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Characteristic Reactions of 4-Siloxy-2,5-dihydrooxepines: Desilylation, [2 + 2] and [4 + 2] Cycloadditions

Bernhard Hofmann[1]a and Hans-Ulrich Reißig*b

Institut für Organische Chemie der Technischen Hochschule Darmstadt[a],
Petersenstraße 22, D-64287 Darmstadt, Germany

Institut für Organische Chemie der Technischen Universität Dresden[b],
Mommsenstraße 13, D-01062 Dresden, Germany

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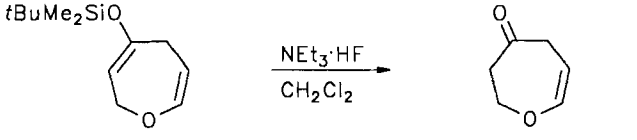
Desilylation of 4-siloxy-2,5-dihydrooxepine **1** with $NEt_3 \cdot HF$ afforded oxepinone **2**. [2 + 2] Cycloadditions of **1** and methyl-substituted derivative **4** to tetracyanoethylene provided bicyclic products **3** and **5**, respectively. Hetero Diels-Alder reactions of 2,5-dihydrooxepines **1** and **9** with 1,1,1-trifluoro-2-nitrosopropene furnished the corresponding bicyclic 1,2-oxazines **8** and **10**, resp., in reasonable yields. The considerably higher reactivity of the silyl enol ether unit compared with the endocyclic enol ether moiety as revealed by these cycloadditions is discussed.

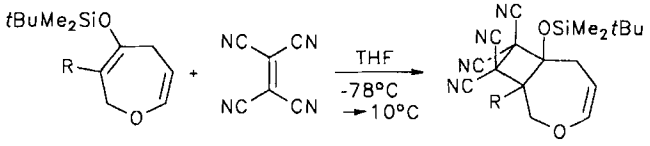
In a preceding publication we reported on the [3,3]-sigmatropic rearrangement of alkenyl-substituted siloxycyclopropanecarboxaldehydes which established an easy and rather flexible route to 4-siloxy-2,5-dihydrooxepines[2]. Subsequently, we studied a few characteristic reactions of these heterocycles containing two enol ether moieties.



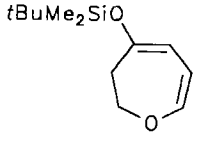
1 2 (51%)

Desilylation of parent compound **1** with tetra-*n*-butylammonium fluoride was not successful and provided only decomposition products. However, use of the weakly acidic $NEt_3 \cdot HF$[3] furnished the expected oxepinone **2**[4] in moderate yield. Thus, it is possible to differentiate between the two enol ether functions with this reagent. It is still more interesting whether this is also the case when stepwise or concerted cycloadditions are attempted. The [2 + 2] cycloaddition reactions of tetracyanoethylene (TCNE) with **1** and the methyl-substituted oxepine **4** afforded cyclobutanes **3** and **5**, respectively, in good yields. The constitution of these cycloadducts was unambiguously established by the NMR data, which are only compatible with products still having the endocyclic enol ether unit. Even in the crude unpurified products there was no indication for the formation of regioisomeric cycloadducts. Apparently, the silyl enol ether moiety undergoes cycloaddition exclusively.

An attempt to trap the 1,3-diene unit of the 2,3-dihydrooxepine **6**[2] with a suitable electron-deficient dienophile such as dimethyl acetylenedicarboxylate was not successful. Even under forced conditions there was no definite cycloaddition of **6** but only decomposition.

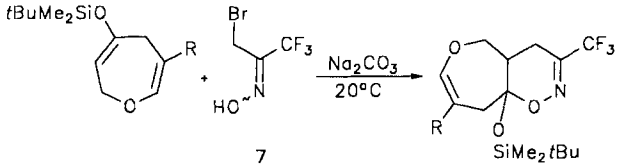


1 (R = H) 3 (53%)
4 (R = Me) 5 (78%)



6

On the other hand, 2,5-dihydrooxepines **1** and **9** smoothly combine with the highly reactive 1,1,1-trifluoro-2-nitrosopropene[5] which was generated in situ by treatment of the corresponding oxime **7** with a base. The [4 + 2] cycloadducts **8** and **10** were isolated in reasonable yields, and again the crude reaction mixtures gave no hints that regioisomers were present which are derived from the reaction of the endocyclic enol ether unit. The structures of the 1,2-oxazines **8** and **10** were proved by the NMR data, in particular by ^1H-^1H-COSY and ^1H-^{13}C-correlated spectra.



7

1 (R = H) 8 (59%)
9 (R = Me) 10 (52%)

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At first glance it was quite surprising that only the silyl enol ether units reacted in the hetero Diels-Alder reactions. Competition experiments had revealed that alkyl enol ethers react with α-nitrosostyrene faster than the corresponding trimethylsilyl enol ethers by a factor of three[6]. This effect can be explained by the weaker donor ability of an siloxy function compared with an alkoxy group which is also evidenced by NMR data and other physical properties[7]. On the other hand, we also found that *cis*-configurated enol ethers and compounds such as dihydropyran are relatively unreactive to nitrosoalkenes as indicated by low yields of the cycloadducts[8]. Apparently, the activation of the 6,7-double bond in **1** and **9** by the endocyclic oxygen is also rather low[9], and the reactivity of the 3,4-double bond is considerably higher since the effect of the exocyclic siloxy group is not restricted.

Similar arguments may be valid for the [2 + 2] cycloaddition reactions with TCNE which should proceed via 1,4-zwitterions as thoroughly established for other examples[10]. For simpler olefins it was found that replacement of an α-H or a β-H by an alkyl group remarkably enhances the rate of the TCNE addition. Therefore, the higher substitution degree of the 3,4-double bond in **1** and **4**, compared with that of the 6,7-double bond should additionally strengthen the preference for the cyloaddition at the silyl enol ether unit.

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Experimental

For general remarks see ref.[11]. $NEt_3 \cdot 3$ HF is commercially available (Riedel-de Haën, 37% HF in NEt_3), tetracyanoethylene was purified by sublimation. For the synthesis of 1-bromo-3,3,3-trifluoro-2-propanone oxime (**7**), see ref.[5]. – NMR: in $CDCl_3$, 300 MHz (^{1}H) and 75.5 MHz (^{13}C).

2,3-Dihydro-4(5H)-oxepinone (**2**): To a solution of 0.673 g (2.97 mmol) of **1** in 20 ml of CH_2Cl_2 was added 9.92 mmol of $NEt_3 \cdot$ HF, prepared by simultaneous addition of 1.60 g (9.92 mmol) of $NEt_3 \cdot 3$ HF and 2.08 g (20.5 mmol) of NEt_3. The mixture was stirred at room temp. for 15 h, before 20 ml of water was added. The layers were separated, and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated in vacuo. The remaining residue, 0.407 g of a pale orange oil, was purified by kugelrohr distillation (35–50°C/0.8 Torr) to furnish 0.170 g (51%) of oxepinone **2**. – ^{1}H NMR: δ = 6.20 (dt, *J* = 7.6/1.5 Hz, 1H, 7-H), 4.35–4.18 (m, 3H, 6,2-H), 3.25 (dd, *J* = 5.7/1.5 Hz, 2H, 5-H), 2.82 (m_c, 2H, 3-H). – ^{13}C NMR: δ = 206.7 (s, C-4), 145.6 (d, C-7), 92.9, (d, C-6), 63.5 (t, C-2), 44.9, 40.4 (2t, C-5,3). – For further characterization see ref.[4].

7-(tert-Butyldimethylsiloxy)-3-oxabicyclo[5.2.0]non-4-ene-8,8,9,9-tetracarbonitrile (**3**): A solution of 0.240 g (1.06 mmol) of **1** in 5 ml of THF was cooled to –78°C. Then a solution of 0.139 g (1.08 mmol) of tetracyanoethylene in 5 ml of THF was added. The mixture was allowed to warm up to 10°C during 15 h and stirred at room temp. for 1 h. The solvent was removed in vacuo, and the remaining orange residue was treated with a small amount of pentane. 0.278 g (71%) of crude **3** was obtained as a yellow-brown solid. For purification, the solid was dissolved in $CHCl_3$, and the solution was filtered through neutral alumina to furnish 0.198 g (53%) of **3** as a yellow brownish solid, m.p. 100–102°C. – ^{1}H NMR: δ = 6.29 (dd, *J* = 7.1/2.7 Hz, 1H, 4-H), 4.42–4.22 (m, 3H, 5,2,1-H), 3.73 (ddd, *J* = 10.8/6.4/1.5 Hz, 1H, 2-H), 3.44 (dt, *J* = 17.3/2.7 Hz, 1H, 6-H), 2.53 (ddd, *J* = 17.3/8.3/1.5 Hz, 1H, 6-H), 0.85 (s, 9H, *t*Bu), 0.20, 0.14 (2 s, 6H, Me_2Si). – ^{13}C NMR: δ = 148.6 (d, C-4), 109.9, 108.9, 108.6, 108.2 (4 s, CN), 98.5 (d, C-5), 82.2 (s, C-7), 67.1 (t, C-2), 54.7 (d, C-1), 48.2 (s, C-8), 33.2 (t, C-6), 31.9 (s, C-9), 25.5, 18.0, –2.3, –2.5 (q, s, 2 q, *t*BuMe$_2$Si). – IR (KBr): $\tilde{\nu}$ = 3020–2810 cm^{-1} (=CH, CH), 2265–2160 (CN), 1655 (C=C), 1475, 1280, 1190, 1115, 850. – $C_{18}H_{22}N_4O_2Si$ (354.5): calcd. C 60.99, H 6.26, N 15.80; found C 60.56, H 6.19, N 15.70.

7-(tert-Butyldimethylsiloxy)-1-methyl-3-oxabicyclo[5.2.0]non-4-ene-8,8,9,9-tetracarbonitrile (**5**): A solution of 0.193 g (0.804 mmol) of **4** in 5 ml of THF was treated with 0.113 g (0.882 mmol) of tetracyanoethylene in 5 ml of THF as described for the synthesis of **3** to furnish 0.230 g (78%) of **5** as a pale yellow solid, m.p. 98–99°C. – ^{1}H NMR: δ = 6.20 (dd, *J* = 7.0/2.5 Hz, 1H, 4-H), 4.63 (d, *J* = 12.2 Hz, 1H, 2-H), 4.37 (ddd, *J* = 8.6/7.0/2.5 Hz, 1H, 5-H), 3.79 (d, *J* = 12.2 Hz, 1H, 2-H), 3.38 (dt, *J* = 17.3/2.5 Hz, 1H, 6-H), 2.45 (dd, *J* = 17.3/8.6 Hz, 1H, 6-H), 1.71 (s, 3H, 1-Me), 0.92 (s, 9H, *t*Bu), 0.26, 0.17 (2s, 6H, Me_2Si). – ^{13}C NMR: δ = 148.2 (d, C-4), 109.6, 109.1, 108.4, (3s, CN, signal at 108.4 of higher intensity), 97.5 (d, C-5), 83.1 (s, C-7), 73.5 (t, C-2), 56.7 (s, C-8), 46.9 (s, C-9), 37.6 (s, C-1), 34.4 (t, C-6), 25.6, 18.4, –2.7 (q, s, q, *t*BuMe$_2$Si), 18.2 (q, 1-Me). – IR (KBr): $\tilde{\nu}$ = 3020–2810 cm^{-1} (=CH, CH), 2265–2160 (CN), 1655 (C=C), 1475, 1280, 1190, 1115, 850. – $C_{19}H_{24}N_4O_2Si$ (368.5): calcd. C 61.93, H 6.56, N 15.20; found C 61.52, H 6.63, N 14.71.

7-(tert-Butyldimethylsiloxy)-10-(trifluoromethyl)-3,8-dioxa-9-azabicyclo[5.4.0]undeca-4,9-diene (**8**): 0.323 g (1.43 mmol) of **1** was dissolved in 100 ml of *tert*-butyl methyl ether, and 1.06 g (10.0 mmol) of freshly powdered Na_2CO_3 was added. Then 0.376 g (1.83 mmol) of **7** was added, and the mixture was stirred for 2.5 d at room temp. For separation from Na_2CO_3, the mixture was filtered through Celite (M*t*B). The solvent was evaporated from the filtrate in vacuo to provide 0.833 g of a yellow oil, which was filtered through neutral alumina (hexane/ethyl acetate, 4:1) to furnish 0.341 g (68%) of crude **8**. Purification was achieved by kugelrohr distillation (100–120°C/0.02 Torr) and led to 0.294 g (59%) of **8** as a colorless solid, m.p. 45–47°C. – ^{1}H NMR: δ = 6.37 (dd, *J* = 6.8/2.2 Hz, 1H, 4-H), 4.76 (dt, *J* = 6.8/4.6 Hz, 1H, 5-H), 3.87 (dd, *J* = 12.4/2.7 Hz, 1H, 2-H), 3.48 (dd, *J* = 12.4/9.6 Hz, 1H, 2-H), 2.74–2.69 (m, 2H, 6,11-H), 2.53 (ddd, *J* = 15.9/4.6/2.2 Hz, 1H, 6-H), 2.54–2.38 (m, 1H, 1-H), 2.12 (dd, *J* = 18.6/3.6 Hz, 1H, 11-H), 0.85 (s, 9H, *t*Bu), 0.22, 0.10 (2 s, 6H, Me_2Si). – ^{13}C NMR: δ = 149.3 (d, C-4), 146.7 (q, J_{CF} = 35 Hz, C-10), 120.4 (q, J_{CF} = 274 Hz, CF_3), 105.3 (d, C-5), 98.9 (s, C-7), 69.9 (d, C-2), 39.4 (d, C-1), 36.2 (t, C-6), 25.5, 17.9, –2.8, –3.8 (q, s, 2 q, *t*BuMe$_2$Si), 20.8 (t, C-11). – MS (EI, 70 eV), *m/z* (%): 353 (<1) [M^+ + 2], 352 (<1) [M^+ + 1], 351 (<1) [M^+], 296 (4), 295 (67), 294 (33), 77 (42), 75 (97) [Me_2SiOH^+], 73 (100) [Me_3Si^+]. – IR (KBr): $\tilde{\nu}$ = 3030–2860 cm^{-1} (=CH, CH), 1665 (C=C), 1635 (C=N), 1340, 1260, 1145 (CF_3), 840. – $C_{15}H_{24}F_3NO_3Si$ (351.5): calcd. C 51.26, H 6.88, N 3.98; found C 51.09, H 6.93, N 3.84.

7-(tert-Butyldimethylsiloxy)-5-methyl-10-(trifluoromethyl)-3,8-dioxa-9-azabicyclo[5.4.0]undeca-4,9-diene (**10**): 0.353 g (1.47 mmol) of **9** was dissolved in 150 ml of *tert*-butyl methyl ether, and 1.16 g (10.9 mmol) of freshly powdered Na_2CO_3 and 0.366 g (1.78 mmol) of **7** were added. Reaction and workup were performed as described for the synthesis of **8** and led to 0.316 g (79%) of crude **10** as a pale yellow oil. Purification was achieved by kugelrohr distillation to furnish 0.227 g (52%) of **10** as a colorless oil, which slowly crystallized to a colorless solid, m.p. 39–41°C. – ^{1}H NMR: δ = 6.32 (quint, *J* = 1.6 Hz, 1H, 4-H), 3.81 (dd, *J* = 12.3/3.8 Hz, 1H, 2-H), 3.35 (dd, *J* = 12.3/10.4 Hz, 1H, 2-H), 2.75–2.62 (m, 2H, 6,11-H), 2.49 (d, *J* = 14.8 Hz, 1H, 6-H), 2.47–2.40 (m, 1H,

1-H), 2.04 (dd, J = 18.6/3.0 Hz, 1H, 11-H), 1.64 (s with fine coupling, 3H, 5-Me), 0.86 (s, 9H, *t*Bu), 0.25, 0.10 (2 s, 6H, Me_2Si). – ^{13}C NMR: δ = 146.4 (q, J_{CF} = 34 Hz, C-10), 144.8 (d, C-4), 120.2 (q, J_{CF} = 285 Hz, CF_3), 118.4 (s, C-5), 97.9 (s, C-7), 70.5 (t, C-2), 41.9 (t, C-6), 39.7 (d, C-1), 25.5, 17.9, −2.3, −3.8 (q, s, 2 q, *t*Bu-Me_2Si), 20.8 (t, C-11), 20.1 (q, 5-Me). – MS (EI, 70 eV), *m/z* (%): 367 (<1) [M^+ + 2], 366 (<1) [M^+ + 1], 365 (<1) [M^+], 309 (28), 308 (53), 294 (14), 277 (10), 184 (10), 183 (11), 89 (17), 77 (28), 75 (99) [Me_2SiOH^+], 73 (100) [Me_3Si^+]. – IR (KBr): $\tilde{\nu}$ = 3030–2860 cm^{-1} (=CH, CH), 1680 (C=C), 1635 (C=N), 1480, 1320, 1200–1135 (CF_3), 850. – $C_{16}H_{26}F_3NO_3Si$ (365.5): calcd. C 52.58, H 7.17, N 3.83; found C 52.37, H 7.29, N 3.72.

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[7] ^1H- and ^{13}C-NMR data indicate a slightly higher negative charge at the β-C of enol ethers compared with those of related silyl enol ethers. There is ample evidence that the oxygen of silyl ethers has a lowered basicity in comparison with alkyl ethers. See: S. Shambayati, J. F. Blake, S. G. Wierschke, W. L. Jorgensen, S. L. Schreiber, *J. Am. Chem. Soc.* **1990**, *121*, 697–703. On the other hand, there is no systematic difference in the reactivity of enol ethers and silyl enol ethers with carbenium ions. See: H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990–1010; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 938–958.
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[9] The folded conformation of the dihydrooxepine ring may prevent an efficient overlap of the oxygen lone pair with the 6,7-double bond.
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