Dihydro-1,3-diazepinones and diazabicyclo[3.2.0]heptenones from pyridyl azides

Ales Reisinger,[a] Rainer Koch[a,b] and Curt Wentrup*,[a]

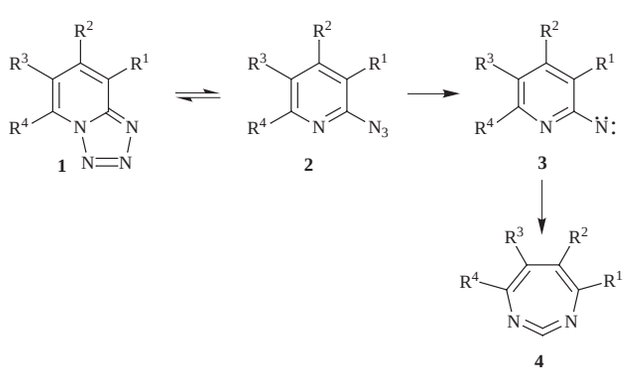
[a] *Department of Chemistry, The University of Queensland, Brisbane, Qld 4072, Australia. E-mail: wentrup@chemistry.uq.edu.au*
[b] *Fachbereich Chemie, Universität Oldenburg, D-26111 Oldenburg, Germany*

1 PERKIN COMMUNICATION

2-Alkoxy-1*H*-1,3-diazepines 5 and 7, 2-dialkylamino-5*H*-1,3-diazepines 6, 2,3-dihydro-1*H*-1,3-diazepin-2-ones 8 and 2,4-diazabicyclo[3.2.0]hepten-3-ones 9 are obtained by photolysis of tetrazolo[1,5-*a*]pyridines or 2-azidopyridines 1/2, including the unsubstituted parent compounds; the relative stabilities of the 2-alkoxy- and 2-dialkylamino-1,3-diazepines 5 and 6 are in excellent agreement with *ab initio* energy calculations.

1,3-Diazepines are little known compounds. Special examples of trifluoromethyl-substituted 1,3-diazepines **5/6** were obtained previously by photolysis of tetrazolo[1,5-*a*]pyridines/2-azidopyridines **1/2** in the presence of the appropriate nucleophile.[1] It appeared that the scope of this synthesis might be severely limited since it was stated that the unsubstituted and simple substituted tetrazolopyridines which do not exist in equilibrium with the azide valence isomers under ordinary conditions were photochemically inert.[2] Nonetheless, we wish to report that this synthesis of 1,3-diazepines **5/6** is in fact general and efficient, also for unsubstituted or simple methyl-substituted tetrazoles **1**, by using quartz optics photolysis. Moreover, we report the efficient synthesis of novel dihydrodiazepinones **8** and their bicyclic valence isomers **9**.

Ar matrix photolysis of **1a** at 10 K gave rise to a strong

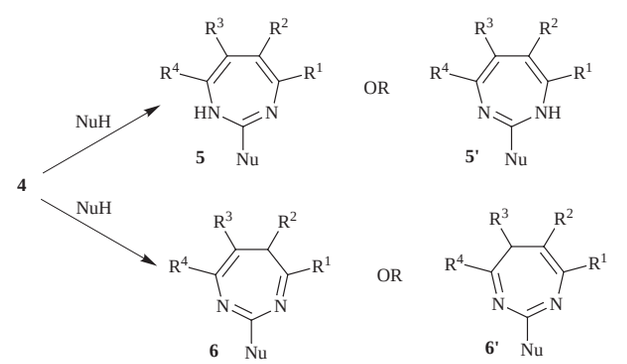


absorption at 1978 cm^{-1}, which is ascribed[3] to the carbodiimide **4a**, formed *via* **3**. The methyl-substituted tetrazoles behaved analogously. Solution photolysis in the presence of the requisite nucleophile afforded the diazepines **5/6** (see Table 1 for representative examples). The alkoxy-substituted diazepines usually exist in the NH form **5**, whereas the amine-substituted derivatives exist in the CH form **6** (although here too, the NH forms can often be isolated). Although at first sight surprising, this dependence of the preferred tautomer on substituents is in excellent agreement with *ab initio* calculations[4] at the G2(MP2, SVP)[5] level of theory, which predict that the 5*H* forms **6** are of lower energy in the 2-unsubstituted and 2-amino cases, whereas the 1*H* isomers **5** are preferred in the 2-alkoxy cases (see Table 2). The non-planar compounds **6** undergo ring inversion with free energies of activation of 34.9 (**6e**), 38.9 (**6f**), or

Table 1 Products of photolysis of tetrazoles **1** in the presence of alcohols and amines

1–6	R^1	R^2	R^3	R^4	Nu	Product	Yield (%)
a	H	H	H	H	OMe	**5a**	53[a,b]
b	H	H	H	H	OEt	**5b**	72[a,b]
c	H	H	H	H	NEt_2	**6c**	*ca.* 60[c]
d	H	H	H	H	$N(Pr^i)_2$	**6d**	67[a,b]
e	CH_3	H	H	H	NMe_2	**6e**	67[a]
f	CH_3	H	H	H	NEt_2	**6f**	68[a]
g	CH_3	H	H	H	$N(Pr^i)_2$	**6g**	46[a]
h	H	H	H	CH_3	NMe_2	**6e**	64[a]
i	H	H	H	CH_3	NEt_2	**6f**	63[a]
j	H	H	H	CH_3	$N(Pr^i)_2$	**6g**	39[a]
k	H	H	H	CH_3	OEt	**5k**	52[a]
l	H	H	H	CH_3	OMe	**5l**	*ca.* 60[c]

[a] Isolated yields, after distillation. [b] The crude product was obtained in >95% yield (estimated from GC and/or NMR data). [c] Yields estimated from ^1H NMR data.



40.3 (**6g**) kJ mol^{-1}, as determined by ^1H NMR coalescence experiments.

When the photochemically produced carbodiimide intermediates **4** are trapped with *tert*-butyl alcohol, the unstable *tert*-butoxydiazepines **7** are formed in high yields. Some of these

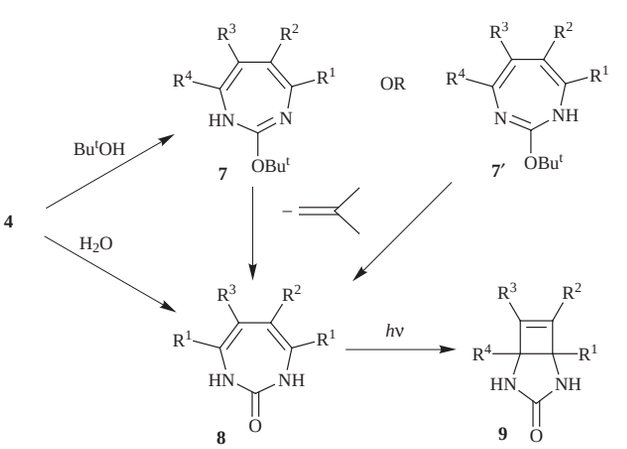


Table 2 Calculated relative energies (kJ mol^{-1}) of 1*H*- and 5*H*-diazepines (**5** and **6**)

1,3-Diazepine (R^1–R^4 = H)	Computational level				
	HF/6-31G*	MP2(fc)/6-31G*	MP2/6-311+G(3df,2p)	QCISD(T)/6-31G	G2(MP2,SVP)
5 (Nu = H)	0.0	0.0	0.0	0.0	0.0
6 (Nu = H)	−19.6	−34.4	−17.2	−27.3	−10.6
5a (Nu = OMe)	0.0	0.0	0.0	0.0	0.0
6a (Nu = OMe)	13.5	−7.4	7.0	−0.7	13.6
5 (Nu = NH_2)	0.0	0.0	0.0	0.0	0.0
6 (Nu = NH_2)	−30.1	−43.6	−25.7	−39.5	−21.6
5 (Nu = NMe_2)	0.0	0.0	0.0	0.0	0.0
6 (Nu = NMe_2)	−34.0	−49.1	−30.3	−44.5	−25.8

Table 3 Photolysis products using Bu^{t}OH and water as nucleophiles

						Product isolated (%)		
7–**9**	R^1	R^2	R^3	R^4	NuH	**7**	**8**	**9**[b]
a	H	H	H	H	Bu^{t}OH	*a*	48	98 ± 2
					H_2O	—	76	—
e	CH_3	H	H	H	H_2O	—	81	98 ± 2
m	H	CF_3	H	H	Bu^{t}OH	*a*	61	98 ± 2
n	CF_3	H	H	H	Bu^{t}OH	94	98 ± 2[b]	98 ± 2
o	CF_3	H	H	CF_3	Bu^{t}OH	67	98 ± 2[b]	98 ± 2
p	CF_3	H	Cl	H	Bu^{t}OH	*a*	73	98 ± 2
q	CF_3	H	CF_3	Cl	Bu^{t}OH	*a*	53	98 ± 2
r	H	H	H	Cl	Bu^{t}OH	*a*	80	—
					H_2O	—	75	—
s	H	H	CH_3	H	H_2O	—	67	98 ± 2

[a] Product not isolated due to facile elimination of isobutene. [b] Yield and purity determined by NMR spectroscopy. All other yields were by isolation.

compounds are isolable and were fully characterized (**7n**,**o**) whereas others were only observed in solution by ^{13}C and ^1H NMR spectroscopy. All the derivatives **7** undergo facile elimination of isobutene, either in the course of their photochemical synthesis, or on distillation, thus affording the novel dihydrodiazepinones **8**, often in nearly quantitative yield. The same dihydrodiazepinones **8** were also conveniently formed by photolysis of the starting tetrazoles/azides **1**/**2** (100 mg) in dioxane–water (100:45 ml) for 2–3 h. These cyclic urea derivatives **8** are stable, crystalline solids. However, on prolonged photolysis, they undergo disrotatory electrocyclization to the diazabicycloheptenones **9**. These, too, are stable solids. Only one isomer of **9** is formed in each case, as determined by ^1H and ^{13}C NMR spectroscopy. Yields of **7**, **8** and **9** are reported in Table 3.

Experimental

General

Melting points were taken on an Electrothermal capillary apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AMX-400 spectrometer, coupling constants *J* are given in Hz. High resolution mass spectra were obtained on a Finnigan 2001 FTMS. Microanalyses were performed on a Carlo Erba elemental analyser. 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.

General procedure for photolysis reactions

All azides/tetrazoles were photolysed in N_2-purged dioxane solutions using quartz vessels and a 1000 W high pressure Hg/Xe lamp. Dihydro-1,3-diazepin-2-ones were photolysed in [$^2H_6$]DMSO solution in 5 mm NMR tubes. Yields are reported in Table 3, and relevant physical and spectral data of **5a**, **6g**, **7o**, **8o** and **9o** are given below.

2-Methoxy-1*H*-1,3-diazepine 5a. Tetrazolo[1,5-*a*]pyridine **1a** (150 mg, 1.25 mmol) was added to a dry and degassed solution of 1,4-dioxane and methanol (90:30 ml) and irradiated for 4 h while cooling the mixture in an ice bath. The solvent was then removed in vacuum and the crude residue was purified by Kugelrohr distillation (80–100 °C/0.5–0.1 mbar) to afford **5a** as a yellow–red solid in 53% yield, mp 37 °C; δ_H(400 MHz, [$^2H_6$]-acetone) 3.70 (s, 3 H, OCH_3), 4.70 (br s, 1 H, N*H*), 5.00 (ddd, 1 H, 6-H, $J_{4,6}$ 0.6, $J_{5,6}$ 5.2, $J_{6,7}$ 7.4), 5.30 (dd, 1 H, 5-H, $J_{4,5}$ 8.2, $J_{5,6}$ 5.2), 5.38 (dd, 1 H, 7-H, $J_{6,7}$ 7.4, $J_{1,7}$ 7.3), 6.18 (dd, 1 H, 4-H, $J_{4,5}$ 8.2, $J_{4,6}$ 0.6); δ_C(400 MHz, [$^2H_6$]acetone) 55 (OCH_3), 112.7 (6-C), 116.6 (5-C), 130.0 (7-C), 139.0 (4-C), 155.2 (2-C) ($C_6H_8N_2O$ requires C, 58.05; H, 6.50; N, 22.57. Found: C, 57.88; H, 6.73; N, 22.39%).

2-Diisopropylamino-4-methyl-5*H*-1,3-diazepine 6g. Prepared as **5a**. 46%, Clear oil, purified by column chromatography (neutral Al_2O_3–diethyl ether); δ_H(400 MHz; $CDCl_3$) 1.24 (d, 12 H, 4 × Me, *J* 6.8), 2.14 (s, 3 H, Me), 2.37 (br, 2 H, 5-H), 4.15 (septet, 2 H, Pr^i, *J* 6.8), 4.61 (q, 1 H, 6-H, $J_{5,6}$ 6.4, $J_{6,7}$ 6.3), 6.63 (d, 1 H, 7-H, $J_{6,7}$ 6.3); δ_H($CDCl_3$) 21 (4 × Me), 24 (4-Me), 36 (5-C), 45 (2 CH, Pr^i), 97 (6-C), 140 (7-C), 157 (4-C), 158 (2-C) ($C_{12}H_{19}N_3$ requires M^+, 207.1732. Found: *M*, 207.1736).

4,7-Bis(trifluoromethyl)-2-*tert*-butoxy-1*H*-1,3-diazepine 7o. Prepared as **5a**. 67%, Yellow–red solid, mp 40–41 °C; δ_H(400 MHz; $CDCl_3$) 1.47 (s, 9 H, 3 × Me), 4.85 (br, 1 H, NH), 5.78 (m, 1 H, 6-H), 5.95 (m, 1 H, 5-H); δ_C($CDCl_3$) 27.6 (3 × Me), 85.1 (OBu^t), 113 (m, 5-C and 6-C), 119.2 (q, 4- or 7-CF_3, $J_{C,F}$ 273), 120.8 (q, 7- or 4-CF_3, $J_{C,F}$ 272), 130 (q, 4-C, J_{C,CF_3} 33), 142 (q, 7-C, J_{C,CF_3} 32), 154 (2-C).

4,7-Bis(trifluoromethyl)-1,3-dihydro-1,3-diazepin-2-one 8o. 50 mg of **7o** was heated neat to about 60 °C until complete disappearance of the yellow–red colour to obtain **8o** as a white solid in 98% yield, mp 166–167 °C; δ_H(400 MHz; [$^2H_6$]DMSO) 6.17 (s, 2 H, 5-H and 6-H), 8.94 (br, 2 H, 1-NH and 3-NH); ([$^2H_6$]DMSO) 113 (q, 5-C and 6-C, J_{C,CF_3} 4), 120 (q, 4-CF_3 and 7-CF_3, $J_{C,F}$ 273), 129.3 (q, 4-C and 7-C, J_{C,CF_3} 33), 163.7 (2-C); ν_{max}(KBr)/cm^{-1} 3274 (NH), 1732 (CO) ($C_7H_4F_6N_2O$ requires C, 34.16; H, 1.64; N, 11.38. Found: C, 33.69; H, 1.64; N, 11.14%).

1,5-Bis(trifluoromethyl)-2,4-diazabicyclo[3.2.0]hept-6-en-3-one 9o. 30 mg of **8o** was dissolved in 1 ml of [$^2H_6$]DMSO in an NMR tube and irradiated until no **8o** could be detected by ^1H NMR spectroscopy (8 h). Solvent was then removed in vacuum and the residue sublimed (0.5 mm Hg/130 °C) to obtain **9o** as a white solid, mp 238–239 °C; δ_H(400 MHz; [$^2H_6$]DMSO) 6.80 (s, 2 H, 6-H and 7-H), 8.47 (br, 2 H, 2-NH and 4-NH); δ_C([$^2H_6$]-DMSO) 68.0 (q, 1-C and 5-C, J_{C,CF_3} 25), 122 (q, 1-CF_3 and 5-CF_3, $J_{C,F}$ 279), 140 (6-C and 7-C), 159 (3-C); ν_{max}(KBr)/cm^{-1} 3212 (NH), 1740 (CO) ($C_7H_4F_6N_2O$ requires C, 34.16; H, 1.64; N, 11.38. Found: C, 34.14; H, 1.58; N, 11.20%).

Acknowledgements

We thank the Australian Research Council for financial support, the Deutsche Forschungsgemeinschaft for a fellowship to R. K., and Ms Julia Stuthe for technical assistance.

References

1 A. Reisinger and C. Wentrup, *Chem. Commun.*, 1996, 813.
2 H. Sawanishi and T. Tsuchiya, *J. Chem. Soc.*, *Chem. Commun.*, 1990, 723.
3 For CF_3-substituted carbodiimides **4**, nitrenes **3**, and further references, *see* R. A. Evans, M. W. Wong and C. Wentrup, *J. Am. Chem. Soc.*, 1996, **118**, 4009.
4 W. J. Hehre, L. Radom, P. v. R. Schleyer and J. A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986; M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. A. Keith, G. A. Peterson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. DeFrees, J. Baker, J. J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, GAUSSIAN 94; Gaussian Inc., Pittsburgh PA, 1995.
5 G2(MP2,SVP) theory: L. A. Curtiss, P. C. Redfern, B. J. Smith and L. Radom, *J. Chem. Phys.*, 1996, **104**, 5148.

Paper 8/04831B
Received 24*th June* 1998
Accepted 24*th June* 1998