Tetrahedron Letters, Vol.31, No.18, pp 2553-2556, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

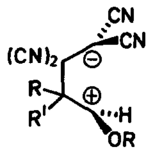
[2+2] CYCLOADDITIONS OF 2,2-BIS(TRIFLUOROMETHYL)ETHYLENE-1,1-DICARBONITRILE WITH ENOL ETHERS, 1,1-DIMETHYLBUTADIENE, AND ALLYLTRIMETHYLSILANE[1]

Rolf Huisgen* and Reinhard Brückner
Institut für Organische Chemie der Universität München
Karlstr. 23, 8000 München 2, West Germany

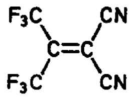
Summary: Vinyl ethers and the title compound (BTF) form cyclobutanes via 1,4-dipoles which can be intercepted with ethanol or acetic acid. *Cis*- and *trans*-1-ethoxypropene react with BTF nonstereospecifically in agreement with a stepwise mechanism. 1,1-Dimethylbutadiene or allyltrimethylsilane undergo [2+2] cycloadditions with BTF, too.

The rules of Woodward and Hoffmann imply that thermal [2+2] cycloadditions other than [${}_\pi 2_s + {}_\pi 2_a$] occur stepwise. In our laboratory, the cycloadditions of tetracyanoethylene (TCNE) to vinyl ethers [2] served as a test case, and an arsenal of mechanistic criteria were in harmony with zwitterionic intermediates **1** [3]: nonstereospecificity [4], reversibility of zwitterion formation [4], interception of **1** by alcohol and its steric course [5], dependence of rate on structure [6], solvent polarity [7], and pressure [8].

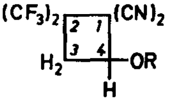
In 1965, Middleton prepared 2,2-bis(trifluoromethyl)ethylene-1,1-dicarbonitrile (**2**, BTF) [9]. We were struck by this author's finding that BTF and methyl vinyl ether form a cyclobutane at -78°C "almost instantaneously", i.e., far below the 20°C required for our [2+2] additions with TCNE. Middleton preferred structure **3**, R = CH_3, to **4** on the basis of an MS peak at 108 corresponding to $(CN)_2C{=}CHOCH_3^{\cdot +}$. We investigated the [2+2] reactivity of BTF in detail and report our results here and in two accompanying papers.



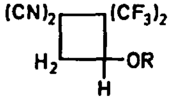
1



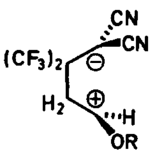
2



3



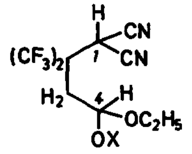
4



5

Addition of 0.9 equivalents of BTF to a 10% solution of ethyl vinyl ether in pentane at -78°C caused the immediate precipitation of a colorless solid which, after low temperature recrystallization, gave **3**, R = C_2H_5, as a homogenous oil (95%) [10]. The ^1H NMR spectrum ($CDCl_3$) shows the d of 3-H_2 at δ 2.93 and the t of 4-H at 4.67, both slightly broadened by H,F coupling; the CF_3 quartets occur at δ(F) -68.3 and -69.5 with J = 10.1 Hz. Adducts **3**, R = butyl, isobutyl, β-chloroethyl, phenyl, were analogously prepared and - coincidentally - likewise reveal A_2X instead of ABX patterns for 3-H_2 and 4-H. In contrast to [2+2] adducts of TCNE, cyclobutanes **3** are distillable in high vacuum. We found no NMR evidence for the occurrence of regioisomers **4** as by-products. Since the order of anion stabilization CN > CF_3 is known from C,H-acids [11], BTF and vinyl ethers react via the cyano stabilized anion **5** rather than via the isomeric 1,4-dipole.

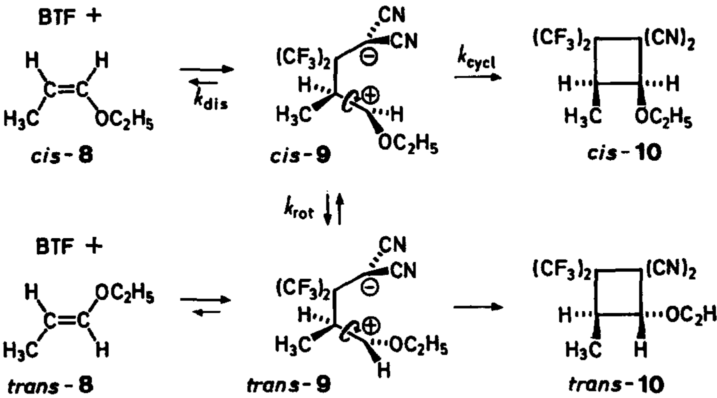
Reaction of cyclobutane **3**, R = C_2H_5, with ethanol (2d, r.t.) and distillation (40°C/0.02 Torr) afforded the diethyl acetal **6** (66%). It results from trapping the 1,4-dipole **5**, R = C_2H_5, which is formed from **3**, R = C_2H_5, in a small equilibrium concentration. The acidic 1-H of **6** gives rise to an s at δ 5.47 and is rapidly replaced by deuterium on exposure to CH_3OD; the pK_a of 2,2-bis(trifluoromethyl)ethane-1,1-dicarbonitrile is 3.09 [12]. An acetal derived from **4** should show its 1-H at higher field and split into a septet due to H,F coupling; 1-H in such an acetal should not be prone to H/D exchange. Hence, the structure of **6** underscores the orientation in zwitterion **5**. The conversion of **6** into a 2,4-dinitrophenylhydrazone and δ(H) 4.74 for the 4-H triplet are consistent with the acetalic nature. The interception of 1,4-dipole **5** occurring alongside **3**, R = C_2H_5, by acetic acid provided acylal **7** (bp 70°C/0.04 Torr, 76%). Not surprisingly, ethanolysis of **7** (1d, r.t.) gave the diethyl acetal **6**.



6 X = C_2H_5

7 X = $\underset{O}{\overset{\|}{C}}-CH_3$

$\mathbf{7}\ X = C(=O)-CH_3$



Cis- and trans-propenyl ethyl ether (**8**) combined with BTF furnishing mixtures of *cis*- and *trans*-**10** which contained mainly the retention products. Recrystallization yielded pure *cis*-**10** (mp 40 - 46.5°C) and pure *trans*-**10** (mp 56.5 - 57°C). Stereochemical assignments rely on δ(H) comparison with **3**, R = C_2H_5. Earlier work in these laboratories had shown that methyl substitution in 4-membered rings moves δ (*cis*-vic-H) to higher field whereas the shift effect is smaller or zero for *trans*-vic-H [13]; *J* values are unreliable for *cis,trans* assignments in cyclobutanes. Accordingly, *trans*-**10** exhibits δ(4-H) at 4.32 and *cis*-**10** at 4.66 as deduced from δ(4-H) = 4.67 observed for **3**, R = C_2H_5 ($CDCl_3$). The resolved dq of 4-H in *cis*-**10** reveals coupling with *one* CF_3 group (0.9 Hz).

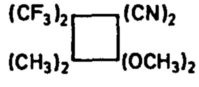
The reactions of BTF (1.1 equiv.) with configurationally pure *cis*- and *trans*-**8** are kinetically controlled. NMR analyses showed 10 - 39% of inversion of configuration (Table 1), somewhat higher than the 4 - 23% observed for TCNE cycloadditions to the same enol ethers [4]. The equilibrium of *cis*-**10** and *trans*-**10** established in ethereal 2M $LiClO_4$ [14] consists of >95% *trans*-**10**. Under kinetic control, more *cis*-**10** is formed from *trans*-**8** - thus "overshooting" the equilibrium concentration - than *trans*-**10** from *cis*-**8**.

Table 1. Steric course of [2+2] additions of BTF with 1-ethoxypropenes; *cis*-**10** : *trans*-**10**

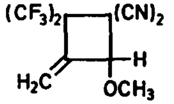
Solvent	from *cis*-**8**	*trans*-**8**
pentane	89 : 11	11 : 89
benzene	87 : 13	10 : 90
ether	90 : 10	13 : 87
ethyl acetate	84 : 16	32 : 68
dichloromethane	79 : 21	34 : 66
acetone	82 : 18	39 : 61
acetonitrile	77 : 23	34 : 66

Rotation about the marked bond of zwitterion **9** and *subsequent* ring closure leads to the cyclobutane with inverted configuration. The stereochemical leakage grows with increasing solvent polarity. Solvation lowers the energy level of **9** more than that of the transition state of cyclization. The extended lifetime of zwitterion **9** results in increased opportunity for rotation. With increase of solvent polarity, the ratio k_{cycl}/k_{rot} is diminished from 9 to 3.3 for *cis*-**9** and from 9 to 1.6 for *trans*-**9**.

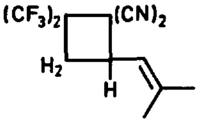
After reacting BTF with a known excess of *cis*-**8** or *trans*-**8**, some *cis,trans* isomerization of the unconsumed donor olefin indicates dissociation of the zwitterion **9**. The ratio k_{dis}/k_{cycl} amounts to ≈ 0.15 for *cis*- and *trans*-**9** in acetonitrile vs. ≈1.0 for TCNE additions to *cis*- and *trans*-1-butenyl ethyl ether [4]. In less polar solvents the dissociation of **9** becomes negligible.



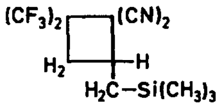
11



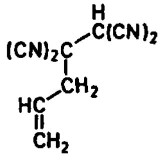
12



13



14



15

Dimethylketene dimethylacetal or methoxyallene plus BTF afforded cyclobutanes **11** (56%) and **12** (mp 61 - 61.5°C, 81%), respectively. The occurrence of $(CN)_2C{=}C(OCH_3)_2^{\bullet +}$ as base peak in the mass spectrum establishes **11** whereas the nonequivalence of the CF_3 groups (^{19}F NMR) and the MS peak of $(CN)_2C{=}CH(OCH_3)^{\bullet +}$ demonstrate the regiochemistry in **12**. In both cases the orientation is consistent with the most stable zwitterionic intermediates.

Certain 1,3-dienes form cyclobutanes with TCNE via dipoles with an allyl cation moiety [15]. Similarly, 1,1-dimethylbutadiene and BTF gave cyclobutane **13** (57%); nonequivalent methyl groups and *one* vinyl proton are noticed in the ^1H NMR spectrum. The same product **13** was found in pentane as solvent. For TCNE and 1,1-dimethylbutadiene, Stewart observed competing [2+2] and Diels-Alder reactions depending on solvent polarity [16].

The propensity of trialkylsilyl groups to stabilize a β-carbenium ion [17] was exploited in combining BTF and allyltrimethylsilane to give cyclobutane **14** (CH_2Cl_2, r.t., mp 46 - 49°C, 77%); the structure was supported by its ^1H NMR spectrum. TCNE and allyltrimethylsilane in CH_2Cl_2 likewise gave rise to the [2+2] cycloadduct; in acetonitrile the S_E2' product **15** was formed [18].

ACKNOWLEDGMENT

We express our gratitude to the *Fonds der Chemischen Industrie*, Frankfurt, for supporting the research program. We thank Drs. *W.J. Middleton* and *H.E. Simmons*, Central Research and Development Department, E.I. du Pont de Nemours Co., Wilmington, for providing hexafluoroacetone required for preparing BTF. The microanalyses were carried out by Mr. *H. Schulz* and Mrs. *M. Schwarz*, and Mr. *H. Huber*'s invaluable help in spectroscopic measurements is gratefully acknowledged.

REFERENCES AND NOTES

1. *This paper is dedicated to the memory of David Ginsburg, Haifa, who did so much for chemistry in Israel.*
2. Williams, J.K.; Wiley, D.W.; McKusick, B.C. *J. Am. Chem. Soc.* **1962**, *84*, 2210.
3. Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117, 199. Huisgen, R.; Schug, R.; Steiner, G. *Bull. Soc. Chim. Fr.* **1976**, 1813.
4. Huisgen, R.; Steiner, G. *J. Am. Chem. Soc.* **1973**, *95*, 5054, 5055.
5. Huisgen, R.; Schug, R.; Steiner, G. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 80, 81. Karle, I.; Flippen, J.; Huisgen, R.; Schug, R. *J. Am. Chem. Soc.* **1975**, *97*, 5285.
6. Huisgen, R.; Steiner, G. *Tetrahedron Lett.* **1973**, 3763.
7. Steiner, G.; Huisgen, R. *J. Am. Chem. Soc.* **1973**, *95*, 5056.
8. Jouanne, J. von; Kelm, H.; Huisgen, R. *J. Am. Chem. Soc.* **1979**, *101*, 151.
9. Middleton, W.J. *J. Org. Chem.* **1965**, *30*, 1402.
10. All new compounds gave satisfactory combustion analyses and ^{1}H NMR spectra (60 MHz).
11. Substituted methanes: Boyd, R.H. *J. Phys. Chem.* **1963**, *67*, 737; Streitwieser, A.; Holtz, D.; Ziegler, G.R.; Stoffer, J.O.; Brokaw, M.L.; Guibé, F. *J. Am. Chem. Soc.* **1976**, *98*, 5229. Pentasubstituted cyclopentadienes: Webster, O.W. *J. Am. Chem. Soc.* **1966**, *88*, 3046; Laganis, E.D.; Lemal, D.M. *J. Am. Chem. Soc.* **1980**, *102*, 6633.
12. Potentiometric titration in 2-methoxyethanol/water (4:1) using the method of Simon, W. *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 661.
13. Cycloadducts of TCNE: Ph. D. Thesis G. Steiner, München 1972. 3-Alkoxycyclobutanones: Mayr, H., Huisgen, R. *Tetrahedron Lett.* **1975**, 1349.
14. Pocker, Y.; Ellsworth, D.L. *J. Am. Chem. Soc.* **1977**, *99*, 2276, 2284. James, D.W.; Mayes, R. E. *Aust. J. Chem.* **1982**, *85*, 1785.
15. Bartlett, P.D. *Quart. Rev.* **1979**, *24*, 473. Huisgen, R.; Plumet Ortega, J. *Tetrahedron Lett.* **1978**, 3975.
16. Stewart, C.A. *J. Am. Chem. Soc.* **1962**, *84*, 117. Rücker, C.; Lang, D.; Sauer, J.; Friege, H.; Sustmann, R. *Chem. Ber.* **1980**, *113*, 1663.
17. Fleming, I. *Chem. Soc. Rev.* **1981**, *10*, 83.
18. Hartmann, G.D.; Traylor, T.G. *Tetrahedron Lett.* **1975**, 939.

(Received in Germany 23 February 1990)