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DONOR-SUBSTITUTED FURANS AND 1,2-BIS(TRIFLUOROMETHYL)ETHYLENE-1,2-DICARBONITRILE: THE HIDDEN CYCLOADDITIONS

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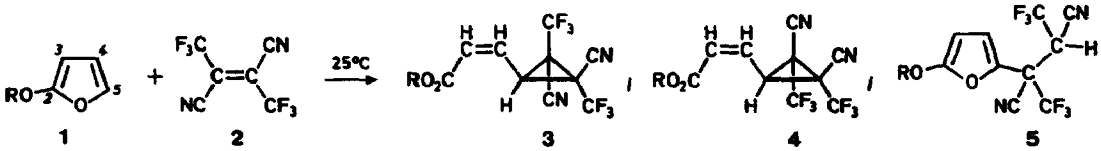
Abstract 2-*p*-Tolyloxyfuran or 2-methoxyfuran and BTE, the title compound, rapidly establish equilibria with [2+2] and/or [4+2] cycloadducts as monitored by ^{19}F NMR analysis; finally, the irreversible opening of the furan ring and concomitant closure of a cyclopropane ring wins. Dissociation constants of four *trans*-adducts and one *cis*-adduct were measured over a temperature range of 90°C; the reaction enthalpies and entropies are discussed.

In the preceding communication, we reported on a novel conversion of donor furans (**1**) with 2,3-bis(trifluoromethyl)fumaronitrile (**2**, *trans*-BTE). After reacting 0.62 M 2-*p*-tolyloxyfuran (**1a**) and 0.49 M *trans*-BTE (**2**) [1] in $CDCl_3$ at 25°C for 14 d, ^{19}F NMR analysis indicated 86% of **3a** + **4a** (76:24), 3% of the substitution products **5** (*threo/erythro* = 70:30) and 6% of unconsumed BTE.



a R = p-$CH_3C_6H_4$ **b** R = CH_3

However, the ^{19}F NMR spectra taken after 10 - 37 min showed that 59% of BTE were consumed; the tiny signals of **3a** + **4a** (1% after 37 min) were dwarfed by a host of signals (Fig. 1), revealing a rapid equilibration of the reactants with new products which we interpret as [2+2] and [4+2] cycloadducts. The integrals of all the signals of Fig. 1 add up to 101% in the spectrum taken after 7 min and to 96% after 14 d. This offers a reliable basis for monitoring the events.

In contrast to *cis-vic* trifluoromethyl groups, *trans*-located CF_3 groups at cyclobutane [2,3] or norbornene rings [3] do not couple each other and appear as pairs of singlets. Four such pairs, matched in the integrals and defined as *trans*-1 to *trans*-4, were found under the proviso that the singlet partner of *trans*-3 coincides with the low-field s at δ_F -64.56 of *trans*-1. Two q with $^5J_{F,F}$ = 12.5 Hz characterize adduct *cis*-1; the high-field absorptions are in accordance with two *cis-vic* hydrogens.

It is plausible that the cycloadducts are formed via the same zwitterionic intermediates **6** as the cyclopropanes **3a** and **4a**. The restriction to *cis*-annellation in the [2+2] cycloadducts **7** leaves us with four racemic diastereoisomers. Ring closure with the 2-position of **6** may furnish four diastereoisomeric 7-oxanorbornenes as [4+2] cycloadducts, illustrated by the *trans,trans* form **8**.

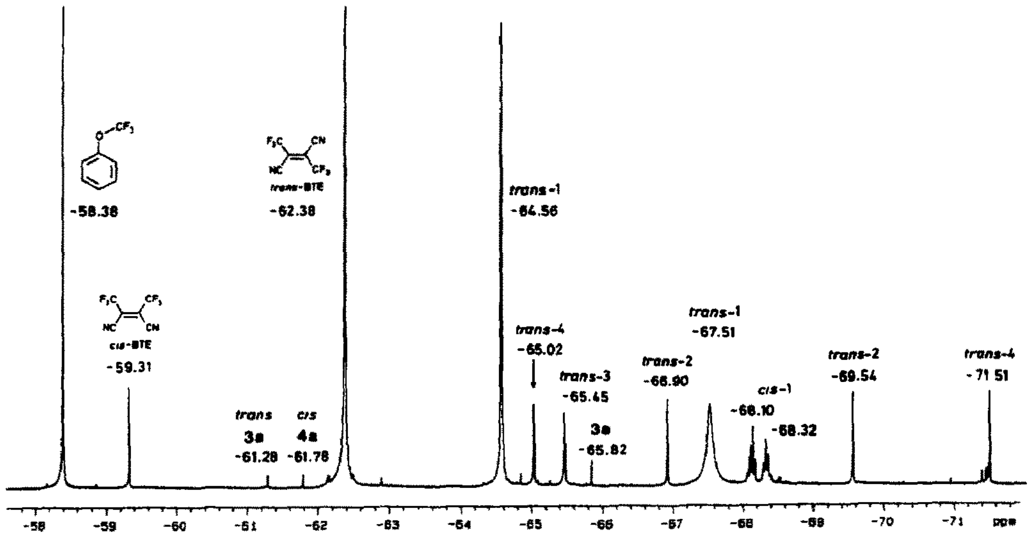
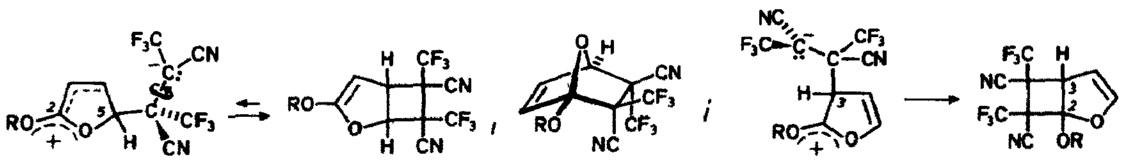


Fig. 1. ^{19}F NMR spectrum (380 MHz, 64 pulses) of the products from 0.62 M **1a** and 0.49 M **2** in $CDCl_3$ at 25°C after 37 min in the presence of 0.12 M trifluoroanisole as a weight standard.

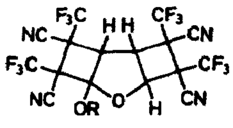


6 **7** **8** *trans,trans* **9** **10**

The 2,3 double bond of the donor furan corresponds to a ketene acetal. Zwitterion **9** could lead to cycloadducts **10**, conceivable in another set of four. In contrast to the cyclobutanes from BTE and vinyl ethers, the cycloadducts of **2** to methylketene dimethylacetal showed weak cycloreversion in solution.[3] Thus, adducts **10** may be energetically less favorable than **7** in which the resonance of the ketene acetal is retained. Bisadducts of type **11** are less likely for the same reason.

Zwitterions from thiocarbonyl ylides and BTE can close the 7-membered ring of cyclic ketene imines under conditions of kinetic control.[4] However, the occurrence of **12** in the equilibrium mixture from **1a** + **2** can be ruled out; an IR absorption in the region of 2000 cm^{-1} was missing.

Structure **13a** fits the ^{19}F NMR data of *cis*-1 (Fig. 1) perfectly, but the NMR information is insufficient for the structural assignment of *trans*-1 to *trans*-4 [5]. What we miss in structural clarity, we gain in thermodynamic insight (see below).



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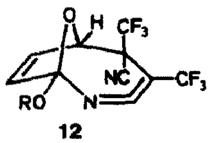
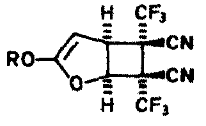
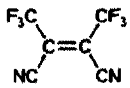


12



13 *cis,trans*

a R = p-$CH_3C_6H_4$;
b R = CH_3



14

Visible in the first 37 min of the reaction is the equilibration of *trans*-BTE with *cis*-BTE (**14**); 3.9% **14** are reached after 37 min and 4.4%, the equilibrium value, after 7 d. The catalysis of the isomerization by **1a** is explained by formation of zwitterion **6**, rotation, and dissociation. Due to the highly mobile equilibrium, *cis*-BTE + **1a** $\rightleftharpoons$ adduct *cis*-**1**, the concentration of *cis*-*1* followed the rise of *cis*-BTE and reached 8% after 37 min. At this time, 41% of BTE was unconsumed, and 40% of the four *trans*-adducts occurred in the ratio 69:10:12:9 (Fig. 1). Slowly, but irreversibly, the opening of the furan ring - only 1% of **3a** + **4a** after 37 min - proceeded affording 70% after 7 d and 86% after 14 d.

$$K^{n}_{diss} = (\textit{trans}\text{-BTE})_e(\mathbf{1a})_e/(\text{Adduct } \textit{trans}\text{-n})_e; \quad (\mathbf{1a})_e = (\mathbf{1a})_o - (\text{BTE})_o + (\text{BTE})_e$$

In experiments with 0.37 M *trans*-BTE, we varied $(\mathbf{1a})_o$ from 0.38 to 1.12 M and found the dissociation constants for the simultaneous equilibria with adducts *trans*-1 to *trans*-4 and the free energy changes (Table 1) fairly reproducible,[6] analogously for *cis*-BTE + **1a** $\rightleftharpoons$ *cis*-1. The law of mass action was fulfilled for a 1:1 reaction. Adduct *trans*-1 owes its dominance to a dissociation constant which is 1/8 of the average for those of *trans*-2 to *trans*-4; the free energy change goes from positive to negative sign. Least dissociated is adduct *cis*-1, and ΔG_{diss} reaches +1.6 kcal mol^{-1}.

In a back-breaking ^{19}F NMR-analytical study, K_{diss} of the five equilibria were measured at 7 temperatures from -35°C to +55°C, i.e., a range of 90°C. On lowering the temperature, the signals became broader due to steric hindrance of CF_3 rotation. The high-field signal of *trans*-1 disappears at -35°C in the underground; even at -15°C it "floods" the nearby quartets (Fig. 1) of *cis*-1. The *trans,cis* isomerization of BTE is frozen below 0°C, but the equilibrium with the five cycloadducts is still mobile at -35°C. The concentration of BTE, 73% at 55°C, goes down to 1.5% at -35°C and the sum of cycloadducts increases from 18% (55°C) to 83% (-35°C), both the result of shrinking K_{diss} values.

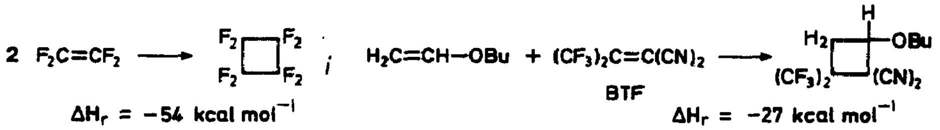
Table 1. Dissociation Constants and Free Energies in $CDCl_3$ at 25°C as well as Dissociation Enthalpies and Entropies for Five Cycloadducts from **1a** (Last Line **1b**) and BTE; ^{19}F NMR Analysis

Cycloadduct	*trans*-1	*trans*-2	*trans*-3	*trans*-4	*cis*-1
K_{diss} (M) at 298 K	0.34	2.5	2.2	3.1	0.064
$\Delta G_{diss,298}$ (kcal mol^{-1})	+0.64	-0.54	-0.48	-0.67	+1.6
ΔH_{diss} (kcal mol^{-1})	14.8 [a]	12.0	13.6	12.1	14.3
ΔS_{diss} (e.u.)	47	42	47	43	43
K_{diss} at 298 K for $OC_6H_4CH_3$	0.28	0.43	2.3	0.41	0.010

[a] The decimal is uncertain and serves only the comparison

100 K_{diss} of adduct *trans*-1 was increased 4600-fold in going from -35°C (0.0802 M) to +55°C (368 M). At -35°C all ΔG_{diss} are positive, at 55°C all negative. In the diagram of ΔG_{diss} versus absol. temperature, excellent straight lines ($r \geq 0.999$) were obtained and evaluated for dissociation entropies and enthalpies (Table 1). The ΔS_{diss} = 43-47 e.u. are in agreement with 45 e.u. for the splitting of cyclobutane into 2 molecules of ethylene.[7] The enthalpies ΔH are in the range of +12 to +15 kcal mol^{-1}.

For comparison with known enthalpies, the *cycloaddition* will be considered. The dimerization of ethylene to cyclobutane is exothermic with -18 kcal mol^{-1}.[7] In the cycloaddition **1a** + BTE $\rightarrow$ **7**, the "resonance energy" of the furan is reduced to that of a ketene acetal and two CN groups lose conjugation. Should we not expect a lower exothermicity than -12 to -15 kcal mol^{-1} for our cycloaddition ?



The dimerization enthalpy of tetrafluoroethylene exceeds that of ethylene by 35 kcal mol^{-1} [8] and suggests that CC bond energies are grossly changed by fluorine substitution. A somewhat lower destabilization of the C=C double bond by CF_3 has been observed.[9] ΔH_r = -27 kcal mol^{-1} was measured for the cycloaddition of BTF, an isomer of BTE, to butyl vinyl ether.[10] The exothermicity is higher by about 14 kcal mol^{-1} than that of the [2+2] cycloadditions of BTE to **1a**. With the empirical "resonance energy" of furan being 16-17 kcal mol^{-1}, [11] the seeming contradiction is dissolved.

When methoxyfuran (**1b**) was reacted with *trans*-BTE in $CDCl_3$ at 25°C, the ^{19}F NMR spectrum revealed an analogous equilibrium with five cycloadducts. The hope that differing δ_F values would disclose the neighborhood of CF_3 and OR - now methoxy instead of *p*-tolyloxy - was in vain. The ^{19}F chemical shifts were very similar; the two q of *cis*-1 coincided at -68.23 to a spectrum of higher order.

Surprisingly, the ^{19}F NMR singlets of *trans*- and *cis*-BTE - razor sharp in the experiments with **1a** - were broadened here. The equilibration of **1b** + *trans*-BTE, mainly with adduct *trans*-1, approaches the rate range of the NMR time scale; **1b** is more nucleophilic than **1a**. Noticeably, K_{diss} of the methoxy-cycloadducts *trans*-2, *trans*-4, and *cis*-1 are only 1/6 of those in the *p*-tolyloxy series (Table 1).

2-Methoxyfuran (**1b**) shows the same reactions with BTE as **1a**, just in a time-lapse. The ring opening to the cyclopropylacrylates **3b** and **4b** (77:23) was 85 times faster than with **1a** ($CDCl_3$, 25°C); the conversion reached 88% in 104 min and 100% after 7 d. When **1a** and *trans*-BTE were mixed in the polar CD_3NO_2, ^{19}F NMR analysis after 7 min revealed neither BTE nor cycloadducts; the whole drama with coming and going of the intermediates was finished and 100% **3b** + **4b** (81:19) was the result.

REFERENCES AND NOTES

Dedicated to Professor Gottfried Märkl, Regensburg, on the occasion of his 65th birthday.

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5. If *one* of the cycloadducts would crystallize, a complete conversion of the whole equilibrium system could be visualized: on dissolving, the crystal would produce the multi-component mixture again. The crystallization did not happen, and our evidence remains limited to the unique 19F NMR information.
6. The estimated error limit of NMR integrals is ±5% relative. Small systematic trends in Kdiss may result from changes of the medium which becomes richer in **1a**. The subscripts e in the equations refer to equilibrium concentrations. The cubic expansion coefficient of chloroform has been taken into account.
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