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DIELS-ALDER REACTIONS WITH 2,2-BIS(TRIFLUOROMETHYL)-ETHYLENE-1,1-DICARBONITRILE AS DIENOPHILE

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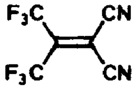
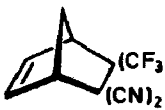
Abstract **In the cycloadditions of the title compound BTF to methylated and phenylated butadienes, NMR spectra of adducts allow to draw the demarcation line between [4+2] and [2+2] cycloadditions. 1-Substituted butadienes accept BTF in the direction less hindered by the bulky CF_3 groups. In rate comparison with TCNE, BTF shows electronic acceleration and steric deceleration.**

The [2+2] cycloadditions of the title compound (BTF) with donor olefins – like those of tetracyanoethylene (TCNE) [2] – proceed via zwitterionic intermediates. The *superelectrophile* BTF exceeds TCNE 2400- and 8200-fold in the rates of cyclobutane formation with butyl vinyl ether [3] and methyl vinyl sulfide [4], respectively. However, the bulky CF_3 groups of BTF generate massive steric hindrance when ß-substituents are introduced into vinyl ethers [3]. Here we compare BTF and TCNE as dienophiles in *normal* Diels-Alder reactions, i.e., those with HO(diene) - LU(dienophile) control.

In 1965 Middleton [5] prepared BTF and described the [4+2] cycloadducts of cyclopentadiene (**1**), 2,3-dimethyl-1,3-butadiene (**2**), and anthracene. We reported on BTF additions to styrene and its derivatives as dienes [6,7]. Methylated 1,3-butadienes served now as model compounds to explore the borderline region between [4+2] and [2+2] cycloadditions as well as the regiochemistry. The discussion of NMR data [8] will be limited to those which allow unequivocal structural assignments.



BTF



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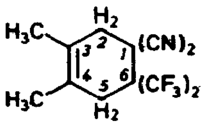

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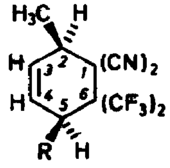
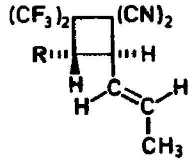
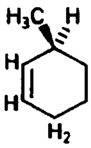




3 R = CH₃ **5**
4 R = H **6**

BTF combined with *(E,E)*-2,4-hexadiene in 1:1 ratio (CH_2Cl_2, 25°C, 20 h) furnishing 86% of **3** [9] after distillation (80°C, 0.02 torr). Two non-vinylic methyls (δ_H 1.58, 1.59) and 2 allylic H are incompatible with the cyclobutane **5**. The vinyl protons at δ 5.77 and 5.79 show $J_{3,4}$ = 10.3 Hz, a *cis* coupling. Fluorine coupling and deshielding by substituents are effected *through space*. The 5-CH_3 signal (δ 1.58) of 3 is split by one CF_3 group with $^4J_{F,H}$ = 2.5 Hz. This CF_3, in turn, is deshielded by 5-CH_3 (δ -62.7) whereas the second CF_3 absorbs "normal" at δ_F -66.6 (cf. -67.7 for **2**).

(E)-1,3-Pentadiene was converted by BTF into 90% of **4** (mp 108.5 - 110°C) in 10 min at 0°C. Again, a *cis* coupling of the vinyl protons ($J_{3,4}$ = 10.2 Hz) was observed. The non-vinylic methyl signal at δ_H 1.56 collapses to s on homodecoupling of the allylic 2-H (3.26). The lack of H,F coupling and two high-field q at δ_F -66.3 and -68.2 ($^4J_{F,F}$ 11.3 Hz) rule out the *regioisomeric* [4+2] cycloadduct **7**.



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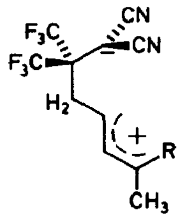
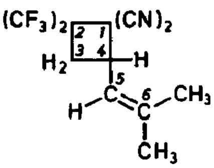


8 R = H

9 R = CH_3



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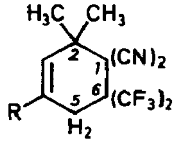
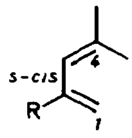




11 R = H **13**

12 R = CH_3 **14**

What favors **4** over **7** in the Diels-Alder reaction ? CN exceeds CF_3 in stabilizing partial negative charge; thus, **4** exemplifies the predilection for "ortho" products. An even stronger directive force is the avoidance of steric interference between CH_3 and CF_3 in the transition state (TS) preceding **7**.

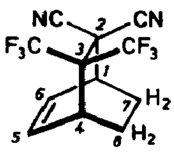
In a twostep pathway, zwitterion **8** [10] is expected to be the favored intermediate from *(E)*-1,3-pentadiene and BTF. The NMR data speak against **6**, the cyclization product of **8**.

The additional methyl group in 4-methyl-1,3-pentadiene shifts the balance in favor of the [2+2] cycloaddition [11] via zwitterion **9**. The reaction in acetonitrile (25 min, 0°C) provided 57% of **10** [12] as an oily distillate. Two vinylic CH_3 appear at δ_H 1.81 and 1.89 and the vinyl-H at 5.33. The high-field CF_3 groups are at δ_F -68.6 and -70.1. When the reaction was run in pentane, **10** still constitutes the major product, but a singlet at δ_H 1.53 and a broad s at 5.67 suggest the concomitant formation of **11**.

Surprisingly, one more methyl group in 2,4-dimethyl-1,3-pentadiene induces a return to the Diels-Alder pattern. The fast reaction (CH_2Cl_2, 0°C, 10 s) afforded 77% of **12** (mp 86 - 87°C) after distillation. A plane of symmetry is revealed by s at δ_H 1.50 for 2-$(CH_3)_2$ and s 2.60 for 5-H_2. Isochronous CF_3 groups are demonstrated by s at δ_F -65.0 and one q at δ_C 123.2 ($^1J_{C,F}$ = 289.3 Hz).

Due to the steric interference of 1-H with *endo*-4-CH_3, the *s-cis* conformation **13** of 4-methyl-1,3-pentadiene occurs only to a small extent in the equilibrium with *s-trans*; the latter conformation, however, is amenable to the [2+2] cycloaddition via **9**. In the ground state of 2,4-dimethyl-1,3-pentadiene, both *s-cis* (**14**) and *s-trans* conformation are sterically hampered; the equilibrium is more balanced, and the predilection for the concerted pathway leads to the cyclohexene derivative **12**.

According to Middleton and Bingham [13], 1,3-cyclohexadiene is dehydrogenated to benzene by BTF. Besides 71% benzene and dihydro-BTF, we isolated 17% of **15** (mp 231-232°C) from a competing Diels-Alder reaction. The ratio of 2:4 of bridge-head (δ_H 3.19, 3.52) and CH_2 protons (1.09 - 2.38) agrees with **15** whereas the [2+2] cycloadduct requires 1:5. Both CF_3 quartets, δ_F -62.4 and -64.5 with $^4J_{F,F}$ = 14.3 Hz, are deshielded; the first is broadened by long-range H,F coupling.



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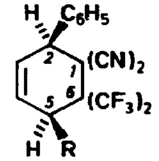
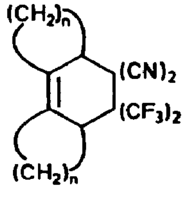


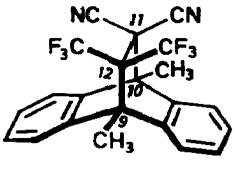
16 R = C_6H_5

17 R = H



18 n = 3

19 n = 4



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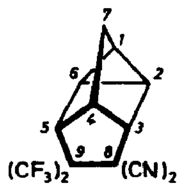

21

The disappearance of the charge-transfer (CT) color of the reactants allowed the visual perception of the cycloaddition. The CT complex of BTF and *(E,E)*-1,4-diphenyl-1,3-butadiene is black and the slow [4+2] addition afforded **16** ($CHCl_3$, 25°C, 21 d, 66%), as established by NMR. *(E)*-1-Phenyl-1,3-butadiene reacted much faster (CH_2Cl_2, 25°C, 30 s); the cycloadduct **17** (78%, mp 150-152°C) displays high-field CF_3 absorptions (δ_F -66.1, -68.0, $^4J_{F,F}$ = 11.4 Hz), indicating the absence of a deshielding cis-vic-C_6H_5 group which the regioisomeric cycloadduct would require.

The red solutions of BTF and 1,1-dicyclopentenyl or 1,1-dicyclohexenyl faded in 1 min or 2 h, respectively. Sublimation provided 90% of **18** (mp 78-80°C) and 70% of **19** (mp 134.5 - 135°C). The ^1H NMR spectra are free of vinyl-H, thus excluding [2+2] cycloadducts.

The blue CT color of BTF and 9,10-dimethylanthracene (CH_2Cl_2, 25°C) disappeared in 6 h. The crystals of **20** (96%) evolved gas on heating above 150°C, and the mp 177-180°C was close to that of dimethylanthracene (181-182°C), thus indicating cycloreversion prior to melting.. The s at δ_F -58.8 reveals strong deshielding of the CF_3 groups by the cis-vic carbon skeleton. The s at δ_H 2.28 for 9-CH_3 is broadened by H,F coupling, that of 10-CH_3 at 2.39 is sharp.

Like TCNE [14], BTF combined with norbornadiene in a homo-Diels-Alder reaction [5]. Structure **21** found support in our ^{13}C NMR data: the strongly shielded doublets at δ_C 12.3, 12.8, and 15.4 disclose the cyclopropane ring. The *endo*-CF_3 signal at δ_F -60.5 is broad and deshielded (*exo*-CF_3 -65.0).

Table 1. Photometric Rate Measurements of the Diels-Alder Reactions of BTF and TCNE (Benzene, 25°C)

1,3-Diene	Adduct formula	10^3k_2 ($M^{-1}s^{-1}$) BTF	TCNE	Ratio
(E)-1,3-Pentadiene	4	170	27	6.3
(E)-1-Phenylbutadiene	17	360	104	3.5
2,3-Dimethylbutadiene	2	330	1570	0.21
(E,E)-2,4-Hexadiene	3	0.91	360	0.0025
4-Methyl-1,3-pentadiene [2+2]	10	12	23	
Cyclopentadiene	1	27400	270 000	0.10
1,3-Cyclohexadiene	15	1.65		
Norbornadiene	21	0.165	0.112	1.5

We based our spectrophotometric rate comparisons [15] of BTF and TCNE on the fading of the CT color (Table 1). In a fundamental study J. Sauer et al. [16] dealt with the reactivity of dienes towards TCNE. Among the divergencies of the BTF and TCNE reactivity scales, steric hindrance by the bulky CF_3 groups is prominent. Butadienes substituted by 1-methyl or 1-phenyl add BTF in the less hindered direction; here BTF exceeds TCNE 6.3- and 3.5-fold in reactivity. However, *(E,E)*-2,4-hexadiene is 190 times slower then *(E)*-1,3-pentadiene in the BTF cycloaddition whereas a 13-fold rate increase was observed for TCNE as the result of a higher HO energy. Thus, an adverse steric effect of ~2500 for the second methyl overcompensates the electronic acceleration, corresponding to $\Delta\Delta G^{\ddagger} = 4.6$ kcal mol^{-1}. Hindrance by the CF_3 groups is smaller in the reactions with 2,3-dimethylbutadiene or cyclopentadiene. In the homo-Diels-Alder reaction with norbornadiene, the rate constant of BTF slightly surpasses that of TCNE.

Why is the advantage of BTF over TCNE in the twostep [2+2] cycloaddition to vinyl ethers so much larger than in the unhindered Diels-Alder reaction ? In the zwitterionic intermediate of cyclobutane formation two CN groups of TCNE have lost conjugation whereas CF_3 groups even prefer bonding to a saturated C-atom [17]. These phenomena affect the late TS of zwitterion formation to a higher extent than the early TS of the conjugated Diels-Alder reaction.

REFERENCES AND NOTES

Dedicated to Professor Alan R. Katritzky, University of Florida, on the occasion of his 65th birthday.

1. New Address: Institut für Organische Chemie der Universität, Tammannstr. 2, D - 37077 Göttingen.
2. Review: Huisgen, R. *Acc.Chem.Res.* **1977**, *10*, 117, 199.
3. Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1990**, *31*, 2557-2560.
4. Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1990**, *31*, 2561-2564.
5. Middleton, W.J. *J.Org.Chem.* **1965**, *30*, 1402-1407.
6. Brückner, R.; Huisgen, R.; Schmid, J. *Tetrahedron Lett.* **1990**, *31*, 7129-7132.
7. Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1990**, *31*, 7133-7136.
8. Representative NMR Spectra ($CDCl_3$). In ^{13}C NMR spectra the multiplicities refer to off resonance, $J_{C,F}$ is listed. **2**: ^1H, δ = 1.74 (s, 2 CH_3), 2.65 and 2.84 (2 s, broadened, 2-H_2 and 5-H_2). ^{13}C, δ = 18.4 (q, 3-CH_3 + 4-CH_3), 30.4 (t sept, 1.6 Hz, C-5), 33.0 (sept, 1.1 Hz, C-1), 39.9 (t sept, 1.1 Hz, C-2), 54.9 (sept, 25.6 Hz, C-6), 112.5 (s, 2 CN), 121.9 and 123.2 (2 s, C-3 and C-4), 122.6 (q, 289 Hz, line broadening by $^3J_{C,F}$). ^{19}F, δ = -67.7 (broad s, 2 CF_3). **3**: ^1H, δ = 1.58 (dq, $J_{H,H}$ = 7.0 Hz, $J_{H,F}$ = 2.5 Hz, 5-CH_3), 1.59 (d, $J_{H,H}$ = 7.0 Hz, 2-CH_3), 2.80-3.16 (m, 2-H + 5-H), 5.57 and 5.79 (dt, AB with J = 10.3 Hz, in addition J_{vic} = J_{allyl} = 1.5 Hz and 3 Hz, 3-H and 4-H). ^{13}C, δ = 16.7 (qq, 2.9 Hz, 5-CH_3), 17.2 (q, 2-CH_3), 32.5 (d, C-2), 37.2 (dq, 1.8 Hz, C-5), 37.9 (broadened, C-1), 56.7 (sept, 24.5 Hz, C-6), 111.9, 112.0 (2 s, 2 CN), 123.2 (q, 288.4 Hz, 2 CF_3), 126.0 (dq, 1.3 Hz, C-4), 131.0 (d, C-3). ^{19}F, δ = -62.7 (q, broadened), -66.6 (q, 12.3 Hz). **4**: ^1H, δ = 1.56 (d, J = 7.1 Hz, 2-CH_3), 2.77 (mc, 5-Hz), 3.11 (mc, 2-H), 5.60 and 5.83 (AB with J = 10.2 Hz on decoupling of 2-H + 5-H_2, 3-H and 4-H). ^{13}C, δ = 16.9 (q, CH_3), 25.4 (t, broadened, C-5), 37.2 (dq, 2.1 Hz, C-2), 39.8 (s, small, C-1), 55.7 sept, 25.7 Hz, C-6), 110.9, 111.5 (2 s, 2 CN), 123.1 (d, C-3), 123.2 (q, broad, 285.7 Hz, 2 CF_3), 128.3 (dq, 1.3 Hz, C-4). ^{19}F, δ = -66.3, -68.2 (2 q, 11.3 Hz). **10**: ^1H, δ = 1.81, 1.89 (2 s, 2 CH_3), 2.66 and 2.79 (AB with J = 14.0 Hz, $J_{3A,4}$ = 10.5 Hz, $J_{3B,4}$ = 9.5 Hz, 3-H_2), 4.05 (q, $J_{3A,4} \sim J_{3B,4} \sim J_{4,5} \sim 9.5$ Hz, 4-H), 5.33 (d, broad, $J_{5,4}$ = 8.5 Hz, 5-H). ^{19}F, δ = -68.6, -70.1 (2 q, 10.2 Hz). **16**: ^1H, δ = 4.18 (s, broadened, 2-H + 5-H), 6.10 (s, broadened, 3-H + 4-H), 7.20 - 7.78 (m, 10 arom. H). ^{19}F, δ = -60.3, -65.2 (2 q, 12.3 Hz). MS (70 eV, 25°C), m/z = 420 (11%, M), 296 (100%, M - BTF), 91 (33%, C_7H_7), 69 (43%, CF_3). **21**: ^{13}C, δ = 12.3 (d, C-2), 12.8 (dq, 3.3 Hz, C-6), 15.4 (d, C-1), 30.0 (t, C-7), 38.7 (s, C-8), 41.1 (dq, 3.0 Hz), 48.1 (d, C-3), 57.1 (d, C-4), 66.0 (sept, 25.3 Hz, C-9), 111.6. 112.8 (2 s, 2 CN), 122.8, 123.1 (2 q, 286.1, 2 CF_3). ^{19}F, δ = -60.5 (q, broad), -65.0 (q, broadened, 13.5 Hz).
9. All new compounds gave satisfactory elemental analyses (CH, N).
10. A 1,4-diradical is not an alternative because zwitterion and diradical are the extremes of a *continuous* scale of tetramethylenes; see Salem, L.; Rowland, C. *Angew.Chem.Int.Ed.Engl.* **1972**, *11*, 92-112.
11. Briefly mentioned by Huisgen, R.; Brückner, R. *Tetrahedron Lett.* **1990**, *31*, 2553-2556.
12. BTF usually gives lower yields of cycloadducts than TCNE; on distillation, some oligomers remain in the residue.
13. Middleton, W.J.; Bingham, E.M. *J.Fluorine Chem.* **1982**, *20*, 397-418.
14. Blomquist, A.T.; Meinwald, Y.C. *J.Am.Chem.Soc.* **1959**, *81*, 667-672.
15. The rates were measured in double runs under pseudo-first order conditions with 20- to 300-fold excess of 1,3-diene, dependent on the rate constants. An exception was cyclopentadiene; the high rate constant required dilute solution of 3-4 equiv diene, 5 cm lightpath (instead of 1 cm), and evaluation by the second-order law. Wherever the extinction of the CT complex was low, 2-methoxynaphthalene was added as a color intensifier.
16. Rücker, C.; Lang, D.; Sauer, J.; Friege, H.; Sustmann, R. *Chem.Ber.* **1980**, *113*. 1663-1690. These authors measured the TCNE rates in CH_2Cl_2 at 20°C; we repeated some in benzene at 25°C (Table 1).
17. Dolbier Jr., W.R.; Medinger, K.S. *Tetrahedron* **1982**, *38*, 2411-2413.

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