

Synthesis of 1,3-diazepines and ring contraction to cyanopyrroles†‡

Ales Reisinger, Paul V. Bernhardt and Curt Wentrup*

Department of Chemistry, School of Molecular and Microbial Sciences,
The University of Queensland, Brisbane, Qld 4072, Australia. E-mail: wentrup@uq.edu.au

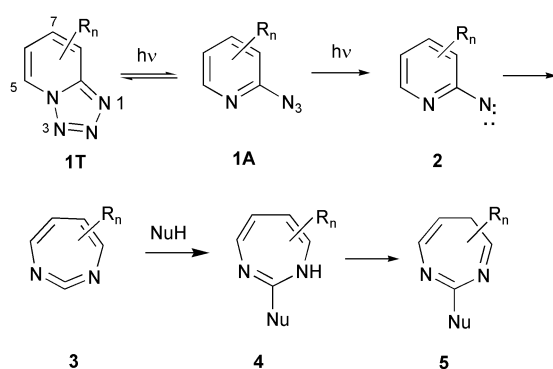
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Several tetrazolo[1,5-*a*]pyridines/2-azidopyridines undergo photochemical nitrogen elimination and ring expansion to 1,3-diazacyclohepta-1,2,4,6-tetraenes (**7**, **10**, **13**, **16**, **19**, **22**) as well as ring cleavage to cyanovinylketenimines (**8**, **17**, **20b**) in low temperature Ar matrices. 6,8-Dichlorotetrazolo[1,5-*a*]pyridine/2-azido-3,5-dichloropyridine **6** undergoes ready exchange of the chlorine in position 8 (**3**) with ROH/RONa. 8-Chloro-6-trifluoromethyltetrazolo[1,5-*a*]pyridine **15** undergoes solvolysis of the CF₃ group to afford 8-chloro-6-methoxycarbonyltetrazolo[1,5-*a*]pyridine **18**. Several tetrazolopyridines/2-azidopyridines afford 1*H*- or 5*H*-1,3-diazepines in good yields on photolysis in the presence of alcohols or amines (**11**, **14**, **23**, **25**). 5-Chlorotetrazolo[1,5-*a*]pyridines/2-azido-6-chloropyridines **21** and **38** undergo a rearrangement to 1*H*- and 3*H*-3-cyanopyrroles **27** and **45**, respectively. The mechanism of this rearrangement was investigated by ¹⁵N-labelling and takes place *via* transient 1,3-diazepines. The structures of 6,8-dichloro-tetrazolo[1,5-*a*]pyridine **6T**, 6-chloro-8-ethoxytetrazolo[1,5-*a*]pyridine **9Tb**, dipyrrolylmethane **28**, and 2-isopropoxy-4-dimethylamino-5*H*-1,3-diazepine **25b** were determined by X-ray crystallography. In the latter case, this represents the first reported X-ray crystal structure of a 5*H*-1,3-diazepine.

Introduction

The photolysis of variously substituted tetrazolo[1,5-*a*]pyridines/2-azidopyridines **1** is a convenient method of synthesis of 1,3-diazepines.^{1,2} The reaction proceeds *via* ring expansion of the first-formed 2-pyridylnitrenes **2** to 1,3-diazacyclohepta-1,2,4,6-tetraenes **3** (Scheme 1), which in several cases have been characterized by matrix-isolation IR spectroscopy.^{3,4} In the presence of a nucleophile, **3** affords the 1*H*- or 5*H*-diazepines **4** and **5** depending on substituents. For Nu = OR the 1*H*-diazepines **4** are invariably formed, and they are calculated to be the most stable, but for Nu = NR₂, the 5*H*-tautomers **5** are more stable.¹ Here we report synthetically useful variants based on chlorotetrazolopyridines as well as the unexpected ring contraction of 1,3-diazepines to pyrroles.



Scheme 1

Results and discussion

Tetrazolo[1,5-*a*]pyridines/2-azidopyridines were prepared from the 2-chloropyridines by exchange of the chlorine with

hydrazine followed by diazotization, or in the case of 6,8-dichlorotetrazolo[1,5-*a*]pyridine **6T** by direct nucleophilic substitution with azide ion. In most cases examined here, the compounds can exist as a tetrazole (**T**) or an azide (**A**). The tetrazole form is usually favoured in the solid state, but equilibria exist in solution (see Experimental section for details). Sublimation of **6T** at 67 °C with matrix deposition of the material in Ar at 12 K affords the azide **6A** (Scheme 2), characterized by a strong absorption at 2141 cm⁻¹. Photolysis of this matrix for 1 min resulted in rapid bleaching of the azide and the appearance of a new, strong absorption at 1984 cm⁻¹, a value typical of seven-membered ring carbodiimides.³ Accordingly, this spectrum is assigned to the carbodiimide **7**. Further photolysis for 1 h caused slower formation of an additional compound absorbing at 3300, strongly at 2029, and weakly at 2220 cm⁻¹, suggesting that ring opening to the ketenimine **8** took place. We have examined such ring opening reactions in several other cases, including cyanopyridylnitrenes,⁵ 1-isoquinolyl-nitrene,⁶ and the unsubstituted 2-pyridylnitrene.⁷ The details of the ring opening reactions of **6**, and those of **15** and **18** mentioned below, are the subjects of ongoing research.⁸ It is noteworthy that 2-pyridylnitrenes carrying electronegative atoms or groups in positions 3 and 5 appear to be particularly prone to ring opening to ketenimines.

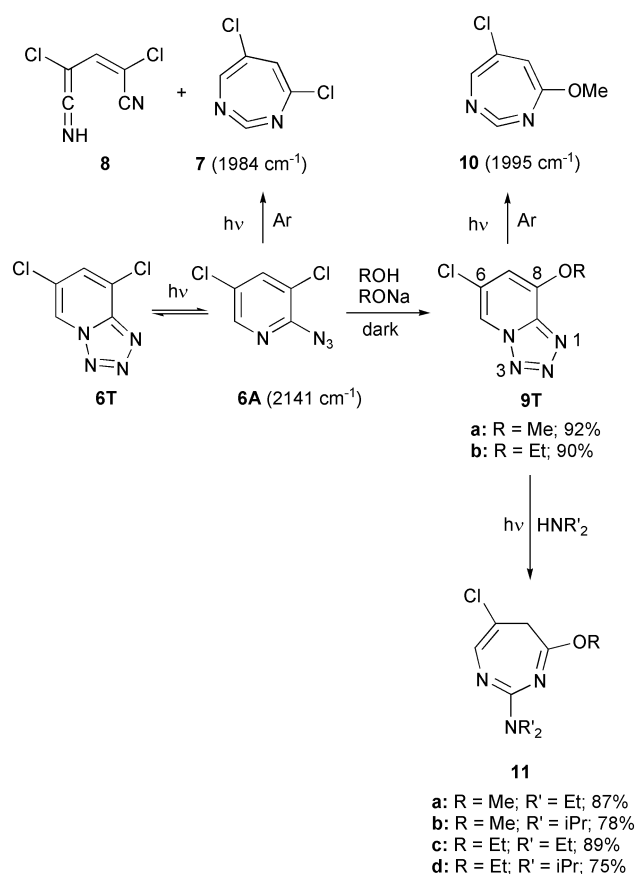
Compound **6** allows the synthesis of several trisubstituted diazepines **11** (75–90 % yield) because the chlorine atom in position 8 in **6** is readily replaced by alkoxy groups in a quantitative dark reaction with sodium alkoxide in alcohol, yielding the new tetrazoles **9**. The photolysis of **9T** (the azide **9A** was not observed) in an Ar matrix at *ca.* 10 K gave rise to a strong absorption at 1995 cm⁻¹, ascribed to the carbodiimide **10**.

The X-ray crystal structures of the new tetrazoles **6T** and **9Tb** are shown in Figs. S3 and S5. In the dichloro compound **6T**, a single molecule on a general site constitutes the asymmetric unit. The aromatic rings are staggered (Fig. S4). The chlorine atom in position 8 is situated above the centre of the five-membered ring of an adjacent, centrosymmetrically related

† Diazepines. Part 2. For Part 1 see ref. 1.

‡ Electronic supplementary information (ESI) available: drawings of the crystal structures of compounds **6T** and **9Tb** (ORTEP); bond lengths and angles for compounds **6T**, **9Tb**, **25b** and **28**, and ¹⁵N NMR spectra of **21**, **30**, **27** and **37**. See <http://www.rsc.org/suppdata/ob/b311247k/>

§ CCDC reference numbers **6T** (222023); **9Tb**, **25b** and **28**: 218060–218062. See <http://www.rsc.org/suppdata/ob/b311247k/> for crystallographic data in .cif or other electronic format.



Scheme 2

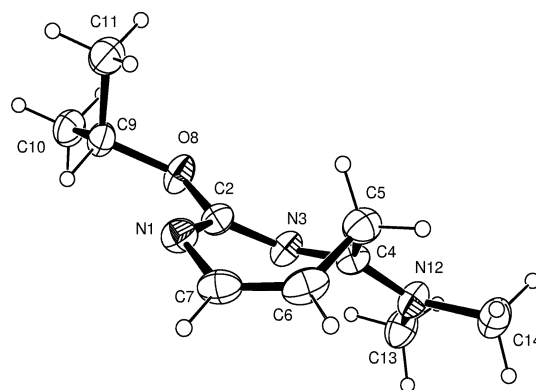
molecule. Compound **9Tb** crystallizes as a π -stacked pair of crystallographically unique molecules (Fig. S6), with some of the intermolecular distances being $\text{N1} \cdots \text{O1}'$ (3.301(4) Å), $\text{N2} \cdots \text{C8}'$ (3.307(5) Å), $\text{N3} \cdots \text{C8a}'$ (3.266(5) Å) and $\text{N4} \cdots \text{N1}'$ (3.280(4) Å). The corresponding bond lengths and angles in the two independent molecules of **9Tb** are similar, so for brevity only bond lengths involving unprimed atoms are mentioned in comparison with **6T**. In the crystal structures of **6T** and **9Tb** the corresponding N–N bond lengths are: N2–N3 (1.295(3) Å for **6T** and 1.309(4) Å for **9Tb**) by comparison with N1–N2 (1.357(3) Å for **6T** and 1.342(4) Å for **9Tb**) and N3–N4 (1.374(3) Å for **6T** and 1.364(4) Å for **9Tb**). Similarly, an unsymmetrical bonding pattern is seen in the six-membered ring, with C5–C6 (1.346(3) Å for **6T** and 1.347(5) Å for **9Tb**) and C7–C8 (1.349(3) Å for **6T** and 1.359(4) Å for **9Tb**) being significantly shorter than C6–C7 (1.426(3) Å for **6T** and 1.406(5) Å for **9Tb**) and C8–C8a (1.408(3) Å for **6T** and 1.416(5) Å for **9Tb**). The two C–N bond lengths within the six-membered ring are essentially the same: N4–C8a (1.357(3) Å for **6T** and 1.351(4) Å for **9Tb**) and N4–C5 (1.365(3) Å for **6T** and 1.374(4) Å for **9Tb**). Evidently substitution of chloro by an ethoxy group in the 8 position has no significant influence on the bond lengths within the bicyclic ring system. The only related published structure is that of 5,7-diphenyl-8-cyano-tetrazolo[1,5-*a*]pyridine,⁹ where a similar bonding pattern was seen.

Compared to the chlorine atom in position 8 in tetrazole/azide **6**, the chlorine atom in position 6 is far less reactive. In agreement with this, the 6-chloro-8-trifluoromethyl analog **12** did not undergo an exchange reaction of the chlorine with NaOMe/MeOH, but on photolysis in alcohols it afforded the diazepine **14**, which can exist in two tautomeric forms, **14** and **14'** (Scheme 3). The ^1H and ^{13}C NMR spectra demonstrated that the equilibrium lies predominantly on the side of **14**. The deposition of **12T** in an Ar matrix afforded the azide **12A** (2146 cm^{-1} ; Ar, 7 K). Photolysis of this material at 7 K afforded the carbodiimide **13**, absorbing strongly at 1991 cm^{-1} .

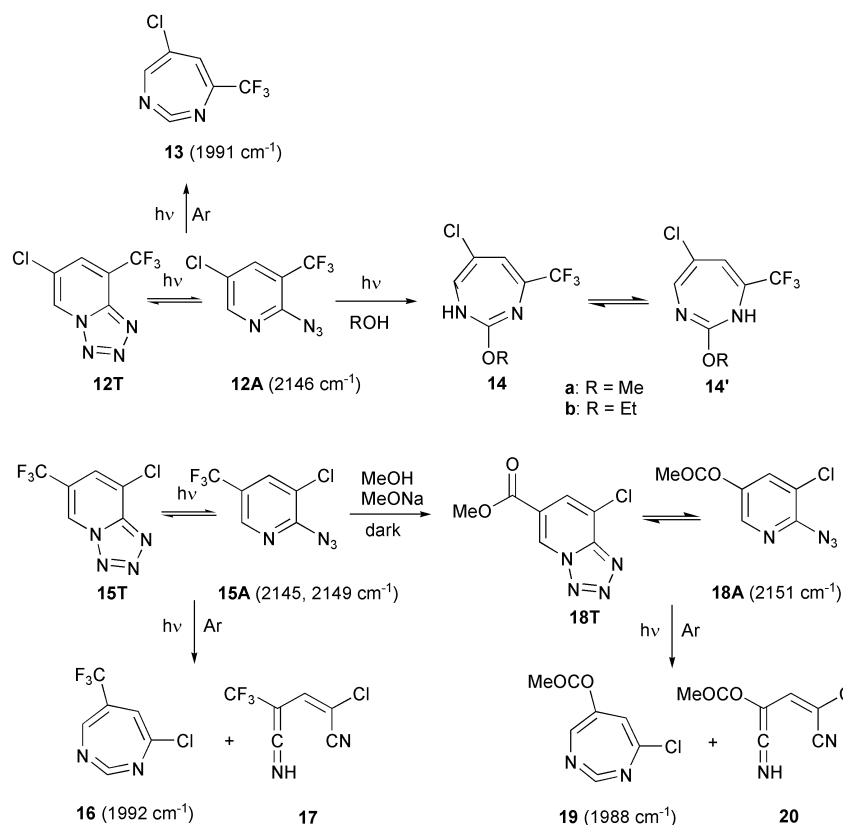
The 6-trifluoromethyl-8-chloro analog **15T** analogously afforded the azide **15A** (2145, 2149 cm^{-1} ; Ar, 7 K), and photolysis of this azide gave rise to a medium-strength absorption at 1992 cm^{-1} , ascribed to carbodiimide **16**. In addition, a relatively strong absorption appeared at 2060 cm^{-1} . This is probably due to ring opening of the pyridylnitrene to ketenimine **17**.⁹ Weak peaks assignable to cyano groups were present at 2220 cm^{-1} , as well as a medium band assigned to NH at 3343 cm^{-1} . Surprisingly, however, compound **15T** did not exchange the chlorine atom on reaction with NaOMe/MeOH in the dark at room temperature. Instead, the trifluoromethyl group solvolysed, presumably *via* the orthoester, to the 6-methoxycarbonyl derivative **18**. Matrix deposition of **18** afforded the azide **18A**, and photolysis afforded the carbodiimide **19** (1988, 1729 cm^{-1}) as well as the ring-opened ketenimine **20** (3355, 2052, 1737 cm^{-1}).⁹ Compound **15** did not give tractable diazepines on photolysis in alcohols in the absence of alkali alkoxides. Neither **12** nor **15** gave tractable diazepines on photolysis in the presence of amines.

The 6-chloro derivative **21** exists as the tetrazole **21T** in the solid state, but a mixture of azide and tetrazole exists in chloroform solution. Heating a KBr pellet containing **21T** to 60–70 °C for 1 min caused complete conversion to the azide **21A**. Deposition of **21** in an Ar matrix also gave rise to **21A**, which photolyzed to a cyclic carbodiimide **22** (1989 cm^{-1} ; Ar, 7 K) (Scheme 4). The chlorine atom in position 5 of compound **21** is readily replaced in photolysis reactions in solution. Thus, photolysis in excess pyrrolidine afforded the disubstituted diazepine **23** as the only isolated product in 33% yield. Photolysis of **21** in the presence of ethanol or methanol followed by addition of a secondary amine *after* the light source had been switched off afforded the 2-alkoxy-4-amino-1,3-diazepines **25** in 52–92% yield, thereby revealing that the chlorine atom must be substituted in the dark at the level of the 2-alkoxy-4-chloro-1,3-diazepine **24** in one of its tautomeric forms. A possible path involving the 4*H*-tautomer **24'**, which is related to **24** by a 1,5-sigmatropic shift, is shown in Scheme 5, but other tautomers of **24** could also be involved.

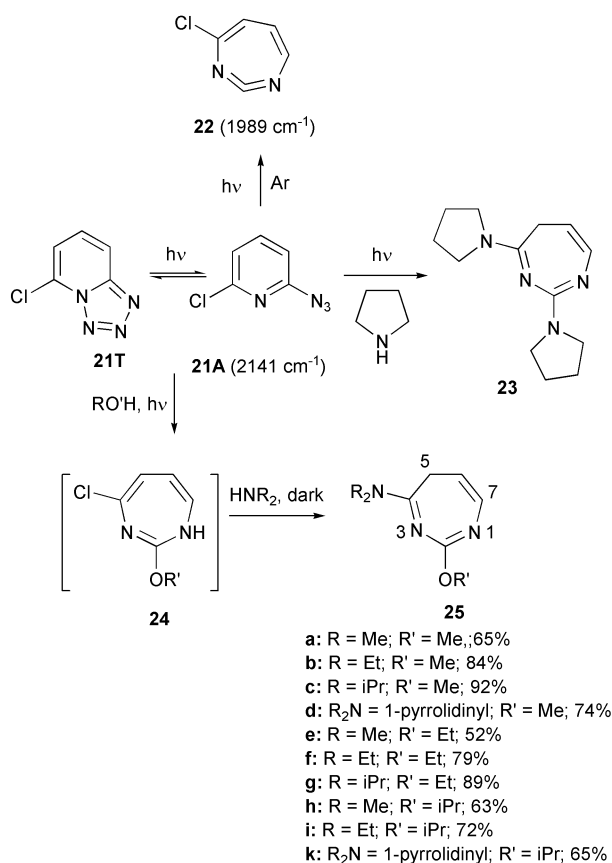
The structure of **25h** was established by X-ray crystallography (Fig. 1).§ The ring has a slightly twisted boat structure. Double bond character is clearly defined for C2–N1 (1.289(2) Å), C4–N3 (1.308(2) Å) and C6–C7 (1.325(3) Å), whereas bonds C2–N3 (1.361(2) Å), C2–O8 (1.359(2) Å) and C4–N12 (1.340(2) Å) fall between typical single and double bonds. There have been no previously published structures of 5*H*-1,3-diazepines. The closest analogue is a tricyclic 3,4-dihydro-1,3-diazepine derivative.¹⁰ Structures of a few 1*H*-1,3-diazepines have been published.^{2,11}

Fig. 1 ORTEP drawing of 5*H*-diazepine **25h**.

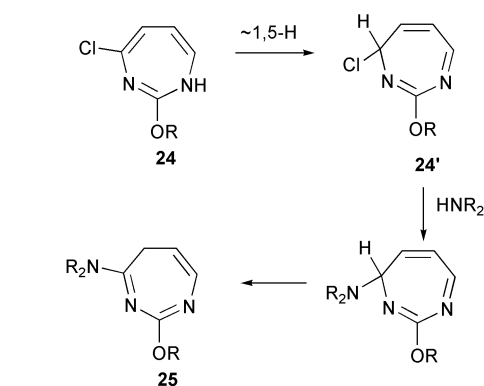
The photolysis of **21** in the presence of diisopropylamine did not afford the expected diazepine **26** (Scheme 6). Instead, a white crystalline material was obtained, the ^1H and ^{13}C NMR data of which indicated that it was either 3-cyano-2-(diisopropylamino)pyrrole **27** or the 2,5-isomer. Derivatization by



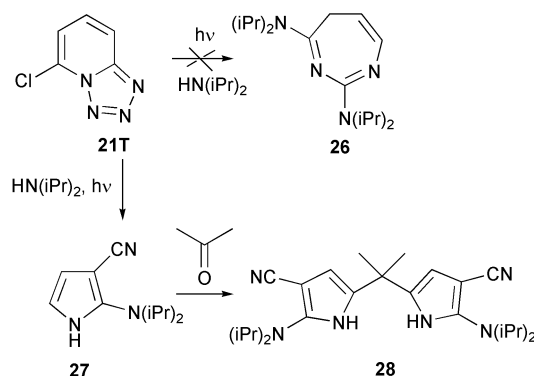
Scheme 3



Scheme 4



Scheme 5



Scheme 6

rapid reaction with acetone afforded the condensation product **28**, whose structure was determined by X-ray crystallography, thereby proving that **27** was the 2,3-disubstituted pyrrole.

The structure of the dipyrlymethane **28** is shown in Fig. 2. Disorder was resolved in three of the four isopropyl groups,

and only one of the many possible conformers is shown. The bond lengths and angles are as expected for a pyrrole derivative. The most closely related structure in the literature is that of the corresponding acetone derivative of ethyl 3,4-dimethylpyrrole-2-carboxylate.¹²

The mechanism of formation of **27** was established in a ¹⁵N-labelling experiment. The doubly labelled hydrazine **29** was

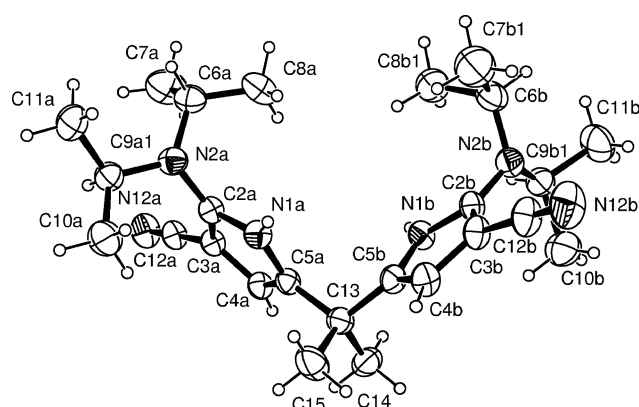
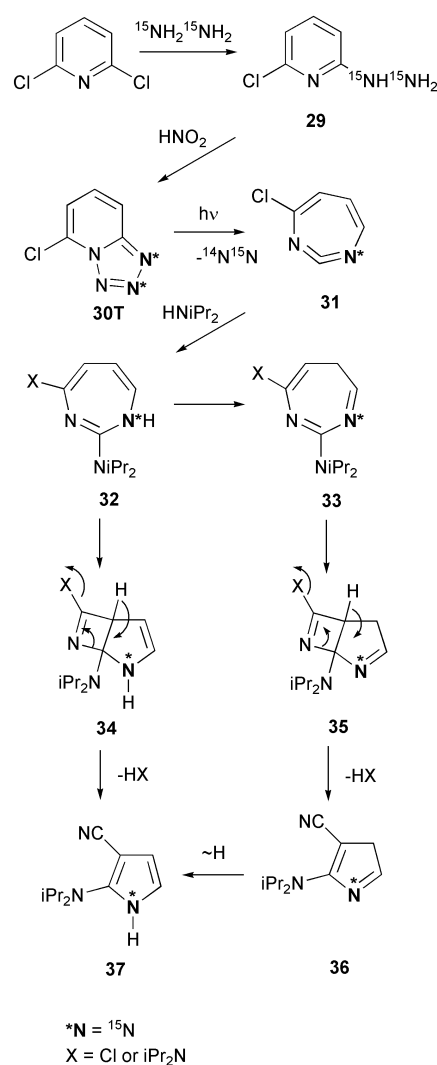


Fig. 2 ORTEP drawing of bispyrrolylmethane **28**.

prepared from 2,6-dichloropyridine and $^{15}\text{N}_2$ -hydrazinium sulfate (96.2% $^{15}\text{N}_2$, diluted with unlabelled material to afford 48.1% $^{15}\text{N}_2$). Diazotization afforded the crystalline $^{15}\text{N}_1^{15}\text{N}_2$ -tetrazole **30T**. In chloroform solution this compound exists largely in the azide form **30A**. In the ^{15}N NMR spectrum of this compound in CDCl_3 solution, the two labelled nitrogen atoms appeared at -260 and -125 ppm referenced to nitromethane. The other two N atoms, N_3 and N_4 were not labelled; they appear at -127 and -85 ppm, respectively, in the natural abundance ^{15}N NMR spectrum of **21A**. Photolysis of **30T/30A** in excess diisopropylamine afforded the labelled 3-cyano-2-(diisopropylamino)pyrrole **37**, which was labelled on the pyrrole-nitrogen only (-198 ppm). This signal remained positive in the DEPT90 spectrum, thereby identifying it as the NH signal. In the natural abundance ^{15}N NMR spectrum of the unlabelled pyrrole **27**, the pyrrole N appears at -198 ppm, the cyano group at -105 ppm, and the tertiary amine-N at -295 ppm.

Following our experience with other 2-amino-1,3-diazepines,¹ reaction of the diazacycloheptatetraene **31** should afford the *1H*-diazepine **32** initially, but, given time, it would be expected to tautomerize to the more stable *5H*-isomer **33** and to exchange the Cl for $\text{N}(\text{iPr})_2$. The labelling results require that either **32** or **33** undergoes a rearrangement to **37**. This can take place as indicated in Scheme 7: a 4π electrocyclicization (disrotatory photochemically) affords transient diazabicyclo[2,3,0]heptadienes **34** or **35**, which can undergo dehydrohalogenation ($\text{X} = \text{Cl}$) or dehydroamination ($\text{X} = \text{N}(\text{iPr})_2$) with ring opening to **36** and **37**. A photochemical cyclization of 1-substituted *1H*-azepines to 2-azabicyclo[2,3,0]heptadienes has been reported.¹³

The bis(trifluoromethyl)-6-chloro derivative **38** exists as the azide **38A** at room temperature (2153 cm^{-1} ; neat film). The compound behaves similarly to **21**. Photolysis in ethanol followed by addition of diisopropylamine in the dark afforded the diazepine **40**, presumably *via* the unobserved intermediate **39** (Scheme 8). Photolysis of **38A** in diisopropylamine afforded the *3H*-pyrrole **45**. In analogy with the mechanism presented in Scheme 7, it is suggested that the initial product is a habitual *1H*-diazepine **41**, which may tautomerise to a *5H*-diazepine **42**. Both of these diazepines can undergo a photochemical (or thermal) 4π electrocyclicization to **43** or **44**, which by elimination of HX ($\text{X} = \text{Cl}$ or $\text{N}(\text{iPr})_2$) will give rise to the isolated product **45**. The structure of **45** is supported by the mass spectrum, the IR spectrum (weak band at 2250 cm^{-1} for an unconjugated nitrile), and in particular by the ^1H and ^{13}C NMR spectra, which show hindered rotation of the congested diisopropyl group, so that the four CH_3 groups and the two CH groups appear as individual signals in the ^{13}C NMR spectrum at 19 – 21 and 50 – 54 ppm, respectively. The two methine CH groups also appear as individual, broad peaks with unresolved couplings at 3.7 and 4.4 in the ^1H NMR spectrum. The two CF_3 groups are characterized by the ^{19}F -couplings, giving rise to quartets around 120 ppm in the ^{13}C NMR spectrum. The quaternary



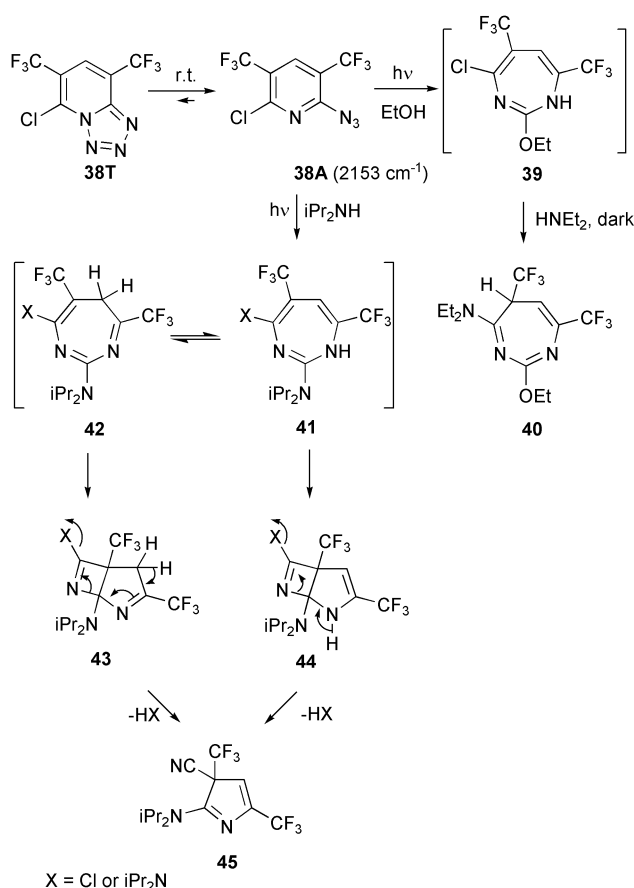
Scheme 7

carbons carrying the CF_3 groups show long range couplings to ^{19}F , causing narrow quartets at 153 (C5) and 57 (C3) ppm. The imine carbon C2 appears at 163 , the vinylic CH(4) at 104 , and the CN group at 110 ppm. The assignments are supported by a DEPT90 spectrum.

We have recorded hindered rotations of dialkylamino groups of the type described above in several 1,3-diazepine derivatives, *e.g.* in **25a–k**, where the free energies of rotation about the C–N bonds were measured by NMR methods as 15 – 16 kcal mol^{-1} .¹⁴ The free energies of activation for ring inversion of the diazepines (9.5 – 12 kcal mol^{-1}) and for the exchange of H between N1 and N3 in diazepines (15.8 – $16.5\text{ kcal mol}^{-1}$) have also been measured¹⁴ and will be the subjects of forthcoming publications.

Conclusion

Tetrazolo[1,5-*a*]pyridines/2-azidopyridines undergo photochemical nitrogen elimination and ring expansion to 1,3-diazacyclohepta-1,2,4,6-tetraenes as well as ring cleavage to cyano-vinylketenimines, both of which are characterized by their Ar matrix IR spectra. The 1,3-diazacyclohepta-1,2,4,6-tetraenes are in many cases trapped by nucleophiles in solution photolysis to afford *1H*- or *5H*-1,3-diazepines in good yields (**11**, **14**, **23**, **25**). 5-Chlorotetrazolo[1,5-*a*]pyridines/2-azido-6-chloropyridines **21** and **38** undergo a rearrangement to *1H*- and *3H*-3-cyanopyrroles **27** and **45**, respectively. The mechanism of this rearrangement was investigated by ^{15}N -labelling and takes place *via* a photochemical electrocyclic ring closure in transient 1,3-diazepines.



Scheme 8

Experimental section

General methods for matrix isolation and photolysis have been reported previously.^{6,15} Ar matrix isolation experiments were carried out at 7–10 K. The unfiltered light from a 1000 W high pressure Hg/Xe lamp was used for the irradiations. IR spectra were recorded with 1 cm^{-1} resolution. ^{15}N NMR spectra were recorded at 40.56 MHz with 30 s delay between scans to minimize NOE; a 30° flip angle was used. The ^{15}N NMR spectra of **21** and **30** were recorded in CDCl_3 (azide forms dominating), and those of **27** and **37** in benzene- d_6 ; 10 M HNO_3 was used as an external reference, and the chemical shifts were recalculated relative to nitromethane. Melting points are uncorrected.

Crystallography

Cell constants were determined by least-squares fits to the setting parameters of 25 independent reflections measured on an Enraf-Nonius CAD4 four-circle diffractometer employing graphite-monochromated Mo $K\alpha$ radiation (0.71073 Å) and operating in the ω -2 θ scan mode. Data reduction was performed with the WinGX package.¹⁶ Structures were solved by direct methods with SHELXS and refined by full-matrix least-squares analysis with SHELXL-97.¹⁷ All non-H atoms were refined with anisotropic thermal parameters. H-atoms were included in estimated positions using a riding model. Drawings were produced with ORTEP.¹⁸

Crystal data

Compound **6T**: $\text{C}_5\text{H}_2\text{Cl}_2\text{N}_4$, $M = 189.01$, monoclinic, space group $P2_1/a$, $a = 7.178(1)$, $b = 13.107(2)$, $c = 8.274(2)$ Å, $\beta = 114.13(8)^\circ$, $U = 710.4(2)$ Å³, $Z = 4$, $D_c = 1.767$ g cm^{-3} , $\mu = 8.41$ cm^{-1} , 1352 reflections measured, 1247 unique ($R_{\text{int}} = 0.0287$), $R_1 = 0.0296$ (for 1065 observed data, $I > 2\sigma$), $wR_2 = 0.0962$ (all data).

Compound **9Tb**: $\text{C}_7\text{H}_{13}\text{ClN}_4\text{O}$, $M = 198.62$, triclinic, space group $P\bar{1}$, $a = 7.792(1)$, $b = 10.213(2)$, $c = 11.8009(3)$ Å, $\alpha = 105.66(2)$, $\beta = 94.91(3)$, $\gamma = 102.04(2)^\circ$, $U = 874.9(3)$ Å³, $Z = 4$, $D_c = 1.508$ g cm^{-3} , $\mu = 3.99$ cm^{-1} , 3313 reflections measured, 3068 unique ($R_{\text{int}} = 0.0380$), $R_1 = 0.0438$ (for 1429 observed data, $I > 2\sigma$), $wR_2 = 0.1235$ (all data).

Compound **25h**: $\text{C}_{10}\text{H}_{17}\text{N}_3\text{O}$, $M = 195.27$, monoclinic, space group $P2_1/a$, $a = 11.185(2)$, $b = 8.1266(4)$, $c = 12.711(3)$ Å, $\beta = 107.343(9)$, $U = 1102.9(3)$ Å³, $Z = 4$, $D_c = 1.176$ g cm^{-3} , $\mu = 0.79$ cm^{-1} , 2052 reflections measured, 1939 unique ($R_{\text{int}} = 0.0114$), $R_1 = 0.0394$ (for 1433 observed data, $I > 2\sigma$), $wR_2 = 0.1190$ (all data).

Compound **28**: $\text{C}_{25}\text{H}_{38}\text{N}_6$, $M = 422.61$, triclinic, space group $P\bar{1}$, $a = 10.9884(9)$, $b = 11.953(1)$, $c = 12.2879(8)$ Å, $\alpha = 65.573(6)$, $\beta = 79.700(6)$, $\gamma = 63.521(6)^\circ$, $U = 1315.2(2)$ Å³, $Z = 2$, $D_c = 1.067$ g cm^{-3} , $\mu = 0.65$ cm^{-1} , 4922 reflections measured, 4622 unique ($R_{\text{int}} = 0.0442$), $R_1 = 0.0577$ (for 2840 observed data, $I > 2\sigma$), $wR_2 = 0.1826$ (all data).

General procedure for the synthesis of 2-hydrazinopyridines

The appropriate 2-chloropyridine (*ca.* 0.04–0.08 moles) was added to a large excess of hydrazine hydrate (30–50 ml), and 20–40 ml of ethanol was then added to make the solution homogeneous. The resulting solution was refluxed (oil bath, 80–90 °C) until TLC analysis (silica gel/dichloromethane) showed no starting 2-chloropyridine remained. The heat was then removed and the volume of the solution was reduced under vacuum. If no crystals appeared during refluxing or cooling, the resultant slurry was extracted with ether (3 × 100 ml), and the combined ether extracts were dried (MgSO_4) and evaporated to give the appropriate 2-hydrazinopyridine. The crude 2-hydrazinopyridines were purified by gentle sublimation (30–50 °C, 0.5–0.1 mbar) or recrystallized from chloroform. The hydrazinopyridines are numbered as the azides/tetrazoles. Thus, for example tetrazole **12T** is made from hydrazine **12H**.

3,5-Bis(trifluoromethyl)-2,6-dichloropyridine was too reactive towards hydrazine hydrate for the above procedure. See the modified procedure under the preparation of 2-hydrazinopyridine **38H**.

General procedure for synthesis of 2-azidopyridines/tetrazolo[1,5-*a*]pyridines from 2-hydrazinopyridines

The appropriate 2-hydrazinopyridine (*ca.* 0.04 moles) was added to 20 ml of ice-cold water, and enough concentrated hydrochloric acid was added to obtain a solution with a pH = 1. Usually, a clear solution was obtained at this acidity. A pre-cooled solution of sodium nitrite (1.2 molar excess) in *ca.* 10 ml of water was added dropwise with stirring. Mild frothing usually occurred on addition of each drop. The pH of the solution was monitored during the reaction, and a few drops of concentrated HCl was added if the acidity significantly decreased. After addition of the sodium nitrite solution, the reaction mixture was extracted with dichloromethane (3 × 30 ml), the combined extracts were dried (MgSO_4) and evaporated to give the appropriate 2-azido/tetrazolo[1,5-*a*]pyridine. The 2-azidopyridines/tetrazolo[1,5-*a*]pyridines were further purified by distillation and/or sublimation (50–100 °C, 0.1–0.5 mbar).

3,5-Dichloro-2-hydrazinopyridine 6H

Obtained from 2,3,5-trichloropyridine as white crystals, mp 179 °C from chloroform; yield 94.5%; ^1H NMR (400 MHz, CDCl_3) δ 8.06 (d, J 1.8 Hz, 1H, 6-H), 7.49 (d, J 1.8 Hz, 1H, 4-H), 6.23 (br s, 1H, NH), 3.95 (br s, 2H, NH); ^{13}C NMR (100 MHz, CDCl_3) δ 154.1, 144.1, 135.9, 120.4, 114.9. Anal. calcd. for $\text{C}_5\text{H}_5\text{N}_3\text{Cl}_2$ C, 33.73; H, 2.83; N, 23.60%. Found C, 33.50; H, 2.78; N, 23.70%.

6,8-Dichlorotetrazolo[1,5-*a*]pyridine 6T

Method 1. The hydrazine **6H** was diazotised as described above to give **6T** as slightly off-white white plates, mp 78–79 °C from 70% ethanol; yield 87%; ¹H NMR (400 MHz, CDCl₃) tetrazole isomer **6T** δ 8.80 (d, *J* 1.5, 1H), 7.69 (d, *J* 1.5, 1H); azide isomer **6A** δ 8.17 (d, *J* 2.2, 1H), 7.64 (d, *J* 2.2, 1H); ratio tetrazole : azide (20 °C) 4 : 1; ¹³C NMR (100 MHz, CDCl₃) tetrazole isomer **6A** δ 145.3, 132.3, 124.8, 123.1, 121.0; azide isomer **6A** δ 149.9, 146.7, 138.0, 127.4, 122.2. In CCl₄ the tetrazole : azide ratio was 1 : 3.7 (20 °C), in pyridine-*d*₅ the tetrazole : azide ratio was 18 : 1 (20 °C), and in DMSO-*d*₆ the tetrazole : azide ratio was 98 : 1 (20 °C) as determined from the ¹H NMR spectra. IR (KBr; only tetrazole **6T** present) ν 3105m, 1537m, 1477vs, 1324m, 1148s, 1070s, 798vs cm⁻¹. Anal. calcd. For C₅H₂N₄Cl₂ C, 31.77, H, 1.07, N, 29.64%. Found C, 31.71; H, 1.01; N, 28.78%.

Method 2. 2,3,5-Trichloropyridine (5.1 g; 0.020 mol) was dissolved in 20 ml of DMF and excess NaN₃ was added. The mixture was stirred at 65 °C for 70 h, cooled, and then slowly added to 100 ml of ice-cold water with stirring. The resulting precipitate was filtered, washed thoroughly with water, dried, and sublimed. Recrystallization from 70% ethanol afforded **6T** in 46% yield.

6-Chloro-8-methoxytetrazolo[1,5-*a*]pyridine 9Ta

A 1 g (0.0053 mol) portion of 3,5-dichlorotetrazolo[1,5-*a*]pyridine **6T** was added to a solution of methanol (30 ml) and 2 M NaOMe/methanol (10 ml), and stirred overnight. When no starting material was detected on a TLC plate (silica gel/chloroform, *ca.* 12 h), concentrated hydrochloric acid was slowly added to neutralize the solution to pH = 7. After filtration, the volume was reduced under vacuum, and the residue was extracted with CH₂Cl₂ (3 × 30 ml) to obtain crude **9Ta**, which was further purified by sublimation (100 °C/0.1–0.5 mbar) to give **9Ta** as a white solid; mp 126 °C; yield: 92%; ¹H NMR (400 MHz, CDCl₃) δ 8.43 (d, 1 H, 6-H, *J*_{4,6} = 2.9 Hz), 6.82 (d, 1 H, 4-H, *J*_{4,6} = 2.9 Hz), 4.06 (s, 3 H, OCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 148.0 (2-C), 131.1 (3-C), 126.2 (5-C), 115.9 (6-C), 109.8 (4-C), 57.2 (OCH₃). The substitution of the chlorine atom on 3-C by the methoxy group was confirmed by an NOE experiment, which showed a 16% enhancement of 4-H on irradiation of the methoxy group at 4.06 ppm. No enhancement was observed for the proton at 6-C. IR (KBr) 3059 w, 2984 m, 1562 vs, 1488 vs, 1474 w, 1456 w, 1436 w, 1415 m, 1401 w, 1357 w, 1333 s, 1289 s, 1210 s, 1196 s, 1123 s, 1102 m, 1077 w, 1004 s, 970 m, 909 m, 878 m, 817 s, 808 m, 765 w cm⁻¹. MS (EI) *m/z* 184 (M⁺, 55%), 155 (51), 141 (42), 129 (61), 114 (100), 101 (56), 86 (25), 77 (10), 64 (12), 53 (28). HRMS, calcd. for ¹²C₆H₅ClN₄O: 184.0135; found: 184.0156. Anal. calcd. for C₆H₅ClN₄O: C, 39.04; H, 2.73; N, 30.35%. Found: C, 39.07; H, 2.65; N, 30.61%.

6-Chloro-8-ethoxytetrazolo[1,5-*a*]pyridine 9Tb

Using sodium ethoxide instead of the methoxide, compound **9Tb** was prepared in the same way as described for **9Ta**. White solid; mp 146 °C; yield: 90%. ¹H NMR (200 MHz, CDCl₃) δ 8.44 (d, 1 H, 6-H, *J*_{4,6} = 1.4 Hz), 6.80 (d, 1 H, 4-H, *J*_{4,6} = 1.4 Hz), 4.33 (q, 2 H, OCH₂CH₃, *J*_{CH₂,CH₃} = 7.0 Hz); 1.54 (t, 3 H, OCH₂CH₃, *J*_{CH₂,CH₃} = 7.0 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 146.9 (2-C), 143.2 (3-C), 125.8 (5-C), 115.5 (6-C), 110.4 (4-C), 66.6 (OCH₂CH₃), 14.2 (OCH₂CH₃); IR (KBr) 3110.5 w, 3061.2 w, 2982.6 w, 2943.3 w, 1560.3 vs, 1490.3 m, 1484.5 m, 1468.8 w, 1447.3 w, 1413.5 w, 1396.3 m, 1367.9 w, 1357.0 w, 1328.6 m, 1290.8 m, 1210.4 s, 1118.9 m, 1098.3 w, 1072.0 w, 1025.4 m, 1003.8 m, 926.5 m, 868.9 m, 828.0 w, 819.3 m, 762 w cm⁻¹; MS (EI) *m/z* 198 (M⁺, 65%), 169 (75), 155 (75), 141 (13), 129 (47), 114 (35), 101 (44), 87 (100), 79 (74), 60 (22), 53 (35), 38 9 (21). HRMS, calcd. for ¹²C₇H₇ClN₄O: 198.0312; found: 198.0308.

Anal. calcd. for C₇H₇ClN₄O: C, 42.33; H, 3.55; N, 28.21%. Found: C, 42.10; H, 3.45; N, 28.42%.

5-Chloro-2-hydrazino-3-trifluoromethylpyridine 12H

Pale yellow solid; mp 79–80 °C; yield 80%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.32 (d, 1 H, 6-H, *J*_{4,6} = 1.8 Hz), 7.90 (br s, 1 H, N-H), 7.82 (d, 1 H, 4-H, *J*_{4,6} = 1.8 Hz), 4.37 (br s, 2 H, NH₂); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 154.3 (q, 2-C, *J*_{C,F} = 1.4 Hz), 149.8 (6-C), 134.6 (q, 4-C, *J*_{C,F} = 5.5 Hz), 123.0 (q, CF₃, *J*_{C,F} = 272.6 Hz), 116.8 (5-C), 107.2 (q, 3-C, *J*_{C,F} = 32.6 Hz); IR (KBr) 3320.4 and 3281.0 br (NH), 1606.2 vs, 1572.8 vs, 1486.4 s, 1458.8 s, 1403.6 m, 1384.6 m, 1347.6 w, 1299.1 vs, 1258.3 w, 1233.4 m, 1156.5 vs, 1138.8 vs, 1121.6 vs, 1050.9 s, 980.0 w, 915.0 m, 883.6 w, 777.0 w, 723.2 w, 662.5 w cm⁻¹; Anal. calcd. for C₆H₅ClF₃N₃: C, 34.06; H, 2.38; N, 19.86%. Found: C, 33.91; H, 2.15; N, 19.90%.

6-Chloro-8-trifluoromethyltetrazolo[1,5-*a*]pyridine 12T

White solid; mp 80–81 °C; yield 71%. ¹H NMR (400 MHz, CDCl₃) tetrazole isomer δ 9.06 (m, 1 H, 6-H), 7.97 (m, 1 H, 4-H); azide isomer **12A** δ 8.38 (d, 1 H, 6-H, *J*_{4,6} = 4.9 Hz), 7.83 (d, 1 H, 4-H, *J*_{4,6} = 4.9 Hz); ¹³C NMR (100 MHz, CDCl₃) tetrazole isomer **12T** δ 143.9 (2-C), 132.4 (q, 4-C, *J*_{C,F} = 5.0 Hz), 126.7 (6-C), 124.3 (5-C), 121.0 (q, CF₃, *J*_{C,F} = 272.0 Hz), 119.2 (q, 3-C, *J*_{C,F} = 38.0 Hz); azide isomer **12A** δ 150.6 (2-C), 150.4 (6-C), 136.0 (q, 4-C, *J*_{C,F} = 5.0 Hz), 127.0 (5-C), 121.5 (q, CF₃, *J*_{C,F} = 271.0 Hz), 116.5 (q, 3-C, *J*_{C,F} = 34.0 Hz); IR (KBr) tetrazole isomer **12T** 3100.1 w, 1641.0 m, 1604.0 s, 1583.4 s, 1490.9 s, 1414.4 w, 1384.5 w, 1364.3 vs, 1341.9 w, 1303.1 s, 1243.0 m, 1227.1 m, 1175.4 vs, 1153.2 vs, 1150.0 vs, 1104.4 w, 1076.4 w, 973.2 m, 919.2 m, 889.7 w, 868.7 w, 803.1 m, 774.9 m, 723.2 m, 667.5 w cm⁻¹; azide isomer **12A** (KBr) after heating the KBr pellet to 60–70 °C for 5 min) 2145.1 (ν_{azide}) s, 1591.0 s, 1575.7 vs, 1520.9 w, 1486.9 w, 1433.2 vs, 1381.9 w, 1357.4 w, 1317.3 w, 1296.3 vs, 1234.8 vs, 1202 m, 1164 w, 1143.9 w, 1132.1 w, 1083.8 w, 1049.3 m, 968.4 w, 908.7 m, 886.6 w, 845.0 m, 809.1 m, 782.3 w, 729.2 w, 720 m, 762.3 w cm⁻¹; MS (EI) *m/z* 222 (M⁺, 62%), 194 (98), 175 (10), 167 (100), 159 (9), 147 (8), 139 (2), 132 (11), 98 (50), 82 (8), 75 (6), 64 (5), 53 (3). HRMS, calcd. for ¹²C₆H₂ClF₃N₄: 221.9920; found: 221.9920. Anal. calcd. for C₆H₂ClF₃N₄: C, 32.38; H, 0.91; N, 25.17%. Found: C, 32.61; H, 1.02; N, 24.72%.

3-Chloro-2-hydrazino-5-trifluoromethylpyridine 15H

White solid; mp 85–86 °C; yield 47%. ¹H NMR (200 MHz, CDCl₃) δ 8.30 (m, 1 H, 6-H, *J*_{4,6} = 2.1 Hz, *J*_{H,F} = 0.9 Hz), 7.61 (dd, 1 H, 4-H, *J*_{4,6} = 2.1 Hz, *J*_{H,F} = 0.4 Hz), 6.79 (br s, 1 H, N-H), 4.09 (br s, 2 H, NH₂); ¹³C NMR (50 MHz, CDCl₃) δ 157.0 (2-C), 143.5 (q, 6-C, *J*_{C,F} = 4.5 Hz), 133.0 (q, 4-C, *J*_{C,F} = 3.2 Hz), 123.0 (q, CF₃, *J*_{C,F} = 269.0 Hz), 116.7 (q, 5-C, *J*_{C,F} = 33.4 Hz), 114.2 (3-C); MS (EI) *m/z* 211 (M⁺, 100%), 192 (21), 183 (16), 182 (14), 181 (54), 147 (9), 146 (39), 141 (8), 127 (5), 126 (13), 85 (8), 83 (6), 76 (11), 75 (15), 69 (18), 52 (6), 28 (15). HRMS, calcd. for ¹²C₆H₅ClF₃N₃: 211.0124; found: 211.0128. Anal. calcd. for C₆H₅ClF₃N₃: C, 34.06; H, 2.38; N, 19.86%. Found: C, 34.05; H, 2.46; N, 19.98%.

8-Chloro-6-trifluoromethyltetrazolo[1,5-*a*]pyridine 15T

White solid; mp 41–42 °C; yield 71%. ¹H NMR (400 MHz, CDCl₃) tetrazole isomer **15T** δ 9.17 (m, 1 H, 6-H), 7.88 (m, 1 H, 4-H); azide isomer **15A** δ 8.50 (m, 1 H, 6-H), 7.89 (m, 1 H, 4-H); ¹³C NMR (100 MHz, CDCl₃) tetrazole isomer **15T** δ 143.7 (2-C), 127.2 (q, 6-C, *J*_{C,F} = 2.0 Hz), 124.5 (3-C), 123.1 (q, 4-C, *J*_{C,F} = 5.4 Hz), 121.8 (q, CF₃, *J*_{C,F} = 272.9 Hz), 121.7 (q, 5-C, *J*_{C,F} = 36.3 Hz); azide isomer **15A** δ 154.9 (2-C), 148.1 (6-C), 135.6 (q, 4-C, *J*_{C,F} = 3.4 Hz), 123.9 (q, 5-C, *J*_{C,F} = 34.3 Hz), 122.8 (q, CF₃, *J*_{C,F} = 272.2 Hz), 120.8 (3-C); IR (KBr) 3105.1 w, 2144.7 (ν_{azide}) w, 1648.3 m, 1610.4 br s, 1414.4 m, 1384.5 w,

1369.4 m, 1335.2 vs, 1245.4 m, 1190.6 m, 1150.7 s, 1128.3 s, 1100.7 w, 1072.0 w, 974.2 w, 893.0 w, 762.6 w, 697.1 m, 661.2 w cm^{-1} ; MS (EI) m/z 222 (M^+ , 45%), 194 (100), 175 (24), 167 (25), 163 (10), 159 (24), 151 (11), 143 (10), 132 (12), 113 (10), 98 (27), 82 (10), 75 (10), 63 (5), 53 (12). HRMS, calcd. for $^{12}\text{C}_6\text{H}_2\text{ClF}_3\text{N}_4$: 221.9923; found: 221.9919. Anal. calcd. for $\text{C}_6\text{H}_2\text{ClF}_3\text{N}_4$: C, 32.38; H, 0.91; N, 25.17%. Found: C, 32.47; H, 0.88; N, 24.96%.

8-Chloro-6-methoxycarbonyltetrazolo[1,5-*a*]pyridine 18T

A 0.5 g (0.0024 mol) portion of 3-chloro-5-trifluoromethyl-tetrazolo[1,5-*a*]pyridine **15T** was dissolved in 20 ml of methanol and 5 ml of 3 M NaOMe in methanol (large excess) was added. The mixture was then stirred overnight at room temperature. After approximately 12 h no **15T** was detected on the TLC plate (silica gel/chloroform). Concentrated hydrochloric acid was slowly added to neutralize the solution to pH = 7. After filtration, the volume was reduced under vacuum, and the residue was extracted with CH_2Cl_2 (3×30 ml) to obtain crude **18T**, which was further purified by sublimation (100 °C/0.1–0.5 mbar) to give **18T** as a white solid; mp 135–136 °C; yield: 71%. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.91 (d, 1 H, 6-H, $J_{4,6} = 1.1$ Hz), 8.29 (d, 1 H, 4-H, $J_{4,6} = 1.1$ Hz), 3.94 (s, 3 H, OMe); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 162.9 (C=O), 148.2 (2-C), 130.9 (6-C), 129.0 (4-C), 120.7 (5 or 3-C), 120.4 (3 or 5-C) 53.2 (CH_3); IR (KBr) 3066.4 m, 3010.7 w, 1725 vs ($\nu_{\text{C=O}}$), 1621.9 m, 1590.1 br m, 1494.7 w, 1436.9 s, 1402.4 w, 1384.6 w, 1369.0 m, 1330.3 m, 1315.3 s, 1241.9 s, 1190.3 w, 1149.6 w, 1109.3 w, 1080.8 m, 995.3 w, 962.5 m, 890.4 w, 765.6 m, 736.7 w cm^{-1} ; MS (EI) m/z 212 (M^+ , 36%), 184 (100), 153 (64), 141 (19), 127 (30), 121 (47), 114 (41), 98 (62), 73 (75), 63 (66), 59 (81), 53 (43), 47 (32), 37 (47). Anal. calcd. for $\text{C}_7\text{H}_5\text{ClN}_4\text{O}_2$: C, 39.55; H, 2.37; N, 26.35%. Found: C, 39.55; H, 2.40; N, 26.36%.

6-Chloro-2-hydrazinopyridine 21H

White crystalline solid; yield 78%; mp. 126–127 °C. ^1H NMR (200 MHz, $\text{DMSO}-d_6$) δ 7.84 (br s, 1 H, N–H), 7.43 (apparent t, 1 H, 4-H, $J = 8$ –8.5 Hz), 6.63 (d, 1 H, 5-H, $J_{4,5} = 8.2$ Hz), 6.50 (d, 1 H, 3-H, $J_{3,4} = 7.2$ Hz), 4.18 (br s, 2 H, NH_2); ^{13}C NMR (50 MHz, $\text{DMSO}-d_6$) δ 162.3 (2-C), 148.2 (6-C), 139.8 (4-C), 110.6 (5-C), 104.3 (3-C); Anal. calcd. for $\text{C}_5\text{H}_6\text{ClN}_3$: C, 41.83; H, 4.21; N, 29.27%. Found: C, 41.74; H, 4.17; N, 29.43%.

6-Chlorotetrazolo[1,5-*a*]pyridine 21T

White crystalline solid; yield 69.8%; mp 78–79 °C. ^1H NMR (400 MHz, CDCl_3) azide isomer (**21A**) δ 7.55 (apparent triplet, 1 H, 4-H, $J = 7$ –8 Hz), 7.03 (dd, 1 H, 5-H, $J_{4,5} = 7.9$ Hz, $J_{3,5} = 0.6$ Hz), 6.69 (dd, 1 H, 3-H, $J_{3,4} = 7.9$ Hz, $J_{3,5} = 0.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 154.5 (2-C), 150.1 (6-C), 140.8 (4-C), 120.1 (3-C), 112.2 (5-C); ^1H NMR (400 MHz, CDCl_3) tetrazole isomer (**21T**) δ 8.00 (d, 1 H, 3-H, $J_{3,4} = 8.3$ Hz), 7.67 (apparent triplet, 1 H, 4-H, $J = 7$ –8 Hz), 7.27 (d, 1 H, 5-H, $J_{4,5} = 8.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 149.7 (2-C), 132.4 (4-C), 119.8 (6-C), 116.4 (3-C), 114.2 (5-C); ^{15}N NMR (CDCl_3 , referenced to external nitromethane) δ –260, –125, –127, –85; IR (KBr): in the solid state at room temperature the tetrazole form predominates; warming the KBr pellet to ca. 60–70 °C for 1 min caused complete conversion of **21T** to the azido-form **21A**, which did not equilibrate back to **21T** after 15 min at room temperature, possibly due to the KBr matrix; tetrazole isomer (**21T**) 3099.1 w, 3070.7 w, 1618.3 s, 1537.5 m, 1489.3 vs, 1353.7 w, 1326.4 s, 1242.4 m, 1230.8 m, 1126.2 w, 1122.4s, 1100.3 vs, 1010.2 m, 989.9 s, 838.4 w, 805.5 vs, 748.8 m cm^{-1} ; azide isomer **21A** (60–70 °C) 2127 vs (ν_{azide}), 1538.8 vs, 1564.4 m, 1498.8 w, 1425.9 vs, 1292.8 s, 1164.1 m, 987.9 w, 900.7 m, 787.6 m, 721.5 w, 658.1 w cm^{-1} ; MS (EI) m/z 154 (M^+ , 78%), 126 (100), 113 (5), 99 (72), 91 (28), 73 (13), 64 (46), 53 (7). HRMS, calcd for $^{12}\text{C}_5\text{H}_3\text{ClN}_4$: 154.0046; found: 154.0046.

Anal. calcd. for $\text{C}_5\text{H}_3\text{ClN}_4$: C, 38.86; H, 1.96; N, 36.25%. Found: C, 38.71; H, 1.91; N, 36.48%.

6-Chloro-2-[$^{15}\text{N}_2$]-hydrazinopyridine 29

1.7 g of [$^{15}\text{N}_2$]-hydrazine sulfate ($\text{H}_2\text{N}-\text{NH}_2 \cdot \text{H}_2\text{SO}_4$, 96.2 atom-% $^{15}\text{N}_2$) was mixed with an equal amount of unlabelled product to obtain 0.026 moles of 48.1% $^{15}\text{N}_2$ hydrazine sulfate to which 2.9 g (0.027 moles) of solid Na_2CO_3 was added. The two compounds were mixed and ground, and 15 drops of H_2O were added to initiate liberation of hydrazine hydrate. When the violent bubbling and frothing ceased, the resulting mixture of hydrazine hydrate and sodium sulfate was diluted with 12 ml of ethanol, and 0.5 g of 2,6-dichloropyridine was added. The mixture was then refluxed for 60 h. Although TLC (silica gel, dichloromethane) showed that starting material was still present, the reaction was stopped due to the appearance of the unwanted by-product 2-chloro-6-hydroxypyridine according to GCMS analysis. Evaporation of the solvent under vacuum left a yellow–brown solid, which was extracted with dichloromethane and washed with a saturated solution of Na_2CO_3 and brine. Evaporation of the extract furnished a yellow solid (0.34 g); this was a mixture of starting material and 2-chloro-6-[$^{15}\text{N}_2$]-hydrazinopyridine (48.1 atom-% $^{15}\text{N}_2$), which was used for the next step without further purification.

During optimization of the reaction using commercially available hydrazine sulfate, it was found that adding small amount of H_2O into the mixture of solid Na_2CO_3 and hydrazine sulfate, as well as carrying out the reaction in a relatively large volume of ethanol (12 ml) improved yields and minimized formation of the unwanted by-product 2-chloro-6-hydroxypyridine. Increasing the amount of 2,6-dichloropyridine above 0.5 g did not improve the yield.

The method for a preparation of hydrazine hydrate from hydrazine sulfate reported by Nenitzescu *et al.*,¹⁹ which uses a boiling solution of sodium acetate and H_2O , was examined and found to be unsuitable for this experiment.

1,2-[$^{15}\text{N}_2$]-5-Chlorotetrazolo[1,5-*a*]pyridine 30T

A 0.34 g portion of the crude 2-chloro-6-[$^{15}\text{N}_2$]-hydrazinopyridine **29** containing ca. 0.15 g of 2,6-dichloropyridine was added to 3 ml of water and diazotized as described above to give 0.22 g of crude **30T**.

3,5-Bis(trifluoromethyl)-6-chloro-2-hydrazinopyridine 38H

The precursor, 3,5-bis(trifluoromethyl)-2,6-dichloropyridine, was found to be very reactive towards hydrazine hydrate. Therefore, the general method was modified. Thus, 5 g (0.018 moles) of 3,5-bis(trifluoromethyl)-2,6-dichloropyridine was dissolved in 30 ml of ethanol and cooled to ca. 10 °C in an water bath. On addition of ca. 1.5 molar excess of hydrazine (2–3 min), the solution turned yellow, and a large amount of a precipitate was formed. The volume was then reduced under vacuum, and the resultant slurry was extracted with ether (3×30 ml). The combined ether extracts were dried (MgSO_4), evaporated, and the crude residue was purified by gentle sublimation (50–60 °C, 0.1–0.5 mm Hg) to afford the hydrazone **38H** as a pale yellow crystalline solid; yield 98%; mp. 96–97 °C. ^1H NMR (200 MHz, CDCl_3) δ 7.92 (s, 1 H, 4-H), 7.03 (br s, 1 H, N–H), 4.16 (br s, 2 H, NH_2); ^{13}C NMR (50 MHz, CDCl_3) δ 156.6 (2-C), 151.7 (6-C), 135.8 (m, 4-C), 122.5 (q, CF_3 , $J_{\text{C,F}} = 269.5$ Hz), 122.0 (q, CF_3 , $J_{\text{C,F}} = 269.0$ Hz), 113.3 (q, 5-C, $J_{\text{C,F}} = 34.1$ Hz), 105.8 (q, 3-C, $J_{\text{C,F}} = 33.5$ Hz); Anal. calcd. for $\text{C}_7\text{H}_4\text{ClF}_6\text{N}_3$: C, 30.07; H, 1.44; N, 15.03%. Found: C, 30.28; H, 1.43; N, 15.26%.

2-Azido-3,5-bis(trifluoromethyl)-6-chloropyridine 38A

Clear oil; purified by distillation (Kugelrohr apparatus, 25 °C, 0.1–0.5 mbar); yield 60%. ^1H NMR (200 MHz, CDCl_3) δ 8.17 (m, 1 H, 4-H, $J_{\text{H,F}} = 0.4$ Hz); ^{13}C NMR (50 MHz, CDCl_3)

δ 154.9 (2-C), 151.5 (6-C), 137.0 (m, 4-C, $J_{C,F} = 5$ Hz), 121.5 (q, CF_3 , $J_{C,F} = 270.5$ Hz), 121.3 (q, CF_3 , $J_{C,F} = 271.5$ Hz), 121.0 (q, 5-C, $J_{C,F} = 34.5$ Hz), 114.2 (q, 3-C, $J_{C,F} = 34.9$ Hz); IR (neat film) 2153 vs (ν_{azide}), 1609 vs, 1561 vs, 1508 w, 1438 m, 1413 m, 1310 vs, 1279 vs, 1266 vs, 1147 vs, 1055 vs, 947 m, 774 w cm^{-1} ; MS (EI) m/z 290 (M^+ , 25%), 262 (100), 243 (15), 227 (14), 212 (9), 172 (21), 167 (15), 156 (13), 150 (7), 141 (14), 132 (8), 127 (7), 120 (10), 112 (8), 98 (10), 89 (7), 86 (6), 82 (6), 75 (9). HRMS, calcd. for $C_7H_1ClF_6N_4$: 289.9797; found: 289.9793. Anal. calcd. for $C_7H_1ClF_6N_4$: C, 28.94; H, 0.35; N, 19.28%. Found: C, 28.84; H, 0.37; N, 19.62%.

General procedures for the synthesis of 1,3-diazepines

The azides/tetrazoles (100–150 mg) were photolysed in N_2 -purged dioxane solutions using a quartz vessel. Alcohols were dried using magnesium metal, amines were refluxed over and distilled from potassium hydroxide, and dioxane was distilled from Na metal immediately prior to use. Products were purified by column chromatography and/or Kugelrohr distillation.

For the synthesis of 2-alkoxy-4-dialkylamino-5*H*-1,3-diazepines the starting azido/tetrazolo[1,5-*a*]pyridine (*ca.* 1 mmol) was dissolved in a mixture of absolute dioxane (120 ml) and the appropriate alcohol (20–30 ml) in a quartz vessel. The mixture was purged with high purity dry nitrogen for about 1 h. The degassed solution was irradiated with the high pressure Hg/Xe lamp while stirring the mixture in an ice bath. Reaction times were usually 1–2 h. The resulting crude reaction mixture was removed from the UV source, divided into two equal portions, and an appropriate amine was added into each half with stirring. When dimethylamine was needed, the gas was passed directly into the reaction mixture, or a saturated solution of dimethylamine (large excess) in dioxane was used. While stirring, the solution was then allowed to warm to room temperature (30 min). The volume was reduced under vacuum, and the resulting oily residue was purified by chromatography on deactivated aluminium oxide (90, neutral). The aluminium oxide was deactivated by aqueous methanol (20%) and then dried in the air overnight at room temperature. The low volatility of these compounds does not usually permit purification by distillation even under very low pressure (10^{-4} – 10^{-5} bar), and mainly decomposition-polymerization occurs at temperatures as low as 80–100 °C.

2-Dialkylamino-5*H*-diazepines were prepared by photolysis of the corresponding tetrazolo[1,5-*a*]pyridines in the presence of the appropriate secondary amine. All products were unstable and slowly decomposed when neat and exposed to air at room temperature, but were more stable in the fridge and/or in solution.

6-Chloro-2-methoxy-4-trifluoromethyl-1*H*-1,3-diazepine 14a

Purified by Kugelrohr distillation (40–60 °C, 0.1–0.5 mm Hg) followed by recrystallization from petroleum ether. Yellow–orange needles; mp 75–76 °C; yield: 49%. 1H NMR (400 MHz, $CDCl_3$) δ 5.89 (br s, 1 H, 5-H), 5.67 (br s, 1 H, 7-H), 4.76 (br s, 1 H, N-H), 3.77 (OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9 (2-C), 139.5 (q, 4-C, $J_{C,F} = 31.6$ Hz), 128.6 (7-C), 120.7 (q, CF_3 , $J_{C,F} = 273.6$ Hz), 117.9 (q, 5-C, $J_{C,F} = 4.7$ Hz), 116.8 (6-C); IR (KBr) 3264 br (NH), 3086.0 m, 3018.7 w, 3000.5 w, 2951.6 m, 1669.2 s, 1652.0 s, 1629.4 s, 1486.4 m, 1459.6 m, 1384.6 m, 1336.2 m, 1291.9 vs, 1278.1 vs, 1206.5 w, 1181.1 m, 1168.4 s, 1156.8 s, 1124.2 vs, 1082.6 m, 1057.7 w, 1009.3 s, 987.6 w, 901.1 m, 845.8 w, 831.3 m, 802.6 m, 767.9 w, 733.1 m, 710.7 m, 684.1 m, 626.8 w cm^{-1} ; MS (EI) m/z 226 (M^+ , 100%), 207 (5), 199 (5), 191 (5), 184 (19), 183 (5), 176 (36), 171 (20), 169 (64), 167 (5), 156 (6), 155 (5), 151 (6), 150 (10), 149 (17), 148 (20), 144 (13), 142 (32), 134 (9), 129 (8), 118 (11), 116 (7), 114 (26), 91 (7), 69 (12), 58 (41), 57 (6), 52 (6), 43 (17). HRMS, calcd. for $^{12}C_7H_6N_2ClF_3O$: 226.01207; found: 226.01233. Anal. calcd. for

$C_7H_6N_2ClF_3O$: C, 37.11; H, 2.67; N, 12.36%. Found: C, 37.06; H, 2.68; N, 12.48%.

6-Chloro-2-ethoxy-4-trifluoromethyl-1*H*-1,3-diazepine 14b

Purified by double Kugelrohr distillation (0.1–0.5 mm Hg, 40–60 °C) to afford yellow–orange crystalline solid, mp 75–76 °C; yield: 57%. 1H NMR (400 MHz, $CDCl_3$) δ 5.88 (s, 1 H, 5-H), 5.68 (d, 1 H, 7-H, $J_{1,7} = 7.0$ Hz), 4.92 (br, 1 H, N-H), 4.20 (q, 2 H, OCH_2CH_3 , $J_{CH_2,CH_3} = 6.9$ Hz), 1.26 (t, 3 H, OCH_2CH_3 , $J_{CH_2,CH_3} = 6.9$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5 (2-C), 139.6 (q, 4-C, $J_{C,F} = 31.6$ Hz), 128.9 (7-C), 121.0 (q, CF_3 , $J_{C,F} = 273.6$ Hz), 117.7 (q, 5-C, $J_{C,F} = 4.7$ Hz), 116.6 (6-C), 65.8 (OCH_2CH_3), 13.8 (OCH_2CH_3); MS (EI) m/z 240 (M^+ , 38%), 212 (66), 197 (11), 177 (26), 176 (34), 169 (36), 157 (17), 149 (49), 143 (30), 122 (15), 115 (100), 114 (26), 87 (13), 79 (17), 69 (26), 52 (26). HRMS, calcd. for $^{12}C_8H_8N_2ClF_3O$: 240.0277; found: 240.0274. Anal. calcd. for $C_8H_8N_2ClF_3O$: C, 39.94; H, 3.35; N, 11.64%. Found: C, 39.78; H, 3.34; N, 11.57%.

4-Chloro-2-diethylamino-4-methoxy-5*H*-1,3-diazepine 11a

The crude residue was chromatographed on deactivated silica gel 100 using $CH_2Cl_2/MeOH$ (20 : 1) as an eluent to give **11a** as a red oil; yield: 87%. 1H NMR (200 MHz, $CDCl_3$) δ 6.69 (s, 1H, 7-H), 3.74 (s, 3H, OCH_3), 3.37 (q, 4H, $N(CH_2CH_3)_2$, $J = 7.0$ Hz), 2.99 (s, 2H, 5-H), 1.08 (t, 6H, $N(CH_2CH_3)_2$, $J = 7.0$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.5 (4-C), 153.3 (2-C), 135.9 (7-C), 102.8 (6-C), 55.1 (OCH_3), 41.7 $N(CH_2CH_3)_2$, 39.5 (5-C), 13.3 $N(CH_2CH_3)_2$; IR (neat film) 2975 m, 2958 m, 1650 vs, 1637 m, 1548 vs, 1523 m, 1407 m, 1391 m, 1379 m, 1369 m, 1324 vs, 1319 s, 1282 s, 1257 s, 1194 m, 1181 m, 1084 w, 1039 m, 909 w, 904 w, 853 w, 801 w, 752 w. MS (EI) m/z 229 (M^+ , 100%), 214 (44), 202 (29), 200 (91), 194 (48), 188 (9), 186 (25), 166 (20), 159 (28), 157 (35), 149 (12), 141 (18), 143 (46), 132 (27), 123 (16), 115 (30), 88 (14), 72 (96), 56 (32), 53 (14). HRMS, calcd. for $^{12}C_{10}H_{16}N_3ClO$: 229.0986; found: 229.0983. Anal. calcd. for $C_{10}H_{16}N_3ClO$: C, 52.29; H, 7.02; N, 18.29%. Found: C, 52.34; H, 7.25; N, 18.18%.

4-Chloro-2-diisopropylamino-4-methoxy-5*H*-1,3-diazepine 11b

The crude residue was chromatographed on deactivated silica gel 100 using hexane/ethyl acetate (10 : 90) or $CH_2Cl_2/MeOH$ (100 : 1) as an eluent to give **11b** as a red oil; yield: 78%. 1H NMR (200 MHz, $CDCl_3$) δ 6.59 (s, 1H, 7-H), 4.10 (br, 2H, *i*Pr, $J = 6.9$ Hz), 3.68 (s, 3H, OCH_3), 2.88 (s, 2H, 5-H), 1.14 (d, 12H, *i*Pr, $J = 6.9$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.8 (4-C), 153.4 (2-C), 136.0 (7-C), 101.5 (6-C), 55.0 (OCH_3), 45.2 (*i*Pr), 39.4 (5-C), 20.8 (*i*Pr); IR (neat film) 2989 m, 2972 m, 1643 vs, 1625 m, 1545 vs, 1511 m, 1442 m, 1409 m, 1389 m, 1372 m, 1363 m, 1360 m, 1319 s, 1282 s, 1252 s, 1192 m, 1187 m, 1154 w, 1070 w, 107 m, 905 w, 890 w, 872 w, 834 w, 754 w. MS (EI) m/z 257 (M^+ , 30%), 214 (100), 200 (30), 178 (15), 166 (18), 159 (20), 157 (61), 145 (24), 136 (22), 132 (28), 117 (11), 115 (22), 100 (9), 97 (10), 88 (16), 80 (19), 69 (42). HRMS, calcd. for $^{12}C_{12}H_{20}N_3OCl$: 257.1295; found: 257.1298. Anal. calcd. for $C_{12}H_{20}N_3OCl$: C, 55.92; H, 7.82; N, 16.30%. Found: C, 55.81; H, 7.67; N, 16.72%.

4-Chloro-2-diethylamino-4-ethoxy-5*H*-1,3-diazepine 11c

The crude residue was chromatographed on deactivated silica gel 100 using $CH_2Cl_2/MeOH$ (20 : 1) as an eluent to give **11c** as a red oil; yield: 89%. 1H NMR (200 MHz, $CDCl_3$) δ 6.74 (s, 1H, 7-H), 4.19 (q, 2H, (OCH_2CH_3), $J = 7.0$ Hz), 3.42 (q, 4H, $N(CH_2CH_3)_2$, $J = 7.0$ Hz), 3.01 (s, 2H, 5-H), 1.30 (t, 3H, OCH_2CH_3), 1.11 (t, 6H, $N(CH_2CH_3)_2$, $J = 7.0$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.5 (4-C), 153.9 (2-C), 135.6 (7-C), 102.6 (6-C), 64.0 (OCH_2CH_3), 41.8 $N(CH_2CH_3)_2$, 39.9 (5-C), 13.9 (OCH_2CH_3), 13.3 $N(CH_2CH_3)_2$; IR (neat film) 2975 m, 2963 m, 1640 vs, 1625 w, 1529 vs, 1429 m, 1405 m, 1373 m, 1370 m, 1318 s, 1284 s, 1251 s, 1194 m, 1189 m, 1080 w, 1039 m, 904 w, 901 w,

857 w, 760 w. MS (EI) m/z 243 (M^+ , 79%), 216 (33), 214 (100), 203 (30), 200 (16), 186 (23), 180 (25), 172 (21), 157 (11), 150 (10), 145 (20), 144 (26), 143 (45), 100 (10), 97 (12), 82 (16), 75 (11), 72 (62), 56 (9). HRMS, calcd. for: $^{12}C_{11}H_{18}N_3OCl$: 243.1136; found: 243.1145. Anal. calcd. for $C_{11}H_{18}N_3OCl$: C, 54.21; H, 7.44; N, 17.24%. Found: C, 53.91; H, 7.65; N, 16.88%.

4-Chloro-2-diisopropylamino-4-ethoxy-5H-1,3-diazepine 11d

The crude residue was chromatographed on deactivated silica gel 100 using $CH_2Cl_2/MeOH$ (95 : 5) as an eluent to give **11d** as a red oil; yield: 75%. 1H NMR (200 MHz, $CDCl_3$) δ 6.68 (s, 1H, 7-H), 4.16 (q, 2H, OCH_2CH_3 , $J = 7.0$ Hz), 4.15 (br, 2H, iPr , $J = 6.8$ Hz), 2.93 (s, 2H, 5-H), 1.27 (t, 3H, OCH_2CH_3 , $J = 7.0$ Hz), 1.20 (d, 12H, iPr , $J = 6.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.5 (4-C), 153.6 (2-C), 135.5 (7-C), 102.2 (6-C), 64.0 (OCH_2CH_3), 45.6 (iPr), 39.9 (5-C), 20.7 (iPr), 14.0 (OCH_2CH_3). IR (neat film) 2977 m, 2959 m, 1651 vs, 1632 m, 1548 vs, 1528 m, 1433 m, 1408 m, 1354 m, 1373 m, 1369 m, 1319 s, 1284 s, 1253 s, 1234 m, 1192 m, 1187 m, 1073 w, 1041 m, 906 w, 901 w, 853 w, 766 w. MS (EI) m/z 271 (M^+ , 29%), 242 (12), 230 (33), 228 (100), 200 (22), 172 (13), 165 (12), 158 (20), 143 (18), 118 (24), 115 (27), 111 (13), 100 (9), 90 (19), 83 (47), 69 (41), 58 (25), 53 (23), 43 (53), 41 (56). HRMS calcd. for: $^{12}C_{13}H_{22}N_3OCl$: 271.1450; found: 271.1456. Anal. calcd. for: $C_{13}H_{22}N_3OCl$: C, 57.45; H, 8.16; N, 15.46%. Found: C, 57.34; H, 8.51; N, 15.29%.

2,4-Dipyrrolidino-5H-1,3-diazepine 23

Purified by column chromatography (Al_2O_3 , dichloromethane/methanol, 3%) and decolourized by charcoal to obtain **23** as a yellow oil; yield 33%. 1H NMR (400 MHz, acetone- d_6) δ 6.55 (d, 1 H, 7-H, $J_{6,7} = 7.6$ Hz), 5.27 (q, 1 H, 6-H, $J_{6,7} = 7.6$ Hz, $J_{5,6} = 7.0$ Hz), 3.75 (t, 4 H, pyrrolidine, $J = 6.7$ Hz), 3.56 (t, 4 H, pyrrolidine, $J = 7.0$ Hz), 3.18 (d, 2 H, 5-H, $J_{5,6} = 7.0$ Hz), 2.02 (quint, 4 H, pyrrolidine, $J = 6.7$ Hz), 1.94 (quint, 4 H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, acetone- d_6) δ 157.4 (2-C), 152.6 (4-C), 129.5 (7-C), 104.3 (6-C), 49.4 and 48.9 (pyrrolidine), 31.6 (5-C), 26.1 and 15.1 (pyrrolidine); IR (neat film) 2974.3 m, 2878.5 m, 1661.9 m, 1615.8 vs, 1579.0 vs, 1575.4 vs, 1516.4 w, 1447.1 vs, 1435 vs, 1374.3 w, 1338.3 m, 1260.2 w, 1244.2 w, 1188.2 w, 1123.1 w, 1019.4 w, 974.8 w, 873.7 w, 695.0 cm^{-1} . MS (EI) m/z 232 (M^+ , 100%), 217 (77), 203 (52), 189 (28), 177 (24), 176 (23), 163 (30), 162 (39), 148 (10), 135 (38), 120 (17), 108 (21), 93 (14), 81 (23), 72 (28), 69 (19), 55 (22), 41 (32), 39 (28). HRMS, calcd. for $^{12}C_{13}H_{20}N_4$: 232.1688; found: 232.1690. Anal. calcd. for: $C_{13}H_{20}N_4$: C, 67.21; H, 8.68; N, 24.12%. Found: C, 67.28; H, 8.41; N, 23.89%.

4-Dimethylamino-2-methoxy-5H-1,3-diazepine 25a

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether, followed by diethyl ether/ethyl acetate (50 : 50) mixture to remove minor impurities. The product, pale yellow oil, was then eluted using ethyl acetate only; yield: 62.5%. 1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.51 (d, 1 H, 7-H, $J_{6,7} = 6.52$ Hz), 4.82 (q, 1 H, 6-H, $J_{6,7} = 6.52$, $J_{5,6} = 7.00$ Hz), 3.60 (s, 3 H, OCH_3), 3.07 (s, 3 H, NCH_3), 2.94 (s, 3 H, NCH_3), 2.73 (d, 2 H, 5-H, $J_{5,6} = 7.00$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 100 MHz) δ 160.3 (2-C), 156.5 (4-C), 139.7 (7-C), 101.9 (6-C), 53.1 (OCH_3), 38.4 (br, $N(CH_3)_2$), 30.0 (5-C); IR (neat) 1605.4 vs, 1583.6 vs, 1524.6 vs, 1438.7 m, 1415.6 m, 1308.1 s, 1281.4 m, 1249.0 s, 1209.4 w, 1154.5 w, 1116.9 w, 1051.3 m, 1003 w, 887.1 w, 778.3 w, 706.2 m, 618.5 cm^{-1} ; MS (EI) m/z 167 (M^+ , 100%), 152 (47), 137 (13), 125 (18), 109 (9), 85 (15), 82 (77), 70 (8), 66 (5), 54 (12). HRMS, calcd. for $^{12}C_8H_{13}N_3O$: 167.1059; found: 167.1054. Anal. calcd. for $C_8H_{13}N_3O$: C, 57.46; H, 7.84; N, 25.13%. Found: C, 57.41; H, 7.53; N, 24.88%.

4-Diethylamino-2-methoxy-5H-1,3-diazepine 25b

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether : hexane (10 : 1). Pale pink oil; yield: 84%. 1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.52 (d, 1 H, 7-H, $J_{6,7} = 6.52$ Hz), 4.78 (q, 1 H, 6-H, $J_{6,7} = 6.52$, $J_{5,6} = 6.80$ Hz), 3.59 (s, 3 H, OCH_3), 3.42 (q, 4 H, NCH_2CH_3 , $^3J = 7.12$ Hz), 2.75 (d, 2 H, 5-H, $J_{5,6} = 6.80$ Hz), 1.18 and 1.05 (t, 6 H, NCH_2CH_3 , $^3J = 7.12$ Hz); ^{13}C NMR (acetone- d_6 , 100 MHz) δ 160.6 (2-C), 155.1 (4-C), 139.8 (7-C), 102.9 (6-C), 53.0 (OCH_3), 43.8 and 44.0 (NCH_2CH_3), 29.9 (C-5), 14.3 and 12.4 (NCH_2CH_3); IR (neat) 2976 m, 2938 w, 1603.9 vs, 1575.3 vs, 1520.4 vs, 1475.7 m, 1429.6 m, 1381.4 w, 1362.2 w, 1312.6 vs, 1275.9 s, 1248.8 vs, 1213.0 vs, 1148.1 m, 1117.1 w, 1080.1 w, 1053.3 m, 1021.3 w, 882.1 m, 805.0 w, 778.0 w, 701.8 cm^{-1} ; MS (EI) m/z 195 (M^+ , 100%), 180 (88), 166 (21), 152 (11), 124 (21), 113 (13), 81 (12), 72 (12), 54 (22). HRMS, calcd. for $^{12}C_{10}H_{17}N_3O$: 195.1373; found: 195.1372. Anal. calcd. for $C_{10}H_{17}N_3O$: C, 61.51; H, 8.78; N, 21.52%. Found: C, 61.59; H, 8.88; N, 21.39%.

4-Diisopropylamino-2-methoxy-5H-1,3-diazepine 25c

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether. Pale yellow solid; mp 46–47 °C; yield: 92%. 1H NMR (acetone- d_6 , 297 K, 500 MHz) δ 6.54 (d, 7 H, 1-H, $J_{6,7} = 6.50$ Hz), 4.71 (q, 6 H, 1-H, $J_{6,7} = 6.50$ Hz), 4.09 br (2 H, $NiPr$), 3.59 (s, 3 H, OCH_3), 2.78 br (2 H, 5-H), 1.23 and 1.12 br (12 H, $NiPr$); ^{13}C NMR (acetone- d_6 , 297 K, 125 MHz) δ 159.6 (2-C), 153.5 br (4-C), 139.6 (7-C), 103.0 (6-C), 53.0 (OCH_3), 48.1 br ($2 \times CH$, $NiPr$), 32.6 (5-C), 21.5 and 20.2 br ($4 \times CH_3$, $NiPr$); IR (KBr) 2980 m, 2963 m, 1605.0 vs, 1561.4 vs, 1510.7 vs, 1482.6 s, 1459.7 m, 1424.9 m, 1385.4 m, 1371.0 s, 1290.4 s, 1247.9 s, 1209.6 s, 1191.8 m, 1180.5 m, 1147.1 s, 1111.9 w, 1059.6 w, 1026.9 w, 1008.6 w, 876.0 w, 777.2 w, 759.8 w, 754.4 w, 702.2 m, 621 w cm^{-1} ; MS (EI) m/z 223 (M^+ , 73%), 208 (10), 180 (100), 166 (15), 143 (14), 138 (39), 124 (13), 123 (24), 108 (8), 98 (9), 81 (16), 70 (9), 57 (23), 54 (15), 43 (23), 41 (16). HRMS, calcd. for $^{12}C_{12}H_{21}N_3O$: 223.1687; found: 223.1678. Anal. calcd. for $C_{12}H_{21}N_3O$: C, 64.54; H, 9.48; N, 18.82%. Found: C, 64.37; H, 9.66; N, 18.64%.

2-Methoxy-4-pyrrolidino-5H-1,3-diazepine 25d

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with ethyl acetate. Yellow oil; yield: 74%. 1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.50 (d, 1 H, 7-H, $J_{6,7} = 6.52$ Hz), 4.82 (q, 1 H, 6-H, $J_{6,7} = 6.52$, $J_{5,6} = 6.92$ Hz), 3.60 (s, 3 H, OCH_3), 3.50 and 3.35 (t, 4 H, pyrrolidine ring, $^3J = 6.88$ Hz), 2.71 (d, 2 H, 5-H, $J_{5,6} = 6.92$ Hz), 1.94 and 1.84 (qnt, 4 H, pyrrolidine ring, $^3J = 6.88$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 100 MHz) δ 160.4 (2-C), 154.5 (4-C), 139.7 (7-C), 101.6 (6-C), 53.0 (OCH_3), 48.4 and 47.9 (pyrrolidine ring), 31.6 (C-5), 26.3 and 25.2 (pyrrolidine ring); IR (neat film) 2971 m, 2962 m, 1615.0 vs, 1567.4 vs, 1511.0 vs, 1483.1 s, 1479.8 m, 1434.1 m, 1382.2 m, 1374.7 s, 1294.4 s, 1249.1 s, 1181.7 m, 1170.1 m, 1156.4 m, 1146.7 s, 1112.3 w, 1061.5 w, 1023.9 w, 1008.6 w, 987.2 w, 787.8 w, 769.1 w, 751.2 w, 734.1 m, 702.9 m, cm^{-1} ; HRMS, calcd. for $^{12}C_{10}H_{15}N_3O$: 193.1215; found: 193.1217. Anal. calcd. for $C_{10}H_{15}N_3O$: C, 62.15; H, 7.82; N, 21.74%. Found: C, 62.41; H, 8.19; N, 21.51%.

4-Dimethylamino-2-ethoxy-5H-1,3-diazepine 25e

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether/hexane (1 : 1) followed by ether to obtain pale red oil; yield: 52%. 1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.50 (d, 1 H, 7-H, $J_{6,7} = 6.52$ Hz), 4.81 (q, 1 H, 6-H, $J_{6,7} = 6.52$, $J_{5,6} = 6.90$ Hz), 4.05 (q, 2 H, OCH_2CH_3 , $J = 7.08$ Hz), 3.06 and 2.93 (s, 6 H, NCH_3), 2.73 (d, 2 H, 5-H, $J_{5,6} = 6.90$ Hz), 1.20 (t, 3 H, OCH_2CH_3 , $J = 7.08$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 100 MHz) δ 159.8 (2-C), 156.4 (4-C), 139.9 (7-C), 101.6

(6-C), 61.4 (OCH_2CH_3), 38.4 (br, $\text{N}(\text{CH}_3)_2$), 29.8 (5-C), 14.9 (OCH_2CH_3); IR (neat) 2977.3 w, 1604.6 vs, 1583.2 vs, 1520.3 vs, 1444.6 m, 1418.9 m, 1361.8 m, 1301.1 s, 1243.2 s, 1207.9 m, 1154.8 w, 1107.5 w, 1052.3 m, 1005.2 w, 883.9 w, 787.3 w, 704.2 m cm^{-1} ; MS m/z 181 (M^+ , 100%), 152 (47), 137 (13), 125 (18), 109 (9), 85 (15), 82 (77), 70 (8), 66 (5), 54 (12). HRMS, calcd. for $^{12}\text{C}_9\text{H}_{15}\text{N}_3\text{O}$: 167.1059; found: 167.1054. Anal. calcd. for $\text{C}_9\text{H}_{15}\text{N}_3\text{O}$: C, 59.64; H, 8.34; N, 23.18%. Found: C, 59.63; H, 8.35; N, 23.18%.

4-Diethylamino-2-ethoxy-5H-1,3-diazepine 25f

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether. Pale red oil; Yield: 79%. ^1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.50 (d, 1 H, 7-H, $J_{6,7} = 6.64$ Hz), 4.77 (q, 1 H, 6-H, $J_{6,7} = 6.64$, $J_{5,6} = 7.08$ Hz), 4.05 (q, 2 H, OCH_2CH_3 , $J = 7.08$ Hz), 3.42 (q, 4 H, NCH_2CH_3 , $J = 7.06$ Hz), 2.75 (d, 2 H, 5-H, $J_{5,6} = 7.08$ Hz), 1.20 (t, 3 H, OCH_2CH_3 , $J = 7.08$ Hz), 1.06 br (t, 6 H, NCH_2CH_3 , $J = 7.06$ Hz); ^{13}C NMR (acetone- d_6 , 100 MHz) δ 160.0 (2-C), 155.1 (4-C), 139.9 (7-C), 102.8 (6-C), 61.4 (OCH_2CH_3), 44.0 and 43.8 (NCH_2CH_3), 30.1 (C-5), 14.9, 14.9 (OCH_2CH_3), 14.3 and 12.5 (NCH_2CH_3); IR (neat film) 2976.8 m, 2934.5 w, 1603.8 s, 1575.4 vs, 1520.2 vs, 1472.3 m, 1381.4 w, 1359.3 m, 1309.4 s, 1271.2 s, 1248.9 vs, 1212.0 vs, 1148.9 m, 1117.3 w, 1080.0 w, 1053.9 m, 881.2 w, 803.5 w, 787.6 w, 700.7 m cm^{-1} ; MS (EI) m/z 209 (M^+ , 100%), 194 (33), 181 (18), 165 (41), 150 (23), 136 (25), 127 (9), 109 (21), 99 (21), 82 (100), 72 (18), 56 (25), 43 (23). HRMS, calcd. for $^{12}\text{C}_{11}\text{H}_{19}\text{N}_3\text{O}$: 209.1525; found: 209.1527. Anal. calcd. for $\text{C}_{11}\text{H}_{19}\text{N}_3\text{O}$: C, 63.13; H, 9.15; N, 20.08%. Found: C, 62.98; H, 9.19; N, 19.85%.

4-Diisopropylamino-2-ethoxy-5H-1,3-diazepine 25g

Purified by column chromatography (Al_2O_3 , 90/ neutral, deactivated) eluting with ether/hexane (3 : 1) mixture. Yield: 87.7%. ^1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.53 (d, 1 H, 7-H, $J_{6,7} = 6.48$ Hz), 4.65 (q, 1 H, 6-H, $J_{6,7} = 6.48$, $J_{5,6} = 6.52$ Hz), 4.11 (app. sep, br, 2 H, $\text{N}(\text{CH}(\text{CH}_3)_2)_2$), 4.06 (q, 2 H, OCH_2CH_3 , $J = 7.08$ Hz), 2.76 (br, 2 H, 5-H), 1.25 (d, br, 12 H, $\text{N}(\text{CH}(\text{CH}_3)_2)_2$, $J = 6.76$ Hz), 1.12 (t, 3 H, OCH_2CH_3 , $J = 7.08$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 100 MHz) δ 159.3 (2-C), 153.5 (4-C), 139.8 (7-C), 102.8 (6-C), 61.3 (OCH_2CH_3), 48.1 ($\text{N}(\text{CH}(\text{CH}_3)_2)_2$), 21.6 and 20.2 (br, $\text{N}(\text{CH}(\text{CH}_3)_2)_2$), 15.0 (OCH_2CH_3); IR (neat film) 2974.2 m, 2934.5 w, 1601.4 s, 1558.9 vs, 1515.8 vs, 1462.4 m, 1370.9 m, 1348.4 m, 1285.3 vs, 1248.5 s, 1202.3 m, 1153.3 m, 1135.2 m, 1107.1 w, 1058.7 m, 1036.4 w, 1006.0 w, 873.6 w, 785.6 w, 766.1 w, 697.0 m, 623 w cm^{-1} ; MS m/z 237 (M^+ , 100%), 222 (9), 208 (6), 194 (99), 180 (9), 166 (14), 152 (19), 138 (7), 123 (33), 108 (41), 82 (δ), 71 (33), 58 (20), 56 (21), 54 (24). HRMS, calcd. for $^{12}\text{C}_{13}\text{H}_{23}\text{N}_3\text{O}$: 237.1849; found: 237.1841. Anal. calcd. for $\text{C}_{13}\text{H}_{23}\text{N}_3\text{O}$: C, 65.88; H, 9.77; N, 17.70%. Found: C, 65.71; H, 9.90; N, 17.41%.

4-Dimethylamino-2-isopropoxy-5H-1,3-diazepine 25h

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether. Pale pink solid, mp 64–65 °C; yield: 63%. ^1H NMR (acetone- d_6 , 301 K, 500 MHz) δ 6.50 (d, 1 H, 7-H, $J_{6,7} = 6.50$ Hz), 4.99 (sep, 1 H, $\text{OCH}(\text{CH}_3)_2$, $J = 6.50$ Hz), 4.78 (q, 1 H, 6-H, $J_{6,7} = 6.50$, $J_{5,6} = 7.00$ Hz), 2.99 (br s, 6 H, $\text{N}(\text{CH}_3)_2$), 2.72 (d, 2 H, 5-H, $J_{5,6} = 7.00$ Hz), 1.20 (d, 6 H, $\text{OCH}(\text{CH}_3)_2$, $J = 6.50$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 125 MHz) δ 159.2 (2-C), 156.3 (4-C), 139.9 (7-C), 101.4 (6-C), 67.3 ($\text{OCH}(\text{CH}_3)_2$), 38.4 (br, $\text{N}(\text{CH}_3)_2$), 29.8 (5-C), 22.3 ($\text{OCH}(\text{CH}_3)_2$); IR (KBr) 3023.2 w, 2971.1 w, 1605.0 vs, 1589.2 s, 1522.9 vs, 1438.0 w, 1416.2 w, 1369.3 w, 1328.2 m, 1294.0 m, 1280.1 s, 1250.9 s, 1206.3 m, 1172.4 w, 1143.3 w, 1108.6 s, 1008.7 m, 929.7 w, 885.1 m, 782.7 w, 701.5 m cm^{-1} ; MS (EI) m/z 195 (M^+ , 60%), 153 (39), 138 (60), 137 (91), 136 (34), 109 (48), 71 (79), 43 (33). HRMS, calcd. for $^{12}\text{C}_{10}\text{H}_{17}\text{N}_3\text{O}$: 195.1374; found:

195.1372. Anal. calcd. for $\text{C}_{10}\text{H}_{17}\text{N}_3\text{O}$: C, 61.51; H, 8.78; N, 21.52%. Found: C, 61.30; H, 8.99; N, 21.58%.

4-Diethylamino-2-isopropoxy-5H-1,3-diazepine 25i

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether. Pale yellow oil; yield: 72%. ^1H NMR (acetone- d_6 , 301 K, 500 MHz) δ 6.49 (d, 1 H, 7-H, $J_{6,7} = 6.50$ Hz), 4.96 (sep, 1 H, $\text{OCH}(\text{CH}_3)_2$, $J = 6.00$ Hz), 4.76 (q, 1 H, 6-H, $J_{6,7} = 6.50$, $J_{5,6} = 7.00$ Hz), 3.41 (q, 4 H, $\text{N}(\text{CH}_2\text{CH}_3)_2$, $J = 7.00$ Hz), 2.74 (d, 2 H, 5-H, $J_{5,6} = 7.00$ Hz), 1.18 (d, 6 H, $\text{OCH}(\text{CH}_3)_2$, $J = 6.00$ Hz), 1.05 (br t, 6 H, NCH_2CH_3 , $J = 7.00$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 125 MHz) δ 159.1 (2-C), 154.7 (4-C), 139.6 (7-C), 102.2 (6-C), 67.0 ($\text{OCH}(\text{CH}_3)_2$), 43.7 ($\text{N}(\text{CH}_2\text{CH}_3)_2$), 29.7 (C-5), 22.1 ($\text{OCH}(\text{CH}_3)_2$), 14.0 and 12.2 (NCH_2CH_3); IR (neat film) 2975.7 m, 2934.6 w, 1602.6 vs, 1575.3 vs, 1520.0 vs, 1471.5 m, 1432.6 m, 1381.3 w, 1368.3 w, 1350.6 m, 1329.3 m, 1305.3 m, 1270.2 vs, 1251.6 vs, 1212.7 vs, 1195.9 w, 1141.0 w, 1111.9 m, 1079.9 m, 1030.6 w, 986.8 w, 936.5 w, 881.8 m, 801.4 w, 783.0 w, 699.6 m cm^{-1} ; MS m/z 223 (M^+ , 83%), 181 (45), 166 (47), 165 (100), 150 (42), 136 (47), 110 (35), 99 (62), 82 (59), 72 (38), 56 (39), 43 (38). HRMS, calcd. for $^{12}\text{C}_{12}\text{H}_{21}\text{N}_3\text{O}$: 223.1688; found: 223.1687. Anal. calcd. for $\text{C}_{12}\text{H}_{21}\text{N}_3\text{O}$: C, 64.54; H, 9.48; N, 18.82%. Found: C, 64.97; H, 9.61; N, 18.60%.

4-Diisopropylamino-2-isopropoxy-5H-1,3-diazepine 25j

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether. Pale yellow oil; yield: 65%. ^1H NMR (acetone- d_6 , 301 K, 400 MHz) δ 6.53 (d, 7 H, 1-H, $J_{6,7} = 6.48$ Hz), 4.96 (sep, 1 H, OiPr, $J = 6.16$ Hz), 4.68 (q, 6 H, 1-H, $J_{6,7} = 6.48$, $J_{6,5} = 6.48$ Hz), 4.12 br (2 H, $\text{N}(\text{iPr})_2$), 2.79 br (2 H, 5-H), 1.25 br (12 H, $\text{N}(\text{iPr})_2$), 1.20 (d, 6 H, OiPr, $J = 6.16$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 100 MHz) δ 158.6 (2-C), 153.4 br (4-C), 139.6 (7-C), 102.6 (6-C), 67.3 (OiPr), 48.0 br (2 \times CH, NiPr), 32.8 (5-C), 22.4 (2 \times CH_3 , OiPr), 21.6 and 20.1 br (4 \times CH_3 , NiPr); IR (KBr) 2974.6 m, 2934.0 m, 1600.7 m, 1557.8 vs, 1505.6 vs, 1463.3 s, 1372.4 s, 1284.5 s, 1251.2 s, 1203.5 m, 1154.8 m, 1108.2 s, 1040.4 w, 936.6 w, 781.5 w, 698.0 w cm^{-1} ; MS (EI) m/z 251 (M^+ , 40%), 209 (19), 208 (16), 193 (38), 178 (28), 166 (53), 152 (11), 150 (38), 123 (40), 120 (32), 118 (90), 116 (100), 111 (15), 108 (89), 85 (35), 84 (27), 83 (44), 82 (47), 81 (52), 59 (48), 58 (45), 43 (59), 28 (42). HRMS, calcd. for $^{12}\text{C}_{14}\text{H}_{25}\text{N}_3\text{O}$: 251.199838; found: 251.199213. Anal. calcd. for $\text{C}_{14}\text{H}_{25}\text{N}_3\text{O}$: C, 66.89; H, 10.02; N, 16.72%. Found: C, 66.71; H, 9.97; N, 16.97%.

2-Isopropoxy-4-pyrrolidino-5H-1,3-diazepine 25k

Purified by column chromatography (Al_2O_3 90/neutral-deactivated) eluting with diethyl ether/methylene chloride (10 : 2) solvent mixture. Yellow oil; yield: 65%. ^1H NMR (acetone- d_6 , 301 K, 500 MHz) δ 6.47 (d, 1 H, 7-H, $J_{6,7} = 6.50$ Hz), 4.96 (sep, 1 H, OiPr, $J = 6.50$ Hz), 4.80 (q, 1 H, 6-H, $J_{6,7} = 6.50$, $J_{5,6} = 7.00$ Hz), 3.49 and 3.34 (t, 4 H, pyrrolidine ring, $J = 7.00$ Hz), 2.70 (d, 2 H, 5-H, $J_{5,6} = 7.00$ Hz), 1.94 and 1.84 (qnt, 4 H, pyrrolidine ring, $J = 7.00$ Hz), 1.18 (d, 6 H, OiPr, $J = 6.50$ Hz); ^{13}C NMR (acetone- d_6 , 301 K, 125 MHz) δ 159.4 (2-C), 154.4 (4-C), 139.8 (7-C), 101.2 (6-C), 67.3 (OiPr), 48.3 and 47.9 (pyrrolidine ring), 31.6 (C-5), 26.3 and 25.2 (pyrrolidine ring), 22.3 (OiPr); IR (neat film) 2974.2 m, 2873.6 w, 1601.9 s, 1575.4 vs, 1520.0 vs, 1483.1 s, 1460.2 m, 1380.8 w, 1368.7 w, 1350.8 m, 1326.8 w, 1280.2 vs, 1248.4 vs, 1189.3 w, 1125.4 w, 1109.9 m, 1020.3 m, 968.4 w, 935.5 w, 884.2 m, 783.4 w, 696.7 m cm^{-1} ; MS (EI) m/z 221 (M^+ , 92%), 179 (55), 164 (64), 163 (99), 162 (53), 131 (78), 119 (100), 110 (23), 109 (32), 100 (32), 97 (40), 82 (45), 70 (85), 55 (56), 43 (40), 41 (39). HRMS, calcd. for $^{12}\text{C}_{12}\text{H}_{19}\text{N}_3\text{O}$: 221.1527; found: 221.1528. Anal. calcd. for $\text{C}_{12}\text{H}_{19}\text{N}_3\text{O}$: C, 65.13; H, 8.65; N, 18.99%. Found: C, 65.32; H, 8.77; N, 18.64%.

5,7-Bis(trifluoromethyl)-4-diethylamino-2-ethoxy-5H-1,3-diazepine 40

Purified by column chromatography (deactivated silica gel 100, hexane/CH₂Cl₂, 90 : 10). White solid; mp 72–73 °C; yield 81%. ¹H NMR (400 MHz, acetone-*d*₆) δ 5.40 (d, 1 H, 6-H, *J*_{5,6} = 9.9 Hz), 5.07 (m, 1 H, 5-H), 4.10 (q, 2 H, OCH₂CH₃, ³*J* = 7.2 Hz), 3.58 (m, 4 H, NCH₂CH₃, ³*J* = 6.8 Hz), 1.23 (t, 3 H, OCH₂CH₃, ³*J* = 7.2 Hz), 1.20 (t, 6 H, NCH₂CH₃, ³*J* = 6.8 Hz); ¹³C NMR (100 MHz, acetone-*d*₆) δ 160.1 (C-2), 149.3 (C-4), 143.8 (q, C-7, *J*_{C,F} = 31 Hz), 125.0 (q, CF₃, *J*_{C,F} = 273 Hz), 122.5 (q, CF₃, *J*_{C,F} = 272 Hz), 96.3 (C-6), 62.8 (OCH₂CH₃), 45.4, 45.1 (NCH₂CH₃), 43.4 (q, C-5, *J*_{C,F} = 31 Hz), 14.6 (OCH₂CH₃), 13.7, 12.1 (NCH₂CH₃). IR (KBr) 3081.0 w, 2991.4 w, 2943.2 w, 2909.6 w, 2882.1 w, 1634.4 m, 1583.0 vs, 1523.8 vs, 1510.1 s, 1477.8 s, 1456.6 m, 1387.2 m, 1360.6 m, 1330.9 m, 1311.8 s, 1279.7 m, 1255.7 vs, 1213.8 m, 1180.8 vs, 1169.7 vs, 1152.7 vs, 1127.3 vs, 1117.0 s, 1097.8 m, 1074.9 m, 1061.9 m, 1029.2 m, 1016.4 m, 983.5 w, 954.8 m, 933.5 w, 898.4 m, 885.0 w, 835.2 m, 806.0 w, 784.4 w, 752.9 w, 744.8 w, 732.1 w, 704.9 w, 685.8 w. MS (EI) *m/z* (M⁺, 100%), 326 (10), 301 (51), 286 (21), 276 (26), 274 (25), 245 (34), 217 (23), 166 (12), 151 (17), 99 (46), 72 (87), 70 (63), 58 (90), 43 (95). HRMS, calcd. for ¹²C₁₃H₁₇N₃OF₆: 345.1276; found: 345.1277. Anal. calcd. for C₁₃H₁₇N₃OF₆: C, 45.22; H, 4.96; N, 12.17%. Found: 44.99; H, 5.12; N, 11.89%.

3-Cyano-2-diisopropylaminopyrrole 27

This compound was obtained from **21T** using the general method for preparation of azepines in the presence of diisopropylamine and purified by distillation/sublimation (~50 °C, 1 × 10⁻² mm Hg); white waxy solid; mp 39–40 °C; yield 52%; ¹H NMR (400 MHz, acetone-*d*₆) δ 10.3 (br, 1 H, N-H), 6.57 (dd, 1 H, 5-H, *J*_{1,5} = 2.7 Hz, *J*_{4,5} = 3.3 Hz), 6.25 (dd, 1 H, 4-H, *J*_{1,4} = 2.6 Hz, *J*_{4,5} = 3.3 Hz), 3.54 (sept, 2 H, *i*Pr, ³*J* = 6.5 Hz), 1.02 (d, 12 H, *i*Pr, ³*J* = 6.5 Hz); ¹³C NMR (100 MHz, acetone-*d*₆) δ 143.1 (C-5), 118.4 (CN), 115.5 (C-2), 110.2 (C-3), 89.7 (C-4), 50.4 (*i*Pr), 21.9 (*i*Pr); ¹⁵N NMR (CDCl₃ referenced to external nitromethane) δ -198 (pyrrole-N), -105 (CN), -295 (amino group); IR (KBr) 3324 br, 2970 s, 2959 m, 2915 w, 2219 vs, 2187 vs, 1618 m, 1605 m, 1564 vs, 1533 m, 1445 s, 1429 s, 1381 s, 1355 m, 1346 s, 1323 m, 1284 m, 1251 m, 1203 w, 1189 m, 1143 m, 1122 m, 1081 m, 961 w, 884 w. MS (EI) *m/z* (M⁺, 51%), 176 (18), 148 (10), 134 (100), 118 (8), 107 (69), 92 (6). 191.1423. Anal. calcd. for C₁₁H₁₇N₃: C, 69.07; H, 8.96; N, 21.97%. Found: C, 69.29; H, 9.23; N, 21.88%.

3,3'-Dicyano-2,2'-diisopropylidimethyldipyrrolylmethane 28

Obtained from **27** by recrystallization from hot acetone; white solid, mp 269–270 °C, yield 98%. ¹H NMR (400 MHz, acetone-*d*₆) δ 10.2 (br, 2 H, N-H), 5.99 (s, 2 H, 3-H), 3.52 (sept, 4 H, *i*Pr, ³*J* = 6.4 Hz), 1.60 (s, 6 H, CH₃), 0.97 (d, 24 H, *i*Pr, ³*J* = 6.4 Hz); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 142.1 (C-5), 135.4 (C-2), 118.2 (CN), 104.9 (C-3), 87.6 (C-4), 48.9 (*i*Pr), 34.4 (C-CH₃), 27.8 (br, CH₃), 21.3 (*i*Pr). IR (KBr) 3251.6 br, 2975.0 m, 2935.6 w, 2987.3 w, 2222.4 vs, 1589.9 s, 1580.1 s, 1517.3 w, 1437.1 m, 1384.0 m, 1365.2 w, 1330.6 w, 1298.4 w, 1255.8 w, 1188.5 m, 1126.7 w, 1106.9 w, 1056 w, 1018.3 w, 924.3 w, 807.0 w, 796.3 m. MS (EI) *m/z* 422 (M⁺, 7%), 407 (3), 238 (18), 232 (28), 194 (10),

192 (14), 191 (100), 190 (6), 188 (16), 180 (5), 176 (12), 174 (9), 149 (6), 148 (9), 134 (14), 107 (4), 106 (7), 43 (19), 41 (7). HRMS, calcd. for ¹²C₂₅H₃₈N₆: 422.3158; found: 422.3157. Anal. calcd. for C₂₅H₃₈N₆: C, 70.09; H, 9.06; N, 19.89%. Found: C, 70.33; H, 9.11; N, 19.58%.

2-Diisopropylamino-3,5-bis(trifluoromethyl)-3H-pyrrole-3-carbonitrile 45

This compound was obtained from **38T** under the general conditions for preparation of diazepines in the presence diisopropylamine; white solid; mp 59–60 °C; 50% yield. ¹H NMR (400 MHz, CDCl₃) δ 5.80 (s, 1H), 4.33 and 3.69 (two broadened singlets due to slow isopropyl rotation, 1H each), 1.5–1.2 (broadened multiplet, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 163 (s, C=N), 153.5 (q, C-CF₃), 121.5 (q, CF₃), 119.2 (q, CF₃), 110.4 (s, CN), 104.10 (s, CH), 104.06 (s, CH), 57.0 (C(q)-CF₃), 53.7 (broadened s, CH), 49.7 (broadened s, CH), 20.9, 19.9, 19.2, 18.6 (four broadened isopropyl CH₃ groups); IR (KBr) ν 2260w cm⁻¹; MS *m/z* 327. Anal. Calcd for C₁₃H₁₅N₃F₆: C, 47.71; H, 4.62; N, 12.84%. Found C, 47.84; H, 4.58; N, 12.32%.

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