1,2-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile: (2 + 2) Cycloadditions with Vinyl Ethers

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Dedicated to the Memory of *Jürgen Sauer*

The title compound (short version: BTE) occurs in (*E*)- and (*Z*)-isomers (both with b.p. of *ca.* 100°) which equilibrate with nucleophilic catalysts. Both undergo (2 + 2) cycloadditions with methyl vinyl ether at 25°. Three stereogenic centers in the cyclobutanes led to four *rac*-diastereoisomers, which were obtained in pure and crystalline state. The structures were elucidated by ^{19}F-NMR spectroscopy and confirmed by two X-ray analyses. The cycloadditions were not stereospecific: *e.g.*, (*E*)-BTE furnished 73% *trans*-adducts (with respect to the CF_3 groups) and 27% *cis*-adducts. The loss of stereochemical integrity occurs in the intermediate *gauche*-zwitterions which can cyclize or rotate, but not dissociate. Under extreme conditions (2M $LiClO_4$ in Et_2O, 70°, 3 months), the thermodynamic equilibrium of the four cyclobutanes was achieved. Considerations of *Coulombic* attraction and conformational strain in the zwitterionic intermediates allow us to rationalize the observed proportions of diastereoisomeric cyclobutanes. Ethyl vinyl ether and butyl vinyl ether furnished cyclobutanes in similar diastereoisomer ratios.

1. Introduction. – 1.1. *(2 + 2) Cycloadditions of Electrophilic and Nucleophilic C=C Bonds.* The dimerization of ethene to give cyclobutane is an equilibrium reaction in which cyclobutane dominates at 25°. However, high temperature is required to surpass the activation barrier, *i.e.*, $E \approx 44$ kcal mol^{-1}, but at 500° the equilibrium shifts to the side of ethene. The process involves the 1,4-tetramethylene biradical as an intermediate.

When electrophilic and nucleophilic C=C bonds are chosen as reactants, the formation of cyclobutanes proceeds at room temperature, as discovered by *Williams et al.* [1] in the *du Pont* Laboratories. The (2 + 2) cycloaddition of ethenetetracarbonitrile (TCNE) with enol ethers serves as an example (*Scheme 1*). Here, a tetramethylene-type 1,4-zwitterion **1** is an attractive intermediate bearing a carboxonium ion at one terminus, and two CN groups stabilizing the anionic charge at the other end.

The intermediacy of the zwitterion has been established by plenty of mechanistic criteria in the Munich Laboratory in the 1970s (for a review, see [2]): low stereo-

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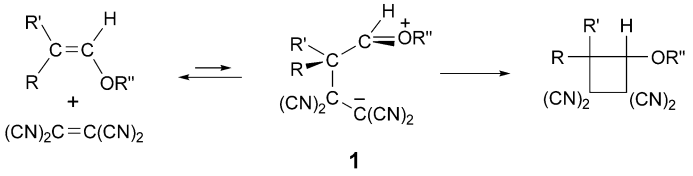
Scheme 1

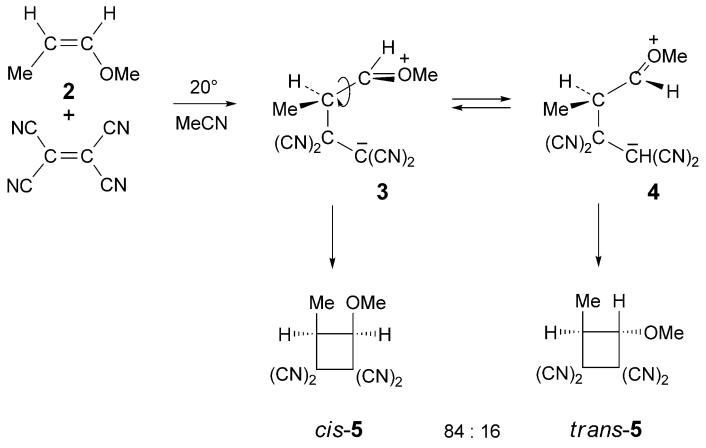


specifity of ring closure, reversibility of zwitterion formation, high influence of solvent polarity on the rate constant, structure–rate relationships. Furthermore, various methods of interception were successful (for a review, see [3]).

A rapid evolution of the $(2+2)$ cycloaddition chemistry took place in the light of a new concept, the *Woodward–Hoffmann* rules for conservation of orbital symmetry (for a review, see [4]). The ${}_{\pi}2_s + {}_{\pi}2_s$ cycloaddition is forbidden to be concerted. In the two-step process, 1,4-biradicals and 1,4-zwitterions occur which are not alternatives, but rather extremes on a continuous scale. It depends on the substitution pattern where a specific tetramethylene has to be located on that scale.

When methyl (*Z*)-prop-1-enyl ether (**2**) was reacted with TCNE, the (*Z*)-geometry of substituents is retained in the main cycloadduct *cis*-**5**. The minor product, *trans*-**5**, goes back to a rotation in the zwitterionic intermediate, **3** ⇌ **4** (*Scheme 2*). In benzene, the cyclobutanes with retention and inversion occurred in a 95 : 5 ratio. The fraction of *trans*-**5** rose with solvent polarity, and reached a *cis*/*trans* ratio of 84 : 16 in MeCN [5].

Scheme 2

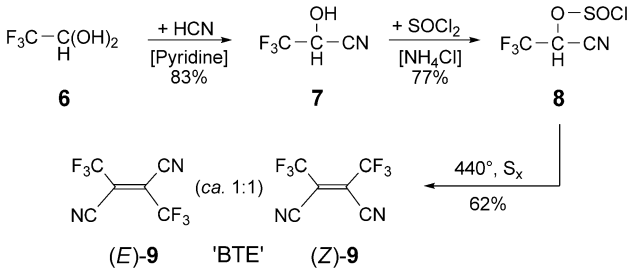


An eventual rotation about the former C=C bond of the acceptor olefin, TCNE, remains hidden, since the pattern of substitution does not give rise to stereogenic centers. We set out to learn about acceptor rotation and to broaden the basis of the project.

1.2. *(*E*)- and (*Z*)-1,2-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile* ((*E*)- and (*Z*)-**9**, resp.) *as an Acceptor-Substituted Ethylene.* The pioneering work on this (*E*)/(*Z*) pair also came from the *du Pont* Laboratories. The synthesis, described by *Cairns* and co-

workers [6][7] and outlined in *Scheme 3*, is not a convenient, but a reproducible procedure. In the last step, the chlorosulfite **8** undergoes eliminattion of SO_2 and HCl in refluxing sulfur at 440°; the ingenuity of the authors is baffling. The assignment of (*E*)- and (*Z*)-**9** mainly rested on the ^{19}F-NMR spectra of the *Diels–Alder* adducts with cyclohexa-1,3-diene.

Scheme 3



Cairns and co-workers studied the (2 + 2) cycloadditions of (*E*)- and (*Z*)-BTE (*i.e.*, (*E*)- and (*Z*)-**9**, resp.) with ethyl vinyl ether and *tert*-butyl vinyl sulfide, and obtained pairs of cycloadducts; the ^{19}F-NMR analysis indicated *high stereospecificity* [6]. It was only in the slower reactions with (*Z*)-prop-1-enyl propyl ether that signals of a minor third adduct appeared in the ^{19}F-NMR spectrum. The slow isomerization of (*Z*)-BTE → (*E*)-BTE in certain solvents was recognized as a complicating factor.

In our hands, all the studied cyclobutane formations from (*E*)- and (*Z*)-BTE with vinyl ethers turned out to be of moderate *stereospecificity*; *e.g.*, the reaction with ethyl vinyl ether gave rise to 21 and 13%, respectively, of inversion products. How did the errors about the steric course come about? Probably, the quality of ^{19}F-NMR analysis in 1963 was not comparable with modern high-resolution technique.

2. Results and Discussion. – 2.1. *Preparation of* BTE, *and of the (*E*)- and (*Z*)-Isomers.* The elimination of SO_2 and HCl from 1-cyano-2,2,2-trifluoroethyl chlorosulfite (**8**; *Scheme 3*) formally generates a carbene which dimerizes; the mechanism is unknown. The thermolysis of **8** in sulfur at 440° described by *Cairns* and co-workers [6] was repeated on a 0.5-mol scale and gave up to 57% of BTE (62% [6]) with an (*E*)/(*Z*) ratio of 55:45. The isomer separation succeeded by vapor-phase chromatography (VPC) on trisiloxane 704 (*Dow Corning*) as a stationary phase.

The elegant (*E*)/(*Z*)-assignment of the BTE isomers *via* the *Diels–Alder* adducts [6] is supplemented here by analysis of the ^{19}F,^{13}C coupling in the NMR spectrum: ^{1}J(C,F) = 280 Hz was observed for (*E*)- and (*Z*)-BTE; only the latter shows an additional F,F coupling between the non-equivalent $^{13}CF_3$ (natural abundance) and $^{12}CF_3$: two *quadruplet*s with ^{5}J(F,F) = 11.1 Hz.

On handling BTE, the volatility (b.p. 101°) and the propensity of isomerization must be considered. The equilibrium (*E*)-BTE ⇌ (*Z*)-BTE, established by nucleophiles, is solvent-dependent and contains the (*Z*)-form as minor fraction: 3.2% in cyclohexane, 4.9% in CH_2Cl_2, and 6.6% in MeCN (slow without catalysis). Previously,

we described a mild catalysis by cyclic azo compounds which allowed the measurement of isomerization rates [8].

A desirable additional access to (*Z*)-BTE was provided by a triplet-sensitized photoisomerization of (*E*)-BTE. Direct irradiation into the UV-absorption band initiated polymerization, but triplet sensitizers established photostationary equilibria which reached nearly a 1:1 ratio of (*E*)- and (*Z*)-BTE. The data compiled in *Table 1* reveal a relation with triplet energies [9].

Table 1. *Triplet-Sensitized Photoisomerization of* (E)*-BTE* (0.20M) *in a Photoreactor of* DURAN 70 *Glass*

Sensitizer (concentration)	Triplet energy [kcal mol^{-1}]	Solvent	Photostationary equilibrium (*Z*) ⇌ (*E*)
Diacetyl (0.046M)	56	Pentane	32 : 68
Naphthalene (0.055M)	61	Pentane	33 : 67
Anthraquinone[a])	62	Pentane	36 : 64
Pyruvic acid (0.045M)	66	Benzene	43 : 57
Benzophenone (0.033M)	69	Pentane	44 : 56
Benzophenone (0.020M)	69	Benzene	49 : 51
Xanthone (0.051M)	74	Benzene	46 : 54

[a]) Saturated solution.

2.2. *BTE and Alkyl Vinyl Ethers.* 2.2.1. *Procedure and Cycloadducts.* The reactions of (*E*)- and (*Z*)-BTE with methyl vinyl ether in CH_2Cl_2 proceeded at 20°, and the yellow color of the charge-transfer (CT) complex disappeared in 3 – 4 days. Thus, BTE is substantially less active than TCNE, where the orange-red CT color fades within 30 min [10]. The cycloadducts **12** of BTE were distilled *in vacuo* and obtained in 90% yield.

Three stereogenic centers in cyclobutane **12** allow four racemic diastereoisomers. All four were present, though in rather different ratios, starting from (*E*)- or (*Z*)-BTE (*Table 2*). The (1*S*)-enantiomers of **12** are chosen as illustrations in *Scheme 4*; *trans* and *cis* refer to the relative positions of CF_3 groups. The two major cycloadducts, **12**(*trans*-1) (52%) from (*E*)-BTE and **12**(*cis*-1) (66%) from (*Z*)-BTE, show *retention* of acceptor structure. By coincidence, adducts with acceptor *inversion* amount to 27% in both reactions.

The major isomers of **12** crystallized from the distilled cycloadducts. The separation of the others succeeded by preparative VPC on dinonyl phthalate as stationary phase. All four *rac*-diastereoisomers of **12** were obtained in pure and crystalline state.

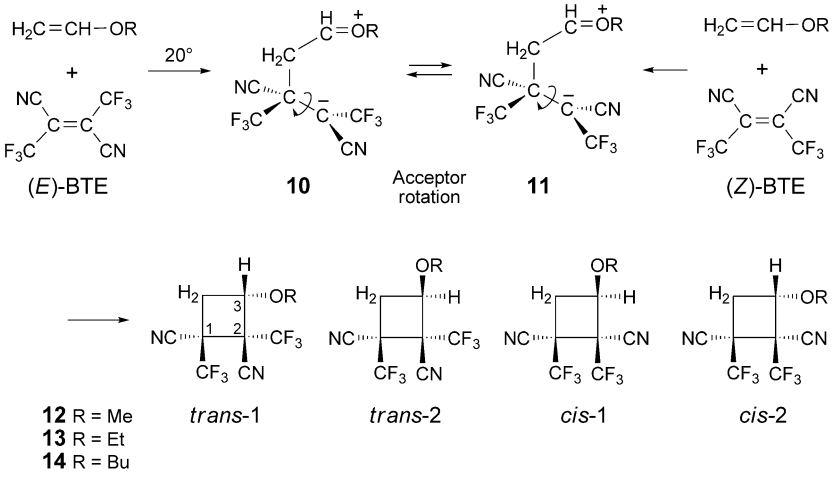
Analogous cycloadditions of (*E*)- and (*Z*)-BTE with ethyl vinyl ether and butyl vinyl ether furnished adducts **13** and **14**, respectively. In *Table 2*, relative yields of the four diastereoisomers are collected. Thus, ethyl vinyl ether does not produce two cycloadducts [6], but rather four *rac*-diastereoisomers with (*E*)- or (*Z*)-BTE. According to the (*R*,*S*) convention, **12**(*cis*-1) is (1*RS*,2*SR*,3*SR*)-3-methoxy-1,2-bis(trifluoromethyl)cyclobutane-1,2-dicarbonitrile.

The loss of stereochemical integrity occurs on the level of the zwitterions **10** and **11** (*Scheme 4*) by rotation about the former C=C bond of BTE. Our system is unsuitable

Table 2. *Cycloadditions of* (E)*- and* (Z)*-BTE with Alkyl Vinyl Ethers in* CH_2Cl_2 *at 20°:* ^{19}*F-NMR Analysis of Cycloadducts*

Cycloadduct			Ratio of diastereoisomeric cyclobutanes [%]			
Compound No.	R	Yield [%]	*trans*-1	*trans*-2	*cis*-1	*cis*-2
Reactions of (E)*-BTE*						
12	Me	89	52	21	1	26
13	Et	89	56	23	2	19
14	Bu	98	59	21	2	18
Reactions of (Z)*-BTE*						
12	Me	90	2	25	66	7
13	Et	90	1	12	81	5
14	Bu	99	2	14	79	3
Equilibrium of cyclobutanes ($LiClO_4$)						
12	Me		23	57	2	18

Scheme 4



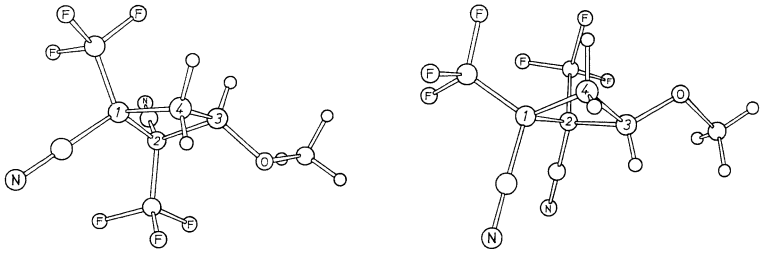
for diagnosing donor rotation (former C=C bond of vinyl ether). The occurrence of two *trans*- and two *cis*-structures goes back to the initial orientation in the CT complex and the formation of the first σ-bond.

2.2.2. *Structure Elucidation by* ^{19}*F-NMR Spectroscopy.* F,F Spin coupling through five bonds is weak (0–2 Hz), but the lone electron pairs at the F-atoms mediate '*coupling through space*'. This term was used by *Petrakis* and *Sederholm* [11] and even applied to *cis*-vicinal and *trans*-vicinal CF_3 groups in cyclobutanes [12]. All the cyclobutanes of *Table 2* with *cis*-CF_3 groups gave rise to two *quadruplet*s with $^5J(F,F) = 11.0–11.5$ Hz in the ^{1}H-decoupled ^{19}F-NMR spectrum; *trans*-CF_3 groups appear as *singlet*s, and only higher resolution reveals *quadruplet*s with $^5J(F,F) = 1.0–1.5$ Hz. Furthermore, in compounds **12**–**14** the ensemble of ^{19}F-chemical shifts allows us to

evaluate the contributions of mutual deshielding by substituents (*Sect. 4.4*) and to allocate the structures to all four diastereoisomers. Two X-ray analyses served as pivotal points.

2.2.3. *X-Ray Structures of Two Cyclobutanes.* The ring of cyclobutane is puckered according to electron diffraction in the gas phase; the folding angle φ amounts to 28°, and the inversion barrier is 1.45 kcal mol^{-1} [13][14]. Numerous X-ray analyses of cyclobutane derivatives brought to light planar structures as well as puckered rings with a variety of angles φ [15]. The puckering angle – also the intracyclic torsion angle is often quoted – is a compromise of angle strain (*Baeyer*) and conformational strain (*Pitzer*).

Crystals of **12**(*trans*-1) and **12**(*cis*-1) were chosen for the X-ray analyses. The ball-and-stick models shown in *Fig. 1* illustrate the dominant influence of the voluminous CF_3 groups on the ring conformation. In **12**(*trans*-1), the CF_3 substituents approach diaxial positions with a torsion angle of 147° at the C(1)–C(2) bond. The puckering angle φ is 22°.



12(*trans*-1) **12**(*cis*-1)

Fig. 1. *X-Ray crystal structures of compounds* **12***(*trans-*1) and* **12***(*cis-*1)*

In **12**(*cis*-1), the *cis*-located CF_3 groups enclose a torsion angle of 30° at the C(1)–C(2) bond. The shortest distance of F-atoms in neighboring CF_3 groups amounts to 267 pm. With a *Van der Waals* radius of 135 pm for the F-atom [16], the F···F distance indicates close contact. This repulsive interaction of the CF_3 groups increases the puckering angle φ to 31°. Another consequence of the ring folding: the sum of the intracyclic angles falls short of 360° by 4.4° for **12**(*trans*-1) and 8.3° for **12**(*cis*-1).

The lengths of the C–C bonds – 155 pm in the cyclobutane parent [13][14] – are increased by number and size of substituents. The tetrasubstituted C(1)–C(2) bond of 157.7 pm in **12**(*trans*-1) and of 158.4 pm in **12**(*cis*-1) (*Table 3*) is substantially longer than C(3)–C(4) bond of 153.5 and 152.4 pm, respectively. The even longer C(2)–C(3) bond, with 158.4 pm for **12**(*trans*-1) and 160.0 pm for **12**(*cis*-1), suggests the participation of a hyperconjugated structure with zwitterionic character.

2.2.4. *The Role of the Zwitterions as Intermediates.* The different diastereoisomer mixtures of **12**–**14**, obtained with (*E*)- and (*Z*)-BTE, do not change composition on distillation or storage of solutions. This is in accordance with kinetic control of cycloadditions. An observation of mechanistic significance: when (*E*)- or (*Z*)-BTE were used in excess over the vinyl ether, the ^{19}F-NMR spectra of the unconsumed BTE after the end of the reaction did not show isomerization. A numerical example: ethyl vinyl ether was reacted in CH_2Cl_2 with 1.2 equiv. of (*Z*)-BTE (isomer purity 99.4%), in

Table 3. *X-Ray Analysis of Cyclobutanes* **12***(*trans-*1) and* **12***(*cis-*1); Selected Bond Lengths and Angles* (standard deviations in parentheses)

	12(*trans*-1)	**12**(*cis*-1)
Bond lengths [pm]		
C(1)–C(2)	157.7(5)	158.4(4)
C(2)–C(3)	158.4(5)	160.0(4)
C(3)–C(4)	153.5(6)	152.4(4)
C(4)–C(1)	156.1(5)	155.7(4)
C(1)–CF3	153.1(5)	151.9(4)
C(2)–CF3	153.3(5)	153.3(4)
C(1)–CN	147.7(6)	148.3(4)
C(2)–CN	149.0(5)	147.5(4)
Bond angles [°]		
C(4)–C(1)–C(2)	89.2(3)	88.4(2)
C(1)–C(2)–C(3)	87.1(3)	85.2(2)
C(2)–C(3)–C(4)	89.9(3)	89.2(2)
C(3)–C(4)–C(1)	89.4(3)	88.9(2)

the course of which 14% *trans*- and 86% *cis*-adducts were formed; however, the (*E*)-content (0.6%) of the excess BTE was virtually undiminished. We must conclude that the zwitterions, once formed, *do not dissociate back* to the reactants. This is in marked contrast with the behavior of TCNE: after the interaction with 1.1 equiv. of (*Z*)-but-2-enyl ethyl ether, the unconsumed 0.1 equiv. of the enol ether showed a (*Z*)/(*E*) ratio of 82:18 and – by coincidence – also a 82:18 ratio for *cis*/*trans*-cycloadduct [17].

Concentrated solutions of $LiClO_4$ in Et_2O resemble a salt melt and belong to the most polar media known [18][19]. In 2M $LiClO_4$ at 70°, the cyclobutane ring of **12** appears to entertain an equilibrium with a small concentration of the zwitterionic rotamers, which, in turn, mediate the equilibration of the four diastereoisomers. Various mixtures of diastereoisomers were heated with ethereal 2M $LiClO_4$ at 70° in sealed NMR tubes for 3 months; the slow isomerizations were followed up by ^{19}F-NMR spectroscopy, as exemplified by *Fig. 2*; the plunge of **12**(*cis*-1) from 52 to 2% is dramatic.

The equilibrium system, established in a medium of high ionic strength, contains 80% **12**(*trans*) and 20% **12**(*cis*), corresponding to $\Delta G = 0.94$ kcal mol^{-1}; the relative shares of the four diastereoisomers are included in *Table 2*. Within the *trans*- and *cis*-pair, the *ortho*-effect between 3-MeO and the bulky *cis*-vic-2-CF_3 is disadvantageous, as 23 *vs.* 57% (*trans*), and 2% *vs.* 18% (*cis*) testify. The high space demand of the CF_3 substituent finds a numerical base in the conformational energies (kcal mol^{-1}): CN, 0.17; MeO, 0.60; CF_3, 2.1 [20][21].

2.2.5. *Which Forces Determine the Steric Pathways?* Our zwitterionic intermediates are substituted tetramethylenes. The parent is a 1,4-biradical, a high-energy intermediate in the thermolysis of cyclobutane; according to calculations [22], it prefers the *anti*-conformation (*zig-zag*). The introduction of substituents (CN, CF_3, OR) stabilizes the tetramethylene, and the electrostatic attraction of the charge centers favors the *gauche*-conformation, as shown in **10** and **11**; the distance of the termini is roughly half that of the *anti*-zwitterion.

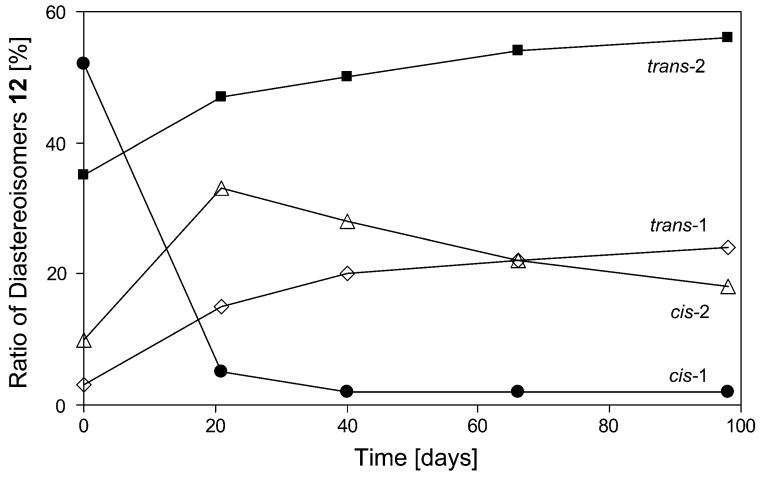
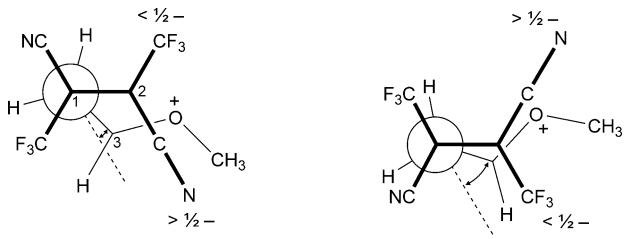


Fig. 2. *Equilibration of the four* rac-*diastereoisomers of* **12** *with* 2M *$LiClO_4$ in Et_2O at 70°*

The *Newman* projection with the bond C(2)–C(3) as axis allows us to recognize the torsion angle between the bond C(1)–C(2), the former C=C bond of the acceptor, and C(3)–C(4), which comes from the vinyl group (*Fig. 3*). Two different configurations of the zwitterion, **15** and **16** (both racemic), emerge from the interaction of (*E*)-BTE and methyl vinyl ether; the π-bonds are omitted in the formulae for the sake of clarity. Due to the *Coulombic* potential, the torsion angle will be less than 60° (staggered). The cationic charge is placed on the O-atom of the carboxonium ion. The CN and CF_3 groups stabilize the carbanion, but to a different extent. In the resonance parameters of *Taft* and co-workers [23], CN (0.49) ranks higher than CF_3 (0.27). Consequently, the center of anionic charge moves below (in **15**) or above (in **16**) the bisector of the acceptor angle, and the torsion angle in **16** comes closer to the *eclipsed* conformation than that in **15**.



(1*R*,2*Si*,3*Si*)-**15** (1*S*,2*Re*,3*Si*)-**16**

Fig. 3. *BTE and methyl vinyl ether: putative conformations of zwitterionic intermediates* **15** *and* **16**

Prelog and *Helmchen* introduced the descriptors of *two-dimensional chirality*, *Re* and *Si* [24]. When the positions are numbered as in the corresponding cyclobutanes, (1*R*,2*Si*,3*Si*) would describe the configuration of **15**, and (1*S*,2*Re*,3*Si*) that of **16**. On 1,4-

cyclization, the more favorable zwitterion **15** furnishes the more hindered cyclobutane and *vice versa* with **16**. This model allows a rationalization of the steric course.

Four zwitterions are shown in *Fig. 4*, all based on the (*S*)-configuration of the initially formed stereogenic center at C(1). The horizontal double arrows indicate rotations about the acceptor bond, the vertical ones are reserved to donor rotations. The rotamers (1*S*,2*Re*,3*Re*)-**15** and (1*S*,2*Si*,3*Si*)-**15** have greater torsion angles than (1*S*,2*Re*,3*Si*)-**16** and (1*S*,2*Si*,3*Re*)-**16**, and offer a more favorable compromise of *Pitzer* strain and *Coulombic* potential. It is plausible that type **15**, due to its energetic advantage, enjoys a preference over type **16** in the formation from (*E*)- and (*Z*)-BTE with methyl vinyl ether.

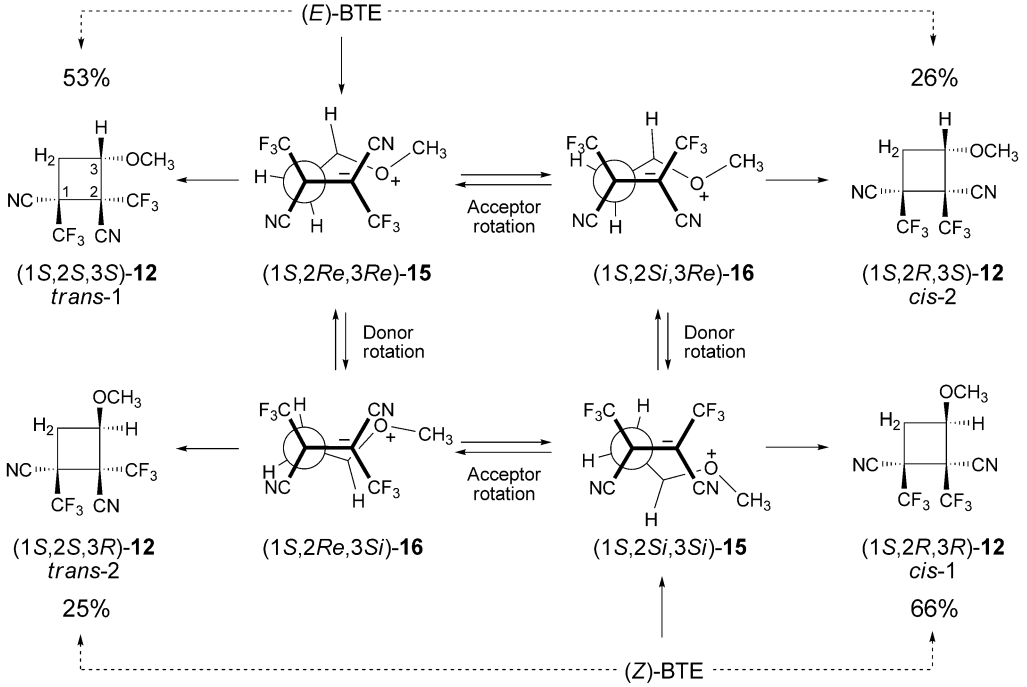


Fig. 4. *Formation of four* rac-*diastereoisomers of* **12** *by (2 + 2) cycloaddition of* (E)- *and* (Z)-*BTE with methyl vinyl ether: proposed steric course*

The zwitterion (1*S*,2*Re*,3*Re*)-**15** produces 53% of **12**(*trans*-1) by direct cyclization and 26% of **12**(*cis*-2) *via* (1*S*,2*Si*,3*Re*)-**16** by rotation about the acceptor bond, *i.e.*, together 79%. The selectivity in the formation of zwitterion (1*S*,2*Si*,3*Si*)-**15** (and its enantiomer) from (*Z*)-BTE appears to be even higher: 66% retention (→**12**(*cis*-1)) and 25% with acceptor rotation (→**12**(*trans*-2)) add up to 91% of the product.

The double arrows between the zwitterions do not indicate established rotamer equilibria. Most of the zwitterions cyclize without rotation (*Table 2*).

2.2.6. *Solvent Polarity and Diastereoisomer Ratios.* The rate-determining step of the cycloaddition is the formation of the zwitterion. The transition state (TS) of establishing this first bond is certainly accompanied by an increase of charge separation

and should respond to solvent polarity. The *Reichardt* parameter E_T is based on solvatochromism and has been proved to be a useful measure of solvent polarity [25].

The influence of solvents on the ratio of diastereoisomeric cyclobutanes was studied for the cycloadditions of (*E*)- and (*Z*)-BTE with ethyl vinyl ether (*Table 4*). The diastereoisomers of **13** (*Scheme 4*) were generated *via* the same set of zwitterions shown in *Fig. 4*, but now with MeO replaced by EtO. We tentatively concluded above that the favored conformations (1*S*,2*Re*,3*Re*) and (1*S*,2*Si*,3*Si*) are the entrance gates to the collection of zwitterions for the reactions of (*E*)- and (*Z*)-BTE, respectively.

Table 4. *(2+2) Cycloadditions of BTE with Ethyl Vinyl Ether: Influence of Solvent Polarity on the Ratio of Diastereoisomeric Cyclobutanes* **13** [%]

Solvent	E_T [kcal mol^{-1}]	**13**(*trans*-1)	**13**(*trans*-2)	**13**(*cis*-1)	**13**(*cis*-2)
(E)-BTE as Reactant					
without		60	20	1	19
C_6D_6	34.3	64	21	1	14
CH_2Cl_2	40.7	56	23	2	19
SO_2	[a])	51	20	3	26
MeCN	45.6	46	14	2	38
(Z)-BTE as Reactant					
without		1	10	83	6
C_6D_{12}	30.9	1	11	85	3
C_6D_6	34.3	1	14	81	4
CH_2Cl_2	40.7	1	13	81	5
MeCN	45.6	3	7	78	12

[a]) Not known.

In the interaction of (*E*)-BTE, direct ring closure of zwitterion (1*S*,2*Re*,3*Re*)-**15** to give **13**(*trans*-1) remains the major pathway, although diminishing with increasing polarity of the solvent from 64% in C_6D_6 to 46% in MeCN; **13**(*cis*-2) profits with a rise from 14 to 38%. In terms of *Fig. 4*, a rotation of the acceptor bond, *i.e.*, (1*S*,2*Re*,3*Re*)-**15** → (1*S*,2*Si*,3*Re*)-**16**, must precede the formation of **13**(*cis*-2). The growth of solvation energy increases the lifetime of the zwitterions as well as the chance of rotation.

Among the diastereoisomers of **13** obtained with (*Z*)-BTE, the direct cyclization of zwitterion, (1*S*,2*Si*,3*Si*)-**15** → **13**(*cis*-1), participates with 85% in C_6D_6 and with 78% in MeCN.

The values compiled in *Table 4* reflect relative rates and are based on substantial ratios of rate constants: $k(\text{MeCN})/k(C_6D_6) = 170$ for (*E*)-BTE and 121 for (*Z*)-BTE, both at 25° [26].

The diastereoisomer ratio did not change during the reaction. As a precaution, ^{19}F-NMR spectra were recorded from minute to minute (30–100% reaction) for BTE + ethyl vinyl ether in MeCN. Thus, even in the polar MeCN, kinetic control remains undisturbed. The zwitterions, once formed, do not dissociate back to the reactants, as described (*Sect. 2.2.4*) for experiments in CH_2Cl_2. When ethyl vinyl ether was reacted with 1.7 equiv. of (*Z*)-BTE (purity 99.7%) *in MeCN*, the ^{19}F-NMR analysis of the unconsumed (*Z*)-BTE showed 99.2% purity, *i.e.*, virtually no dissociation of zwitterions either.

Experimental Part

1. *General.* See [8]. Prep. VPC was carried out with an instrument *APG 402*, *Fa. Hupe & Busch*, with inserted evaporation chamber; for stationary phases, see below. A *Varian Aerograph 1440* instrument served anal. VPC (injection of sample directly on column), combined with *Varian CDS 111 Integrator* (high sensitivity for purity of (*E*)- and (*Z*)-BTE). IR Spectra: The C≡N str. frequency of the cycloadducts is either missing or tiny; this is an old experience for nitriles with adjacent electron-attracting substituents. ^{1}H-NMR Spectra were recorded with *Varian XL 100* (100 MHz) or *Bruker WP 200* (200 MHz), and ^{13}C-NMR spectra with *Bruker WP 80 DS* (20.15 MHz) or *Bruker WP 200* (50.29 MHz); for ^{19}F-NMR spectra, usually ^{1}H-decoupled, *Varian XL 100* (94.1 MHz) or *Jeol FX 90* (84.29 MHz) were used with $FCCl_3$ as internal standard (negative sign for CF_3 in cycloadducts).

2. *Materials.* Methyl vinyl ether (*Baker*, 99.9%) was distilled over $LiAlH_4$. Ethyl vinyl ether (*Merck*) and butyl vinyl ether (*EGA*), likewise distilled over solid $LiAlH_4$, were fractionated with a *Vigreux* column (20 cm). Org. solvents were usually *p.a.* or *Uvasol* quality (mostly *Merck*); for purification, see [27]. Standards for quant. ^{19}F-NMR analysis: fluorobenzene (*Fluka*) and trifluoromethylbenzene (*Merck*), passed through a column of basic Al_2O_3, were dried over molecular sieves, and rectified under Ar; 1,1-dichloro-2,2,2-trifluoroethylbenzene [28], b.p. 91°/37 Torr, was stored under Ar at 0°.

3. *1,2-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile* (=*2,3-Bis(trifluoromethyl)but-2-enedinitrile*; BTE; **9**). 3.1. *Trifluoroacetaldehyde Hydrate* (=*2,2,2-Trifluoroethane-1,1-diol*; **6**) [29]. Trifluoroacetic acid (4.2 mol) in abs. Et_2O (1 l) was cooled to −78°, and a suspension of $LiAlH_4$ (1.25 mol) in Et_2O (1 l) was slowly added; fract. distillation gave **6** (83%); b.p. 101–104° (103–105° [29]).

3.2. *Trifluoroacetaldehyde Cyanohydrin* (=*3,3,3-Trifluoro-2-hydroxypropanenitrile*; **7**). The conversion of **6** → **7** according to [30] gave 76% of **7** with b.p. 53–54°/12 Torr; with a drop of conc. H_2SO_4 added, **7** could be stored at 0°.

3.3. *1-Cyano-2,2,2-trifluoroethyl Chlorosulfite* (**8**). For the reaction with $SOCl_2$, the presence of some NH_4Cl [6] is mandatory, though its function is unclear. $SOCl_2$ (3.6 mol, *Merck*, freshly distilled) and NH_4Cl (1.3 g) were refluxed for 15 min. Compound **7** (0.99 mol) was dropwise introduced into the ice-cooled, stirred $SOCl_2$. After refluxing (bath 90°) for 12 h, distillation over a *Vigreux* column (60 cm) removed the excess of $SOCl_2$, and the yellow **8** followed at 45°/14 Torr (50%): 76%. B.p. 41–42°/10 Torr [6]). Compound **8** is of limited storability.

3.4. *Thermolysis of* **8** *at 440°.* A failed experiment of pyrolysis of **8** in an Ar stream suggests a protective role of sulfur. The apparatus described in [6] was only slightly modified. The elemental sulfur (230 g) was refluxed in a double-necked flask in a salt bath regulated at 460–465°. Two vertical tubes (60 cm, 3-cm-wide) acted as air coolers for the sulfur vapor, one bearing a jacketed, water-cooled dropping funnel, the other leading to the cooled (CO_2/acetone) trap. The chlorosulfite **8** (0.496 mol) was introduced into the boiling sulfur with a rate of *ca.* 1 drop/s. After evaporation of the condensed SO_2, **9** was twice distilled (the second time over a 20-cm column) and obtained as a colorless liquid, b.p. 101–102°, which consisted of (*E*)-**9**/(*Z*)-**9** 55:45. Yield variable, up to 57% ([6]: 62%).

3.5. *Separation of (*E*)- and (*Z*)-BTE. Cairns et al.* [6] used VPC with a 'silicone fluid' on diatomaceous earth at 53°. We found *Dow Corning 704* (1,3,3,5-tetramethyl-1,1,5,5-tetraphenyltrisiloxane) suitable. Acid-washed kieselgur (*Merck 9697*; 250 g) was mixed with *DC 704* (45 g) in pentane (1 l). The solvent was removed in the rotatory evaporator (20°), the material was dried at 20°/10 Torr, filled into a U-shaped column (2 m, ∅ 3 cm), and fit into the VPC instrument *APG 402*. BTE was injected in 300 µl portions into the column kept at 35°, inlet and outlet at 90°, and with N_2 stream 400 ml/min. Retention times (t_R): 15 min for (*E*)-BTE and 27 min for (*Z*)-BTE; base line was reached in between. A total of 6.8 g of isomer mixture furnished 2.8 g of (*E*)-BTE and 2.3 g of (*Z*)-BTE (75%); purity control was conducted by ^{19}F-NMR or anal. VPC. For storage and reactions of BTE, acid-washed glassware was employed, and the experimenter should be aware of the fact that BTE (mol. mass 214) has virtually the same volatility as H_2O.

3.6. *Photostationary Equilibrium of (*E*)- and (*Z*)-BTE* (*Table 1*). *a*) The soln. of (*E*)-BTE (2.14 g, 10.0 mmol) and benzophenone (0.91 g, 5.0 mmol) in pentane (150 ml) was irradiated in a water-cooled reactor made of *DURAN 50* glass (non-transparent in the absorption range of BTE) with a Hg high-pressure arc (*HANAU Q700*, 500 W) for 8 h under Ar; the ^{19}F-NMR *singlet*s indicated an (*E*)/(*Z*) ratio

of 51:49. On cooling the soln. to $-78°$, BTE and benzophenone crystallized, and they were isolated by suction; distillation provided the BTE mixture + little pentane.

b) The soln. (1.0 ml) of (*E*)-BTE (0.20M) and benzophenone (0.049M) in benzene was irradiated in a NMR tube, and periodically ^{19}F-NMR spectra were recorded. Hours (fraction of (*Z*)-**9**): 1.5 (9%), 4 (20%), 10 (37%), 40 (49%). For workup, benzene as solvent is unsuitable.

3.7. *Characterization of BTE. a*) (*E*)-BTE ((*E*)-**9**) crystallized in colorless thin leaflets (recryst. from pentane or sublimation at 25°/12 Torr). M.p. 60.5–61.5° (closed cap.). UV (CH_2Cl_2): λ_{max} (log ε) 227 (4.10). ^{13}C-NMR ($CDCl_3$, 20.2 MHz, ^{1}H-decoupled): 107.3 (*s*, slightly broadened, 2 C≡N); 117.6 (*q*, ^1J(C,F) = 280, 2 CF_3); 123.9 (*q*, ^2J(C,F) = 40.3, 2 olefin. C). ^{19}F-NMR (CH_2Cl_2, 94.1 MHz): −62.1 (*s*, 2 CF_3); −60.8, −63.8 (2*s*, ^{13}C-satellites, ^1J(C,F) = 280). MS (70 eV, 30°): 214 (31, M^+), 195 (11, [M − F]$^+$), 145 (36, [$M - CF_3$]$^+$), 69 (100, CF_3).

b) *(Z)-BTE* ((*Z*)-**9**). Purity by anal. VPC: 99.27% (*Z*), 0.73% (*E*). UV (CH_2Cl_2): λ_{max} (log ε) 232 (3.98). ^{13}C-NMR ($CDCl_3$, 20.2 MHz): 109.2 (*s*, 2 C≡N); 117.1 (*q*, ^1J(C,F) = 279, 2 CF_3); 123.9 (*q*, ^2J(C,F) = 40, 2 olefin. C). ^{19}F-NMR (CH_2Cl_2, 94.1 MHz): −59.1 (*s*, 2 CF_3); −57.7, −60.7 (2*q*, ^{13}C-satellites, ^1J(C,F) = 280, ^5J(C,F) = 11.1, 2 CF_3). Anal. calc. for $C_6F_6N_2$ (214.08): C 33.66, N 13.09; found: C 33.81, N 13.12.

4. *(2+2) Cycloadditions of BTE and Methyl Vinyl Ether.* 4.1. *(*E*)-***9***.* Methyl vinyl ether (68 mg, 1.17 mmol) was condensed into a NMR tube at −78°, closed with a septum, and weighed. After injection of the soln. of (*E*)-**9** (221 mg, isomer purity >99.9%) in CH_2Cl_2 (0.5 ml) at −78°, the tube was cooled with liquid N_2 and melted off at the tapered position.

The yellow soln. (CT complex color) at r.t. became colorless in 4 d. A ^{19}F-NMR spectrum was recorded, before the content of the tube was transferred into a microflask and distilled at 60°/0.02 Torr: **12** as a colorless, partially crystalline oil (248 mg, 89%); a weighed amount of standard – 1,1-dichloro-2,2,2-trifluoroethylbenzene (δ −78.2) – was added for the quant. ^{19}F-NMR analysis in CH_2Cl_2. The diastereoisomer ratios of **12** remained constant in weeks at r.t. and were determined by the following ^{19}F-NMR signals: −62.6 (*q*, 2-CF_3, *cis*-1); −66.3, −71.6 (2*s*, *trans*-1); −67.7 (*q*, 2-CF_3, *cis*-2); −70.3 (*s*, 2-CF_3, *trans*-2). The integrals were added up, and the relative amounts are collected in *Table 2*. Anal. calc. for $C_9H_6F_6N_2O$ (272.15): C 39.72, H 2.22, N 10.29; found for isomer mixture: C 40.00, H 2.37, N 10.26.

Besides **12**, the ^{19}F-NMR spectrum before distillation indicated 7% of 1:2 adducts [31]. In another experiment with 1.79 mmol of methyl vinyl ether and 0.96 mmol of (*E*)-**9** in CH_2Cl_2 (0.5 ml), 11% of 1:2 adducts and 89% of 1:1 adducts (unchanged isomer ratio) were formed (rel. yields). An experiment without solvent gave a slightly varied isomer composition (*Table 4*).

4.2. *(*Z*)-***9***.* A specimen (1.17 mmol) with 99.2% (*Z*)- and 0.8% (*E*)-content was reacted with methyl vinyl ether (1.10 mmol) in CH_2Cl_2 (0.5 ml), as described above. The distillation at 60°/0.05 Torr furnished oil and crystals (270 mg, 90%). The ^{19}F-NMR spectrum (CH_2Cl_2) was unchanged after 4 weeks at r.t. and confirmed kinetic control of the cycloaddition. The ratios of the diastereoisomers listed in *Table 2* do not include the 0.8% admixture of (*E*)-**9**. The weight standard for the ^{19}F-NMR analysis was fluorobenzene with δ −113.7. Anal. of diastereoisomer mixture: calc. for $C_9H_6F_6N_2O$ (272.15): C 39.72, H 2.22, N 10.29; found: C 39.84, H 2.16, N 10.47.

4.3. *Separation of Cyclobutanes* **12**. The column (8 m, ∅ 1 cm) for the prep. VPC was filled with acid-washed kieselgur (*Anakrom A*; 0.15–0.18 mm; *Fa. Antechnika*) and charged with 10% of dinonyl phthalate (*Fa. Merck*); column temp., 60°; inlet temp., 95°; detector temp., 115°; N_2 pressure, 1.1 atm. t_R: 22.0 h for *cis*-1, 22.4 h for *cis*-2, 19.0 h for *trans*-2, and 20.1 h for *trans*-1; 5 portions of 30–60 mg of the mixture, obtained from (*E*)-**9**, were used for the isolation of *trans*-1, *trans*-2, and *cis*-2, whereas the cryst. product from (*Z*)-**9** was an ample source of *cis*-1.

4.4. *Note on Structural Assignment by ^{19}F-NMR Spectroscopy.* The F,F coupling is limited to *cis*-located CF_3 groups (J(F,F) ≈ 11). A second criterion of differentiation comes from a net of mutual deshielding effects by substituents. The size of this effect on δ(F) varies and allows a consistent attribution:

cis-vic-MeO > *trans*-vic-MeO > *cis*-vic-CF_3 > *trans*-vic-CF_3 > 1,3-*cis*-MeO > 1,3-*trans*-MeO

4.5. *(1*RS,*2*RS,*3*RS*)-3-Methoxy-1,2-bis(trifluoromethyl)cyclobutane-1,2-dicarbonitrile* (**12**(*trans*-1)). This is the main constituent (52%) of the oil and crystals from (*E*)-**9** and the unsaturated ether. The oil was adsorbed by filter paper; repeated recrystallization of the solid from CH_2Cl_2/pentane and subsequent sublimation at 35°/0.05 Torr gave colorless prisms. M.p. 78.5–79° (sealed cap.). IR (KBr): 714*s*, 810*w*, 996*m*, 1077*m*, 1089*m*; 1136*s*, 1143*s*, 1198*vs* + 1210*vs* (br.), 1285*s* (C–F, C–O str.), no C≡N str. visible; 2845*w* (MeO), 2920*w*, 2950*w* (C–H, sharp). ^{1}H-NMR (100 MHz, $CDCl_3$, F-decoupled): 3.85 (*s*, MeO); the *ABX* system of ring-H was simulated with the program *LAME* [32]: 3.32, 3.40 (*AB*, CH_2(4)); 4.81 (*X*, H–C(3)); $^2J_{AB}$ = 13.8, $^3J_{AX}$ = 9.1, $^3J_{BX}$ = 8.9. ^{13}C-NMR (50.3 MHz, ^{1}H-decoupled): 36.6 (*s*, C(4)); 39.9 (*q*, ^2J(C,F) = 34, C(1)); 51.6 (*q*, ^2J(C,F) = 29, C(2)); 60.0 (*s*, MeO); 77 (C(3), overlap with $CDCl_3$); 111.0, 111.3 (2*s*, 2 CN); 121.6 (*q*, ^1J(C,F) = 284, CF_3); 122.4 (*q*, ^1J(C,F) = 283, CF_3). ^{19}F-NMR ($CDCl_3$, 94.1 MHz): −66.5 (br. *s*, 2-CF_3); −71.2 (br. *s*, 1-CF_3); on ^{1}H-decoupling 2 sharp *s*).

4.6. *(1*RS,*2*RS,*3*SR*)-Isomer* (**12**(*trans*-2)). The fraction of VPC was distilled at 60°/0.1 Torr and crystallized at 0°. M.p. *ca.* 20°. IR: 726*m* (sharp), 921*m*, 985*m*; 1057*s* (C–O); 1202*vs* + 1262*vs* (br. (C–F, C–O)), no C≡N; 2850*w*, 2950*w* (C–H). ^{1}H-NMR ($CDCl_3$, 100 MHz, F-decoupled): 3.54 (*s*, MeO), *ABX* system calc. with the method of effective *Larmor* frequencies [33]: 2.90, 3.06 (*AB* part, $^2J_{AB}$ = 13.4, H_A–C(4), H_B–C(4)); 4.49 (*X*, $^3J_{AX}$ = 8.1, $^3J_{BX}$ = 7.9, H–C(3)). ^{19}F-NMR (CH_2Cl_2, 94.1 Hz): −68.9 (br. *s*, 2-CF_3), −71.6 (*s*, structured, 1-CF_3); ($CDCl_3$): −69.0 (br. *s*, 2-CF_3), −70.5 (*d*, partially resolved, ^5J(F,F) = 1.5, 1-CF_3).

4.7. *(1*RS,*2*SR,*3*SR*)-Isomer* (**12**(*cis*-1)). The colorless leaflets, obtained by VPC, were sublimed at 40°/0.05 Torr. M.p. 78.0–78.5° (pentane). IR: 731*m*, 747*m*, 993*m*, 1030*m*, 1043*m* (all sharp); 1174*s*, 1183*m*, 1193*s*, 1202*s*, 1238*m*, 1261*s*, 1303*s* (all C–O, C–F str.); 2255v*w* (C≡N non-conjug.), 2840v*w* (C–H of MeO); 2950*w*, 2980*w*, 3035*w* (C–H, sharp). ^{1}H-NMR ($CDCl_3$, 100 MHz, F-decoupled): 3.02 (br. *d*, ^3J(3,4) = 9.0, CH_2(4)); 3.60 (*s*, MeO); 4.69 (*t*, ^3J(3,4) = 9.0, H–C(3)); (F-coupled): 3.02 (*dq*, ^4J(H,F) = 0.9, CH_2(4)); 4.69 (*tq*, ^4J(H,F) = 1.9, H–C(3)). ^{13}C-NMR ($CDCl_3$, 50.3 MHz, ^{1}H-decoupled): 36.2 (*s*, C(4)); 42.3 (*q*, ^2J(C,F) = 30, C(1)); 53.6 (*q*, ^2J(C,F) = 31, C(2)); 59.9 (*s*, MeO); 77 (below C–D signals, C(3)); 112.4 (*q*, ^3J(C,F) = 3.5, CN); 113.4 (*q*, ^3J(C,F) = 1.5, CN); 120.6 (*q*, ^1J(C,F) = 281, CF_3); 121.1 (*q*, ^1J(C,F) = 284, CF_3). ^{19}F-NMR ($CDCl_3$, ^{1}H-decoupled): −62.9 (br. *q*, ^5J(F,F) = 11.0, 2-CF_3); −68.9 (*q*, ^5J(F,F) = 11.4, 1-CF_3).

4.8. *(1*RS,*2*SR,*3*RS*)-Isomer* (**12**(*cis*-2)). Distillation of the product (288 mg), which was obtained from (*E*)-**9** and methyl vinyl ether in MeCN, furnished oil and crystals, which were separated by filter paper. Colorless needles (23 mg) were obtained from pentane. M.p. 77.5–78.0°. IR: 720*m*, 743*m*, 985*s*, 1043*m* (all sharp); 1109*s*, 1179v*s* + 1220v*s* (br.), 1290*s* (br., C–O, C–F), 2255v*w* (C≡N, uncertain). ^{1}H-NMR ($CDCl_3$, 100 MHz, ^{19}F-decoupled): 3.82 (*s*, MeO); *ABX* calc. with effective *Larmor* frequencies [33]: 3.26, 3.35 (*AB*, J_{AB} = 13.4, CH_2(4)); 4.73 (*X*, ^3J(3,4*A*) = 8.8, ^3J(3,4*B*) = 7.7, H–C(3)); (fully coupled): 33.0, 33.2 (2 apparent *dqq*, *J*(H,F) = 0.8 and 0.6, CH_2(4)); 3.82 (*q*, ^6J(H,F) = 0.3, MeO); 4.74 (apparent *tq*, ^4J(H,F) = 0.8, H–C(3)). ^{13}C-NMR ($CDCl_3$, 50.3 MHz, ^{1}H-decoupled): 35.4 (*s*, C(4)); 41.4 (*q*, ^2J(C,F) = 37, C(1)); 57.3 (*q*, ^2J(C,F) = 37, C(2)); 58.7 (*s*, MeO); 73.1 (*s*, C(3)); 109.9, 112.1 (br. 2*s*, 2 CN); 120.3 (*q*, ^1J(C,F) = 276, CF_3); 121.9 (*q*, ^2J(C,F) = 281, CF_3). ^{19}F-NMR ($CDCl_3$, 50.3 MHz, H-decoupled): −67.9, −68.8 (2*q*, ^5J(F,F) = 11.4, further split, 2 CF_3); (CH_2Cl_2): −67.8, −68.8 (2*q*, ^5J(F,F) = 11.2, 2 CF_3).

4.9. *Equilibration of Cyclobutanes* **12**. $LiClO_4$ (*p.a.*) was dried at 160°/0.3 Torr for 4 h and dissolved in abs. Et_2O. The 2M soln. (0.5 ml) and the diastereoisomers of **12** (114 mg, *ca.* 0.40 mmol, obtained with (*E*)-**9**), in a sealed NMR tube, were heated in a thermostat at 70°; in a second tube, a specimen of **12**, prepared from (*Z*)-**9**, was treated correspondingly with 2M $LiClO_4$. *Fig. 2* shows the slow isomerization; after 143 d, the two isomer mixtures have become identical within the limits of the ^{19}F-NMR analysis. No BTE signals were observed. Beginning decomposition was noticed after 160 d.

5. *(2 + 2) Cycloadditions of BTE* (**9**) *with Ethyl Vinyl Ether.* 5.1 *(*E*)-***9***.* The procedure was similar to that described above; a brief description of one example would be sufficient. Ethyl vinyl ether (70 mg, 0.97 mmol) and (*E*)-**9** (246 mg, 1.15 mmol) in CH_2Cl_2 (4 ml) showed a light-yellow CT complex color which slowly faded. After 8 d at r.t., the solvent was removed, and distillation at 55°/0.3 Torr furnished **13** as a colorless oil (248 mg, 89%); *Table 2* shows the ratio of the four diastereoisomers. The quant. ^{19}F-NMR analysis was based on the following signals: −71.6, −66.4 (2*s*) for **13**(*trans*-1), −70.3 (*s*) for **13**(*trans*-2), −62.7 (*q*) for **13**(*cis*-1), and −67.7 (*q*) for **13**(*cis*-2). As described above, the elemental

analysis was carried out for the isomer mixture. Anal. calc. for $C_{10}H_8F_6N_2O$ (286.18): C 41.97, H 2.82, N 9.79; found: C 41.94, H 2.92, N 9.75.

Further cycloaddition experiments were carried out in other solvents. The fast reaction in MeCN was virtually complete for (*E*)-**9** after 13 min and for (*Z*)-BTE after 4.5 min.

In the reaction of (*Z*)-**9** without solvent, the deep-yellow color disappeared in 20 min; the ^{19}F-NMR analysis (*Table 2*) was performed with fluorobenzene (−113.7 in CH_2Cl_2) as a weight standard. The distilled oil (65%/0.02 Torr) showed the same isomer composition as before. Anal. calc. for $C_{10}H_8F_6N_2O$ (286.18): C 41.97, H 2.82, N 9.79; found: C 42.03, H 2.82, N 9.89.

5.2. *Separation of the Isomers of Cyclobutanes* **13** *and Assignment.* Only partial separation was achieved with VPC on dinonyl phthalate or bis(2-ethylhexyl) sebacate as stationary phases. The major products were **13**(*trans*-1) (52%) from (*E*)-**9** and **13**(*cis*-1) (66%) from (*Z*)-**9**. Besides the F,F-coupling of *cis*-located CF_3 groups, the mutual deshielding effects of substituents (*Sect. 4.4*) established the structures.

5.3. *(1*RS,*2*RS,*3*RS*)-3-Ethoxy-1,2-bis(trifluoromethyl)cyclobutane-1,2-dicarbonitrile* (**13**(*trans*-1)). The compound partially crystallized from the distilled mixture, obtained with (*E*)-**9**. Oily constituents were removed by pressing between filter papers. Colorless prisms crystallized from pentane. M.p. 28.5–29.5°. IR: 714*m* (sharp, CF_3 deform.), 1200*vs* and 1282*s* (very br., C–O, C–F str.); no clear C≡N vibr. ^{1}H-NMR ($CDCl_3$, 100 MHz, F-decoupled): 1.25 (*t*, ^3J = 7.0, Me of EtO); 3.5–3.9 (*m*, CH_2 of EtO); 3.03, 3.08 (*AB* from *Larmor* frequencies, $^2J(4A,4B)$ = 13.8, H_A–C(4), H_B–C(4)); 4.58 (*X* of *ABX*, $^3J(3,4A)$ = 10.2, $^3J(3,4B)$ = 7.8, H–C(3)). ^{19}F-NMR ($CDCl_3$, 94.1 MHz, ^{1}H-decoupled): −71.9, −66.7 (2*s*, 2 CF_3); in CH_2Cl_2: −71.6, −66.4.

5.4. *(1*RS,*2*SR,*3*SR*)-Isomer* (**13**(*cis*-1)). This compound crystallized from the dist. material (experiment with (*Z*)-**9**). M.p. 35.0–35.5° (pentane). IR: 732*m*, 749*w* (both sharp); 1031*m*, 1045*m*, 1167*s*,

Table 5. *X-Ray Crystallographic Data of Compounds* **12**(trans-*1) and* **12**(cis-*1)*

	12(*trans*-1)	**12**(*cis*-1)
CCDC	856014	856015
Molecular formula	$C_9H_6F_6N_2O$	$C_9H_6F_6N_2O$
Molecular mass	272.15	272.15
Temp. [K]	153	153
Space group, *Z*	*C*2/*c*, 8	*P*21/*c*, 4
Crystal size [mm]	0.30 × 0.24 × 0.35	0.30 × 0.28 × 0.42
Unit cell dimensions:		
a [Å]	20.047(6)	7.091(2)
b [Å]	7.754(3)	15.378(4)
c [Å]	14.106(4)	10.238(3)
β [°]	98.54(2)	103.69(3)
Volume [Å^3]	2232.7(18)	2168.3(13)
Density calc. [g/cm^3]	1.619	1.667
Wave number (MoK_a) [mm^{-1}]	1.72	1.72
2*θ* Range [°]	2–40	2–50
Reflex width [°]	1.0	1.2
Measurement speed [°/min]	1.3–29.3	1.5–29.3
Reflections collected	1284	2269
Control reflections	52	108
Reflections unique with $I > 3\sigma(I)$	1109	1902
	930	1563
Parameters refined	181	186
Final *R*	0.069	0.058
wR^2	0.057	0.058

1206*vs* (br.), 1236*s* (br.), 1273*s* (br., C–O, C–F str.); no distinct CN band. ^{1}H-NMR ($CDCl_3$, 100 MHz, F-decoupled): 1.27 (*t*, $^3J = 7.0$, Me of EtO); 3.02 (2 *d*, $^3J = 9.0$, $CH_2(4)$); 3.3–3.9 (*m*, diastereotopic CH_2 of EtO); 4.74 (*t*, $^3J(3,4) = 9.0$, H–C(3)); (fully coupled): 3.02 (*dq*, $^4J(H,F) = 1.0$, only partially resolved, $CH_2(4)$); 4.74 (*tq*, $^4J(H,F) = 1.7$, H–C(3)). ^{19}F-NMR ($CDCl_3$, 94.1 MHz, ^{1}H-decoupled): −63.0 (br. *q*, $^5J(F,F) = 11.4$, 2-CF_3); −69.1 (*q*, $^5J(F,F) = 11.4$, 1-CF_3).

6. *3-Butoxy-1,2-bis(trifluoromethyl)cyclobutane-1,2-dicarbonitrile* (**14**). The cycloaddition of (*E*)-**9** to butyl vinyl ether in CH_2Cl_2 at r.t. was complete after 3 d; the solvent was removed, and (trifluoromethyl)benzene (^{19}F-NMR, δ −63.1) was added in a weighed amount. The yield of the four diastereomeric adducts **14** was 99% (for composition, see *Table 2*). Distillation at 65°/0.3 Torr gave a colorless oil. The separation was not attempted. Anal. calc. for $C_{12}H_{12}F_6N_2O$ (314.23): C 45.86, H 3.85, N 8.92; found: C 46.00, H 3.92, N 9.15.

The color of the deep-yellow soln. of (*Z*)-**9** (0.59 mmol) and butyl vinyl ether (0.51 mmol) in CH_2Cl_2 (0.5 ml) faded in 16 h. Evaporation of the solvent left **14** as a colorless oil (158 mg, 99%). The elemental analysis confirmed the purity. Anal. calc. for $C_{12}H_{12}F_6N_2O$ (314.23): C 45.86, H 3.85, N 8.92; found: C 46.12, H 3.87, N 9.00.

Without separation of the diastereoisomers of **14**, the close relation of the ^{19}F-NMR spectrum with those of **12** and **13** allowed the structural assignments. ^{19}F-NMR (CH_2Cl_2, 94.1 MHz, H-decoupled): −66.2 (*s*) and −71.6 (*s*) for **14**(*trans*-1), −68.8 (*s*) and −70.3 (*s*) for **14**(*trans*-2), −62.6 (*q*, $J = 11.5$) and −68.9 (*q*, $J = 11.5$) for **14**(*cis*-1), and −67.6 and −68.6 (2*q*, $J = 11.0$) for **14**(*cis*-2).

7. *X-Ray Analyses of* **12**(trans-*1*) *and* **12**(cis-*1*). For details, see *Table 5*. Crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 IEZ, UK, with deposition numbers CCDC-856014 for **12**(*trans*-1) and 856015 for **12**(*cis*-1).

REFERENCES

[1] J. K. Williams, D. W. Wiley, B. C. McKusick, *J. Am. Chem. Soc.* **1962**, *84*, 2210.
[2] R. Huisgen, *Acc. Chem. Res.* **1977**, *10*, 117.
[3] R. Huisgen, *Acc. Chem. Res.* **1977**, *10*, 199.
[4] R. B. Woodward, R. Hoffmann, *Angew. Chem.* **1969**, *81*, 797; *Angew. Chem., Int. Ed.* **1969**, *8*, 781.
[5] R. Huisgen, G. Steiner, *J. Am. Chem. Soc.* **1973**, *95*, 5054.
[6] S. Proskow, H. E. Simmons, T. L. Cairns, *J. Am. Chem. Soc.* **1963**, *85*, 2341 (communication); *J. Am. Chem. Soc.* **1966**, *88*, 5254 (full paper).
[7] S. Proskow; *E. I. du Pont de Nemours & Co.*, US Pat. No. 3,133,155; *Chem. Abstr.* **1964**, *61*, 25019.
[8] R. Huisgen, G. Mlostoń, E. Langhals, T. Oshima, *Helv. Chim. Acta* **2002**, *85*, 2668.
[9] J. A. Barltrop, J. D. Coyle, in 'Principles of Photochemistry', John Wiley & Sons, New York, 1978, p. 130.
[10] R. Huisgen, G. Steiner, *Tetrahedron Lett.* **1973**, 3763.
[11] L. Petrakis, C. H. Sederholm, *J. Chem. Phys.* **1961**, *35*, 1241.
[12] S. Ng, C. H. Sederholm, *J. Chem. Phys.* **1964**, *40*, 2090.
[13] A. Almenningen, O. Bastiansen, P. N. Skancke, *Acta Chem. Scand.* **1961**, *15*, 711.
[14] T. Egawa, T. Fukuyama, S. Yamamoto, F. Takabayashi, H. Kambara, T. Ueda, K. Kuchitsu, *J. Chem. Phys.* **1987**, *86*, 6018.
[15] F. H. Allen, *Acta Crystallogr., Sect. B* **1984**, *40*, 64.
[16] L. Pauling, 'The Nature of the Chemical Bond', Cornell University Press, 1948, p. 187.
[17] R. Huisgen, G. Steiner, *J. Am. Chem. Soc.* **1973**, *95*, 5055.
[18] K. Ekelin, L. G. Sillén, *Acta Chem. Scand.* **1953**, *7*, 987.
[19] Y. Pocker, R. F. Buchholz, *J. Am. Chem. Soc.* **1970**, *92*, 2075; Y. Pocker, D. L. Ellsworth, *J. Am. Chem. Soc.* **1977**, *99*, 2276.
[20] J. A. Hirsch, *Topics Stereochem.* **1967**, *1*, 199, 205.
[21] E. W. Della, *Tetrahedron Lett.* **1966**, *7*, 3347.
[22] G. A. Segal, *J. Am. Chem. Soc.* **1974**, *96*, 7892.
[23] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165.

[24] V. Prelog, G. Helmchen, *Angew. Chem.* **1982**, *94*, 614; *Angew. Chem., Int. Ed.* **1982**, *21*, 567.
[25] C. Reichardt, 'Solvent Effects in Organic Chemistry', VCH Weinheim, 1979; C. Reichardt, *Chem. Rev.* **1994**, *94*, 2319.
[26] T. Oshima, R. Huisgen, in preparation.
[27] J. A. Riddick, W. B. Burger, 'Organic Solvents', Vol. II of 'Techniques of Chemistry', 3rd edn., Ed. A. Weissberger, J. Wiley and Sons, 1970.
[28] S. G. Cohen, H. T. Wolosinski, P. J. Scheuer, *J. Am. Chem. Soc.* **1949**, *71*, 3439.
[29] D. R. Husted, A. H. Ahlbrecht, *J. Am. Chem. Soc.* **1952**, *74*, 5422.
[30] S. H. Burstein, H. J. Ringold, *Can. J. Chem.* **1961**, *39*, 1848.
[31] R. Huisgen, G. Urrutia Desmaison, in preparation.
[32] C. W. Haigh, *Annu. Rep. NMR Spectrosc.* **1971**, *4*, 311.
[33] H. Günther, 'NMR Spectroscopy', John Wiley & Sons, New York, 1980, p. 162.

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