, MeO, MMP′), 3.85 + 3.86 (together 1H, 2 dd, J 15.0, 6.5, 3″-H^B), 3.99 (1H, dd, J 15.4, 6.0, 3′-H^B), 5.94 + 5.95 (together 1H, 2 dd, J 6.0, 2.7, 2′-H), 6.23 + 6.24

---

‡‡ Primed characters are used for the left-hand side, doubly primed characters for the right-hand side, and unprimed characters for the central part of the molecular formula of compound **5a** oriented as shown above.

(together 1H, 2 dd, J 6.5, 3.0, 2″-H), 6.65 (1H, ddd, J 8.2, 2.5, 1.0, 4-H, MMP″), 6.71 (1H, ddd, J 8.2, 2.3, 1.0, 4-H, MMP′), 6.76 (1H, ddd, J 8.0, 2.1, 1.0, 6-H, MMP″), 6.78 + 6.79 (together 1H, 2 ddd, J 8.0, 2.1, 1.0, 6-H, MMP′), 7.00 (1H, dd, J 2.5, 2.1, 2-H, MMP″), 7.02 (1H, dd, J 2.3, 2.1, 2-H, MMP′), 7.18 (1H, dd, J 8.2, 8.0, 5-H, MMP″), 7.23 (1H, dd, J 8.2, 8.0, 5-H, MMP′), 7.36 (1H, dd, J 7.4, ≈0.5, 6-H), 8.47 + 8.48 (together 1H, 2 d, J 7.4, 7-H); NOE: 7.36 (6-H)→8.47 (7-H), 7.02 (2-H, MMP′), 6.79 (6-H, MMP′), 5.94 (2′-H), 3.16 (3′-H^A); 8.47 (7-H)→7.36 (6-H), 7.00 (2-H, MMP″), 6.76 (6-H, MMP″), 6.23 (2″-H), 3.01 (3″-H^A); δ_C ‡‡ (CDCl$_3$) 42.4 (two lines within less than 0.1 ppm; C3″), 45.05 (C3′), 49.0 (two lines within less than 0.1 ppm; C2′), 55.4 + 55.5 (2 × MeO), 56.7 (two lines within less than 0.1 ppm; C2″), 103.1 (C2, MMP″), 103.2 (two lines within less than 0.1 ppm; C2, MMP′), 108.6 (two lines within less than 0.1 ppm; C6, MMP′), 108.9 (C6, MMP″), 110.1 (C4, MMP″), 110.5 (two lines within less than 0.1 ppm; C4, MMP′), 113.4 (C6), 121.4 (two lines within less than 0.1 ppm; C8), 130.0 (C5, MMP″), 130.6 (C5, MMP′), 135.6 (C7), 137.8 (C1, MMP″), 138.6 (C1, MMP′), 142.0 (C5), 147.3 (C8a), 160.3 (C3, MMP″), 160.6 (C3, MMP′), 162.2 (C4″), 162.5 (C4′), 190.7 (two lines within less than 0.1 ppm; CO).

1-(3-Methoxyphenyl)-4-[pyrazol-3(5)-ylcarbonyl]azetidin-2-one 6a.

Work-up: Method C, mp 139–142 °C; HRMS, Found: M$^{·+}$, 271.0950. C$_{14}$H$_{13}$N$_3$O$_3$ requires M, 271.0957; v_{max}/cm^{-1} (KBr) 3220br (NH), 1760 (CO), 1680 (CO); δ_H (CDCl$_3$) 3.11 + 3.50 (together 2H, ABM, J 15.2, 2.8, 5.5, 3-H$_2$), 3.76 (3H, s, MeO), 5.53 (1H, ABM, J 2.8, 5.5, 4-H), 6.63 (1H, m, 4-H, MMP), 6.78 (1H, m, 6-H, MMP), 6.95 [1H, d, J 2.5, 5(3)-H, pyrazole], 7.02 (1H, m, 2-H, MMP), 7.17 (1H, m, 5-H, MMP), 7.67 (1H, d, J 2.5, 4-H, pyrazole), 11.0 (1H, br s, NH).

1-(3-Methoxyphenyl)-5-propiolylpyrrolidin-2-one 4b.

Work-up: Method A (solvent used in CC: DCM–acetone, 10 : 0.1), mp 114 °C; HRMS, Found: M$^{·+}$, 243.0886. C$_{14}$H$_{13}$NO$_3$ requires M, 243.0895; v_{max}/cm^{-1} (KBr) 3200 (≡CH), 2100 (C≡C), 1700 (CO), 1680 (CO); δ_H (CDCl$_3$) 2.25 + 2.46–2.80 (together 4H, 2 m, 3-H$_2$ + 4-H$_2$), 3.36 (1H, s, ≡CH), 3.80 (3H, s, MeO), 4.83 (1H, dd, J 9.5, 3.3, 5-H), 6.74 (1H, ddd, J 1.0, 2.5, 8.5, 4-H, MMP), 6.92 (1H, ddd, J 1.0, 2.0, 8.2, 6-H, MMP), 7.20 (1H, dd, J 2.0, 2.5, 2-H, MMP), 7.25 (1H, dd, J 8.2, 8.5, 5-H, MMP).

1-(3-Methoxyphenyl)-5-[pyrazol-3(5)-ylcarbonyl]pyrrolidin-2-one 6b.

Work-up: Method C;§§ mp 164–165 °C (from EtOH); HRMS (FAB), Found: (M + H)$^+$, 286.1206. C$_{15}$H$_{16}$N$_3$O$_3$ requires m/z, 286.1192; v_{max}/cm^{-1} (KBr) 3200br (NH), 1700sh (CO), 1680 (CO); δ_H (CDCl$_3$) 2.15 + 2.54–2.82 (together 4H, 2 m, 3-H$_2$ + 4-H$_2$), 3.72 (3H, s, MeO), 5.90 (1H, m, 5-H), 6.67 (1H, ddd, J 8.2, 2.5, 0.8, 4-H, MMP), 6.88 [1H, d, J 2.5, 5(3)-H, pyrazole], 6.98 (1H, ddd, J 8.0, 2.0, 0.8, 6-H, MMP), 7.17 (1H, dd, J 8.2, 8.0, 5-H, MMP), 7.25 (1H, dd, J 2.5, 2.0, 2-H, MMP), 7.57 (1H, d, 2.5, 4-H, pyrazole), 10.3 (br, 1H, NH).

Ethynyl phenyl ketone 8a.

Work-up: Method A (solvent used in CC: DCM–hexane, 1 : 1), mp 47–48 °C (lit.,[23] 49–50 °C); the IR and ^{1}H NMR spectra were identical with those reported.[24]

Phenyl propyn-1-yl ketone 8b, 2-benzoylprop-1-enyl acetate 9b, 2-benzoyl-2-hydroxypropyl acetate 10b and 2-benzoyl-2-hydroxypropyl acetoxyacetate 11b.

Work-up: Method B1 (solvent used in TLC: DCM).

Compound 8b. Oil, the IR and ^{1}H NMR spectra were essentially identical with those reported.[25]

Compound 9b. Oil; HRMS (FAB), Found: (M + H)$^+$, 205.0870. C$_{12}$H$_{13}$O$_3$ requires m/z, 205.0865; v_{max}/cm^{-1} (film) 1760 (ester), 1630 (CO), 1200 (ester), 1120 (ester); δ_H (CDCl$_3$) 2.01 (3H, d, J 1.4, =CMe), 2.25 (3H, s, OAc), 7.43 (2H, m, 3-H + 5-H, Ph), 7.52 (1H, m, 4-H, Ph), 7.64 (2H, m, 2-H + 6-H, Ph), 7.87 (1H, q, J 1.4, CH=CMe); DIFNOE: 2.01→7.87, 7.64; 7.87→7.64, 2.01, 2.25.

Compound 10b. Oil; v_{max}/cm^{-1} (film) 3470br (OH), 1730 (ester), 1680 (CO, 1250 (ester), 1050 (ester); δ_H (CDCl$_3$) 1.60 (3H, s, Me), 1.99 (3H, s, OAc), 4.11br (1H, OH), 4.36 + 4.57 (together 2H, 2 d, J 11.7, CH_2OAc), 7.46 (2H, m, 3-H + 5-H, Ph), 7.58 (1H, m, 4-H, Ph), 8.00 (2H, m, 2-H + 6-H, Ph); δ_C (CDCl$_3$) 20.6 (MeCO$_2$), 23.7 (Me), 69.9 (CH$_2$O), 78.4 (C–OH), 128.6 + 129.3 + 133.2 + 134.3 (Ph), 170.7 (COO), 202.0 (CO).

Compound 11b. Oil; v_{max}/cm^{-1} (film) 3450 (OH), 1760sh + 1750 + 1740sh (COOs), 1675 (CO); δ_H (CDCl$_3$) 1.61 (3H, s, Me), 2.07 (3H, s, OAc), 4.1 (1H, br, OH), 4.51 + 4.60 (together 2H, 2 d, J 11.4, CH$_2$O), 4.52 + 4.55 (together 2H, 2 d, J 16.0, COCH_2OAc), 7.48 + 7.59 + 8.00 (together 5H, 3 m, Ph); δ_C (CDCl$_3$), 20.3 (MeCO$_2$), 23.6 (Me), 60.6 (COCH_2OAc), 70.4 (CCH$_2$OAc), 78.3 (COCOH), 128.7 (C3 + C5, Ph), 129.4 (C2 + C6, Ph), 133.3 (C4, Ph), 134.0 (C1, Ph), 167.5 (OCOCH$_2$), 170.4 (MeCO$_2$), 201.6 (PhCO).

1-Benzoyl-1-(1-methyltetrazol-5-yl)methyl acetate 12d, (E)-(1-methyltetrazol-5-yl)-[2-(1-methyltetrazol-5-yl)-1-phenylvinyl-oxy]methyl phenyl ketone 13d, 2,3-bis(1-methyltetrazol-5-yl)-1,4-diphenylbutane-1,4-dione 14d (as a mixture of the racemic and *meso* forms), and 2,3-bis(1-methyltetrazol-5-yl)-1,4-diphenylbut-2-ene-1,4-dione 15d.

Work-up: the filtrate of the reaction mixture, combined with the EtOAc washings, was evaporated to dryness and the residue was dissolved in EtOAc. On storage for 12 h in a refrigerator, compound 15d separated in the form of colorless crystals. The filtrate was evaporated to dryness, and the residue was taken up in a small amount of DCM and worked up by PLC (solvent: DCM–acetone, 7 : 2) to yield compounds 12d, 14d and 13d in order of increasing polarity.

Compound 12d. Oil, HRMS, Found: M$^{·+}$, 260.0906. C$_{12}$H$_{12}$N$_4$O$_3$ requires M, 260.0909; v_{max}/cm^{-1} (film) 1760 (ester), 1700 (CO), 1200 (ester), 1070 (ester); δ_H (CDCl$_3$) 2.27 (3H, s, OAc), 4.14 (3H, s, NMe), 7.47 (1H, s, COCHO), 7.48 (2H, m, 3-H + 5-H, Ph), 7.62 (1H, m, 4-H, Ph), 8.09 (2H, m, 2-H + 6-H, Ph); δ_C (CDCl$_3$) 20.2 (MeCOO), 35.1 (NMe), 68.0 (COCHO), 129.1 + 129.2 (C2 + C6 and C3 + C5, Ph), 132.8 (C1, Ph), 135.0 (C4, Ph), 148.9 (C5, tetrazole), 168.7 (MeCOO), 189.0 (PhCO).

Compound 13d. Oil, HRMS (FAB), Found: (M + H)$^+$, 403.1647. C$_{20}$H$_{19}$N$_8$O$_2$ requires m/z, 403.1631; v_{max}/cm^{-1} 1700 (CO); δ_H¶¶ (CDCl$_3$) 4.00 (3H, s, N′Me), 4.25 (3H, s, NMe), 5.85 (1H, s, =CH), 7.19 (1H, s, COCH), 7.34 (2H, m, 3-H + 5-H, Ph), 7.4–7.5 (3H, m, 3-H + 4-H + 5-H, Ph′), 7.52 (1H, m, 4-H, Ph), 7.53 (2H, m, 2-H + 6-H, Ph′), 7.75 (2H, m, 2-H + 6-H, Ph); NOE 4.00 (N′-Me)→5.85 (=CH); 4.25 (NMe)→7.19 (COCH), 7.75 (2-H + 6-H, Ph), 7.53 (2-H + 6-H, Ph′), 5.85 (=CH); 5.85 (=CH)→4.00 (N′Me), 7.53 (2-H + 6-H, Ph′); 7.19 (COCH)→7.75 (2-H + 6-H, Ph), 4.25 (NMe), 7.53 (2-H + 6-H, Ph′), 5.85 (=CH); δ_C¶¶ (CDCl$_3$) 33.6 (N′Me), 35.4 (NMe), 73.1 (COCH), 93.1 (=CH), 127.9 (C2 + C6, Ph′), 128.7 (C2 + C6, Ph), 129.0 (C3 + C5, Ph), 129.3 (C3 + C5, Ph′), 131.1 (C4, Ph′), 132.6 (C1, Ph′), 132.8 (C1, Ph), 134.8 (C4, Ph), 149.5 (C5, tetrazole), 149.8 (C5, tetrazole′), 161.2 (PhC=), 181.8 (PhC=O).

Compound 14d. A 2 : 1 mixture of stereoisomers A and B, mp 187–196 °C; HRMS (FAB), Found: (M + H)$^+$, 403.1651.

$C_{20}H_{19}N_8O_2$ requires m/z, 403.1631; ν_{max}/cm^{-1} (KBr) 1690 (CO); stereoisomer A, δ_H (CDCl$_3$) 4.03 (6H, s, 2 × NMe), 6.34 (2H, s, 2 × COCH), 7.50 (4H, m, 3-H + 5-H, 2 × Ph), 7.62 (2H, m, 4-H, 2 × Ph), 7.97 (4H, m, 2-H + 6-H, 2 × Ph); NOE: 6.34 (COCH)→7.97 (2-H + 6-H, Ph), 4.03 (NMe); δ_C (CDCl$_3$) 34.4 (NMe), 43.9 (COCH), 128.7 (C2 + C6, Ph), 129.3 (C3 + C5, Ph), 134.7 (two lines within less than 0.1 ppm; C4, Ph and C1, Ph), 150.4 (C5, tetrazole), 192.0 (C=O); stereoisomer B, δ_H (CDCl$_3$) 4.29 (6H, s, 2 × NMe), 6.20 (2H, s, 2 × COCH), 7.44 (4H, m, 3-H + 5-H, 2 × Ph), 7.58 (2H, m, 4-H, 2 × Ph), 7.80 (4H, m, 2-H + 6-H, 2 × Ph); NOE: 6.20 (COCH)→7.80 (2-H + 6-H, Ph), 4.29 (NMe); δ_C (CDCl$_3$) 34.4 (NMe), 44.3 (COCH), 128.3 (C2 + C6, Ph), 129.3 (C3 + C5, Ph), 134.7 (C4, Ph), 134.9 (C1, Ph), 151.2 (C5, tetrazole), 192.8 (C=O).

Compound 15d. Mp 230–236 °C; HRMS, Found: M·⁺, 400.1383. $C_{20}H_{16}N_8O_2$ requires M, 400.1396; ν_{max}/cm^{-1} (KBr) 1680 (CO); δ_H (CDCl$_3$ + DMSO-d$_6$) 3.97 (6H, s, 2 × NMe), 7.55 (4H, m, 3-H + 5-H, 2 × Ph), 7.68 (2H, m, 4-H, 2 × Ph), 7.95 (4H, m, 2-H + 6-H, 2 × Ph); δ_C (CDCl$_3$ + DMSO-d$_6$) 35.2 (NMe), 129.4 (C2 + C6, Ph),|||| 129.5 (C3 + C5, Ph),|||| 134.4 (C1, Ph), 135.3 (C4, Ph), 136.9 (>C=), 149.3 (C5, tetrazole), 189.7 (C=O).

Phenyl phenylethynyl ketone 8e. Work-up: Method B2, mp 44 °C (lit.,[26] 46.5–48 °C); ν_{max}/cm^{-1} (KBr) 2200 (C≡C), 1645 (CO), identical with the reported spectrum;[27] δ_H (CDCl$_3$) *** 7.48 (2H, m, 3-H + 5-H, Ph″), 7.49 (1H, m, 4-H, Ph″), 7.69 (2H, m, 2-H + 6-H, Ph″), 7.52 (2H, m, 3-H + 5-H, Ph′), 7.63 (1H, m, 4-H, Ph′), 8.23 (2H, m, 2-H + 6-H, Ph′), essentially identical with the reported spectrum;[27] δ_C (CDCl$_3$) *** 86.9 (COC≡), 93.1 (≡CPh″), 120.2 (C1, Ph″), 128.7 (two lines within less than 0.1 ppm; C3 + C5, Ph′ and Ph″), 129.6 (C2 + C6, Ph′), 130.8 (C4, Ph″), 133.1 (C2 + C6, Ph″), 134.1 (C4, Ph′), 137.0 (C1, Ph′), 178.0 (C=O).

(4-Methoxyphenyl)ethynyl phenyl ketone 8f. Work-up: Method B1 (solvent used in TLC: DCM–acetone, 10 : 0.1); mp 81–85 °C (lit.,[28] 81–82 °C); ν_{max}/cm^{-1} (KBr) 2195 (C≡C), 1625 (CO), identical with the reported spectrum;[28] δ_H (CDCl$_3$) 3.85 (3H, s, MeO), 6.93 + 7.64 (4H, AA′BB′, PMP), 7.51 (2H, m, 3-H + 5-H, Ph), 7.61 (1H, m, 4-H, Ph), 8.22 (2H, m, 2-H + 6-H, Ph).

(4-Nitrophenyl)ethynyl phenyl ketone 8g. Work-up: Method B1 (solvent used in TLC: DCM–acetone, 10 : 0.5), the least polar component of the mixture; mp 152–154 °C (lit.,[28] 148–148.5 °C); ν_{max}/cm^{-1} (KBr) 2200 (C≡C), 1650 (CO) identical with the reported spectrum;[28] δ_H (CDCl$_3$) 7.55 (2H, m, 3-H + 5-H, Ph), 7.67 (1H, m, 4-H, Ph), 8.20 (2H, m, 2-H + 6-H, Ph), 7.84 + 8.29 (4H, AA′BB′, J 8.8, nitrophenyl).

(E)-{2-[8-Benzoyl-8-(4-nitrophenyl)-3,6-dioxanon-7-en-1-yl]-tetrazol-5-yl}-(4-nitrophenyl)methyl acetate 16g. From a mixture of the other compounds accompanying compound **8g** as a highly polar component by two successive PLC separations, using a Merck coated glassplate (20 × 20 cm; thickness of adsorbent layer 2.5 mm) for the second separation; oil, HRMS, Found: M·⁺, 602.1734. $C_{29}H_{26}N_6O_3$ requires M, 602.1761; δ_H (CDCl$_3$) ††† 2.17 (3H, s, OAc), 3.67 + 4.12 (2 × 2H, 2 m, 4′-H$_2$ + 5′-H$_2$, respectively), 4.03 (2H, t, J 5.4, 2′-H$_2$), 4.74 (2H, m, 1′-H$_2$), 7.14 (1H, s, CHOAc), 7.28 (1H, s, 7′-H), 7.40 (2H, m, 3-H + 5-H, Ph), 7.50 (1H, m, 4-H, Ph), 7.52 (2H, m, 2-H + 6-H, PNP), 7.61 (2H, m, 2-H + 6-H, Ph), 7.68 (2H, m, 2-H + 6-H, PNP′), 8.18 (2H, m, 3-H + 5-H, PNP), 8.20 (2H,

m, 3-H + 5-H, PNP′); NOE 7.28 (7′-H)→7.61 (2-H + 6-H, Ph), 4.12 (5′-H$_2$); 7.14 (CHOAc)→7.68 (2-H + 6-H, PNP′), 2.17 (OAc); δ_C (CDCl$_3$) ††† 20.8 (OOCMe), 53.0 (C1′), 68.3 (C2′), 68.4 (CHOAc), 69.9 (C4′), 74.3 (C5′), 119.4 (C8′), 123.2 (C3 + C5, PNP), 124.0 (C3 + C5, PNP′), 128.4 (two lines within less than 0.1 ppm; C2 + C6, PNP′ and C3 + C5, Ph), 129.2 (C2 + C6, Ph), 130.9 (C2 + C6, PNP), 131.9 (C4, Ph), 138.9 (C1, Ph), 140.6 (C1, PNP), 143.2 (C1, PNP′), 146.5 (C4, PNP), 148.2 (C4, PNP′), 162.3 (C7′), 164.3 (C5, tetrazole), 169.4 (OOCMe), 194.7 (C9′).

Cyclohexyl ethynyl ketone 8h. Work-up: Method B1 (solvent used in TLC: DCM), oil, ν_{max}/cm^{-1} (film) 3250 (≡C–H), 2090 (C≡C), 1680 (C=O), identical with the reported spectrum;[29] δ_H (CDCl$_3$) 1.15–1.50 (5H, m, 2-H to 5-H cyclohexyl, axial), 1.60–2.05 (5H, m, 2-H to 5-H, cyclohexyl, equatorial), 2.43 (1H, tt, J_{aa} 11.0, J_{ae} 3.6, 1-H, cyclohexyl, axial), 3.21 (1H, s, ≡CH), essentially identical with the reported spectrum.[29]

Ethyl pyrazole-3(5)-carboxylate 18i. Work-up: Method C, mp 152–154 °C (lit.,[30] 154–157 °C); ν_{max}/cm^{-1} (KBr) 3240 (NH), 1690 (C=O), identical with the spectrum reported.[31]

Benzyl propiolate 8j. Work-up: Method B2 (only solvent used for CC: DCM–hexane, 1 : 2), oil; ν_{max}/cm^{-1} (film) 3280 (≡C–H), 2110 (C≡C), 1710 (C=O), 1220 (ester); δ_H (CDCl$_3$) 2.83 (1H, s, ≡CH), 5.20 (2H, s, OCH$_2$), 7.30–7.40 (5H, m, Ph), essentially identical with the CCl$_4$ spectrum described in ref. 32.

Propiolanilide 8k. Work-up: Method A (solvent used for CC: DCM), mp 85–86 °C (lit.,[33] 82–83 °C); ν_{max}/cm^{-1} (KBr) 3260 (≡C–H), 2100 (C≡C), 1620 (Amide I), essentially identical with the spectrum reported.[33]

N-Methylpropiolanilide 8l. Work-up: Method B1 (solvent used for TLC: DCM–acetone, 7 : 1); mp 83–85 °C (lit.,[34] 78–79 °C); ν_{max}/cm^{-1} 3330 (≡C–H), 2120 (C≡C), 1630 (Amide I), identical with the spectrum reported for a CHCl$_3$ solution.[34]

N-(3-Methoxyphenyl)but-2-ynamide 8n. Work-up: Method A (solvent used for CC: DCM); mp 79–83 °C; HRMS, Found: M·⁺, 189.0788. $C_{11}H_{11}NO_2$ requires M, 189.0790; ν_{max}/cm^{-1} 3200–2800br (NH), 2210 (C≡C), 1620 (Amide I); δ_H (CDCl$_3$) 1.98 (3H, s, ≡CMe), 3.79 (3H, s, OMe), 6.67 (1H, br dd, J 2.0, 8.0, 4-H, MMP), 7.00 (1H, br dd, J 2.0, 8.0, 6-H, MMP), 7.20 (1H, t, J 8.0, 5-H, MMP), 7.25 (1H, t, J 2.0, 2-H, MMP), 7.56 (1H, br s, NH); δ_C (CDCl$_3$) 3.7 (≡CMe), 55.3 (OMe), 75.4 (COC≡), 84.5 (≡CMe), 105.7 (C2, MMP), 110.5 (C4, MMP), 112.0 (C6, MMP), 129.7 (C5, MMP), 138.6 (C1, MMP), 151.1 (C3, MMP), 160.1 (C=O).

9-Methoxy-4-methyl-4H-tetrazolo[1,5-a][1,5]benzodiazepin-5(6H)-one 19o and 4-acetoxy-9-methoxy-4-methyl-4H-tetrazolo-[1,5-a][1,5]benzodiazepin-5(6H)-one 20o. Work-up: Method B1 (solvent used for TLC: DCM–acetone, 7 : 1). The resulting crude compound **19o** was taken up in DCM (1 ml) and subjected to purification by TLC (solvent: DCM–EtOAc, 7 : 1).

Compound 19o. Mp 260–262 °C; HRMS, Found: M·⁺, 245.0917. $C_{11}H_{11}N_5O_2$ requires M, 245.0913; ν_{max}/cm^{-1} (KBr) 3190br (NH), 1680 (Amide I); δ_H (CDCl$_3$ + DMSO-d$_6$) 1.68 (3H, d, J 7.0, Me), 3.77 (1H, q, J 7.0, 4-H), 3.89 (3H, s, MeO), 7.12 (1H, dd, J 9.0, 2.8, 8-H), 7.32 (1H, d, J 9.0, 7-H), 7.39 (1H, d, J 2.8, 10-H), 10.50 (1H, br, NH).

Compound 20o. Mp 198–205 °C (from Et$_2$O); HRMS, Found: M·⁺, 303.0957. $C_{13}H_{13}N_5O_4$ requires M, 303.0968; ν_{max}/cm^{-1} (KBr) 3200br (NH), 1756 (ester), 1688 (Amide I), 1224 (ester), 1068 (ester); δ_H (CDCl$_3$) 1.63 (3H, s, OAc), 2.26 (3H, s, Me), 3.92 (3H, s, MeO), 7.09 (1H, dd, 8-H), 7.18 (1H, d, 7-H), 7.50 (1H, d, 10-H), 8.10 (1H, br s, NH); NOE: 8.10→7.18; 3.92→7.50, 7.09; δ_C (CDCl$_3$) 18.2 (Me), 19.9 (MeCO$_2$), 56.1

|||| The reverse assignation is equally possible.

*** Primed characters are used for the phenyl group adjacent to the carbonyl group, doubly primed characters for the phenyl group adjacent to the triple bond.

††† The 4-nitrophenyl groups on the left- and right-hand side of the formula are denoted by PNP and PNP′, respectively.

(MeO), 75.1 (C4), 107.1 (C10), 117.6 (C8), 121.9 (C6a), 123.0 (C7), 126.5 (C10a), 151.9 (C3a), 157.6 (C9), 165.7 (C5), 168.1 (MeCO_2).

N-Propinoylpiperidine 8p.‡‡‡ Work-up: Method B1 (solvent used for TLC: DCM–acetone, 10 : 2); oil; HRMS, Found: M$^{\cdot+}$, 137.0836. $C_8H_{11}NO$ requires *M*, 137.0841; ν_{max}/cm^{-1} (film) 3200 ($\equiv$C–H), 2100 (C$\equiv$C), 1625br (Amide I); δ_H (CDCl$_3$) 1.50–1.75 (6H, m, 3-H$_2$ + 4-H$_2$ + 5-H$_2$), 3.09 (1H, s, $\equiv$CH), 3.58 + 3.71 (4H, 2 t, 2-H$_2$ + 6-H$_2$).

ESR measurements

The solvent THF used was pretreated by refluxing for *ca.* 3 h over LiAlH$_4$. THF solutions (0.1 cm^3) of *N*-(*tert*-butyl)-α-phenylnitrone (0.1 g cm^{-3}) were added to saturated THF solutions (1 cm^3) of compounds **2b** and **7d**, and the mixtures were thoroughly homogenized. After the spectrometer was set to measuring conditions, suspensions of LTA in THF were added dropwise to the solutions placed into the spectrometer at −20 °C and room temperature, respectively, whereby mixing took place due to gravitational forces. The measurements were carried out in air. In the absence of the nitrone no ESR signals were detected.

Acknowledgements

‡‡‡ This compound had been obtained by a different route before[34] but no physical or spectral data were disclosed.

References

1 L. T. Giang, J. Fetter, M. Kajtár-Peredy, K. Lempert, F. Bertha, G. M. Keserű, G. Czira and T. Czuppon, *Tetrahedron*, 1999, **55**, 8457.
2 L. T. Giang, J. Fetter, M. Kajtár-Peredy, K. Lempert, F. Bertha, G. M. Keserű and G. Czira, *J. Chem. Res. (S)*, 2000, 204; L. T. Giang, J. Fetter, M. Kajtár-Peredy, K. Lempert, F. Bertha, G. M. Keserű and G. Czira, *J. Chem. Res. (M)*, 2000, 601.
3 J. Elguero, R. Jacquier and H. C. N. Tien Duc, *Bull. Soc. Chim. Fr.*, 1966, 3727.
4 (*a*) R. Criegee, *Angew. Chem.*, 1958, **70**, 173; (*b*) G. W. Rotermund, in *Methoden der Organischen Chemie* ("Houben-Weyl"), ed. E. Müller, Thieme, Stuttgart, 4th edn., 1975, vol. IV/1b, pp. 207, 223 *et seq.*, 242.
5 K. Ichikawa and Y. Yamaguchi, *J. Chem. Soc. Jpn.*, 1952, **73**, 415.
6 W. Cocker and J. C. P. Schwarz, *Chem. Ind.*, 1951, 390.
7 G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 1955, 4426.
8 M. J. Harrison and R. O. C. Norman, *J. Chem. Soc. (C)*, 1970, 728 and earlier references cited.
9 Ref. 4*b*, pp. 274–276.
10 E. Hecker and R. Lattrell, *Justus Liebigs Ann. Chem.*, 1963, **662**, 48.
11 H. Behringer and M. Matner, *Tetrahedron Lett.*, 1966, 1663.
12 E. G. Janzen and B. J. Blackburn, *J. Am. Chem. Soc.*, 1968, **90**, 5909; E. G. Janzen and B. J. Blackburn, *J. Am. Chem. Soc.*, 1969, **91**, 4481.
13 Ch. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Bell, London, 1953, p. 555.
14 (*a*) R. B. Woodward and R. A. Olofson, *Tetrahedron Suppl. 7*, 1966, 415; (*b*) R. T. Chakrasali, H. Ila and H. Junjappa, *Synthesis*, 1988, 453.
15 W. G. Finnegan, R. A. Henry and R. Lofquist, *J. Am. Chem. Soc.*, 1958, **80**, 3908.
16 K. H. Boltze, O. Brendler, H. Jacobi and W. Opitz, *Arzneim.-Forsch.*, 1980, **30**, 1314.
17 J. Diago-Meseguer, A. L. Palomo-Coll, J. R. Fernandez-Lizarbe and A. Zugaza-Bilbao, *Synthesis*, 1980, 547.
18 C. Arnold, Jr. and D. N. Thatcher, *J. Org. Chem.*, 1969, **34**, 1141.
19 M. Augustin, W. Jahreis and D. Rudolf, *Synthesis*, 1977, 472.
20 A. Dornow and H. Grabhöfer, *Chem. Ber.*, 1958, **91**, 1824.
21 A. Miyashita, Y. Suzuki, Y. Okamura and T. Higashino, *Chem. Pharm. Bull.*, 1996, **44**, 252.
22 J. Speziale and P. C. Hamm, *J. Am. Chem. Soc.*, 1956, **78**, 5580.
23 R. R. France and W. Faulconer, *J. Org. Chem.*, 1971, **36**, 2048.
24 M. Noro, T. Masuda, A. S. Ichimura, N. Koga and H. Iwamura, *J. Am. Chem. Soc.*, 1994, **116**, 6179.
25 J. Suffet and D. Toussaint, *J. Org. Chem.*, 1995, **60**, 3550.
26 M. S. Newman and B. C. Ream, *J. Org. Chem.*, 1966, **31**, 3861.
27 J. B. Hendrickson and S. Hussain, *Synthesis*, 1989, 217.
28 W. F. Winecoff and D. W. Boykin, Jr., *J. Org. Chem.*, 1973, **38**, 2544.
29 R. D. Dillard and D. E. Pavey, *J. Org. Chem.*, 1971, **36**, 749.
30 E. Schweizer and C. S. Labaw, *J. Org. Chem.*, 1973, **38**, 3069.
31 Y. Nakano, M. Hamaguchi and T. Nagai, *J. Chem. Res. (M)*, 1991, 1701.
32 L. Balas, B. Jaisseaume and B. Langwort, *Tetrahedron Lett.*, 1989, **30**, 4525.
33 S. Puertas, R. Brieva, F. Rebolledo and V. Gotor, *Tetrahedron*, 1993, **49**, 4007.
34 B. Kanner and U. K. Pandit, *Tetrahedron*, 1982, **38**, 3597.