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Studies on Seven-Membered Heterocycles. XXXIII.[1] Synthesis of Fully Unsaturated 1,2,5-Triazepines by Photochemical Ring Expansion of 4-Azidopyridazines

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Photolysis of the 3-methoxy-4-azidopyridazines (11) in the presence of a base such as methoxide ion and diethylamine resulted in ring-expansion to produce the 1*H*-1,2,5-triazepines (12 and 27), which were too unstable to be isolated, but tautomerized to the stable 4*H*-isomers (13 and 28) on further treatment with sodium methoxide and were converted to the stable 1-acetyl-1*H*-1,2,5-triazepines (14 and 29) by acetylation with acetyl chloride. The products 12—14 and 27—29 are the first examples of fully unsaturated 1,2,5-triazepines and were characterized by means of spectral analyses and some chemical reactions.

Keywords 4-azidopyridazine; 1*H*-1,2,5-triazepine; 4*H*-1,2,5-triazepine; photolysis; ring-expansion; pyridazinyl nitrene; azirine intermediate

Syntheses of new fully unsaturated seven-membered heterocyclic rings with two or more heteroatoms have recently been widely studied.[2] With regard to monocyclic triazepines,[3] 1,2,4-triazepines have been prepared by the cycloaddition of 1-azirines to 1,2,4,5-tetrazines[4] or by a photochemical walk-rearrangement of 3,4,7-triaza-2,4-norcaradienes.[5] However, the other three possible isomers due to the isomeric positions of the three nitrogen atoms, 1,2,3-, 1,2,5-, and 1,3,5-triazepines, have remained unknown, although some reactions[3,6] involving such triazepines as unisolable intermediates and the syntheses[2,3] of di- and per-hydrotriazepines have been reported. Therefore, we were interested in the synthesis of new triazepines and report here the synthesis of the first examples of fully unsaturated 1,2,5-triazepines.[7]

The singlet arylnitrenes generated from arylazides either by photolysis or by thermolysis are known to undergo ring-expansion.[8] We have already reported[9] that the photolysis of the 4-azidopyridines (1) in the presence of methoxide ion resulted in ring-expansion to give the 6*H*-1,4-diazepines (3) *via* the azirine intermediates **2** formed from the initially generated 4-pyridylnitrenes. In the case of 3-azidopyridines (**4**),[10] 2-unsubstituted compounds give the 5*H*-1,3-diazepines (**6**) *via* the azirines (**5**), while 2-substituted compounds afford the 2*H*-1,4-diazepines (**8**) *via* the different azirines (**7**). These results prompted us to examine the photolysis of 4-azidopyridazines.

The synthetic route to the starting 4-azidopyridazines (**11a**—**f**) used in the present work is shown in Chart 2. The known 4-nitropyridazine 1-oxides (**9a**—**f**) were treated with sodium azide to give the 4-azidopyridazine 1-oxides (**10**: 80—90% yields), which were deoxygenated by treatment with phosphorus trichloride to afford the 4-azidopyridazines (**11**) in 50—70% yields.

Irradiation (400 W, high-pressure Hg lamp; Pyrex filter) of the 3-methoxy-4-azidopyridazines (**11a**—**c**: *ca.* 0.5 g) in methanol–dioxane (1 : 1; 150 ml) containing a large excess of sodium methoxide (*ca.* 10 mol eq) until almost all of the starting azides had been consumed (for 60—90 min) gave the desired 4*H*-1,2,5-triazepines (**13a**—**c**) in 50—60% yields *via* the 1*H*-isomers **12**, as the sole ring-expansion products. In order to confirm the initial formation of the 1*H*-isomers **12**, the azides (**11a**, **b**) were irradiated in the presence of equimolecular amounts of sodium methoxide under ice-cooling for 50—60 min to form the expected 1*H*-1,2,5-triazepines (**12**) together with the 4*H*-isomers **13**. The product mixtures containing **12** and **13** in the ratios of 3—4 : 1 (based on proton nuclear magnetic resonance (^{1}H-NMR) spectral analysis) were chromatographed to give

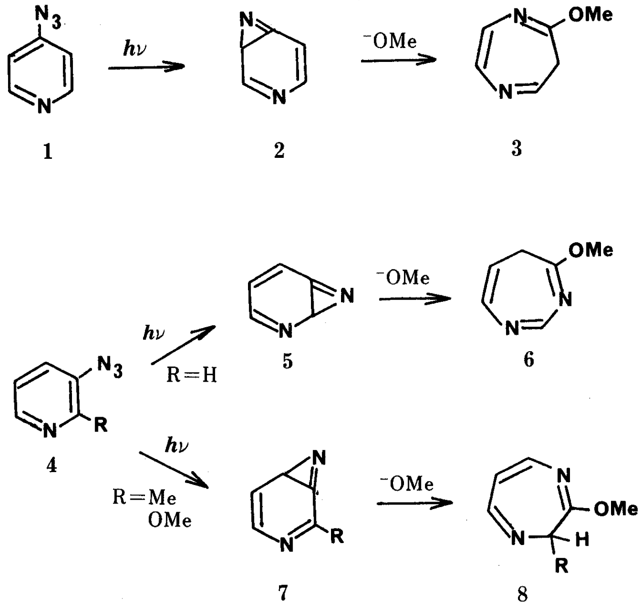
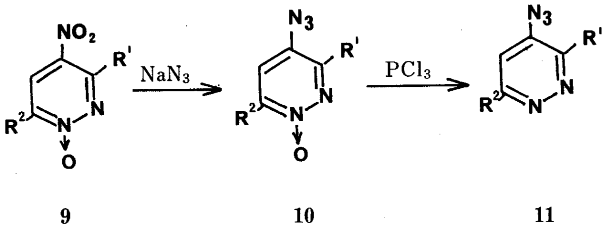


Chart 1



	R^1	R^2
a	OMe	H
b	OMe	Me
c	OMe	OMe
d	H	H
e	H	Me
f	Me	Me

Chart 2

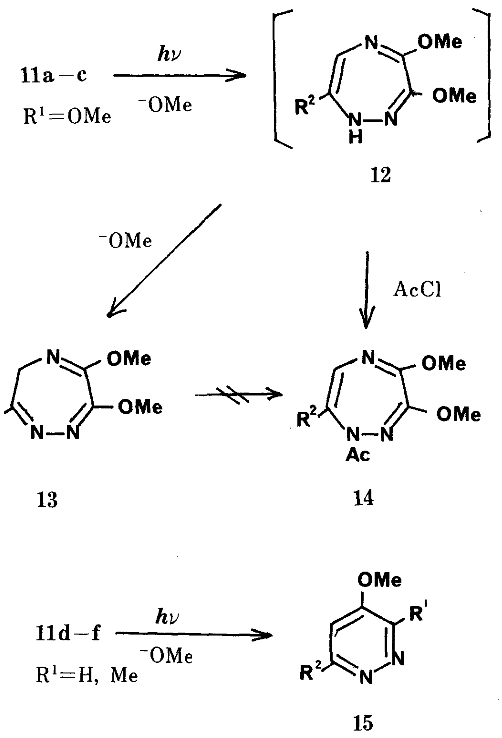


Chart 3

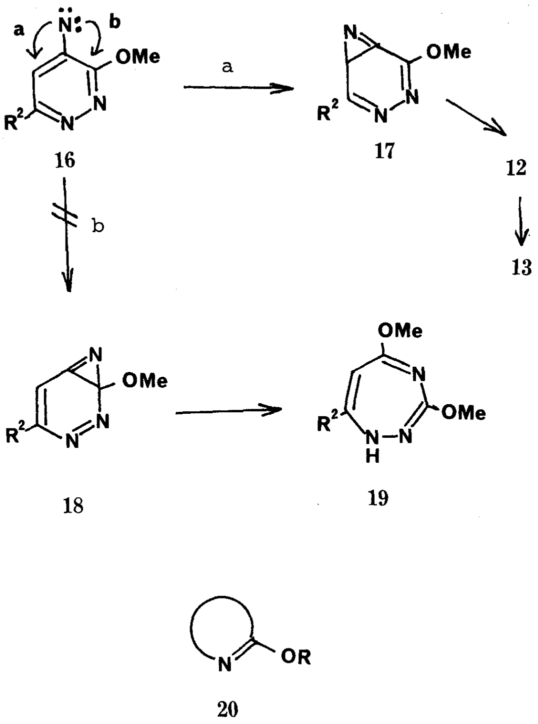


Chart 4

only the 4*H*-isomers **13** in low yields (**13a**: 15%; **13b**: 27%), but were further treated with a large excess of sodium methoxide in methanol for 3—5 h at room temperature to give **13** in higher yields (**13a**: 45%; **13b**: 51%). These results clearly indicate that the 1*H*-isomers **12** initially formed are unstable and readily decomposed when passed through a silica gel or alumina column, but tautomerize to the more stable 4*H*-isomers **13** on treatment with sodium methoxide, by analogy with the case of 1*H*-1,4-benzodiazepines.[11] Therefore, the structures of **12** were confirmed by means of ^{1}H-NMR spectral analysis of the product mixtures without isolation and by the following chemical study. The photolysed product mixtures containing the 1*H*-isomers **12** obtained from **11a,b** were treated with acetyl chloride in pyridine to give the desired 1-acetyl-1*H*-1,2,5-triazepines (**14a**: 26%; **14b**: 46%) as stable crystals. It is known that the CH-forms of diazepines such as 4*H*-1,2-,[12] and 6*H*-1,4-diazepines[9] and 3*H*-1,4-[11] and 5*H*-2,3-benzodiazepines[13] undergo acetylation with tautomerization, giving rise to the corresponding N-acetyl derivatives. However, attempts to convert the 4*H*-isomers **13** into the 1-acetyl-1*H*-triazepines (**14**) have been unsuccessful, resulting only in decomposition. These results show that the acetyl compounds **14** are directly fromed form the 1*H*-isomers **12**.

It should be noted that, on the contrary, the 4-azidopyridazines (**11d**—**f**) having no methoxy group, upon irradiation under similar conditions, gave only the substitution products **15**, 4-methoxypyridazines, in low yields (10—20%) and no ring-expansion products.

The formation of the 1,2,5-triazepines (**12**) from the azides (**11**) may proceed *via* the azirine intermediates **16**, but that of 1,2,4-triazepines such as **19** expected from the other possible azirine intermediates **18** was not observed in the present photolysis. This direction of azirine formation is analogous to that of 2-substituted phenylnitrenes[14] and 3-pyridylnitrenes,[10] which are known to cyclize preferentially at the vacant α-position. Although the effect of the methoxy group is not clear, we assume that the strong electron-donating methoxy group may provide assistance for the cyclization of the initially formed pyridazinylnitrenes (**16**) to the azirines (**17**), and for stabilization of the triazepine ring obtained. It has been observed that azepine and diazepine rings are stabilized by an iminoether structure **20**.[9,10]

The ^{1}H-NMR spectra of the a-series of the 1*H*-triazepines showed AB pairs of doublets (**12a**: δ 5.80 and 5.97, $J=6$ Hz; **14a**: δ 6.20 and 6.34, $J=6$ Hz) assignable to 7-H and 6-H and, in the case of **12a**, a broad NH signal at δ 5.15, in addition to methoxy and acetyl proton signals, while that of the 4*H*-isomer **13a** showed a methylene proton signal at δ 3.72 (2H, d, $J=5$ Hz) due to 4-H_2 and a triplet signal at δ 7.50 ($J=5$ Hz) due to 3-H. The ^{13}C-NMR spectra of **13a**—**c** exhibited signals due to sp^3 ring carbon atoms at around δ 45 (t), whereas those of **14** showed no sp^3 ring carbon signals. These spectral data and the results of the following chemical studies are consistent with the proposed 1,2,5-triazepine structures for **12**—**14**.

$LiAlH_4$ reduction of the 4*H*-triazepines (**13a, b**) afforded the dihydro compounds **21** in moderate yields (**21a**: 87%; **21b**: 51%). Treatment of **21a** with acetyl chloride in pyridine gave 1-acetyl-3,4-dimethoxy-6,7-dihydro-1*H*-1,2,5-triazepine (**22**: 41% yield), which was also obtained from the 1-acetyl-1*H*-triazepine (**14a**) by hydrogenation over Pd–C in 73% yield. Heating **14a** in *o*-dichlorobenzene at 190—200 °C for 65 h in a sealed tube resulted in isomerization to give the 6-acetylaminopyrazine (**24**) in 76% yield, presumably *via* the diaziridine intermediate **23**, This thermal behavior, including the mode of the diaziridine ring fission and the substituent effect, is similar to that observed in the thermolysis of 1,2- and 1,3-triaze-

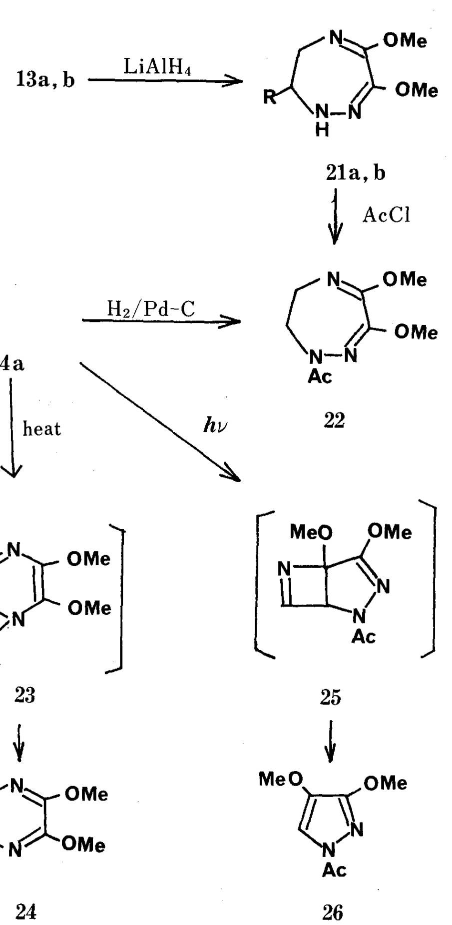


Chart 5

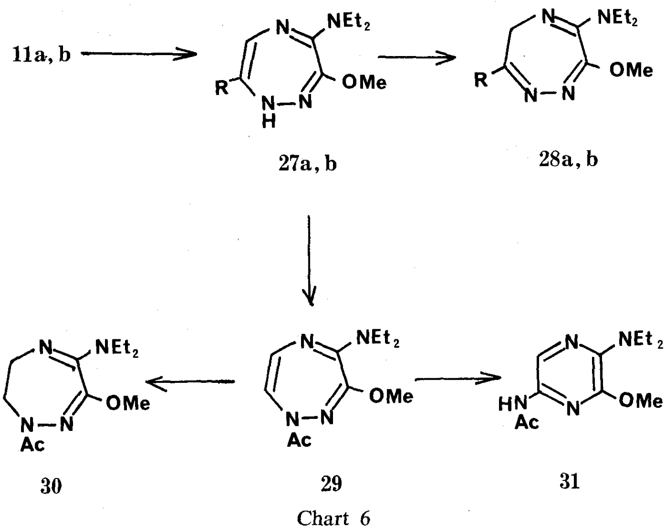


Chart 6

pines.[9,10,15] Irradiation of **14a** in benzene for 4.5 h gave 1-acetyl-3,4-dimethoxypyrazole (**26**) in 71% yield, probably *via* the bicyclic intermediate **25**. This photochemical behavior is also analogous to those observed for a variety of fully unsaturated seven-membered heterocyclic rings.[2,16]

Next, when an amine was used as a base instead of sodium methoxide in the present photolysis, similar results were obtained. Irradiation of the azides (**11a, b**) in diethylamine–dioxane (1 : 1) for 70—80 min formed the unstable 1*H*-triazepines (**27**) and the stable 4*H*-isomers (**28**) in the ratios of 3—5 : 1. These product mixtures were treated with sodium methoxide in methanol, and then chromatographed on alumina to give the 4*H*-1,2,5-triazepines (**28**) in *ca.* 40% yields. The photolysed mixture obtained form **11a** was acetylated with acetyl chloride in pyridine to give the 1-acetyl compound **29** in 46% yield. Hydrogenation of **29** over Pd–C afforded the 6,7-dihydro compound **30** in 79% yield and the thermolysis of **29** at 190—200 °C gave the pyrazole derivative **31** in 62% yield.

In conclusion, the products **12**—**14** and **27**—**29** are the first examples of fully unsaturated 1,2,5-triazepines.

Experimental

Melting points were measured on a Yanagimoto micro melting point hot stage apparatus and are uncorrected. Infrared (IR) spectra were determined with a Hitachi 270—30 spectrometer and mass spectra (MS) were measured with a JEOL DX-300 instrument. ^{1}H-NMR spectra were recorded on a JEOL JNM-MH100 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard unless otherwise stated; spectral assignments were confirmed by spin-decoupling experiments and, in the case of NH protons, by exchange with D_2O. ^{13}C-NMR spectra were recorded on a JEOL FX-100 spectrometer in $CDCl_3$. Microanalyses were performed in the Microanalytical Center of this faculty by Mrs. R. Igarashi. Photolyses were carried out under a nitrogen atmosphere in an immersion apparatus equipped with a 400 W high-pressure Hg lamp and a Pyrex filter, which was cooled internally with running water. Kieselgel 60 (70—230 mesh, Merck) was used for silica gel column chromatography. For alumina column chromatography, Aluminiumoxid 90 standardisiert (Activitätsstufe II—III, 70—230 mesh, Merck) was used.

Starting Materials The 4-nitropyridazine 1-oxides (**9a**,[17] **9b**,[18] **9c**,[19] **9d**,[20] **9e**,[21] and **9f**[22]) were prepared by the reported methods.

4-Azidopyridazine 1-Oxides (10a—f) General Procedure: A solution of sodium azide (3—5 mol eq) in water (3—5 ml) was added to a solution of **9** (2—8 g) in EtOH (50—150 ml) with stirring at room temperature. The mixture was refluxed for 4—6 h and then evaporated *in vacuo*. The residue was extracted with CH_2Cl_2 and the extract was washed with water, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2 as an eluent to give **10**.

10a: 93% yield, mp 140—141 °C, pale yellow needles [from isopropyl ether (IPE)]. IR (KBr): 2136 (N_3) cm^{-1}. ^{1}H-NMR δ: 4.10 (3H, s, 3-OMe), 7.03 (1H, d, 5-H), 7.84 (1H, d, 6-H), $J_{5,6}=6$ Hz. *Anal.* Calcd for $C_5H_5N_5O_2$: C, 35.93; H, 3.02; N, 41.91. Found: C, 36.20; H, 2.91; N, 40.16.

10b: 78% yield, mp 103—105 °C, pale yellow needles (from hexane–CH_2Cl_2). IR (KBr): 2120 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.40 (3H, s, 6-Me), 4.06 (3H, s, 3-OMe), 6.99 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7N_5O_2$: C, 39.78; H, 3.89; N, 38.66. Found: C, 40.03; H, 3.79; N, 38.52.

10c: 90% yield, mp 93—94 °C, pale yellow needles (from IPE). IR (KBr): 2120 (N_3) cm^{-1}. ^{1}H-NMR δ: 4.05 and 4.06 (each 3H, s, 3- and 6-OMe), 7.03 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7H_5O_3$: C, 36.55; H, 3.58; N, 35.52. Found: C, 36.72; H, 3.61; N, 35.39.

10d: 90% yield, mp 125—126 °C (lit.[23] mp 123—124 °C).

10e: 81% yield, mp 139—140 °C, pale yellow needles (from hexane–CH_2Cl_2). IR (KBr): 2132 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.48 (3H, s, 6-Me), 7.20 (1H, d, 5-H), 8.04 (1H, d, 3-H), $J_{3,5}=3$ Hz, *Anal.* Calcd for $C_5H_5N_5O$: C, 39.73; H, 3.33; N, 46.34. Found: C, 39.80; H, 3.25; N, 46.59.

10f: 82% yield, mp 143—144 °C, pale yellow needles (from hexane–CH_2Cl_2). IR (KBr): 2124 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.36 (3H, s, 3-Me), 2.48 (3H, s, 6-Me), 7.22 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7N_5O$: C, 43.63; H, 4.27; N, 42.41. Found: C, 43.88; H, 4.22; N, 42.12.

4-Azidopyridazines (11a—f) General Procedure: The procedure[23] for the preparation of **11d** was employed. Phosphorus trichloride (*ca.* 3 mol eq) was added dropwise with stirring to a solution of **10** (2—5 g) in $CHCl_3$ (50—150 ml) in an ice bath. The mixture was stirred for 4—8 h at room temperature and then poured into ice-water (50—100 ml). The aqueous mixture was made alkaline with $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with brine, dried, and evaporated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2 as an eluent to give **11** as colorless needles (from IPE).

11a: 73% yield, mp 70.5—71.5 °C. IR (KBr): 2136 (N_3) cm^{-1}. ^{1}H-NMR δ: 4.22 (3H, s, 3-OMe), 6.94 (1H, d, 5-H), 8.71 (1H, d, 6-H), $J_{5,6}=5$ Hz. *Anal.* Calcd for $C_5H_5N_5O$: C, 39.73; H, 3.33; N, 46.34. Found: C, 39.53;

H, 3.19; N, 46.10.

11b: 60% yield, mp *ca.* 20 °C. MS *m/z*: 165 (M^+). IR (KBr): 2124 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.53 (3H, s, 6-Me), 4.14 (3H, s, 3-OMe), 6.72 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7N_5O$: C, 43.63; H, 4.27; N, 42.41. Found: C, 43.69; H, 4.01; N, 42.16.

11c: 45% yield, mp 74—75 °C. IR (KBr): 2128 (N_3) cm^{-1}. ^{1}H-NMR δ: 3.97 (3H, s, 6-OMe), 4.07 (3H, s, 3-OMe), 6.41 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7N_5O_2$: C, 39.78; H, 3.89; N, 38.66. Found: C, 39.91; H, 3.82; N, 38.60.

11d: 70% yield, mp 63—65 °C (lit.[23]) mp 62—64 °C).

11e: 51% yield, mp *ca.* 15 °C. MS *m/z*: 135 (M^+). IR (neat): 2120 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.70 (3H, s, 6-Me), 6.93 (1H, d, 5-H), 8.68 (1H, d, 3-H), $J_{3,5}=3$ Hz. *Anal.* Calcd for $C_5H_5N_5$: C, 44.44; H, 3.73; N, 51.83. Found: C, 44.21; H, 3.92; N, 51.56.

11f: 69% yield, mp 86—87 °C. IR (KBr): 2128 (N_3) cm^{-1}. ^{1}H-NMR δ: 2.52 (3H, s, 3-Me), 2.64 (3H, s, 6-Me), 6.98 (1H, s, 5-H). *Anal.* Calcd for $C_6H_7N_5$: C, 48.31; H, 4.73; N, 46.96. Found: C, 48.20; H, 4.63; N, 46.67.

Photolysis of 11a—c in the Presence of Sodium Methoxide: Formation of the 4*H*-1,2,5-triazepines (13) *via* the 1*H*-isomers (12). i) In the Presence of a Large Excess of Sodium Methoxide General Procedure: A solution of **11** (*ca.* 0.5 g) in MeOH–dioxane (1 : 1, 150 ml) containing a large excess of NaOMe (*ca.* 10 mol eq) was irradiated with a 400 W high-pressure Hg lamp under a nitrogen atmosphere. The photolysis was followed in terms of the disappearance of the spot of the starting azide on thin-layer chromatography, and was complete in 60—90 min. After removal of the solvent *in vacuo*, ice-water (20—30 ml) was added to the residue and the aqueous mixture was extracted with benzene. The extract was washed with brine, dried, and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2 as an eluent to give the 6,7-dimethoxy-4*H*-1,2,5-triazepines (**13**).

13a: 52% yield, pale yellow viscous oil. MS *m/z*: 155 (M^+). IR (neat): 1666 and 1646 (C=N) cm^{-1}. ^{1}H-NMR δ: 3.72 (2H, br d, 4-H_2), 3.72 and 3.92 (each 3H, s, 6- and 7-OMe), 7.50 (1H, t, 3-H), $J_{3,4}=5$ Hz. ^{13}C-NMR δ: 43.7 (t, 4-C), 54.0 (q), 54.3 (q), 151.3 (d, 3-C), 152.4 (s), 154.5 (s). *Anal.* Calcd for $C_6H_9N_3O_2$: C, 46.44; H, 5.85; N, 27.08. Found: C, 46.60; H, 5.83; N, 26.81.

13b: 60% yield, mp *ca.* 15 °C, colorless prisms (from IPE–hexane). MS *m/z*: 169 (M^+). IR (neat): 1646 (C=N) cm^{-1}. ^{1}H-NMR δ: 2.21 (3H, s, 3-Me), 3.72 (2H, s, 4-H_2), 3.72 and 3.90 (each 3H, s, 6- and 7-OMe). ^{13}C-NMR δ: 23.5 (q), 47.7 (t, 4-C), 53.9 (q), 54.1 (q), 152.2 (s), 155.0 (s), 160.2 (s). *Anal.* Calcd for $C_7H_{11}N_3O_2$: C, 49.69; H, 6.55; N, 24.84. Found: C, 49.58; H, 6.56; N, 24.66.

13c: 60% yield, mp 66—68 °C, colorless prisms (from IPE–hexane). MS *m/z*: 185 (M^+). IR (KBr): 1654 (C=N) cm^{-1}. ^{1}H-NMR δ: 3.84 (2H, s, 4-H_2), 3.76, 3.82, and 3.94 (each 3H, s, 3-, 6-, and 7-OMe). ^{13}C-NMR δ: 46.2 (t, 4-C), 54.1 (q), 54.4 (q), 55.2 (q), 153.4 (s), 155.7 (s), 160.7 (s). *Anal.* Calcd for $C_7H_{11}N_3O_3$: C, 45.40; H, 5.99; N, 22.69. Found: C, 45.36; H, 6.08; N, 22.50.

ii) In the Presence of Equimolecular Amounts of Sodium Methoxide The azides (**11a—c**: 0.4—0.5 g) were irradiated in the presence of NaOMe (*ca.* 1.1 mol eq) and worked up as described for i). In the cases of **11a** and **11b**, the ^{1}H-NMR spectrum of the residue obtained from the extract showed that the product was a mixture of **12** and **13** (4 : 1 for **a**; 2 : 1 for **b**), but the residue obtained from **11c** contained only **13c**. The 1*H*-isomers (**12a, b**) were unstable and readily decomposed during isolation by chromatography, and therefore were characterized only by the following ^{1}H-NMR spectral data. **12a**: δ 3.68 (3H, s, OMe), 3.80 (3H, s, OMe), 5.15 (1H, br, NH), 5.80 (1H, d, 7-H), 5.97 (1H, d, 6-H), $J_{6,7}=6$ Hz. **12b**: δ 1.84 (3H, s, 7-Me), 3.72 (3H, s, OMe), 3.80 (3H, s, OMe), 5.2 (1H, br, NH), 6.36 (1H, s, 6-H). The residue was chromatographed on alumina or silica gel to give only the 4*H*-isomer **13** in a low yield (**13a**: 15%; **13b**: 27%; **13c**: 37%). However, the residue was dissolved in MeOH containing a large excess of NaOMe and the solution was stirred for 3—5 h at room temperature, and then poured into ice-water. The aqueous mixture was extracted with benzene. The extract was washed, dried, and evaporated *in vacuo*. The residue showed no signals due to **12** in the ^{1}H-NMR spectrum was chromatographed on alumina to give **13** in a higher yield (**13a**: 45%; **13b**: 51%; **13c**: 47%).

1-Acetyl-1*H*-1,2,5-triazepines (14a, b) The azides (**11a,b**: *ca.* 0.5 g) were photolysed in the presence of NaOMe (*ca.* 1 mol eq) and worked up as described for the photolysis of **11a—c** (ii). The residue, containing a mixture of **12** and **13** was dissolved in pyridine (3—4 ml). AcCl (0.4 g) was added to the ice-cold pyridine solution and the mixture was stirred for 5—6 h at room temperature, and then poured into ice-water (*ca.* 20 ml). The aqueous mixture was extracted with CH_2Cl_2 and the extract was successively washed with saturated $NaHCO_3$ and water, and then dried and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2–Et_2O (10 : 1) as an eluent to give **14**.

14a: 26% yield, mp 112–113 °C, pale yellow plates (from hexane). MS *m/z*: 197 (M^+). IR (KBr): 1684 (C=O) cm^{-1}. ^{1}H-NMR δ: 2.21 (3H, s, 1-COMe), 3.82 and 3.89 (each 3H, s, 3- and 4-OMe), 6.20 (1H, d, 6-H), 6.34 (1H, d, 7-H), $J_{6,7}=6$ Hz. ^{13}C-NMR δ: 21.1 (q), 54.1 (q), 55.9 (q), 120.9 (d), 128.4 (d), 157.2 (s), 158.0 (s), 172.3 (s). *Anal.* Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.68; H, 5.67; N, 21.35.

14b: 46% yield, mp 101.5—103.5 °C, pale yellow plates (from hexane). MS *m/z*: 211 (M^+). IR (KBr): 1678 (C=O) cm^{-1}. ^{1}H-NMR δ: 2.06 (3H, s, 7-Me), 2.12 (3H, s, 1-COMe), 3.80 and 3.90 (each 3H, s, 3- and 4-OMe), 6.32 (1H, s, 6-H). *Anal.* Calcd for $C_9H_{13}N_3O_3$: C, 51.17; H, 6.20; N, 19.90. Found: C, 51.40; H, 6.05; N, 19.86.

Photolysis of 11d—f The azides (**11d—f**: 0.3—0.5 g) were photolysed in the presence of a large excess of NaOMe and worked up as described for **11a—c** to give 4-methoxypyridazines (**15**) and no triazepines.

15d: 8% yield, mp 42—44 °C (lit.[24]) mp 43—44 °C).

15e: 16% yield, viscous oil. MS *m/z*: 124 (M^+). ^{1}H-NMR δ: 2.64 (3H, s, 6-Me), 3.89 (3H, s, 4-OMe), 6.74 (1H, d, 5-H), 8.73 (1H, d, 3-H), $J_{3,5}=3$ Hz. *Anal.* Calcd for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 57.89; H, 6.54; N, 22.31.

15f: 8% yield, mp 73—75 °C, colorless needles (from IPE). MS *m/z*: 138 (M^+). ^{1}H-NMR δ: 2.50 and 2.60 (each 3H, s, 3-and 6-Me), 3.87 (3H, s, 4-OMe), 6.63 (1H, s, 5-H). *Anal.* Calcd for $C_7H_{10}N_2O$: C, 60.85; H, 7.30; N, 20.28. Found: C, 60.83; H, 7.46; N, 20.01.

$LiAlH_4$ Reduction of 13a, b $LiAlH_4$ (2—3 mol eq) was added in small portions to a solution of **13** (0.1—0.2 g) in dry Et_2O (10 ml) with stirring in an ice bath. The mixture was stirred for a further 1 h at room temperature. After addition of saturated NaCl (0.5 ml) to decomposed excess reagent, the reaction mixture was dried over $MgSO_4$ and filtered. The filtrate was evaporated and the residue was chromatographed on alumina using CH_2Cl_2–benzene (1 : 1) as an eluent to give the 6,7-dihydro-1*H*-1,2,5-triazepines (**21**).

21a: 87% yield, mp 73—74 °C, colorless needles (from hexane). MS *m/z*: 157 (M^+). IR (KBr): 3352 (NH), 1676 (C=N) cm^{-1}. ^{1}H-NMR δ: 3.32 (2H, t, 7-H_2), 3.68 and 3.72 (each 3H, s, 3- and 4-OMe), 3.80 (2H, t, 6-H_2), 5.36 (1H, br, 1-NH), $J_{6,7}=5$ Hz. ^{13}C-NMR δ: 50.2 (t, 7-C), 51.7 (t, 6-C), 53.3 (q), 54.0 (q), 143.2 (s), 151.1 (s). *Anal.* Calcd for $C_6H_{11}N_3O_2$: C, 45.85; H, 7.05; N, 26.74. Found: C, 45.83; H, 7.11; N, 26.52.

21b: 51% yield, colorless viscous oil. MS *m/z*: 171 (M^+). IR (neat): 3360 (NH), 1666 (C=N) cm^{-1}. ^{1}H-NMR δ: 1.20 (3H, d, 7-Me), 3.2—3.4 (1H, m, 7-H), 3.68 and 3.72 (each 3H, s, 3- and 4-OMe), 3.70 (2H, d, 6-H_2), 4.90 (1H, br, 1-NH), $J_{6,7}=5$, $J_{7,7\text{-Me}}=6$ Hz. ^{13}C-NMR δ: 18.2 (q), 53.2 (q), 54.0 (q), 55.9 (t, 6-C), 57.1 (d, 7-C), 143.9 (s), 151.3 (s). *Anal.* Calcd for $C_7H_{13}N_3O_2$: C, 49.11; H, 7.65; N, 24.55. Found: C, 49.01; H, 7.69; N, 24.31.

Acetylation of 21a with Acetyl Chloride AcCl (75 mg, 1.3 mol eq) was added dropwise to a solution of **21a** (100 mg) in pyridine (2 ml) with stirring in an ice bath. The mixture was stirred for a further 5 h at 0—5 °C and then ice-water (*ca.* 20 ml) was added. The aqueous mixture was extracted with CH_2Cl_2 and the extract was successively washed with saturated $NaHCO_3$ and brine, and then dried and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2 as an eluent to give 1-acetyl-3,4-dimethoxy-6,7-dihydro-1*H*-1,2,5-triazepine (**22**): 54 mg, 41% yield, mp 64—65 °C, colorless needles (from IPE–CH_2Cl_2). MS *m/z*: 199 (M^+). IR (KBr): 1680 (C=O) cm^{-1}. ^{1}H-NMR δ: 2.28 (3H, s, 1-COMe), 3.77 and 3.80 (each 3H, s, 3- and 4-OMe), 3.80 and 4.05 (each 2H, t, 6- and 7-H_2), $J_{6,7}=4$ Hz. *Anal.* Calcd for $C_8H_{13}N_3O_3$: C, 48.23; H, 6.58; N, 21.10. Found: C, 48.25; H, 6.86; N, 21.07.

Hydrogenation of 14a The 1-acetyl compound **14a** (65 mg) was hydrogenated over 5% Pd–C (100 mg) in MeOH (15 ml) under atmospheric pressure at room temperature for 3 h. The catalyst was filtered off and the filtrate was evaporated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–MeOH (10 : 1) as an eluent to give the dihydro compound (48 mg, 73% yield), which was identical with **22** obtained from **21a** by acetylation.

Thermolysis of 14a A solution of **14a** (33 mg) in *o*-dichlorobenzene (0.5 ml) was heated at 190—200 °C in a sealed NMR tube until the ^{1}H-NMR signals due to starting **14a** disappeared (for 65 h). After cooling, the solution was chromatographed on silica gel using CH_2Cl_2–Et_2O (5 : 1) as an eluent to give 6-acetylamino-2,3-dimethoxypyrazine (**24**): 25 mg, 76% yield, mp 184—185 °C, colorless needles (from hexane–CH_2Cl_2). MS *m/z*: 197 (M^+). IR (KBr): 3260 (NH), 1652 (C=O) cm^{-1}. ^{1}H-NMR δ: 2.24 (3H, s, COMe), 3.99 and 4.04 (each 3H, s, 2- and 3-OMe), 7.60 (1H, br, NH), 8.52 (1H, s, 3-H). ^{13}C-NMR δ: 24.2 (q), 54.0 (q), 54.2 (q), 121.5 (d), 138.0 (s), 146.9 (s), 148.3 (s), 167.9 (s). *Anal.* Calcd for $C_8H_{11}N_3O_3$: C. 48.72; H, 5.62; N, 21.31. Found: C, 48.70; H, 5.68; N, 21.19.

Photolysis of 14a A solution of **14a** (350 mg) in benzene (130 ml) was irradiated for 4.5 h and then evaporated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2 as an eluent to give 1-acetyl-3,4-dimethoxypyrazole (**26**): 212 mg, 71% yield, mp 96—97 °C, colorless plates (from hexane). MS *m/z*: 170 (M^+). IR (KBr): 1706 (C=O) cm^{-1}. ^{1}H-NMR δ: 2.50 (3H, s, COMe), 3.79 and 3.84 (each 3H, s, 3- and 4-OMe), 7.60 (1H, s, 5-H). ^{13}C-NMR δ: 20.5 (q), 56.5 (q), 59.0 (q), 110.1 (d), 138.2 (s), 156.8 (s), 168.5 (s). *Anal.* Calcd for $C_7H_{10}N_2O_3$: C, 49.40; H, 5.92; N, 16.46. Found: C, 49.48; H, 5.79; N, 16.43.

Photolysis of 11a, b in the Presence of Diethylamine A solution of **11** (*ca.* 0.5 g) in Et_2NH–dioxane (1 : 1, 150 ml) was irradiated for 70—80 min and then evaporated *in vacuo*. The ^{1}H-NMR spectrum of the residue showed that the residue contained the 1*H*-1,2,5-triazepine (**27**) and the 3*H*-isomer (**28**) in a ratio of 3—5 : 1. However, the residue was chromatographed on alumina using CH_2Cl_2–Et_2O (1 : 1) as an eluent to give only **28** in a low yield (5—10%), indicating that the 1*H*-isomers (**27**) are too unstable to be isolated. Therefore, they were characterized only by the following ^{1}H-NMR spectral data. **27a**: δ 1.12 and 3.1—3.4 (6H, t, and 4H, m, 4-NEt$_2$), 3.60 (3H, s, 3-OMe), 4.88 (1H, br, 1-NH), 5.76 (1H, d, 7-H), 6.10 (1H, d, 6-H), $J_{6,7}=6$ Hz. **27b**: δ 1.08 and 3.0—3.4 (6H, t, and 4H, m, 4-NEt$_2$), 1.84 (3H, s, 7-Me), 4.04 (3H, s, 3-OMe), 4.9 (1H, br, NH), 6.52 (1H, s, 6-H).

The above residue was dissolved in MeOH (10 ml) containing NaOMe (*ca.* 0.5 g) and the solution was stirred for 10 h at room temperature, and then evaporated *in vacuo*. Ice-water (5—10 ml) was added to the residue and the aqueous mixture was extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2–Et_2O (1 : 1) as an eluent to give the 4*H*-1,2,5-triazepines (**28**) as colorless viscous oils.

28a: 36% yield. MS *m/z*: 196 (M^+). IR (neat): 1634 (C=N) cm^{-1}. ^{1}H-NMR δ: 1.04 and 2.95—3.35 (6H, t, and 4H, m, 6-NEt$_2$), 3.80 (3H, s, 7-OMe), 3.8 (2H, br d, 4-H$_2$), 7.40 (1H, t, 3-H), $J_{3,4}=6$ Hz. ^{13}C-NMR δ: 13.1 (q, 2×C), 42.8 (t, 2×C), 44.9 (t, 4-C), 53.5 (q), 152.4 (s), 154.9 (d, 3-C), 155.7 (s). *Anal.* Calcd for $C_9H_{16}N_4O$: C, 55.08; H, 8.22; N, 28.55. Found: C, 54.87; H, 8.23; N, 28.32.

28b: 41% yield. MS *m/z*: 210 (M^+). IR (neat): 1630 (C=N) cm^{-1}. ^{1}H-NMR δ: 1.08 and 3.0—3.4 (6H, t, and 4H, m, 6-NEt$_2$), 2.16 (3H, s, 3-Me), 3.5 (2H, br, 4-H$_2$), 3.98 (3H, s, 7-OMe). *Anal.* Calcd for $C_{10}H_{18}N_4O$: C, 57.11; H, 8.63; N, 26.65. Found: C, 56.98; H, 8.61; N, 26.40.

1-Acetyl-4-diethylamino-3-methoxy-1*H*-1,2,5-triazepines (29) A mixture of the residue obtained by the photolysis of **11a** (0.5 g) in the presence of Et_2NH, acetyl chloride (0.3 g), and pyridine (5 ml) was stirred for 10 h at room temperature, and then ice-water (10 ml) was added to the mixture. The aqueous mixture was extracted with CH_2Cl_2 and the extract was washed with water, dried, and evaporated *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2–Et_2O (1 : 1) as an eluent to give **29**: 46% yield, mp 60—61 °C, yellow plates (from hexane). MS *m/z*: 238 (M^+). IR (KBr): 1680 (C=O) cm^{-1}. ^{1}H-NMR δ: 1.16 and 3.32 (6H, t, and 4H, q, 4-NEt$_2$), 2.16 (3H, s, 1-COMe), 3.87 (3H, s, 3-OMe), 6.03 (1H, d, 6-H), 6.50 (1H, d, 7-H), $J_{6,7}=6$ Hz. *Anal.* Calcd for $C_{11}H_{18}N_4O_2$: C, 55.44; H, 7.61; N, 23.52. Found: C, 55.58; H, 7.41; N, 23.49.

1-Acetyl-4-diethylamino-3-methoxy-6,7-dihydro-1*H*-1,2,5-triazepine (30) Compound **29** (100 mg) was hydrogenated over 5% Pd–C and worked up as described for the hydrogenation of **14** to give **30**: 80 mg, 79% yield, mp 51.5—53 °C, colorless needles (from IPE). MS *m/z*: 240 (M^+). IR (KBr): 1660 (C=O) cm^{-1}. ^{1}H-NMR δ: 1.14 (6H, t, NEt$_2$-Me$_2$), 3.1—3.5 [6H, m, NEt$_2$-(CH$_2$)$_2$ and 7-H$_2$], 2.08 (3H, s, 1-COMe), 3.84 (2H, t, 6-H$_2$), 3.96 (3H, s, 2-OMe). ^{13}C-NMR δ: 13.2 (q, 2×C), 21.8 (q), 42.1 (t, 2×C), 45.5 (t, 7-C), 51.1 (t, 6-C), 54.7 (q), 155.1 (s), 160.4 (s), 171.9 (s). *Anal.* Calcd for $C_{11}H_{20}N_4O_2$: C, 54.98; H, 8.39; N, 23.32. Found: C, 55.07; H, 8.36; N, 23.37.

Thermolysis of 29 A solution of **29** (130 mg) in *o*-dichlorobenzene was heated at 190—200 °C and worked up as described for the thermolysis of **14a** to give 6-acetylamino-3-diethylamino-2-methoxypyrazine (**31**): 80 mg, 62% yield, mp 121—122 °C, colorless needles (from hexane). MS *m/z*: 238 (M^+). IR (KBr): 3152 (NH), 1706 (C=O) cm^{-1}. ^{1}H-NMR δ: 1.12 and 3.46 (6H, t, and 4H, q, 3-NEt$_2$), 2.20 (3H, s, COMe), 3.92 (3H, s, 2-OMe). 7.50 (1H, br, NH), 8.54 (1H, s, 5-H). *Anal.* Calcd for $C_{11}H_{18}N_4O_2$: C, 55.44; H, 7.61; N, 23.52. Found: C, 55.63; H, 7.54; N, 23.48.

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