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1*H*-1,3-Diazepines, 5*H*-1,3-diazepines, 1,3-diazepinones, and 2,4-diazabicyclo[3.2.0]heptenes †, ‡

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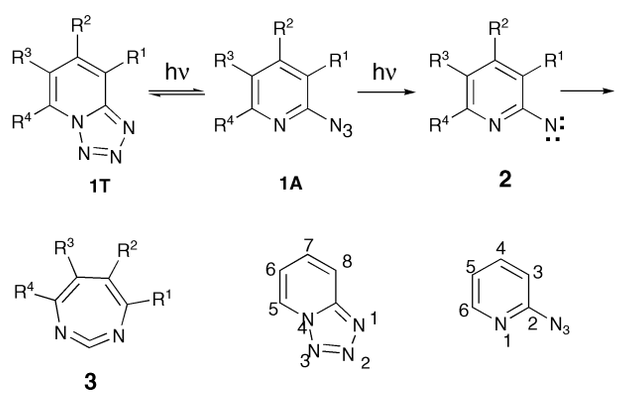
Tetrazolo[1,5-*a*]pyridines/2-azidopyridines **1** undergo photochemical nitrogen elimination and ring expansion to 1,3-diazacyclohepta-1,2,4,6-tetraenes **3**, which react with alcohols to afford 2-alkoxy-1*H*-1,3-diazepines **4** (**5**), with secondary amines to 2-dialkylamino-5*H*-1,3-diazepines **16**, sometimes *via* isolable 2-dialkylamino-1*H*-1,3-diazepines **15**, and with water to 1,3-diazepin-2-ones **19**. The latter are also obtained by elimination of isobutene or propene from 2-*tert*-butoxy- or 2-isopropoxy-1*H*-1,3-diazepines **4** or **5**. 1,3-Diazepin-2-one **22B** and 1,3-diazepin-4-one **24** were obtained from hydrolysis of the corresponding 4-chlorodiazepines. Diazepinones **19** undergo photochemical ring closure to diazabicycloheptenones **25** in high yields. The 2-alkoxy-1*H*-1,3-diazepines **4** and **5** interconvert by rapid proton exchange between positions N1 and N3. The free energies of activation for the proton exchange were measured by the Forsén–Hoffman method as $\Delta G^{\ddagger}_{298} = 16.2 \pm 0.6$ kcal mol^{-1} as an average for **4a**–**c** in CD_2Cl_2, acetone-d_6, and methanol-d_4, and 14.1 ± 0.6 kcal mol^{-1} for **4c** in acetone/D_2O. The structures of 2-methoxy-5,6-bis(trifluoromethyl)-1*H*-1,3-diazepine **4k**, 1,2-dihydro-4-diethylamino-5*H*-1,3-diazepin-2-one **22bB**, and diazabicycloheptanone **26** were determined by X-ray crystallography. The former represents the first reported X-ray crystal structure of any monocyclic *N*-unsubstituted 1*H*-azepine.

Introduction

1,4-Diazepines are well known for their many pharmaceutical properties. In contrast, 1,3-diazepines are relatively little known.[3] Some 1,3-diazepin-2-ones and other cyclic ureas have received considerable attention recently as potential anti-AIDS drugs.[4] In previous communications we have described the photolysis of variously substituted tetrazolo[1,5-*a*]pyridines **1T**/2-azidopyridines **1A** as 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**, which in several cases have been characterized by matrix-isolation IR spectroscopy (Scheme 1).[2,5] Here we report full details of the syntheses of the title compounds by nucleophilic trapping of **3** as well as the first X-ray crystal structure of an *N*-unsubstituted 1*H*-azepine.



Scheme 1

Results and discussion

1 1*H*-1,3-Diazepines

Photolysis of tetrazoles/azides (**1T/1A**) in 1,4-dioxan solution in the presence of alcohols afforded 2-alkoxy-1,3-diazepines **4** (**5**) as indicated in Scheme 2 and Table 1. Most of these diazepines are distillable, yellow to orange compounds, often crystalline in the solid state. Unsymmetrical diazepines of this kind can exist in two *NH* tautomeric forms, **4** and **5**, of which the isomers with the substituent the farthest away from the NH site usually dominates. For each of the isomeric tetrazole/azide pairs **6** and **7**, **8** and **9**, and **10** and **11**, the same cyclic carbodiimide intermediate **3** is formed.[5a] Consequently, nucleophilic trapping affords the same diazepines **4** (**5**) for each pair. The compounds and yields are listed in Table 1. The chemical shifts and coupling patterns in the proton NMR spectra clearly identify these compounds as the 1*H*, not the 4*H* or 5*H*, isomers. The proton attached to the carbon atom next to the NH function couples with the NH proton. Decoupling of the NH proton by double irradiation or by addition of a drop of D_2O causes a corresponding reduced multiplicity of the CH signal. The ^{1}H NMR spectra were fully assigned in several cases by means of homonuclear decoupling experiments. The ^{13}C NMR spectra were fully assigned in several cases by means of 2-D HMBC experiments (*e.g.* for **4b**), or by means of short- and long-range C–F couplings in the compounds containing CF_3 groups.

† Preliminary reports on parts of this work have been published in ref 1. This paper is Diazepines, Part 3. For Part 2, see ref 2.

‡ Electronic supplementary information (ESI) available: NMR spectra of **4a**, **4c**, **19v** ⟶ **20**, **19a** ⟶ **25a**, and **19g** ⟶ **25g** (Fig. S1–S6), Arrhenius and Eyring plots for H-exchange in **4b**,**c** (Fig. S7), views of the X-ray crystal structures of compounds **26** and **22bB** (Fig. S8–S9), bond lengths and angles for compounds **4k**, **22bB** and **26**, preparative procedures and characterization data for all compounds not described in the Experimental section, and computational data (Cartesian coordinates, absolute energies, IR, ^{1}H and ^{13}C NMR) for **20a**–**c**, **21a**–**b**, **22aA**–**F** and **22aB** dimer. See http://www.rsc.org/suppdata/ob/b3/b317099c/

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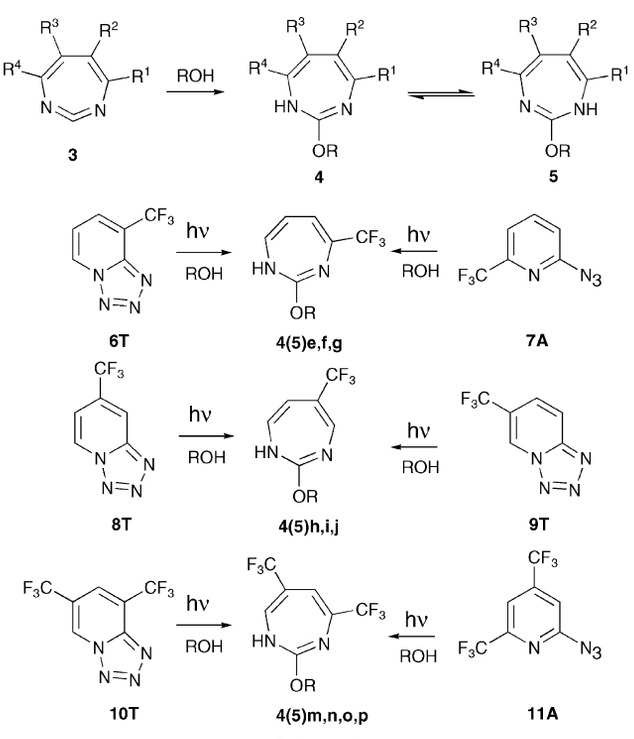
Table 1 1*H*-1,3-Diazepines **4**(**5**) from reaction of tetrazoles/azides **1T/1A** with alcohols ROH

	R^1	R^2	R^3	R^4	OR	Yield (%)
a	H	H	H	H	OMe	53[a,b]
b	H	H	H	H	OEt	72[a,b]
c	H	H	H	H	OiPr	53[a]
d	H	H	H	H	OtBu	[c]
e	CF_3	H	H	H	OMe	92[a] from **7a**[d,e], 47[a] from **6T**
f	CF_3	H	H	H	OEt	89[a] from **7a**[e]
g	CF_3	H	H	H	OtBu	94[a] from **7a**[e]
h	H	CF_3	H	H	OMe	72[a] from **8T**[d], 69[a] from **9T**[d,e]
i	H	CF_3	H	H	OEt	74[a] from **8T**
j	H	CF_3	H	H	OtBu	[c]
k	H	CF_3	CF_3	H	OMe	80[f,g]
l	H	CF_3	CF_3	H	OEt	60[a]
m	CF_3	H	CF_3	H	OMe	95[a] from **11A**, 67[a] from **10T**
n	CF_3	H	CF_3	H	OEt	93[a] from **11A**, 64[a] from **10T**
o	CF_3	H	CF_3	H	OiPr	95[a] from **11A**
p	CF_3	H	CF_3	H	OtBu	89[a]
q	CF_3	H	H	CF_3	OMe	93[a]
r	CF_3	H	H	CF_3	OEt	90[a]
s	CF_3	H	H	CF_3	OtBu	67[a]
t	CH_3	H	H	H	OMe	60[h]
u	CH_3	H	H	H	OEt	52[a]
v	H	H	H	Cl	OtBu	[c]
x	CF_3	H	Cl	H	OtBu	[c]
y	CF_3	H	CF_3	Cl	OEt	[i]
z	CH_3	H	CF_3	Cl	OtBu	[c]

[a] Isolated yield, after distillation. [b] Crude yield >95% by NMR and/or GC [c] Not isolable due to elimination of isobutene, affording **19** (see Table 4). [d] Two precursors, see Scheme 2. [e] The major isomer **4** is listed; this is in equilibrium with the minor isomer **5**. [f] Isolated by preparative TLC. [g] X-ray crystal structure, see Fig. 5. [h] Yield estimated by ^{1}H NMR. [i] Not isolated; see Ref. 2.



Scheme 2

In some cases, individual signals for **4** and **5** can be observed in the NMR spectra, *e.g.* for **4h/5h** and **4i/5i** (see experimental data in the ESI material for details ‡), but in most cases only one set of signals is observed. In the case of **4h/5h** the isomer ratio is 2 : 1. Irradiation of one of the ^{1}H NMR signals of **4h**, for example, not only allows identification of the proton with which it couples; it also causes the complete disappearance of the corresponding peak of **5h**. Therefore, the two isomers exist in a fast equilibrium. Compounds substituted only on 2-C exhibit individual signals for 4-H, 5-H, 6-H and 7-H, as seen for example in the ^{1}H NMR spectrum of **4b** in Fig. 1a. However, if one proton in **4b** is irradiated, *e.g.* 4-H, the signal for 7-H disappears as well (Fig. 1b). If 5-H is irradiated, the signal for 6-H disappears too (Fig. 1e–f). Therefore, there is fast and degenerate interconversion of **4b** and **5b**, presumably by exchange of H between 1-N and 3-N. However, the rate of exchange was not experimentally accessible using conventional coalescence technique.[6] Line broadening occurred in the ^{1}H NMR spectrum on heating the solution of **4a** to 130 °C, but the coalescence temperature was not reached (Fig. S1 in the ESI material ‡). Therefore, we used the Forsén–Hoffman double resonance saturation transfer method[7] to determine the free energies of activation for the H-exchange interconverting **4** and **5**.

The Forsén–Hoffman method is limited to cases where the rate of exchange approximately equals the longitudinal spin–lattice relaxation time T_1. Nuclear Overhauser effects in proton NMR can limit the accuracy of the method when the two exchanging nuclei are in the same molecule. Observing a ^{13}C nucleus instead of ^{1}H overcomes this problem. Saturation of a site, *e.g.* ν_b, by irradiation with a strong radiofrequency field causes perturbation of its spin distribution, which is transferred to the site ν_a which is being observed. The lifetime τ_a of this site depends on the relaxation time T_1 and the rate constant for the exchange, k_a. Therefore, T_1 must be determined by the standard inversion–recovery technique using the pulse sequence $(T_D$–π–τ–$\pi/2)n$. τ_a and k_a are then obtained from the equations

$$\tau_a = T_1 \times \{M_z^a(\infty)/M_z^a(0) - (M_z^a(\infty)\} \quad (1)$$

and

$$k_a = 1/\tau_a \quad (2)$$

where $M_z^a(\infty)$ is the measured intensity of magnetization at site ν_a, and $M_z^a(0)$ is the measured intensity of magnetization in the absence of irradiation. Knowing k_a, activation parameters can then be obtained from the Arrhenius and Eyring equations.[6]

Fig. 2 shows an example of a saturation–transfer experiment using the 2-isopropoxy-1,3-diazepine **4c** in CD_2Cl_2 solution.

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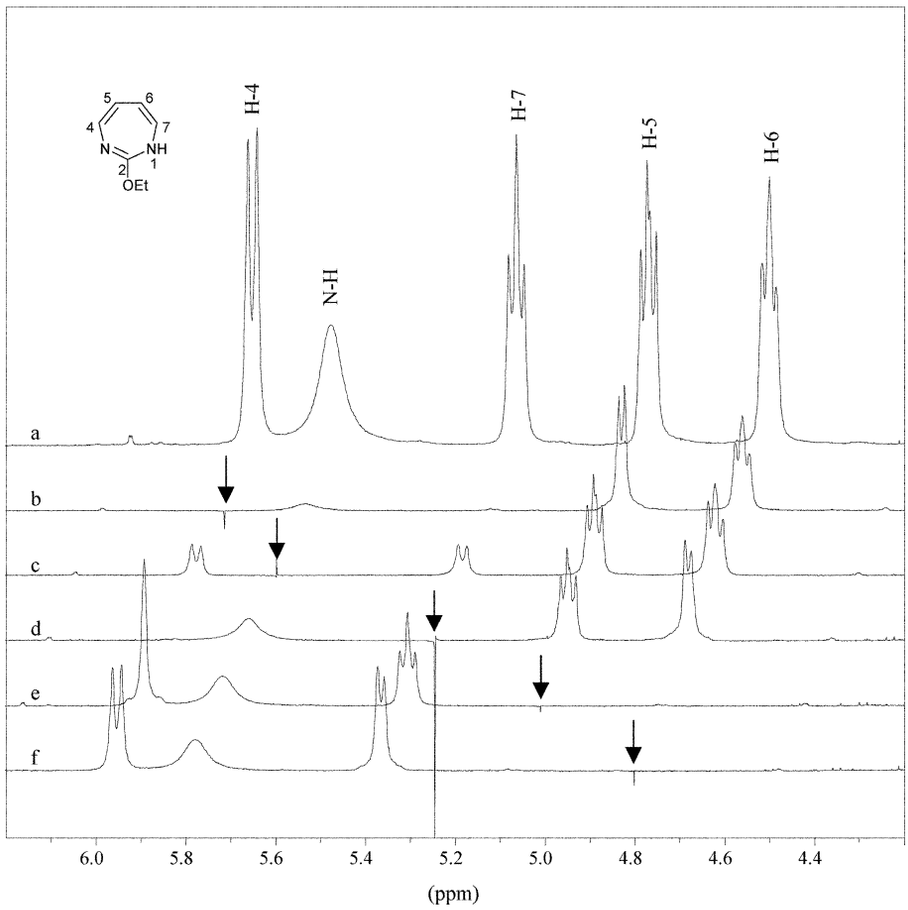

Fig. 1 Decoupling experiments on **4b**. ^{1}H homonuclear decoupling with selective irradiation at each resonance as indicated by arrows.

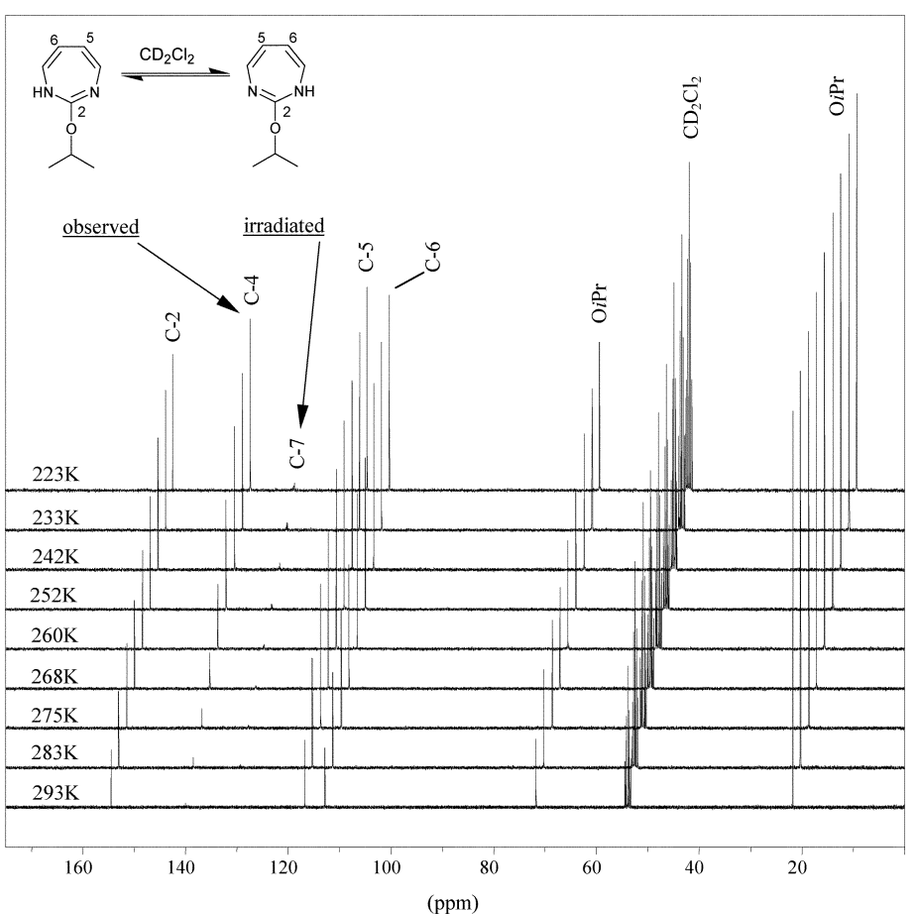

Fig. 2 Saturation–transfer experiment: stacked ^{13}C NMR spectra (100 MHz) of 2-propoxy-1*H*-1,3-diazepine **4c** obtained as a function of temperatures in CD_2Cl_2 solution. Carbon C-7 was irradiated and carbon C-4 observed. 32 Scans were collected in each run.

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Table 2 Activation parameters for hydrogen exchange between N1 and N3 in 2-alkoxy-1*H*-1,3-diazepines **4**[a]

Compd	Solvent	E_a/kcal mol^{-1}	A/s^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}_{298}$/kcal mol^{-1}
4a[a]	CD_2Cl_2	7.9 ± 0.3	3.2×10^6	7.3	−30.8	16.5 ± 0.3
4b[a]	Acetone-d_6	7.9 ± 1.1	2.3×10^7	8.3	−26.9	16.3 ± 1
4c[a]	CD_2Cl_2	9.2 ± 0.2	2.8×10^7	8.6	−24.5	15.9 ± 0.2
4c[a]	Acetone-d_6	11.4 ± 0.1	4.1×10^9	10.8	−16.5	15.8 ± 0.1
4c[a]	CD_3OD	12.3 ± 0.1	8.7×10^9	11.7	−15.0	16.2 ± 0.1
4c[b]	Acetone-d_6/D_2O	—	—	—	—	14.1 ± 0.6

[a] Forsén-Hoffman method. [b] Coalescence experiment, T_c = 308 ± 0.5 K.

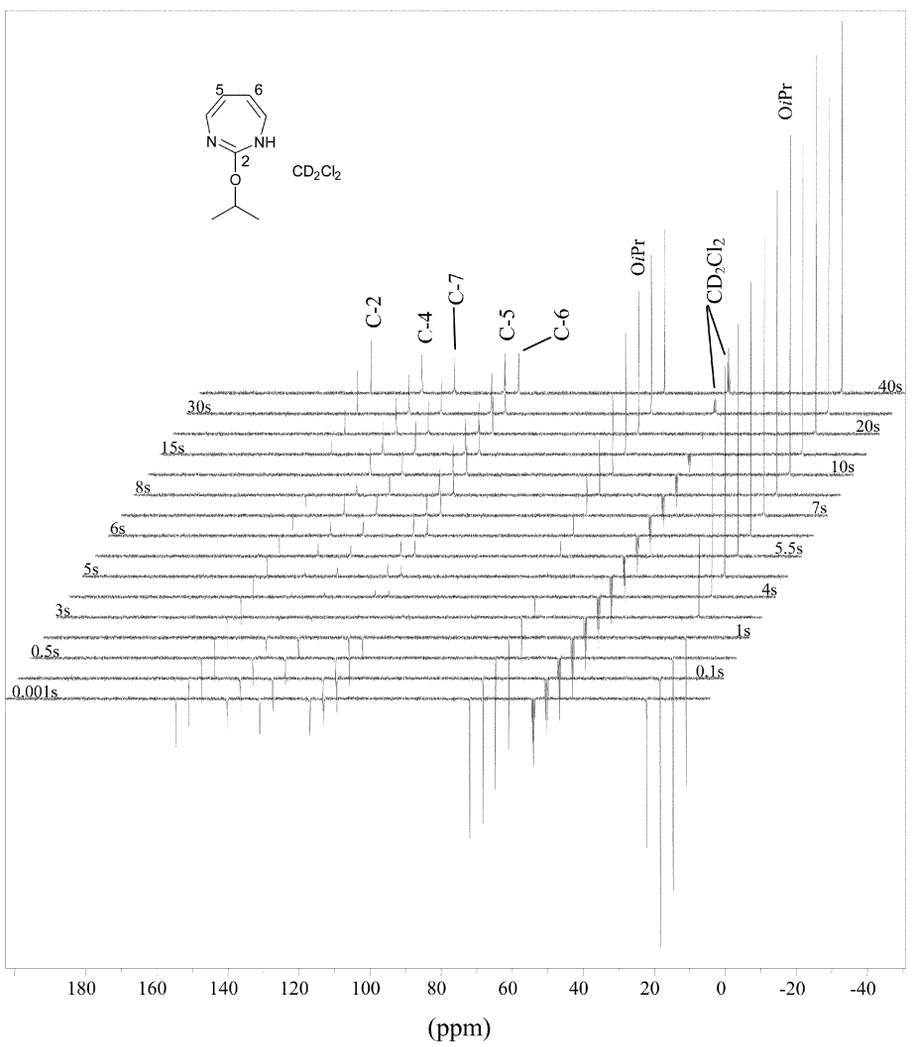

Fig. 3 Inversion–recovery experiment on **4c**. ^{13}C NMR at 125 MHz in CD_2Cl_2. The times indicated in each spectrum are the delay times in s after which the 90° sampling pulse was applied after the inversion. The derived spin–lattice relaxation times T_1 are C2, 20.37; C4, 5.51; C7, 5.29; C5, 4.76; C6, 4.84; OiPr(CH), 7.59; OiPr(CH_3), 4.04 s.

The corresponding inversion–recovery experiment with determination of T_1 is shown in Fig. 3. Analogous experiments were carried out with **4c** in acetone-d_6 and methanol-d_4, with **4a** in CD_2Cl_2 and with **4b** in acetone-d_6. In all cases, excellent Arrhenius and Eyring plots were obtained,[8] and the resulting activation parameters are given in Table 2. The average free energy of activation, $\Delta G^{\ddagger}_{298}$ = 16.2 ± 0.6 kcal mol^{-1}, for the three diazepines **4a**–**c** reveals that there is hardly any structural or solvent effect in the three solvents used (average $\Delta H^{\ddagger}$ = 9.3 ± 2 kcal mol^{-1}; $\Delta S^{\ddagger}$ = 22.7 ± 8 cal K^{-1} mol^{-1}). The most likely mechanism is intermolecular H-transfer between neighbouring diazepine molecules (Fig. 4). Only by using acetone/D_2O as a solvent was a decrease in the activation free energy to 14.1 ± 0.6 kcal mol^{-1} observed (Table 2). The deuterium isotope effect can be expected to cause a slightly *decreased* rate of exchange (*cf.* data for CD_3OD in Table 2), but the net rate increase

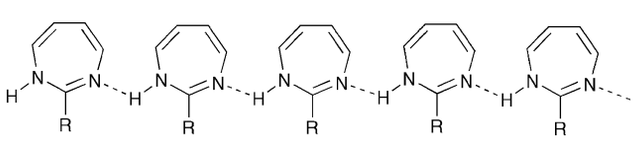

Fig. 4 1,3-H-exchange in hydrogen bonded 1,3-diazepine molecules.

observed with D_2O indicates intermolecular H(D)-exchange between diazepine and (deuterated) water molecules, whereas in the other solvents the exchange is between diazepine molecules (Fig. 4). The exchange rate was fast enough for **4c** in acetone/D_2O to be measured by the conventional coalescence technique (Fig. S2 in the ESI material‡). The coalescence temperature for H4/H7 was 308 ± 0.5 K, from which the free energy of activation was calculated.

The structures of the 1,3-diazepines are boat-like. The

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Table 3 1*H*- and 5*H*-1,3-Diazepines **15** and **16** from reaction of tetrazoles/azides **1T/1A** with amines HNR_2 [a]

	R^1	R^2	R^3	R^4	NR_2	Yield 1*H* **15** (%)	Yield 5*H* **16** (%)
a	H	H	H	H	NEt_2	—	61 [b]
b	H	H	H	H	$N(iPr)_2$	—	67 [b,c]
e	CF_3	H	H	H	$N(iPr)_2$	64 [b]	20 [b,d]
t	CH_3	H	H	H	NMe_2	—	67 from **17**, 63 from **18** [b,c]
u	CH_3	H	H	H	NEt_2	—	64 from **17**, 68 from **18** [b,e]
ua	CH_3	H	H	H	$N(iPr)_2$	—	46 from **17**, 39 from **18** [b,e]
v	H	H	H	Cl	$N(iPr)_2$	—	[f]

[a] Other 5*H*-1,3-diazepines have been reported.[2] [b] Isolated yields after distillation or chromatography. [c] Crude yield >95% by ^1H NMR. [d] This compound exists in the 7-trifluoromethyl-5*H*-form. [e] Two precursors; see Scheme 4. [f] Rearranges to 2-(diisopropylamino)pyrrole-3-carbonitrile;[2] *cf.* Scheme 11.

structure of the 1*H*-1,3-diazepine **4k** was determined by single crystal X-ray structure (Fig. 5).§ This is the first reported crystal structure of any monocyclic *N*-unsubstituted azepine. A few polycyclic 1*H*-1,3-diazepines[9] and 1-benzoyl-1,3-diazepines,[1b,10] including **12e**,[1b] have been reported, and a 5*H*-1,3-diazepine[2] was described recently. The bond lengths and angles are as expected; the C2–N3 (1.275(3) Å) and C2–N1 (1.382(3) Å) bonds are consistent with a proton residing at N1, and this was confirmed by its identification from difference maps during refinement. The C–C single (C5–C6 1.487(4) Å) and double bonds (C4–C5 1.325(4) Å and C6–C7 1.328(4) Å) within the seven-membered ring are also clearly defined.

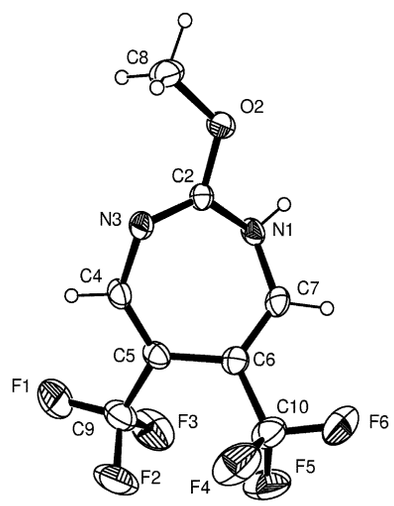
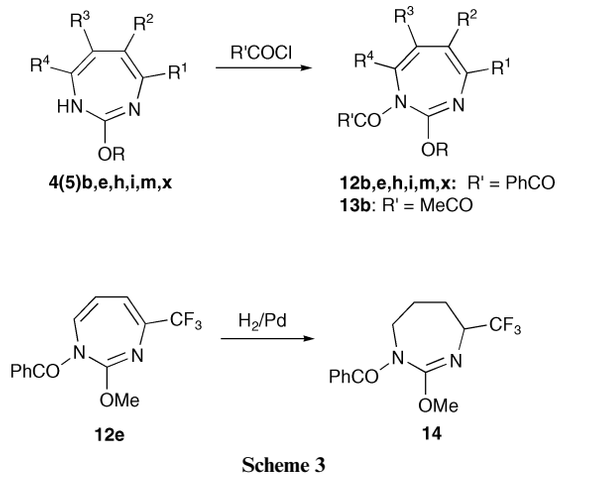
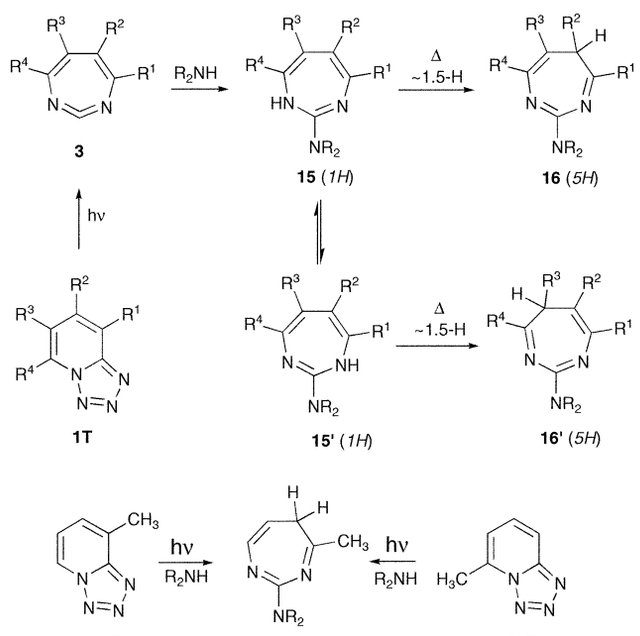


Fig. 5 ORTEP view of 1*H*-1,3-diazepine **4k** (30% ellipsoids).

The 1*H*-diazepines react with acid chlorides to afford 2-benzoyl derivatives **12b**,**e**,**h**,**i**,**m** and the 2-acetyl derivative **13b**. Catalytic hydrogenation of this compound affords the tetrahydro-derivative **14**. The amidine structure being very stable, this compound could not be reduced further (Scheme 3).



Scheme 3



Scheme 4

2. 3*H*-1,3-Diazepines

Analogous photolysis of the tetrazoles/azides **1** in the presence of secondary amines presumably also affords the 1*H*-1,3-diazepine as the initial product, which was isolable for the first time in the case of **15e**. This compound was fully characterised but isomerised to the 5*H* isomer **16e** on heating, best by gas chromatography at 130 °C, and partially on flash vacuum thermolysis at 600 °C. In all other cases the 5*H* isomers **16** were obtained directly in the photolysis reactions. The isolated compounds are listed in Scheme 4 and Table 3. In agreement with the experimental observations, theoretical calculations showed that the 2-alkoxy-1,3-diazepines are most stable in the 1*H*-form, but 2-dialkylamino-1,3-diazepines are usually more stable in the 5*H*-form.[1a] We have not found any limitation in the kind of substituent that can be used. The unsubstituted 2-dialkylamino-5*H*-1,3-diazepines **16a**–**c** are reported here, as well as trifluoromethyl- and methyl-substituted analogs. Several chloro- and alkoxy-substituted 2-dialkylamino-5*H*-1,3-diazepines have been described previously,[2] and cyano-substituted analogs will be reported.[11]

The 1*H*- and 5*H*-isomers **15** and **16** are related by 1,5-sigmatropic shifts of hydrogen. Substituted derivatives can in principle exist in two isomeric forms, **15′** and **16′** (Scheme 4). Unlike the alkoxy-substituted 1*H*-derivatives **4**(**5**) and the single

§ CCDC reference numbers: **4k**: 225886; **22bB**: 226705 **26**: 225887. See http://www.rsc.org/suppdata/ob/b3/b317099c/ for crystallographic data in cif or other electronic format.

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Table 4 Diazepinones **19** and diazabicycloheptenones **25**

	R^1	R^2	R^3	R^4	ROH	Yield **19** (%)	Yield **25** (%)[c]
a	H	H	H	H	H_2O[a]	76	98
a	H	H	H	H	tBuOH[b]	48	—
g	CF_3	H	H	H	tBuOH	98[d]	98
j	H	CF_3	H	H	tBuOH[b]	61	98
p	CF_3	H	CF_3	H	tBuOH	98[d]	98
s	CF_3	H	H	CF_3	tBuOH	100[e]	98
t	CH_3	H	H	H	H_2O[a]	81	98
v	H	H	H	Cl	tBuOH[b]	80	—
v	H	H	H	Cl	H_2O[a]	75	—
x	CF_3	H	Cl	H	tBuOH[b]	73	98
z	CF_3	H	CF_3	Cl	tBuOH[b]	53	98
aa	H	CH_3	H	H	H_2O[a]	67	98

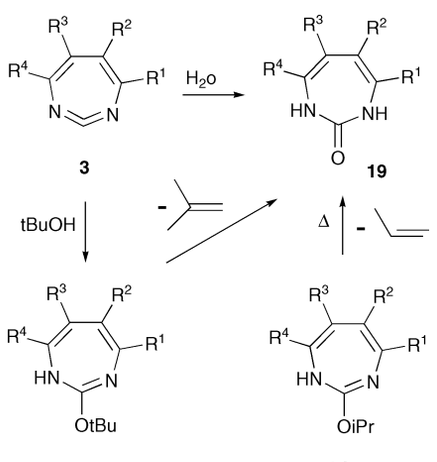
[a] By photolysis of **1T** in the presence of water. [b] By photolysis of **1T** in the presence of tBuOH. [c] By photolysis of **19** for 7–8 h. [d] By heating **4g** or **4p** at 100–120 °C for 30 min. [e] By heating **4s** at 70–80 °C for 15 min.

isolated amino-substituted 1*H*-derivative **15e**, the amino-substituted 5*H*-derivatives **16** tend to exist preferably with a substituent at C4 next to the methylene group at C5 (*e.g.* **16t**,**u**,**ua** (Scheme 4)). **16e** is an exception (Table 3). Isomeric tetrazolopyridines **1T** afford the same carbodiimides **3** and the same diazepine product. Thus, tetrazoles **17** and **18** both afforded the same diazepines **16** (Scheme 4 and Table 3).

The barriers to hindered rotations of the dialkylamino groups about the C–N single bonds in several 2-dialkylamino-5*H*-1,3-diazepine derivatives have been measured by NMR methods ($\Delta G^{\ddagger}_{298}$ = 15–16 kcal mol^{-1}).[8] The free energies of activation for ring inversion of the 5*H*-1,3-diazepines (9.5–12 kcal mol^{-1}) have also been measured[8] and will be the subject of a forthcoming publication.

3. 1,3-Diazepinones

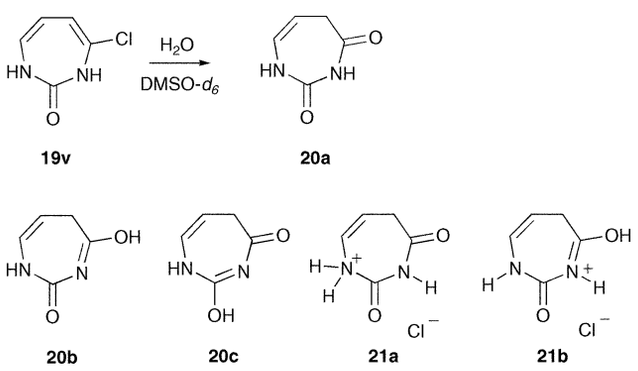
We found that all the 2-*tert*-butoxy-1,3-diazepines **4** reported in Table 1 as well as some of the 2-isopropoxy derivatives (**4c**,**o**) were thermally unstable and eliminated isobutene or propene, respectively, to furnish 1,3-diazepin-2-ones **19** (Scheme 5 and Table 4). In several cases the 2-*tert*-butoxy-1,3-diazepines were not isolable because they underwent isobutene elimination already during the initial photochemical preparation from **3**. When the isolable *tert*-butoxy derivative **4s** was heated above its melting point (40–41 °C), the melt suddenly solidified at *ca.* 80 °C to give white, crystalline diazepinone **19s**. When the thermal reaction of **4p** was monitored by ^{1}H NMR spectroscopy (DMSO-d_6 solution) at 87 °C, isobutene was readily observed at 1.67 and 4.64 ppm along with peaks due to **19s**. The reaction was complete in 45 min. The analogous elimination of propene from **4o** in DMSO-d_6 solution had a half-life of *ca.* 4 h at 130 °C.



Scheme 5

Moreover, the diazepinones **19** are conveniently obtained in high yields by photolysis of the appropriate tetrazoles/azides **1** in the presence of water (Scheme 5 and Table 4). Except for the 4-chloro derivative **19v** described below, they are stable, crystalline compounds, and they have all been fully characterized.

Although prepared by trapping of **3v** in dioxan/water solution, once isolated, the 4-chlorodiazepinone **19v** is sensitive to moisture. Its reaction with H_2O in DMSO-d_6 solution was investigated *in situ* by ^{13}C NMR spectroscopy as shown in Fig. S6 in the ESI material.‡ Compound **19v** gradually disappeared to be replaced by a new compound, which features two new quaternary carbons at 170 and 153 ppm, two further sp^{2}methine carbons at 125 and 106 ppm, and a CH_2 group at 34 ppm (verified in a DEPT-135 experiment). The corresponding ^{1}H NMR signals were a doublet of doublets at 6.0 (7-H), a quartet typical of 5*H*-1,3-diazepines at 5.1 (6-H), and a doublet at 2.95 ppm (CH_2). The ^{13}C NMR spectrum is in excellent agreement (sum of deviations 15.8 ppm) with the calculated spectrum of the diazepinedione **20a** (Scheme 6). NMR calculations were carried out at the B3LYP/6–31+G**//MP2/6–31G* level, which was previously established as the most accurate for this type of molecules.[12] The other hypothetically possible tautomers **20b** and **20c** have calculated energies 16.4 and 19.1 kcal mol^{-1} higher than **20a**, respectively. Energies were calculated at the MP2/6–31G* level of theory. Since HCl is formed in the reaction, the compound could also exist as the salt **21** (Scheme 6), or in equilibrium with this salt. Of the two tautomers **21a** and **21b**, the former is calculated to be 8.5 kcal mol^{-1} lower in energy. The calculated ^{13}C NMR spectra for these tautomers are in poorer agreement with the experimental spectrum than that of **20a** (sum of deviations 29.7 and 50.7 kcal mol^{-1}, respectively). The computational data are tabulated in the ESI material (Tables S4–S10).‡



Scheme 6

In order to obtain rigorous information on the nature of the substitution products derived from **19v**, the reaction with amines was investigated. This could in principle give rise to any

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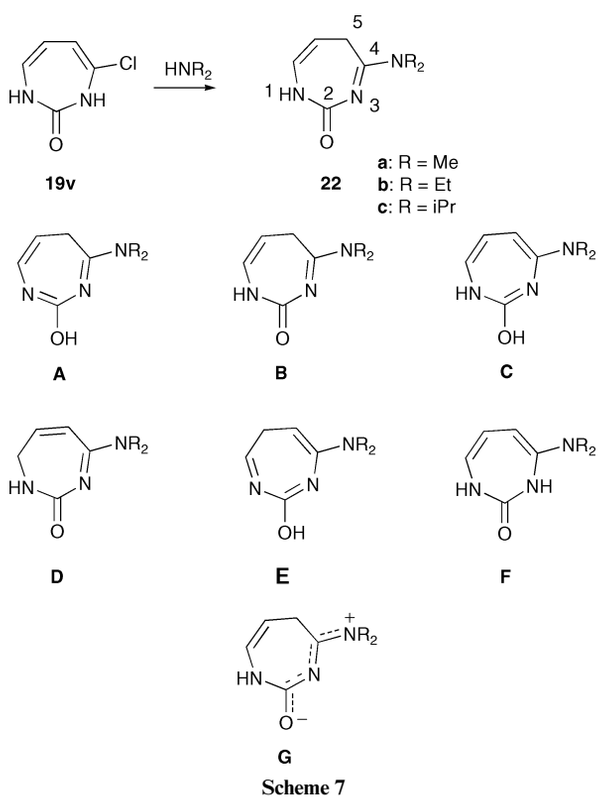
Table 5 Calculated relative energies (kcal mol^{-1}; 0 K) of structures **20a–c**, **21a–b** and tautomers **22aA–F** at various levels of theory with inclusion of scaled ZPVE (*cf.* Schemes 6 and 7)

	HF/6–31G*	B3LYP/6–31G*	MP2/6–31G*[a]
20a	0.0		0.0
20b	18.3		16.2
20c	20.1		18.7
21a	0.0		0.0
21b	−15.3		8.2
22aA	0.0	0.0	0.0
22aB	−11.6	−10.3	−9.8
22aC	11.3	12.0	13.1
22aD	−8.8	−5.7	−6.6
22aE	10.6	8.7	9.3
22aF	−9.4	−6.2	−5.8

[a] the ZPVE from the HF/6–31G* calculation was used.

of the six tautomers of **22 A–F** (Scheme 7). *Ab initio* calculations (HF/6–31G*, MP2/6–31G* and B3LYP/6–31G*) confirmed chemical intuition that **B** is the most stable tautomer, followed by **D, F, A, E** and **C** in the order of increasing energy (Table 5 and Table S8). The compounds **22** obtained show a CH_2 group in the proton and carbon NMR spectra. Tautomers **C**, **E**, and **F** are in discord with the ^{1}H NMR spectra. Tautomer **B** is in excellent accord with the calculated ^{13}C and ^{1}H NMR data (for full details see the ESI material, Tables S6–S7‡). However, the urea-type structures **B**, **D**, and **F** have calculated C=O stretching vibrations at 1717, 1725 and 1740 cm^{-1}, respectively (for **22a** in the gas phase at the B3LYP/6–31G* level; for full details see Table S5). In contrast, the highest experimental wavenumbers that come into consideration for a carbonyl group are in the low-to-middle 1600 cm^{-1} range. Therefore, at first sight, the 2-hydroxy tautomer **A** appeared to fit the IR spectroscopic data better than tautomer **B**.



Scheme 7

However, the IR spectra in KBr clearly show highly hydrogen bonded NH or OH groups absorbing between 3600 and 2800 cm^{-1}, and a weak and broad signal near 8.5 ppm in the ^{1}H NMR could be due to either NH or OH. Strong hydrogen bonding would make the experimental IR spectra of tautomers **A** or **B** more similar and lower the C=O stretching frequency in **B**. A B3LYP/6–31G* calculation of a H-bonded dimer of **22aB** moved the carbonyl group vibration closer to the experimental frequency (calculated: 1676; experimental: 1621 cm^{-1} with a weak shoulder at 1650 cm^{-1}; for the full calculated IR data see Table S5 in the ESI material‡).

The problem was resolved by recording the IR spectra in Ar matrices at 20 K, where discrete molecules, devoid of intermolecular H-bonding, are observed. The IR spectrum of **22a** showed no band due to OH, but bands at 3444 (NH), 1690 (C=O), 1654, and 1612 cm^{-1}, and the appearance was in very good agreement with the calculated spectrum for **22aB** in the gas phase (B3LYP/6–31G*). Therefore, the discrete molecules exist in the most stable tautomeric form, **B**.

An X-ray crystal structure determination of **22b** confirmed that the molecule crystallizes as a centrosymmetric H-bonded dimer of **22bB** (Fig. 6 and Fig. S8). The H atom was located on N1 and refined without any constraints. There is a strong and short hydrogen bond (N1–H1 ⋯ O2′ 2.04(2) Å, 174(2)°, O2′ symmetry code $1-x, 2-y, 1-z$), and a correspondingly long C=O double bond (1.245(2) Å). Also of note is the trigonal planar coordination geometry of the exocyclic amino group N4 (dihedral angles N3–C4–N4–C8 1.3(3)° and C5–C4–N4–C1 1.2(3)°); the C4–N4 bond length (1.340(2) Å) is intermediate between single and double bonds, and the N4–C4–N3–C2–O2 moiety is almost planar. Thus, the compound has some degree of zwitterionic character with a partial positive charge on N4 and a partial negative charge on O2 (see structure **G** in Scheme 7).

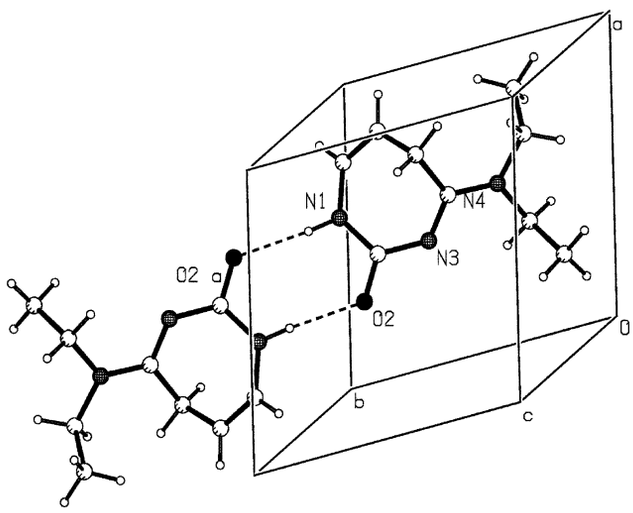


Fig. 6 ORTEP view of 1,3-diazepin-2-one **22bB** (30% ellipsoids).

The chlorine atom in the 2-ethoxydiazepine **5y/4y** is also prone to substitution.[2] This compound is generated by photolysis of the azidopyridine **1Ay** in the presence of ethanol (Scheme 8). The facile dark reaction with diethylamine to furnish **23** in 81% yield has been described.[2] Compound **5y/4y** reacts with water to give a 57% yield of the 1,3-diazepin-4-one **24**, which features a carbonyl group at 162 ppm (1705 cm^{-1}) and an NH function at 7.8 ppm (broad) in the ^{1}H NMR (Scheme 8).

4 Diazabicycloheptenes

The cyclic ureas **19** all undergo electrocyclic photocyclization, formally disrotatorily, to afford 2,4-diazabicyclo[3.2.0]hepten-3-ones **25** in virtually quantitative yield (Scheme 9 and Table 4). Several NMR spectra showing this transformation are reproduced in the ESI material (Fig. S4–S6‡). This typically requires 12 h of photolysis, *i.e.* the photocyclization is much slower than

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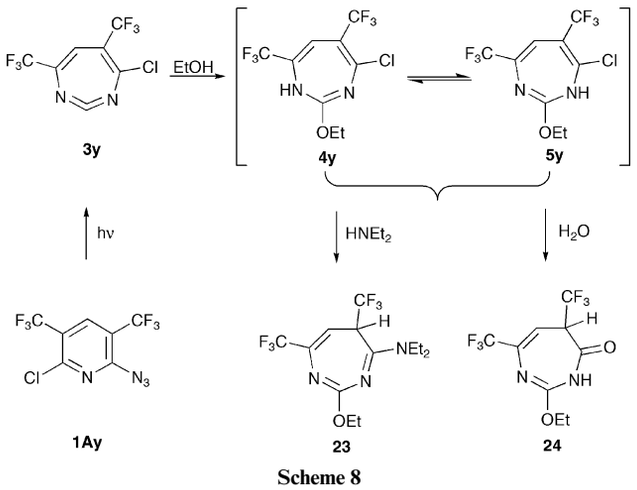
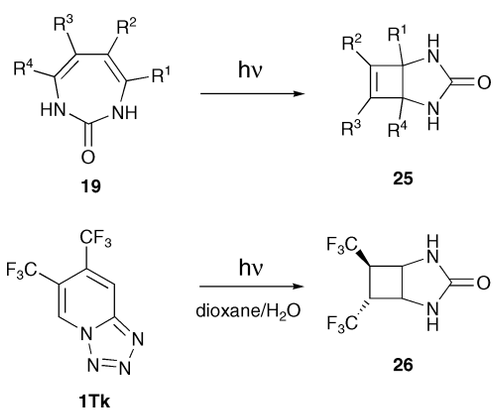


Scheme 8

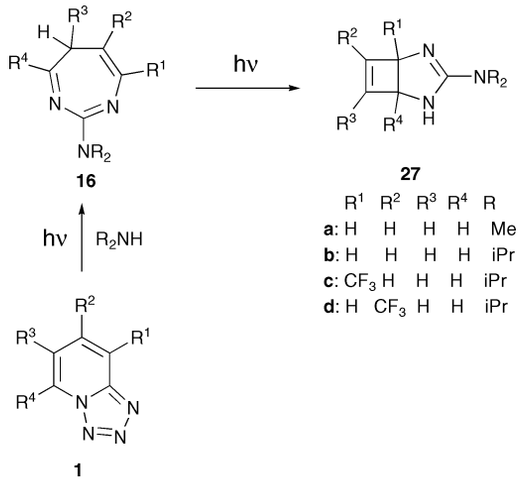


Scheme 9

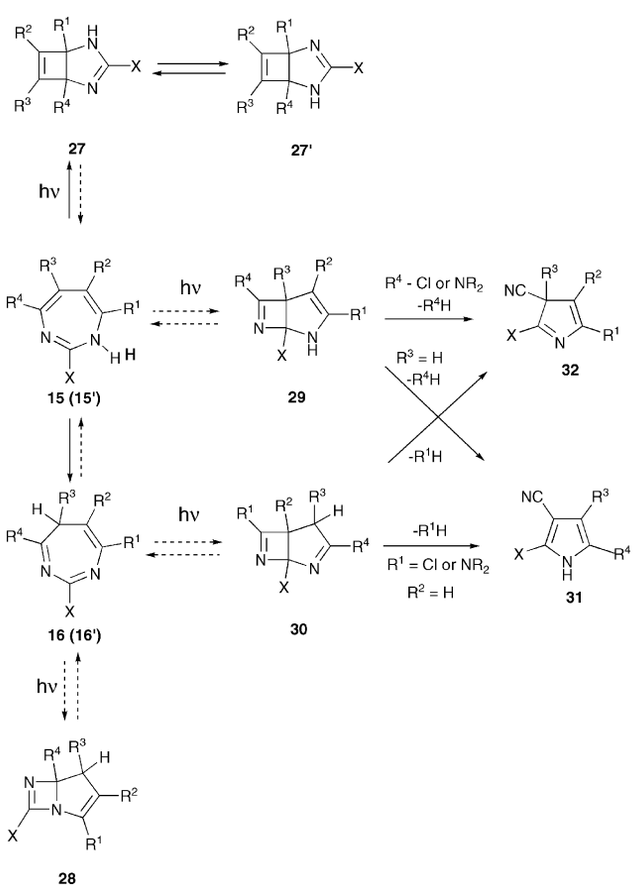
the synthesis of the diazepinones **19**, thereby allowing the latter to be prepared. In the case of the photolysis of 6,7-bis(trifluoromethyl)tetrazolo[1,5-*a*]pyridine **1Tk** in dioxane/water for 2 h and 40 min, the diazabicycloheptanone **26** was unexpectedly obtained in 48% yield. The mechanism of this presumed photoreduction reaction had not been investigated, but the structure of **26** was unequivocally established by X-ray crystallography,‡ thereby lending further support to the structural characterization of the bicycloheptenones **25**. The crystal structure and essential data for **26** are given in the ESI material (Fig. S9). We have observed an unexpected photoreduction/photocyclization in another case, *viz.* the formation of 3-ethoxy-2*H*-2,4-diazabicyclohept-3-ene on photolysis of tetrazole **1Tk** in the presence of ethanol, but this reaction was not investigated further.¶

Prolonged photolysis of some of the tetrazoles/azides **1T/1A** in the presence of amines without isolation of the 2-dialkylamino-1,3-diazepines **15** or **16** also caused photocyclization to 3-substituted 2,4-diazabicycloheptadienes **27**, which were isolated in modest yields in several cases (Scheme 10). This presumably takes place *via* the 1*H* tautomers **15** (isolable in the case of **15e**, *vide supra*) and it suggests that there is a dynamic equilibrium between **16** and **15** (Scheme 11).

The vinylic and aliphatic cyclobutene protons give rise to only one signal each in the ^{1}H NMR spectra of **27a**,**b**, thereby implying rapid H-exchange between the N-atoms of the



Scheme 10



Scheme 11

imidazole moiety. The ^{1}H and ^{13}C NMR data rule out the alternative 4π electrocyclizations in **15** or **16** leading to 1,6- or 2,7-diazabicyclo[3.2.0]heptadienes **28**–**30**, which would have been analogous to the photocyclizations reported for 2-dialkylamino-3*H*-azepines[13a] and 2,5-bis-*tert*-butoxy-3*H*-azepine.[13b] Nevertheless, we know from previous work that photocyclizations of the type **15** ⟶ **29** or **16** ⟶ **30** do take place when appropriate substituents are present to drive the reaction forward to the 3-cyanopyrroles **31** or **32**.[2] In the present case, it is likely that a photoequilibrium exists between all the possible electrocyclization paths, in which the imidazole derivative **27** becomes the dominant product (Scheme 11).

Conclusion

Photolysis of tetrazolo[1,5-*a*]pyridines/2-azidopyridines **1T/1A** gives rise to nitrogen elimination and formation of 1,3-diaza-

¶ Other unexpected reactions have been observed in this work, *e.g.* the acquisition of an extra carbon atom with formation of 2-formylamino-3,5-dichloropyridine from 6,8-dichlorotetrazolo[1,5-*a*]pyridine in a dark reaction with diethylamine or dipropylamine. After stirring the tetrazole with an amine for several days in cyclohexane or in dioxane the crude residue showed the presence of the starting material and about 20% (by GCMS) of 3,5-dichloropyridine-2-N=CHNEt$_2$ and -2-N=CHNPr$_2$, respectively. These two products were not isolated, as they decomposed on silica gel to give 2-formylamino-3,5-dichloropyridine, whose structure was verified by X-ray crystallography.

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cyclohepta-1,2,4,6-tetraenes **3**. In the presence of alcohols, **3** is trapped to afford 2-alkoxy-1*H*-1,3-diazepines **4**(**5**) in good to excellent yields. The 1*H*-1,3-diazepines **4**(**5**) undergo rapid hydrogen exchange between positions 1 and 3, with free energies of activation $\Delta G^{\ddagger}_{298}$ of the order of 16.2 ± 0.6 kcal mol^{-1} with little or no solvent effect; most likely, this process takes place by intermolecular H-exchange between neighbouring diazepine molecules (Fig. 4). A lower free energy of activation of 14.1 ± 0.6 kcal mol^{-1} for **4c** in acetone/D_2O indicates H-exchange between diazepine and water molecules in this case. X-ray crystallography of **4k** reveals a twist-boat type structure of this molecule.

Trapping of the 1,3-diazacyclohepta-1,2,4,6-tetraenes **3** with amines affords 2-dialkylamino-5*H*-1,3-diazepines **16**, but the corresponding 2-diisopropylamino-1*H*-1,3-diazepines **15e** was isolated in one case and underwent partial isomerization to **16e** on heating. *Ab initio* calculations confirmed that the 2-alkoxy-1,3-diazepines are more stable in the 1*H* form, whereas the 2-dialkylamino-1,3-diazepines are usually more stable in the 5*H*-form.[1a]

Trapping of the 1,3-diazacyclohepta-1,2,4,6-tetraenes **3** with water affords the novel 1,3-diazepin-2-ones **19** in high yields. The same compounds are also obtained by very easy thermal elimination of isobutene from the 2-*tert*-butoxy-1*H*-1,3-diazepines **4**(**5**) or less readily from the 2-isopropoxy analogues. Reaction of **19v** with water affords the 4-dialkylamino-1,3-diazepin-2-ones **22B**, which exist as hydrogen bonded dimers in solution and in the solid state.

Prolonged photolysis of the 1,3-diazepin-2-ones **19** causes electrocyclization to 2,4-diazabicyclo[3.2.0]hept-6-en-2-ones **25** in virtually quantitative yields. In some cases unexpected photoreduction to diazabicycloheptane derivatives such as **26** takes place.

In some cases, prolonged photolysis of tetrazoles/azides **1T/1A** in the presence of amines, *i.e.* conditions expected to lead to diazepines **15** and/or **16**, also causes cyclization to 3-dialkylamino-2*H*-2,4-diazabicyclohepta-3,6-dienes **27**.

Computational methods

Standard *ab initio* molecular orbital calculations[14] were carried out using the Gaussian 98 system of programs.[15] Geometry optimisations were performed with the polarised split-valence 6-31G* basis set at the Hartree–Fock (HF), second-order Møller-Plesset pertubation (MP2) and the hybrid density functional theory B3LYP levels of theory. The frozen-core approximation was employed for all correlated calculations. Harmonic frequencies were calculated at the HF/6–31G* and the B3LYP/6–31G* levels in order to confirm the stationary points as minima and to evaluate zero-point vibrational energies (ZVPEs). The directly calculated ZVPEs were scaled by 0.9135 (HF/6-31G*)[16] and 0.9806 (B3LYP/6-31G*)[17] to account for their overestimation at this level of theory. ^{13}C and ^{1}H NMR chemical shifts were calculated at the B3LYP/6-31+G**//MP2/6-31G* level using TMS as a reference.[12] The calculated harmonic frequencies are required to be scaled to account for the neglect of anharmonicity effects in the theoretical treatment. For the B3LYP/6–31G* IR spectra reported herein, a factor of 0.9614 has been used.[17]

Experimental

The unfiltered light from a 1000 W high pressure Hg/Xe lamp was used for all irradiations. Tetrazolo[1,5-*a*]pyridines/2-azidopyridines were prepared as previously described,[2,5a] except 2-azido-3,6-bis(trifluoromethyl)pyridine **1Aq**, which is described in the ESI material. ‡ Preparative details and characterization data for most of the compounds prepared are given in the ESI material. ‡ Only the general experimental procedure and data for representative and new types of diazepines, diazepinones and diazabicyclo[3.2.0]heptenes are reported below. Melting points are uncorrected.

Exchange kinetics

The variable temperature saturation transfer experiments using the Forsén–Hoffman double resonance method[7] were performed on a Bruker AMX400 spectrometer operating at 400.136 MHz for ^{1}H and 100.614 MHz for ^{13}C. The probe was temperature calibrated using methanol as standard. The reported temperatures are estimated to be accurate to ±0.5 °C. All solutions were prepared by dissolving 50–60 mg in 1 ml of the appropriate deuterated solvent and degassing by three freeze–pump–thaw cycles. The single frequency irradiation, which was used to irradiate the selected exchanging carbon peak, was set to the frequency of that carbon resonance. Irradiation at this frequency was switched on for 40 seconds (equal to approximately $5 \times T_1$), and with the minimal delay of 24 microseconds a 70° pulse was applied followed by collection of 64K data points. The irradiation power was selected such that the irradiated resonance was fully saturated but was not high enough to irradiate the magnetized resonance. The ^{1}H Waltz decoupler was switched on all the time. The solution was allowed to equilibrate for at least 10–15 minutes before 32 scans were collected at each temperature. The probe tuning and shimming was adjusted for each temperature. The intensity of the magnetized resonance was measured directly as the absolute value. The rates of exchange k were measured over the temperature range 312–296 K.

The ^{13}C NMR spectra of **4c** in CD_2Cl_2 at various temperatures are shown in Fig. 2. When the C-7 carbon was irradiated at 293 K, the C-4 carbon was fully saturated, and hence no signal was observed for this site. Lowering the temperature slowed down the exchange, and already at 283 K a small signal for C-4 was observed. Gradually lowering the temperature to 223 K resulted in complete recovery of the C-4 signal. Hence the rate of exchange at this temperature must equal zero on the NMR time scale. The exchange rate for the process was then calculated from eqns. (1) and (2) above. The relaxation times T_1 for C-4 and all other carbon atoms were obtained by standard inversion–recovery experiments and are given in the caption of Fig. 3. The intensity of the magnetized resonance C-4 in the absence of irradiation, $M_z^{C4}(0)$, and in the presence of irradiation, $M_z^{C4}(8)$, were measured, and the spin lifetime τ(C-4) was calculated for each temperature following eqn. (1). The exchange rate k at each temperature was then calculated from eqn. (2). The data are presented in Table 6. Measurements of T_1 and k were performed in a similar manner for **4c** in acetone-d_6 (Table 6), for **4b** in acetone-d_6 and for **4a** in CD_2Cl_2. Relaxation times of all carbons were slightly longer in acetone-d_6 (for **4c** 24.2, 5.6, 5.7, 5.1, 5.1, 8.4 and 4.1 s for C-2, C-4, C-7, C-5, C-6, OiPr(CH) and OiPr(CH_3), respectively).

In the case of **4c** in acetone-d_6/D_2O, 2 drops of D_2O was added to the acetone-d_6 solution that had been used previously for kinetic measurements. This resulted in broadening of all carbon signals except that of C-2, and therefore saturation by irradiation was not possible. Increasing the temperature to 308 K caused further broadening of the protonated ring carbon signals and their complete disappearance in the spectral baseline. Cooling to 263 K slowed the rate of exchange so that the peaks became just visible. Further cooling to 243 K resulted in full recovery of all carbon signals, now indicating slow exchange (Fig. S2). This experiment indicated that the coalescence temperature should be *ca.* 308 K. Measurements of the ^{1}H NMR spectra as a function of temperature confirmed the coalescence temperature as 308 ± 0.5 K, from which $\Delta G^{\ddagger}$ for N,N–D exchange was calculated (Table 2).[6]

In the case of **4c** in methanol-d_4 the initial ^{1}H NMR spectrum at 301 K showed very broad signals for all protons. Unlike the previous experiment in acetone-d_6/D_2O, warming to 330 K did

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Table 6 Exchange rates k/s^{-1} and spin state lifetimes τ/s for C-4 or C-7 at temperatures T/K ± 0.5 K for **4c** in various solvents

CD_2Cl_2			Acetone-d_6			Methanol-d_4		
T	k	τ(C4)	T	k	τ(C7)	T	k	τ(C4)
283	1.396	0.716	273	2.73	0.366	285	2.877	0.348
275	1.040	0.962	263	1.16	0.858	280	1.849	0.541
268	1.154	0.866	253	0.55	1.813	275	1.404	0.712
260	0.735	1.361	248	0.37	2.684	270	0.911	1.098
252	0.245	4.089	243	0.23	4.380	263	0.507	1.971
242	0.116	8.589	238	0.14	7.050	258	0.306	3.262
233	0.079	12.809	233	0.082	12.25	253	0.212	4.726
223	0.023	44.209	228	0.044	22.84	247	0.111	9.034
213	0.0078	128.72	223	0.022	45.95	240	0.0464	21.53
						234	0.0245	40.82

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not result in further broadening but marginal sharpening of the signal. In contrast, upon renewed cooling to 298 K sharpening to fully resolved and coupled peaks occurred. This was an irreversible phenomenon caused by initial fast NH,N exchange, followed by H–D exchange (accelerated and completed on warming to 330 K), and a slower ND,N exchange in the resulting N-deuterated diazepine. H-7 had become a doublet due to coupling with H-6 and uncoupling from the now deuterated NH function. A Forsén–Hoffmann saturation transfer experiment could now be carried out on this solution, where each of the four ring carbon atoms could be irradiated while its partner was being observed. On irradiation of C-4 at 139.9 ppm above 290 K the C-7 resonance at 132.6 ppm was fully saturated, indicating fast exchange. Gradual cooling caused an increased intensity of the C-7 peak till 243 K (slow exchange). T_1, τ and k for the ND,N exchange were obtained as described above (Table 6). Except for C-2, the T_1 values were shorter in methanol-d_4 than either acetone-d_6 or CD_2Cl_2 (28.5, 4.3, 4.1, 4.2, 4.4, 6.0 and 3.3 s for C-2, C-4, C-7, C-5, C-6, OiPr(CH) and OiPr(CH_3), respectively).

Arrhenius and Eyring parameters were derived in the usual manner[6] by plotting ln k *vs.* $1/T$ and ln (k/T) *vs.* $1/T$, respectively (Fig. S7 in the ESI material). The r^2 values for the Arrhenius and Eyring plots were 0.980 (**4c** in CD_2Cl_2), 0.997 (**4c** in acetone-d_6), 0.990 (**4c** in methanol-d_4), 0.980 (**4a** in CD_2Cl_2), and 0.990 (**4b** in acetone-d_6). All resulting activation parameters are collected in Table 2.

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 Kα radiation (0.71073 Å) and operating in the ω–2θ scan mode. Data reduction was performed with the WinGX package.[18] Structures were solved by direct methods with SHELXS and refined by full-matrix least-squares analysis with SHELXL-97.[19] All non-H atoms were refined with anisotropic thermal parameters. Hydrogens attached to N-atoms were located from difference maps then restrained in these positions using a riding model. All other H-atoms were included at calculated positions and again allowed to ride on their parent C-atom. Drawings were produced with ORTEP.[20] Crystallographic data in CIF format have been deposited with the Cambridge Crystallographic Data Centre.§ Essential structural parameters are listed in the ESI material.‡

General procedures for the synthesis of 1,3-diazepines

The azides/tetrazoles (100–150 mg) were photolysed in dry, distilled, N_2-purged 1,3-dioxane ("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.

For the synthesis of 2-alkoxy-5*H*-1,3-diazepines and 1,3-diazepin-2-ones 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 or water (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. Dialkylaminodiazepines were prepared analogously. 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. After the end of the reaction (monitored by nitrogen evolution and thin layer chromatography, usually 1–2 h) 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. Compounds were purified by Kugelrohr distillation, column or preparative thin layer chromatography.

5,6-Bis(trifluoromethyl)-2-methoxy-1*H*-1,3-diazepine 4k

Purified by preparative TLC (silica gel 100, CH_2Cl_2–MeOH 97 : 3). Crystallized from petroleum ether, yellow–orange crystals, mp 120–121 °C. The crystals were suitable for X-ray data collection (see below). Yield: 80%. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.12 (q, 1 H, 4-H, $J_{H,F}$ = 1.80 Hz), 6.42 (dq, 1 H, 7-H, $J_{1,7}$ = 6.34 Hz, $J_{H,F}$ = 1.40 Hz), 5.15 (br, 1 H, N-*H*), 3.81 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 157.0 (2-C), 146.5 (q, 4-C, $J_{C,F}$ = 7.8 Hz), 139.5 (q, 7-C, $J_{C,F}$ = 7.6 Hz), 122.5 (q, CF_3, $J_{C,F}$ = 270.5 Hz), 122.1 (q, CF_3, $J_{C,F}$ = 270.5 Hz), 115 (q, 5-C, $J_{C,F}$ = 31.2 Hz), 113.2 (q, 6-C, $J_{C,F}$ = 32.4 Hz), 56.8 (OCH_3); MS (EI) *m*/*z* 260 (M^+, 100%), 241 (30), 218 (39), 203 (85), 184 (92), 177 (34), 156 (11), 153 (25), 148 (26), 121 (24), 120 (22), 98 (62), 76 (23), 75 (22), 69 (91), 58 (98), 42 (17). HRMS, calcd. for $^{12}C_8H_6N_2F_6O$: 260.0367; found: 260.0390. Anal. calcd. for $C_8H_6N_2F_6O$: C, 36.94; H, 2.33; N, 10.77%. Found: C, 36.96; H, 2.26; N, 10.73%.

Crystal data. $C_8H_6F_6N_2O$, M = 260.15, monoclinic, space group $P2_1/c$, a = 9.642(7), b = 10.277(7), c = 10.081(7) Å, β = 91.89(3)°, U = 998(1) Å^3, Z = 4, D_c = 1.731 g cm^{-3}, μ = 1.91 cm^{-1}, 1854 reflections measured, 1746 unique (R_{int} = 0.0213), R_1 = 0.0494 (for 1331 observed data, $I > 2\sigma$), wR_2 = 0.1637 (all data). Crystallographic data in cif format have been deposited with the Cambridge Crystallographic Data Centre.§ Essential structural parameters are listed in the ESI material.‡

2-Diisopropylamino-4-trifluoromethyl-1*H*-1,3-diazepine 15e

Purified by Kugelrohr distillation (~50 °C, 10^{-4} mbar); red oil. Yield: 64%. ^{1}H NMR (benzene-d_6, 400 MHz) δ 5.90 (d, 1 H, 5-H, $J_{5,6}$ = 5.7 Hz), 5.61 (dd, 1 H, 7-H, $J_{6,7}$ = 7.2, $J_{1,7}$ = 4.6 Hz), 5.40 (m, 1 H, 6-H), 4.30 (br s, 1 H, N-H), 3.91 (sept, 2 H, N*i*Pr), 1.13 (d, 12 H, N*i*Pr), ^{13}C NMR (benzene-d_6, 100 MHz) δ 157.9 (2-C), 137.1 (q, 4-C, $J_{C,F}$ = 32.4 Hz), 134.6 (7-C), 123.1 (CF_3,

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$J_{C,F}$ = 273 Hz), 118.2 (5-C), 110.4 (6-C), 44.9 (N*i*Pr), 20.2 (N*i*Pr); IR (neat film) 3398 br, 2954 m, 2946 w, 2913 w, 1611 s, 1553 vs, 1525 s, 1456 m, 1364 m, 1328 vs, 1295 vs, 1254 s, 1232 vs, 1151 m, 1137 m, 1100 m, 1052 m, 1035 w, 1016 w, 985 m, 932 w, 902 w, 893 w, 862 w, 796 w, 741.0 m, 634 w cm^{-1}; MS (EI) *m*/*z* 261 (M^+, 100%), 247 (8), 246 (29), 232 (14), 202 (33), 201 (12), 189 (6), 150 (49), 148 (13), 105 (21), 104 (8), 87 (36), 78 (13), 77 (22), 56 (6), 54 (5), 44 (7), 42 (11). HRMS, calcd. for $^{12}C_{12}H_{18}F_3N_3$: 261.14528; found: 261.14544. Anal. calcd. for $C_{12}H_{18}F_3N_3$: C, 55.16; H, 6.94; N, 16.08%. Found: C, 55.44; H, 5.66; N, 16.61%.

2-Diethylamino-5*H*-1,3-diazepine 16a

Purified by distillation (Kugelrohr, 50–70 °C/0.5 mmHg). Pale red oil. Yield: 61%. ^{1}H NMR (acetone-d_6, 301 K, 400 MHz) δ 6.88 (d, 1 H, 4-H, $J_{4,5}$ = 5.00 Hz), 6.64 (d, 1 H, 7-H, $J_{6,7}$ = 6.46), 4.53 (q, 1 H, 6-H, $J_{6,7}$ = 6.46, $J_{5,6}$ = 6.47, $J_{4,6}$ = 0.88 Hz), 3.41 (q, 4 H, N(CH_2CH$_3$)$_2$, J = 7.04), 2.24 br (2 H, 5-H), 1.01 (t, 6 H, NCH$_2$$CH_3$, J = 7.04 Hz); the assignments were confirmed by homonuclear decoupling experiments; ^{13}C NMR (100 MHz, acetone-d_6) δ 159.0 (2-C), 147.7 (4-C), 142.1 (7-C), 95.7 (6-C), 43.3 and 41.2 (N(CH_2CH$_3$)$_2$), 32.8 (5-C), 13.7 and 13.6 (N-(CH$_2$$CH_3$)$_2$); IR (KBr) 3010 w, 2972 m, 2931 m, 2871 w, 1622 vs, 1599 s, 1588 s, 1575 s, 1557 m, 1520 vs, 1516 vs, 1460 m, 1446 m, 1422 m, 1376 m, 1356 s, 1318 m, 1286 m, 1254 m, 1228 w, 1209 w, 1161 m, 1096 w, 1080 m, 1015 w, 916 w, 883 w, 847 w, 783 w, 753 w, 722 w, 701 w cm^{-1}; MS (EI) *m*/*z* 165 (M^+, 11%), 136 (5), 110 (3), 109 (10), 108 (7), 95 (9), 94 (13), 93 (17), 92 (5), 83 (7), 82 (8), 81 (43), 80 (7), 72 (35), 71 (5), 69 (10), 68 (28), 67 (100), 66 (11), 56 (17), 55 (12), 54 (12), 53 (10), 44 (11), 42 (10), 41 (12), 39 (18). HRMS, calcd. for $^{12}C_9H_{15}N_3$: 165.1265; found: 165.1266. Anal. calcd. for $C_9H_{15}N_3$: C, 65.42; H, 9.15; N, 25.43%. Found: C, 65.02; H, 9.19; N, 25.39%.

2-Diisopropylamino-7-trifluoromethyl-5*H*-1,3-diazepine 16e

Prepared and purified by preparative GC of **15e** at 130 °C. Red oil, yield: 20%. Decomposes on silica gel and Al_2O_3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (t, 1 H, 4-H, $J_{4,5}$ = 5.2 Hz), 4.90 (t, 1 H, 6-H, $J_{5,6}$ = 6.7 Hz), 3.95 (br, 2 H, *i*Pr$_2$), 1.65 (br, 2 H, 5-H), 1.11 (br, 12 H, *i*Pr); the assignments were confirmed by homonuclear decoupling experiments; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0 (2-C), 157.6 (4-C), 147.7 (4-C), 141.7 (q, 7-C, $J_{C,F}$ = 31.6 Hz), 123.0 (q, CF_3, $J_{C,F}$ = 273 Hz), 95.9 (q, 6-C, $J_{C,F}$ = 3.4 Hz), 46.0 (*i*Pr$_2$), 31.5 (5-C), 20.6 (*i*Pr); IR (neat) 2974 m, 2956 w, 2935 w, 1622 m, 1595 vs, 1542 w, 1520 w, 1511 w, 1487 w, 1472 w, 1398 w, 1370 m, 1322 w, 1301 s, 1206 m, 1164 s, 1118 s, 1071 w, 1021 w, 1008 w, 956 w, 839 w, 757 w, 697 w, 672 w cm^{-1}. MS (EI) *m*/*z* 261 (M^+, 49%), 242 (11), 218 (100), 203 (12), 201 (8), 175 (64), 161 (14), 150 (10), 149 (38), 148 (6), 126 (33), 117 (10), 107 (12), 83 (11), 69 (7), 58 (12), 54 (3), 43 (25), 41 (37). HRMS, calcd. for $^{12}C_{12}H_{18}F_3N_3$: 261.14528; found: 261.14551. Anal. calcd. for $C_{12}H_{18}F_3N_3$: C, 55.16; H, 6.94; N, 16.08%. Found: C, 54.91; H, 6.58; N, 15.75%.

1,2-Dihydro-4-diethylamino-5*H*-1,3-diazepin-2-one 22bB

This compound was prepared in a similar manner as described for **22aB** using diethylamine. The product was crystallized from an ether–dichloromethane (10%) mixture placed into a closed vessel containing hexane. After 12 h, one large crystal (30–40 mg) separated from the solution; a fraction of this was used for X-ray crystallography. More hexane was added into the mother liquor to afford more product as small white cubes. Yield: 61%, mp 118–119 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.3 (br s, 1 H), 6.22 (d, 1 H, 7-H, $J_{6,7}$ = 7.2 Hz), 4.98 (q, 1 H, 6-H, $J_{6,7}$ = 7.2 Hz, $J_{5,6}$ = 7.2 Hz), 3.44 (q, 4 H, N(CH_2CH$_3$)$_2$, $J_{CH3,CH2}$ = 7.2 Hz), 3.01 (d, 2 H, 5-H, $J_{5,6}$ = 7.2 Hz), 1.19 and 1.07 (br, 6 H, N(CH$_2$$CH_3$)$_2$, $J_{CH3,CH2}$ = 7.2 Hz); all proton signals were identified from homonuclear decoupling experiments; ^{13}C NMR (100 MHz, acetone-d_6) δ 159.9 (2-C), 158.4 (4-C), 130.7 (7-C), 102.9 (6-C), 44.1 and 43.5 (NCH_2CH$_3$)$_2$, 29.3 (5-C), 14.7 and 12.5 (NCH$_2$$CH_3$)$_2$; IR (KBr) 3600–2800 vbr. (ν_{max} 3425 and 3189), 2977 w, 2939 w, 1650 w sh, 1629 s, 1568 vs, 1464 m, 1454 m, 1437 m, 1396 m, 1382 w, 1366 w, 1322 s, 1270 m, 1245 m, 1204 w, 1188 w, 1147 w, 1127 w, 1097 w, 1078 w, 1068 m, 1017 w, 929 w, 823 m, 807 w, 778 w, 760 w, 715 m cm^{-1}; MS (EI) *m*/*z* (M^+, 100%), 154 (8), 153 (9), 152 (13), 139 (6), 138 (7), 125 (10), 110 (14), 109 (54), 97 (17), 90 (12), 83 (15), 82 (23), 72 (36), 70 (31), 69 (17), 65 (59), 64 (22), 63 (17), 58 (25) 56 (17), 55 (14), 54 (18), 45 (20), 44 (17), 32 (17), 30 (18). HRMS, calcd. for $^{12}C_9H_{15}N_3O$: 181.120963; found: 181.121575. Anal. calcd. for $C_9H_{15}N_3O$: C, 59.64; H, 8.34; N, 23.19%. Found: C, 59.98; H, 8.63; N, 22.82%.

Crystal data. $C_9H_{15}N_3O$, *M* 181.24, triclinic, space group $P\bar{1}$, a = 7.607(2), b = 8.040(2), c = 8.369(1) Å, α = 96.79(2), β = 98.36(3), γ = 104.70(2)°, U = 483.4(2) Å^3, Z = 2, D_c = 1.245 g cm^{-3}, μ = 0.84 cm^{-1}, 1839 reflections measured, 1697 unique (R_{int} = 0.0242), R_1 = 0.0434 (for 1181 observed data, $I > 2\sigma$), wR_2 = 0.1244 (all data). Crystallographic data in cif format have been deposited with the Cambridge Crystallographic Data Centre.§ Essential structural parameters are listed in the ESI material.‡

6,7-Bis(trifluoromethyl)-2,4-diazabicyclo[3.2.0]heptan-3-one 26

This compound was obtained unexpectedly when 250 mg of 6,7-bis(trifluoromethyl)tetrazolo[1,5-*a*] pyridine **1Tk** was photolysed in dioxane/H_2O (120/30 ml) solution for 2 h and 40 min. Solvent was removed under vacuum, and the residue was chromatographed on silica gel 100 (70–230 mesh ASTM, $CHCl_3$/EtOH 85 : 15) to afford 120 mg (48%) of crystalline solid, mp 80–81 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.15 (br s, 1 H, N-*H*), 7.05 (br s, 1 H, N-*H*), both protons exchange with D_2O, 4.45 (m, 1 H, 1 or 5-H, $J_{1,5}$ = 8.2 Hz), 4.27 (m, 1 H, 5 or 1-H, $J_{1,5}$ = 8.2 Hz), 3.58 (m, 1 H, 6 or 7-H), 3.34 (m, 1 H, 7 or 6-H). Upon addition of D_2O to simplify the spectrum, a homonuclear decoupling experiment showed that the proton at 4.45 couples with the proton at 3.58 ppm, and the proton at 4.27 couples with the proton at 3.34 ppm. Even under such conditions (N*H* decoupled), all signals were observed as complex multiplets due to H–F coupling. ^{13}C NMR (100 MHz, acetone-d_6), 163.5 (3-C), 125.3 (q, CF_3, $J_{C,F}$ = 275 Hz), 124.9 (q, CF_3, $J_{C,F}$ = 275 Hz), 50.4 (q, 1- or 5-C, $J_{C,F}$ = 3 Hz), 48.7 (q, 5- or 1-C, $J_{C,F}$ = 4 Hz), 46.2 (q, 6- or 7-C, $J_{C,F}$ = 26 Hz), 39.8 (q, 7- or 6-C, $J_{C,F}$ = 27 Hz), DEPT-135 indicated protonated carbons at 50.4, 48.7, 46.2 and 39.8 ppm. IR (KBr) 3265 br (N-*H*), 1710 vs, 1661 vs, 1455 m, 1413 m, 1361 s, 1319 s, 1300 w, 1265 m, 1249 vs, 1235 m, 1211 vs, 1202 s, 1166 s, 1135 s, 1124 m, 1094 vs, 953 w, 928 w, 845 w, 798 w, 738 w cm^{-1}; MS (EI) *m*/*z* 249 (M^+ + 1, < 1%), 229 (1), 111 (6), 95 (4), 91 (3), 84 (100), 69 (10), 56 (20), 28 (17), MS (CI) *m*/*z* 249 (M^+ + 1, 100%), 85 (3), 84 (36); HRMS calcd. for $^{12}C_7H_7N_2F_6O$: 249.045707; found: 249. 046065. Anal. Calcd for $C_7H_6N_2F_6O$: C, 33.88; H, 2.44; N, 11.31; found: C, 33.88; H, 2.49; N, 11.31.

Crystal data. $C_7H_6F_6N_2O$, *M* = 248.14, monoclinic, space group $P2_1/c$, a = 13.243(3), b = 5.6585(5), c = 13.304(3) Å, β = 116.61(1)°, U = 891.3(3) Å^3, Z = 4, D_c = 1.849 g cm^{-3}, μ = 2.09 cm^{-1}, 1668 reflections measured, 1561 unique (R_{int} = 0.0396), R_1 = 0.0423 (for 928 observed data, $I > 2\sigma$), wR_2 = 0.1223 (all data). Crystallographic data in cif format have been deposited at the Cambridge Crystallographic Data Centre.§ The crystal structure and essential bond lengths and angles are reported in the ESI material (Fig. S7).‡

3-Diisopropylamino-5-trifluoromethyl-2*H*-2,4-diazabicyclo-[3.2.0]hepta-3,6-diene 27e

A solution of 2-azido-6-trifluoromethylpyridine **7A** (100 mg; 0.47 mmol) in 100 ml of dioxan and 5 ml of diisopropylamine

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was photolysed for 12 h. Evaporation of the solvent gave a yellow oil, purified by distillation at 45–50 °C/0.5 mbar. ^{1}H NMR (acetone-d_6) δ 6.38 (1 H), 6.32 (1 H), 4.48 (1 H), 3.90 (septet, 2 H, iPr), 1.23 (d, 12 H, iPr); ^{13}C NMR (acetone-d_6) δ 164 (C=N), 142.3 (C=C), 141.0 (C=C), 126.1 (q, CF_3), 62.0 (m, C1 and C5), 47.5 ($CH(CH_3)_2$), 21.5 (CH_3); MS *m/z* 261 (M^+, 35%). Anal. Calcd for $C_{12}H_{18}N_3F_3$ C, 55.14; H, 6.95; N, 16.09; found C, 55.37; H, 7.16; N, 16.08.

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