Reactions of Methyl Diazoacetate with (*E*)- and (*Z*)-1,2-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile: Novel and Unanticipated Pathways[1])

by **Rolf Huisgen***, **Grzegorz Mlostoń**[2]), **Peter Pöchlauer**[3]), **Lubor Fišera**[4]), and **Henry Giera**[5])

Department Chemie und Biochemie der Ludwig-Maximilians-Universität München, Butenandtstrasse 5–13 (Haus F), D-81377 München

Dedicated to *Mordecai Rubin*, Technion, Haifa, on the occasion of his 80th birthday

The cycloadditions of methyl diazoacetate to 2,3-bis(trifluoromethyl)fumaronitrile ((*E*)-**BTE**) and 2,3-bis(trifluoromethyl)maleonitrile ((*Z*)-**BTE**) furnish the 4,5-dihydro-1*H*-pyrazoles **13**. The retention of dipolarophile configuration proceeds for (*E*)-**BTE** with >99.93% and for (*Z*)-**BTE** with >99.8% ($CDCl_3$, 25°), suggesting concertedness. Base catalysis (1,4-diazabicyclo[2.2.2]octane (DABCO), proton sponge) converts the cycloadducts, *trans*-**13** and *cis*-**13**, to a 94:6 equilibrium mixture ($CDCl_3$, r.t.); the first step is *N*-deprotonation, since reaction with methyl fluorosulfonate affords the 4,5-dihydro-1-methyl-1*H*-pyrazoles. Competing with the *cis*/*trans* isomerization of **13** is the formation of a bis(dehydrofluoro) dimer (two diastereoisomers),

$$2\ C_9H_4F_6N_4O_2\ (\mathbf{13}) \rightarrow C_{18}H_6F_{10}N_8O_4\ (\mathbf{22}) + 2\ HF,$$

the structure of which was elucidated by IR, ^{19}F-NMR, and ^{13}C-NMR spectroscopy. The reaction slows when DABCO is bound by HF, but F^- as base keeps the conversion to **22** going and binds HF. The diazo group in **22** suggests a common intermediate for *cis*/*trans* isomerization of **13** and conversion to **22**: reversible ring opening of *N*-deprotonated **13** provides **18**, a derivative of methyl diazoacetate with a carbanionic substituent. Mechanistic comparison with the reaction of diazomethane and dimethyl 2,3-dicyanofumarate, a related tetra-acceptor-ethylene, brings to light unanticipated divergencies.

1. Introduction. – '*The Astounding Reaction of Diazomethane with Dimethyl 2,3-Dicyanofumarate*' was the title of a paper published by the Munich Laboratory in 1986 [2]. The mentioned reaction gave rise to no less than 14 products, depending on stoichiometry, temperature, and solvent. The elucidation of their mechanistic interrelations came close to a mystery novel. Some essential features (*Scheme 1*) will serve as

[1]) 1,3-Dipolar Cycloadditions, Part 135; Part 134: [1]. In parts presented at the *14th European Symposium on Fluorine Chemistry*, Poznań, 2004; Book of Abstracts A-P-76.

[2]) Present address: University of Łódź, Section of Heteroorganic Compounds, Narutowicza 68, PL-90-136 Łódź.

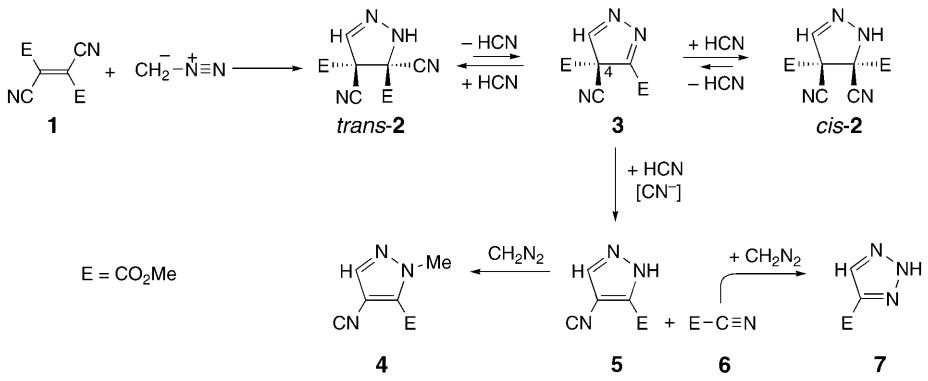
[3]) Present address: DMS Fine Chemicals, Austria GmbH, St. Peter-Str. 25, A-4021 Linz.

[4]) Present address: Department of Organic Chemistry, Slovak Technical University, Radlinského 9, 81237 Bratislava, Slovak Republic.

[5]) Present address: Fachhochschule München, Fachbereich 05, Lothstrasse 34, D-80335 München.

counterpart to the present study which deals with another tetra-acceptor-substituted ethylene as dipolarophile.

Scheme 1

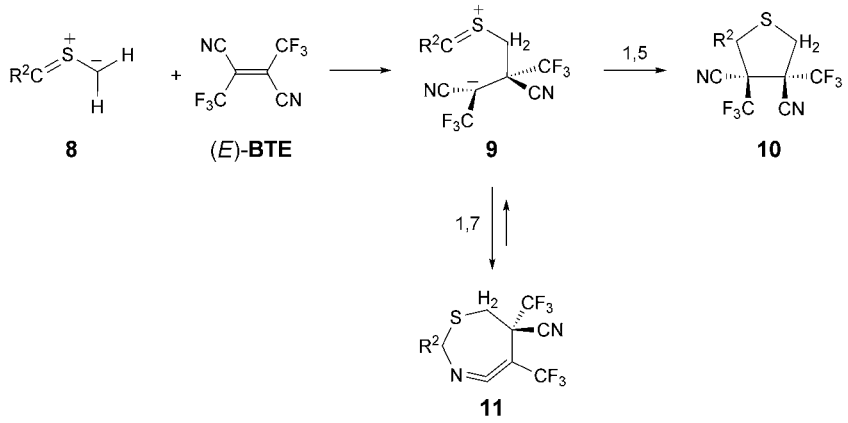


Dimethyl 2,3-dicyanofumarate (**1**) and 1.0 equiv. of diazomethane at 0° afford the *trans*-cycloadduct **2** *via* a 4,5-dihydro-3*H*-pyrazole. A *trans* ⇌ *cis* equilibration, *trans*-**2** ⇌ *cis*-**2** (40 : 60), is base-catalyzed. A second molecule of diazomethane can deprotonate the rather acidic NH of **2**, and a reversible elimination of CN^- mediates the stereoisomerization, *trans*-**2** ⇌ *cis*-**2**. The (not isolable) 4*H*-pyrazole **3** is the key intermediate which – in a competing irreversible attack by CN^- on the *C(4)*-methoxycarbonyl group – gives rise to the 1*H*-pyrazole **5** and methyl cyanoformate (**6**). The latter, in turn, is a chameleon of reactivity: as a methylating agent, it can convert **5** to **4** and – in an acylation – transfer the methoxycarbonyl group to the nitrogen of pyrazole **5**. Moreover, **6** is an excellent dipolarophile which adds diazomethane and forms methyl 1,2,3-triazole-4-carboxylate (**7**). Excess of diazomethane leads to conversion of **5** and **7** to five *N*-methyl derivatives; *Scheme 1* is still simplifying. Nine of the 14 products mentioned come from the second act of the reaction drama which begins with the irreversible deacylation, **3** + HCN (CN^-) → **5** + **6** [2][3].

1,2-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile (**BTE**; *Scheme 2*) has turned out to be a valuable model for mechanistic studies. (*E*)-**BTE** and (*Z*)-**BTE** have the volatility of water, and nucleophilic catalysis leads to a 95 : 5 equilibrium; in neutral medium the (*E*)- and (*Z*)-isomers are fairly stable. First prepared by *Cairns et al.* in 1966 [4], **BTE** hardly found the deserved attention, probably due to a somewhat inconvenient access; the last step consists of the pyrolysis of a chlorosulfite in the gas phase over refluxing sulfur at 460° [4][5].

In the two-step cycloaddition of thiocarbonyl ylide **8** to ethenetetracarbonitrile or **1**, a short-lived seven-membered ketene imine is passed [6][7]. With **BTE** as dipolarophile, the cyclic ketene-imine **11** becomes isolable [8][9]. The 'perfluoroalkyl effect' stabilizes strained ring systems and appears to be kinetic in nature [10]. The zwitterionic intermediate **9** concurrently undergoes a reversible 1,7-cyclization to give **11** and an irreversible 1,5 ring closure furnishing thiolane **10**.

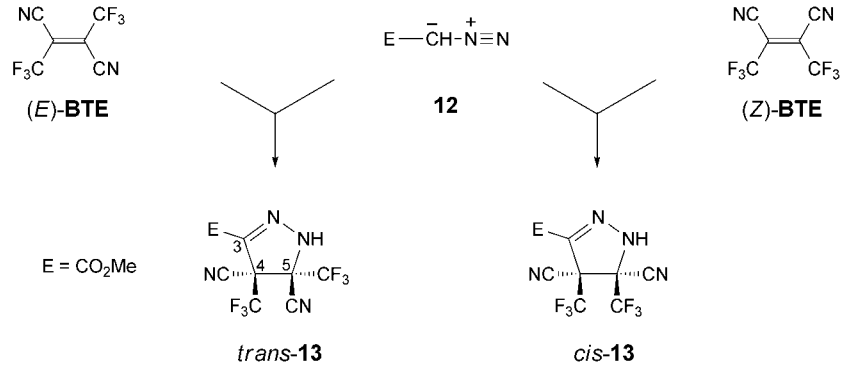
Scheme 2



We are dealing here with the reaction of methyl diazoacetate (**12**) with **BTE** as a contrast program. Some common features and even more divergencies will stimulate mechanistic considerations.

2. Results and Discussion. – 2.1. *Preparation of Cycloadducts.* The reaction of (*E*)-**BTE** with 1.2 equiv. of methyl diazoacetate (**12**) in $CDCl_3$ at 0–25° afforded the crystalline 4,5-dihydro-1*H*-pyrazole *trans*-**13** (90%); the ^{1}H-NMR analysis of the reaction solution with weight standard indicated a virtually quantitative yield. Analogously, (*Z*)-**BTE** and **12** furnished *cis*-**13**, which shows lower crystallization tendency (*Scheme 3*). The IR spectra exhibit the NH bond, and the C=N frequency occurs at 1570 and 1583 cm^{-1}, respectively. The tautomerization of the 4,5-dihydro-3*H*-pyrazoles, expected as primary cycloadducts, to the more stable 4,5-dihydro-1*H*-pyrazolines is usually fast when electron-attracting substituents increase the acidity.

Scheme 3



The CF_3 groups appear in the ^{19}F-NMR spectrum of *trans*-**13** as *singlet*s, whereas those of *cis*-**13** couple with each other: two *quadruplet*s with $^5J = 12.3$ Hz were

observed. This coupling pattern simulates that of other *trans,cis* pairs obtained by cycloaddition of nitrile oxides and nitrones to (*E*)- and (*Z*)-**BTE** [11]. F,F-Coupling is mainly transmitted through space, and the CF_3 groups of *trans*-cycloadducts probably occupy *pseudo*-axial positions.

2.2. *Kinetics of Cycloadditions.* We were interested in testing the stereospecificity of the cycloadditions of **12** to (*E*)- and (*Z*)-**BTE**. In the light of the *cis,trans* isomerization of **13** (see *Sect. 2.4*), it was mandatory to know the rate constants of cycloadditions. The ^{1}H-NMR analysis of the time-dependent concentrations was based on the decrease of the CH integral of **12** and the increase of the MeO integral of *trans*-**13** and *cis*-**13**. The data excellently fit the second-order law, and furnished $k_2 = 2.50 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$] for (*E*)-**BTE** and $1.16 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$] for (*Z*)-**BTE** in $CDCl_3$ at 36°. An illustration: 0.4M (*E*)- or (*Z*)-**BTE** and 0.7M **12** reach 90% reaction after 35 and 76 min, respectively.

The competition constant, $k_E/k_Z = 2.16$, is rather small. Comparative figures for other 1,3-dipolar cycloadditions to (*E*)/(*Z*)-isomeric tetra-acceptor-ethylenes are not known. Larger values for k_E/k_Z result when steric interference of (*Z*)-substituents weakens conjugation, as found for dimethyl fumarate *vs.* dimethyl maleate [12]. This difference between (*E*)- and (*Z*)-isomers is less pronounced in tetrasubstituted ethylenes.

2.3. *Retention of Dipolarophile Configuration*. Fortunately, neither methyl diazoacetate nor the cycloadducts **13** catalyzed the equilibration of the **BTE** isomers. The reaction of (*E*)-**BTE** with 1.2 equiv. of **12** ($CDCl_3$, 25°) was monitored by ^{19}F-NMR spectroscopy. At 80% reaction, a tiny *singlet* for (*Z*)-**BTE** at δ −59.3 appeared. After **BTE** was completely consumed by the excess of **12**, a small *quadruplet* indicated 0.07% of *cis*-**13**. With a yield of 98% for *trans*-**13**, the stereospecificity amounts to 99.93%. However, with high probability the small *cis*-share comes from (*Z*)-**BTE**, *i.e.*, the retention of configuration in the cycloaddition must be >99.93%.

The liquid (*Z*)-**BTE** is harder to purify than the crystalline (*E*)-isomer; the sample of (*Z*)-**BTE** contained 2.04% of (*E*)-**BTE**. A small increase of the '*trans*-concentration', *i.e.*, the sum of *trans*-**13** + (*E*)-**BTE**, indicated a retention of >99.8% (see *Exper. Part*).

Only top analytical conditions allow the determination of higher values of stereospecificity in 1,3-dipolar cycloadditions. The two record examples previously achieved in our laboratory afforded retention values above 99.99% (for a review, see [13]). In two-step cycloadditions, the intermediate can undergo the ring closure before or after rotation; k_{rot}/k_{cycl} offers the key to the differing activation free energies in the two processes. A retention of >99.997% (diazomethane + methyl angelate [14]) would impose an improbably high rotational barrier on the intermediate; a barrier that exceeds $\Delta G^{\neq}$ of cyclization by >6.2 kcal mol^{-1}. It is a reasonable conclusion that no intermediate capable of rotation occurs on the cycloaddition pathway.

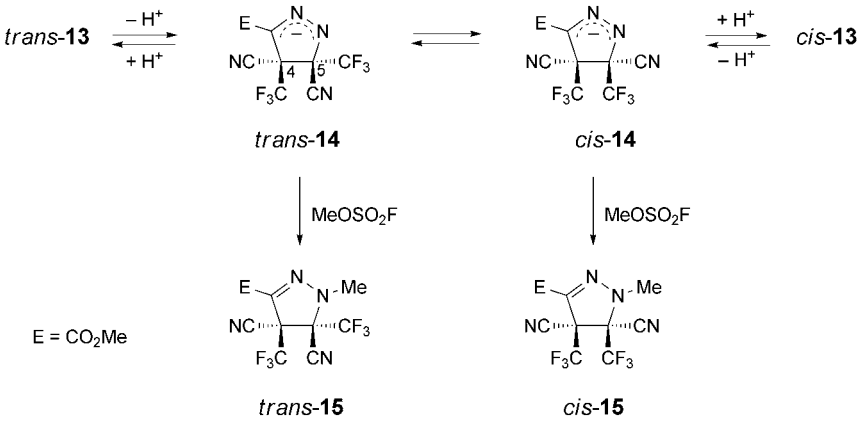
The retention values observed for **12** + *trans*-**BTE** and *cis*-**BTE** would correspond to $\Delta G^{\neq}_{rot} - \Delta G^{\neq}_{cycl} > 4.3$ and >3.7 kcal mol^{-1}, respectively. In our opinion, the steric course indicates concertedness. Substantial or complete loss of stereospecificity was observed in the cycloadditions of thiocarbonyl ylides to dimethyl 2,3-dicyanofumarate (**1**) and dimethyl 2,3-dicyanomaleate, characterizing authentic two-step processes [7][15][16].

2.4. *Base-Catalyzed* cis/trans-*Isomerization of Cycloadducts* **13**. When *cis*-**13** in C_6D_6 was stored at room temperature for one week, no change of the ^{19}F-NMR spectrum was observed. At 80°, however, an isomerization to *trans*-**13** was noticed and reached 50%

after *ca*. 70 h. In polar solvents, the isomerization was faster, *e.g.*, in CD_3CN at 80° the equilibration proceeded with a half-life of *ca*. 3 min and reached a *trans*-**13**/*cis*-**13** ratio of 91 : 9 from both sides. After the base catalysis of the stereoisomerization was recognized, the poorly reproducible thermal reactions can be ascribed to autoprotolysis and/or basic impurities.

When *cis*-**13** (0.14M) was treated with 7 mol-% of triethylenediamine (1,4-diazabicyclo[2.2.2]octane (DABCO)) in C_6D_6 at 25°, the equilibrium, *trans*-**13**/*cis*-**13** 92 : 8, was established with a half-reaction time of *ca*. 5 min. The even faster equilibration, induced by 'proton sponge' (1,8-bis(dimethylamino)naphthalene), left no doubt that the deprotonation of **13** is the initiating step. The active role of the dihydropyrazolide anions **14** (*trans* and *cis*) was confirmed by the conversion of *trans*-**13** to the *N*-methyl compound *trans*-**15** with 1 equiv. each of proton sponge and methyl fluorosulfonate (*Scheme 4*); MeI reacted more slowly. The ^{1}H-NMR *singlet* at δ 3.45 was assigned to MeN, and the MeO signal (δ 3.93) closely corresponds to MeO of *trans*-**13**. As in *trans*-**13**, the CF_3 groups of *trans*-**14** do not couple.

Scheme 4

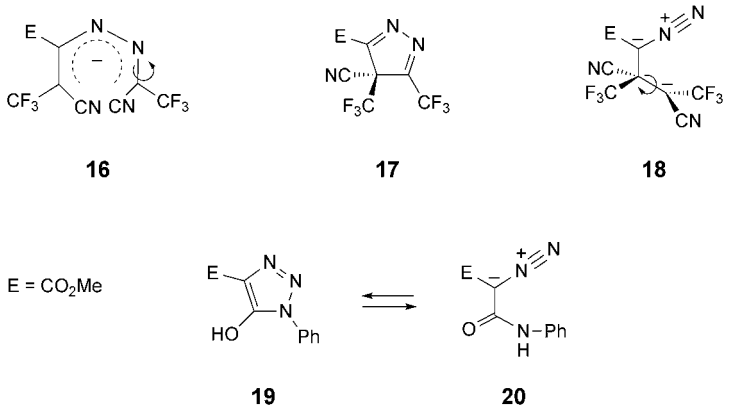


By the reaction of *cis*-**13** with proton sponge, followed by methyl fluorosulfonate, a mixture of *N*-methyl derivatives, *trans*-**15**/*cis*-**15** 65 : 35, was obtained. When methyl fluorosulfonate was first added, followed by the base, *cis*-**15** at least prevailed in the product, *i.e.*, *trans*-**15**/*cis*-**15** 40 : 60. Thus, the *cis*/*trans* isomerization of **14** keenly competes with the methylation. As expected, the *N*-methyl derivatives **15** are no longer prone to base-catalyzed *cis*/*trans* isomerization.

No simple rotation or prototropy can equilibrate the dihydropyrazolides *trans*-**14** and *cis*-**14**; the cleavage of a bond must precede. We are aware of three pathways worth discussing (*Scheme 5*).

The reversible electrocyclic ring opening in positions 4 and 5 of the dihydropyrazolide **14**, would give rise to an open-chain diazapentadienyl anion **16**. This *disrotatory* process – **16** should come from *cis*-**14** – belongs to the type cyclopentenyl anion⇌pentadienyl anion which is of great importance in heterocyclic chemistry

Scheme 5



(for a review, see [17]). The system **14** ⇌ **16** would be an example of twofold isoionic exchange.

In the ring-opened species **16**, a rotation about the C–C or C–N bond temporarily diminishes the anionic delocalization from pentadienyl to allyl; a substantial barrier has to be overcome. Anion **16** could also be reached by a one-step conrotation from *trans*-**14**, *i.e.*, a reaction forbidden by orbital symmetry. 'Forbidden processes' may occur, but they require high activation energies, improbable for a *cis*/*trans* isomerization of **14** which rapidly proceeds at room temperature.

A second mechanism consists of the reversible elimination of a CN^- ion from **14** whereby the 4*H*-pyrazole **17** occurs as an intermediate. The analogous elimination–addition process was considered as most likely for the *cis*/*trans* isomerization *trans*-**2** ⇌ **3** ⇌ *cis*-**2** in the previous study [2][3] (*Scheme 1*).

Finally, a ring opening of **14** at the bond N(1)–C(5) should afford **18**, *i.e.*, a diazoacetate with a carbanionic substituent. Rotation and reclosure would effect *cis*/*trans* isomerization of **13**. The reversal, **18** → **14**, is an *intramolecular* azo coupling with a stabilized carbanion. *Intermolecular* coupling reactions of diazocarbonyl compounds with enolate ions have been known for over hundred years [18][19]. A formal analogy is offered by *O. Dimroth*'s classic study of ring-chain tautomerism, **19** ⇌ **20** [20], in which the carbanion is replaced by the isoelectronic amino group (*Scheme 5*).

Additional evidence on the nature of the *cis*/*trans* isomerization of **13** is obtained from further study of dihydropyrazolides **14** and their reactions.

2.5. *The Dihydropyrazolides* **14** *as Intermediates.* The colorless solutions of **13** (*trans* or *cis*) in $CHCl_3$ turn yellow upon addition of DABCO or proton sponge. The IR spectrum in $CHCl_3$ showed no diazo band in the region of 2100 cm^{-1}.

According to the ^{19}F-NMR spectra, the equilibration of the pyrazolines **13** with their anions **14** (*Scheme 4*) is fast on the NMR time scale; the frequencies of the CF_3 signals continuously change with the ratio of neutral and deprotonated species. When the solution of *trans*-**13** ($CDCl_3$, 25°) is successively treated with 0.5–2.0 equiv. of DABCO, the signal height (sharpness) goes through a minimum. At low temperature, coalescence phenomena were observed.

Upon addition of DABCO or proton sponge (0.5 equiv.) to *trans*-**13** in $CDCl_3$, the *trans* ⇌ *cis* equilibrium was rapidly established. Under identical conditions (2.0 equiv. of DABCO, $CDCl_3$, 25°), *trans*-**13** and *cis*-**13** gave rise to the same ratio *trans*-**14**/*cis*-**14** 97:3. Nevertheless, the *cis*/*trans* isomerization is slow on the NMR timescale. Discrete signals – *quadruplet*s with $J(F,F) = 12.5$ Hz for the *cis*-anion, and *singlet*s for the *trans*-anion – were discerned.

The deprotonation of *trans*-**13** and *cis*-**13** is accompanied by distinct negative shifts of $\delta(F)$ for the high-frequency signals, whereas the low-frequency absorptions change in the positive direction by smaller margins (*Table 1*). The N(1)-atom bears more of the allylanionic charge of *trans*-**14** and *cis*-**14** than C(3). Therefore, we expected a stronger shielding for the neighboring CF_3–C(5) than for CF_3–C(4). However, an even better argument for the opposite assignment will be offered in *Sect. 2.7*. *trans*- and *cis*-cycloadducts have been prepared from six further diazoalkanes with (*E*)-**BTE** and (*Z*)-**BTE** [21]. The comparison of their $\delta(F)$ values did not provide a convincing argument for the assignment.

Table 1. *^{19}F-NMR Chemical Shifts of* trans-**13** *and* cis-**13** (0.70 mM) *without and with Added Triethylenediamine* (DABCO) *in $CDCl_3$ at 25°* (*vs.* $PhOCF_3$ as secondary frequency standard)

Equiv. of DABCO	*trans*-Series		*cis*-Series	
	CF_3–C(4)	CF_3–C(5)	CF_3–C(4)	CF_3–C(5)
0	−68.93	−75.74	−66.63	−68.81
0.5	−70.16	−75.65	−67.80	−68.70
1.0	−71.26	−75.33	−69.92	−68.26
2.0	−71.74	−75.16	−70.55	−68.04
Δ [ppm]	−2.81	+0.58	−3.92	+0.77

The data of *Table 1* suggest that the deprotonation of **13** was still incomplete when 2 equiv. of DABCO were employed. Interestingly, $\delta(CF_3$–C(4)) in the *cis* series 'overtakes' $\delta(CF_3$–C(5)) between the additions of 0.5 and 1.0 equiv. of DABCO.

2.6. *Competition of* cis/trans *Isomerization with Formation of a Bis(dehydrofluoro) Dimer*. By using lower base concentrations, the rate of *cis*/*trans* isomerization became measurable. When *cis*-**13** (0.72M, $CDCl_3$, 25°) was treated with 3.1 mol-% of DABCO, ^{19}F-NMR monitoring indicated that the rate of *cis* ⇌ *trans* equilibration did not fulfil pseudo-first-order kinetics. The rate constant continuously decreased, due to a deactivation of the catalyst. The base catalyzed not only the stereoisomerization, *cis* ⇌ *trans*, but likewise the conversion of the dihydropyrazoles **13** to a new product, according to the stoichiometry

$$2\ C_9H_4F_6N_4O_2\ (\mathbf{13}) \rightarrow C_{18}H_6F_{10}N_8O_4\ (\mathbf{22}) + 2\ HF.$$

However, the competing reactions did not stop, after equivalence of base and eliminated HF was reached, but proceeded at a reduced rate.

The baffling phenomenon is illustrated in *Table 2* for an experiment with *trans*-**13** and 14 mol-% of DABCO as catalyst. After 7 d, the concentration of **13** (*trans*/*cis* 94:6) was diminished to 21%; nearly 78% of the C_{18} compound was observed, exceed-

ing the DABCO concentration 5.6-fold. Where has the excess of the eliminated HF gone? 4,5-Dihydro-1*H*-pyrazolines and the product $C_{18}H_6F_{10}N_8O_4$ are weak bases, and no shift of the ^{19}F-NMR frequencies suggested protonation. The second basicity constant of triethylenediamine (DABCO) is smaller than the first by 10^6 (pK_s I 2.97, II 8.92 in H_2O). The F^- ion appears to be the culprit; known as a rather strong base in inert media, it may well be the acceptor for the excess of HF. *Primary*, *secondary*, and *tertiary* ammonium fluorides form poly(hydrogen fluoride) complexes. Pyridinium fluoride + 70 wt-% HF (pyridine/HF 1:9) afford a straw-colored solution which is stable up to 55° [22–24] and is used for hydrofluorinations (THF, 0°). The anion $F(HF)_x^-$ is certainly a weaker base than the monomeric F^-, but might still be capable of generating a small equilibrium concentration of the dihydropyrazolide **14**.

Table 2. *Competing Reactions of* trans-**13** (0.407M) *and Triethylenediamine* (DABCO, 0.056M, 14 mol-%) *in* $CDCl_3$ *at 25°* (^{19}F-NMR analysis[a]), 376 MHz)

Reaction time	*trans*-**13** [μmol]	*cis*-**13** [μmol]	% **13** (*trans* + *cis*)	$C_{18}H_6F_{10}N_8O_4$ (**22**)		
				[μmol]	%	**A**/**B**
30 min	306.2	14.9	78.8	21.3	10.4	72:28
30 min	295.2	16.5	76.5	24.8	12.2	
7 d	79.3	5.0	20.7	158.1	77.6	57:43
26 d	74.9	4.9	19.3	150.7	74.0	58:42

[a]) Decimals not rounded.

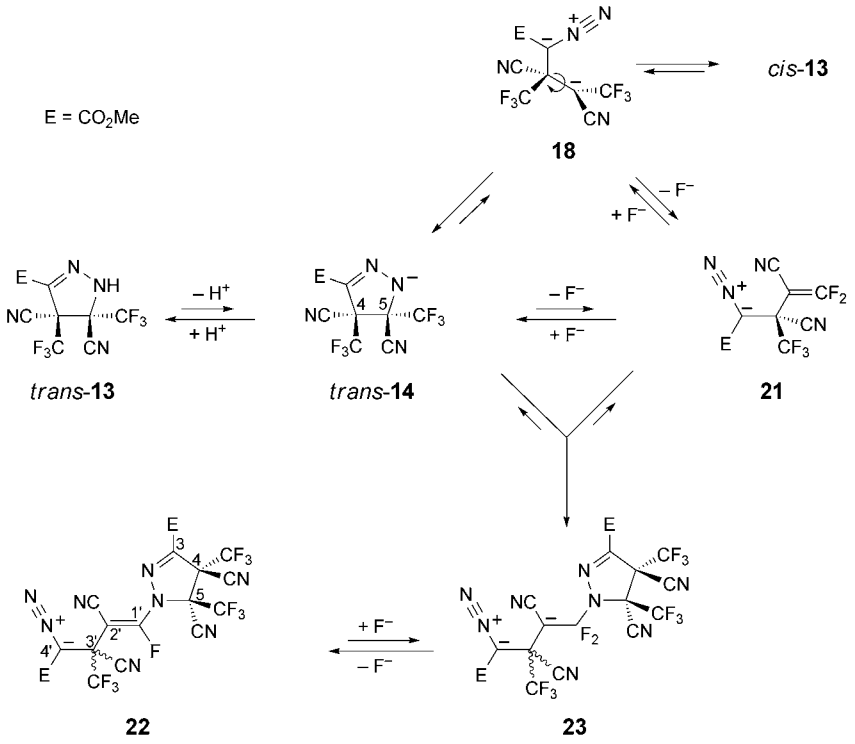
Elemental analyses and the molecular-mass peak (*m*/*z* 588) secure the formula $C_{18}H_6F_{10}N_8O_4$. The new compound occurs in two diastereoisomers, **22A** and **22B**. *Table 2* reveals a further complication: the ratio **A**/**B** changes in the course of the reaction.

An even simpler access to **22** was offered by adsorption of *trans*-**13** on silica gel; the colorless zone turned yellow within 1 h, and elution furnished the crystalline C_{18} compound (**22A**/**22B** 67:33) in 73% yield. Silica gel is usually regarded as a slightly acidic adsorbent. However, in a previous study in our laboratory, commercial silica gels showed a variable capacity to deprotonate a *sec*-nitroalkane group, clearly a function of basic centers. An alleged violation of configurational retention in a cycloaddition was traced to a subsequent *cis* → *trans* conversion on silica gel [25].

2.7. *Structure and Formation of the Bis(dehydrofluoro) Dimer* **22**. In the plausible mechanistic *Scheme 6*, both the *cis*/*trans* isomerizaton of **13** and the path to **22** require the ring opening of the dihydropyrazolide **14** to the derivative **18** of methyl diazoacetate, which bears a carbanionic substituent. The loss of fluoride from **18** generates the α,β-unsaturated nitrile **21** which contains a terminal difluoromethylene group. Moreover, *Scheme 6* shows a conceivable one-step shortcut from *trans*-**14** to **21**: an *E*1-type elimination at the C(5)–CF_3 bond. Nucleophilic addition of a second dihydropyrazolide *trans*-**14** to the unsaturated nitrile of **21** furnishes anion **23**, and another F^- loss gives rise to the isolated C_{18} compound **22**.

Before accumulating the spectroscopic evidence for **22**, it may be underscored that *Scheme 6* presents several pathways for the *cis*/*trans* isomerization of dihydropyrazoles

Scheme 6



13: rotation in **18** (about the former C=C bond of **BTE**) and recyclization, or the fluoride addition to **21**, which converts the planar olefinic C-atom to two pyramidal conformations of the carbanionic C-atom of **18**. The concerted process **21** → **14** offers a variant of the second path.

The spectroscopic similarity of **22A** and **22B** suggests diastereoisomerism. Structure **22** reveals four stereogenic elements: three tetrahedral centers and a tetrasubstituted C=C bond. Since the separation of **A** and **B** did not succeed, an X-ray analysis is not available. The configuration around the C=C bond is determined by the loss of F^-, **23** → **22**, whereby the two big substituents assume (*E*)-positions. The F,F coupling of the vinylic fluorine with *two* CF_3 groups confirms the (*Z*)-relation of F-atom and diazo side chain at the C=C bond. Both **22A** and **22B** harbor the intact dihydropyrazole structure of *trans*-**13**. The *trans*-relation of the CF_3 groups in the dihydropyrazole ring reduces the number of stereogenic centers to two. Thus, **A** and **B** differ in the relative configuration at C(3).

The strong IR absorption at 2121 cm^{-1} indicates an aliphatic diazo group. The pale-yellow color of **22** is no surprise; electron-attracting substituents have a hypsochromic effect on the light absorption of diazomethane [26].

The ^{19}F-NMR spectra offer the basic support. The integrals reveal three CF_3 groups and one C–F for each **A** and **B** (*Fig.*). As shown in *Sect. 2.1*, the CF_3 groups of *trans*-**13** do not couple with each other, whereas those of *cis*-**13** appear as *quadruplet*s with

^5J(F,F) = 12.3 Hz. No *quadruplet*s occur among the CF_3 signals of **22**. The CF_3 *singlet*s at δ(F) −68.34 (**A**) and −68.62 (**B**) correspond to the CF_3−C(4) (−68.93) of *trans*-**13** (*Table 1*), whereas the *doublet*s at −73.35 and −73.39 come close to the *singlet* of CF_3−C(5) (−75.74) in *trans*-**13**. Only the CF_3−C(5) of **22** can couple with F−C(1′); that, in turn, establishes the assignments of the CF_3 groups in *trans*-**13** (*Sect. 2.5*). The CF_3 *doublet*s at −71.01 and −71.12 (^5J(F,F) = 7.4 and 9.5) for **22A** and **22B** are attributed to CF_3−C(3′). The ^{19}F signal of F−C(1′) is expected to be a *quadruplet* of *quadruplet*s; the broad *multiplet*s are only partially resolved. It is worth mentioning that the δ(F) values of **A** and **B** differ here the most (−69.64 and −70.41).

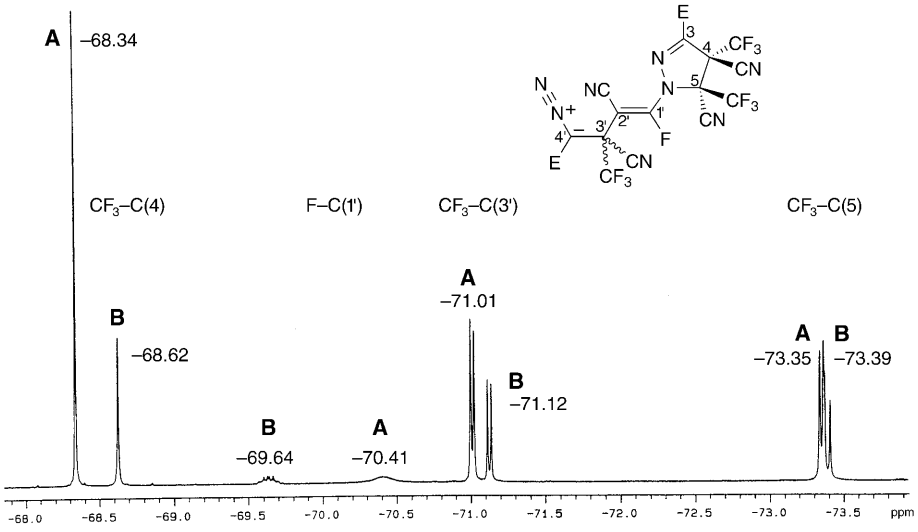


Figure. *^{19}F-NMR Spectrum* (376 MHz) *of Compound* $C_{18}H_6F_{10}N_8O_4$ (**22A** and **22B** in the ratio 66:34) *in* C_6D_6 *at 25°*

The ^{13}C-NMR parameters are in full agreement with structure **22**, and the heights of each **A**,**B** pair of signals reflect the isomer ratio **22A**/**22B**. The δ(^{13}C) values of *trans*-**13** reappear in those of **22** within narrow limits. The δ(^{13}C=O) values of the two ester groups are singled out and compared with methyl benzoate (166.8 ppm, MeO_2C at sp^2-hybridized C-atom). N(1) in dihydropyrazole **13** releases electronic density to the ester carbonyl by resonance, and δ(^{13}C=O) values of 157.7 (*trans*-**13**) and 157.5 (*cis*-**13**) show the upfield shift. This absorption is observed in **22** at 155.8 (**A**) and 157.4 ppm (**B**). The second ester group in **22**, CO_2Me−C(2), resonates at 162.3 (**A**) and 162.4 ppm (**B**).

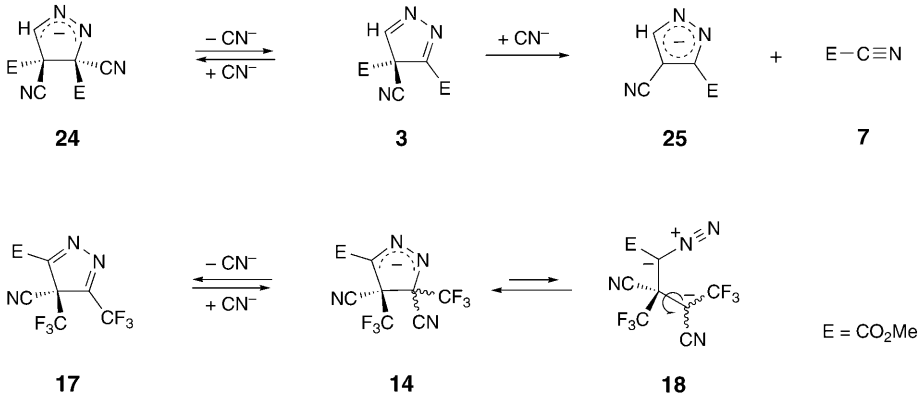
Although the ^{13}C-NMR spectrum was run with a high number of pulses, the low-intensity signal of C(2) is a blemish. The *multiplet* at δ 56.26 – two overlapping *quadruplet*s – is the most likely assignment for the C-atom of the diazoalkane group. Diazomethane resonates at δ 23.1, and methyl diazoacetate at 46.2 [27]. The large upfield shift, when compared with olefinic C-atoms, is the consequence of the partial carbanionic charge (for discussion, see [28]).

The mass spectrum of **22** displays, besides the molecular ion (15%), the usual fragmentation pattern: the N_2 extrusion is followed by loss of CF_3, CN, or CO_2Me. The radical ion *m*/*z* 247 (42%, $C_9H_3F_4N_2O_2^+$) suggests the loss of $N_2 + \mathbf{13} - H$.

Apparently the isomer ratio **22A**/**22B** changes when kept in the reaction solution for a longer time (*Table 2*). That suggests reversibility of all the steps of *Scheme 6* back to the anion *trans*-**14**. Puzzling at first, on closer scrutiny, however, there is no reaction step to be found which appeared irreversible.

3. Comments and Conclusions. – 3.1. **BTE** vs. *Dimethyl 2,3-Dicyanofumarate* (**1**) *as Dipolarophile.* In the reaction of diazomethane with **1**, the 4*H*-pyrazole **3** plays a key-role (see *Introduction* and *Scheme 1*). Nine of the 14 products observed were formed after the take-over of the $CO_2Me-C(4)$ by CN^- giving rise to the pyrazolide anion **25** + methyl cyanoformate (**7**). According to *Scheme 7*, **3** is produced from the dihydropyrazolide anion **24** by reversible loss of CN^-, thus mediating the *cis*/*trans* isomerization of cycloadduct **2**. The conversion of **24** to 4*H*-pyrazole **3** + CN^- profits from a gain of π conjugation energy (estimate: *ca.* 3 kcal mol^{-1}).

Scheme 7



Even in basic medium, the cycloadducts **13** from **12** and **BTE** do not undergo elimination of HCN; neither the 4*H*-pyrazole **17** nor any secondary products were observed. In contrast to the *stabilization* of a C=N bond by conjugation with CO_2Me, the adjacent C=N bond of **17** is *destabilized* by CF_3. Admittedly, thermochemical data (heats of hydrogenation) are available only for the interaction of CF_3 with the C=C bond: the destabilization amounts to *ca.* 3 kcal mol^{-1} [29].

Both dihydropyrazoles **2** and **13**, which are cycloadducts of **1** and **BTE**, respectively, are prone to base-catalyzed *cis* ⇌ *trans* equilibration. The *a priori* presumption of a common mechanism appears to be incorrect. The exchange of CO_2Me by CF_3 makes the path *via* 4*H*-pyrazole **17** unattractive. Instead, the reversible ring opening of the dihydropyrazolide **14** furnished the diazo-carbanion **18** (*Scheme 7*), which is capable of configurational rotation, *i.e.*, a fundamentally different process.

3.2. *Stereospecific and Nonstereospecific Cycloadditions.* The high retention of stereochemical integrity in the cycloadditions of methyl diazoacetate (**12**) with (*E*)- and

(*Z*)-**BTE** (see *Sect. 2.3*) suggests concertedness. In contrast, the additions of thiocarbonyl ylide **8** and related 1,3-dipoles with dimethyl 2,3-dicyanofumarate or dimethyl 2,3-dicyanomaleate proceed with low or zero stereospecificity [7][16], and the reaction with **BTE** reveals intermediates **9** and **11** (*Scheme 2*) [8][9]. How do these facts fit into the general reactivity scheme of 1,3-dipolar cycloadditions?

A puzzling multitude of rate and regiochemistry phenomena found an elegant solution in the MO perturbation treatment by *Sustmann* in 1971 [30][31]. The reactivity sequences of dipolarophiles are 1,3-dipole-specific and depend on the energy separation of the frontier orbital pairs. 1,3-Dipoles can be classified by the relative energy contributions of their two HO–LU interactions with dipolarophiles (for reviews, see [32][33]).

1,3-Dipoles of *Sustmann*'s type I as thiocarbonyl ylide **8** react only with electron-poor double bonds, *i.e.*, in PMO terms, the interaction HO(1,3-dipole)–LU(dipolarophile) dwarfs the contribution by LU(1,3-dipole)–HO(dipolarophile). The latter still suffices to warrant concerted additions of **8** to dimethyl fumarate (retention $>99.97\%$) or maleonitrile (99.95%) [16]. However, this second HO–LU contribution dwindles in the reactions with tetra-acceptor-substituted ethylenes as **1** or **BTE**, *i.e.*, the mechanism switches to a two-step path with zwitterionic intermediate.

The well-balanced reactivity profile of methyl diazoacetate (**12**) reveals *Sustmann*'s type II; a U-shaped curve results, when log k_2 is plotted *vs.* the ionization potential of the dipolarophilic π-bond [34]. Diazoacetate undergoes fast cycloadditions with electron-deficient double bonds; vinyl ether occurs as rate minimum, whereas the growing electron density of enamine double bonds leads to increasing rate constants. From the high retention values of the cycloadditions to (*E*)- and (*Z*)-**BTE**, we deduce that both HO–LU interactions still 'count', and concertedness is the outcome. In the enamine branch of the U-function, however, azo couplings *via* zwitterions were observed besides cycloadditions [35][36].

We express our thanks to Prof. *Herbert Mayr*, Munich, and to Prof. *Christian Reichardt*, Marburg, for helpful discussions. The support by the *Fonds der Chemischen Industrie*, Frankfurt, is gratefully acknowledged. The help of Dr. *David Stephenson* and *Helmut Huber* in the NMR measurements has been essential. The elemental analyses were carried out by *Helmut Schulz* and *Magdalena Schwarz*.

Experimental Part

1. *General.* Materials: for (*E*)- and (*Z*)-2.3-Bis(trifluoromethyl)ethene-1,2-dicarbonitrile, abbreviated as (*E*)- and (*Z*)-**BTE**, resp., see [4][5][8]. PLC is prep. layer chromatography: 20×20 cm glass plates, 2-mm *Merck* silica gel *60 PF_{254}*. ^{1}H-NMR Spectra were recorded on *Varian XR400S* (400 MHz for ^{1}H, 100.6 MHz for ^{13}C, and 376.3 MHz for ^{19}F) or on *Bruker WP80CW* (80 MHz for ^{1}H) and *WP80DS* (20.15 MHz for ^{13}C; multiplicities from comparison with off-resonance spectra). Solvent was acid-free $CDCl_3$, stored over dry K_2CO_3, if not stated otherwise. The weight standards applied for quantitative ^{1}H- and ^{19}F-NMR analysis (usually $\pm5\%$, relative) are specified below; repeatedly taken machine integrals were averaged. ^{19}F chemical shifts are based on Cl_3CF, some on $PhOCF_3$ as secondary standard (δ -58.38). The MS are EI spectra with 70 eV, recorded on a *Finnigan MAT90* instrument; intensities of isotope peaks are reported as, *e.g.*, ^{13}C % calc./% found.

2. *Cycloadditions of Methyl Diazoacetate to (*E*)-***BTE*** and (*Z*)-***BTE***.* 2.1. *Methyl* trans-*4,5-Dicyano-4,5-dihydro-4,5-bis(trifluoromethyl)-1*H-*pyrazole-3-carboxylate* (*trans*-**13**). Freshly distilled *methyl diazoacetate* (**12**, 560.0 mg, 5.60 mmol) in $CDCl_3$ (2 ml) was added dropwise to the stirred soln. of (*E*)-**BTE**

(1.01 g, 4.70 mmol) in $CDCl_3$ (5 ml) at 0°. After storing at r.t. for 24 h in the dark, the solvent was evaporated. The oily residue crystallized was digested with hexane at −18° for 1 h and filtered: *trans*-**13** (1.328 g, 90%), m.p. 87–89°; the anal. sample, recrystallized from pentane/Et_2O, showed m.p. 90°. An ^{1}H-NMR anal. experiment in $CDCl_3$ in the presence of $Cl_2CH-CHCl_2$ as weight standard indicated 99% of *trans*-**13**. IR (KBr): 711*m*, 745*m*; 1043*m*, 1156*m*, 1212v*s* (br.), 1346*s* (CF_3 stretch.); 1452*s*; 1570*s* (C=N), 1735v*s* (C=O), 2262v*w* (C≡N), 3215*s* (br., N–H). ^{1}H-NMR (400 MHz): 3.98 (*s*, MeO); 8.35 (br. *s*, NH). ^{13}C-NMR (20.2 MHz): 53.9 (*q*, MeO); 58.4 (*q*, ^2J(C,F) = 33.7, C(4)); 70.1 (*q*, ^2J(C,F) = 33.1, C(5)); 106.5, 107.9 (2*q*, ^3J(C,F) = 1.2, 2 CN); 120.4 (*q*, ^1J(C,F) = 290.3, CF_3); 120.6 (*q*, ^1J(C,F) = 289.5, CF_3); 131.1 (*s*, C(3)); 157.7 (*s*, C=O). ^{19}F-NMR (376 MHz): −68.93 (*s*, CF_3–C(4)); −75.74 (*s*, CF_3–C(5)). MS (40°): 314 (5, $M^{+\cdot}$), 294 (14, $[M-HF]^+$), 287 (4, $[M-MeO]^+$), 245 (7, $[M-CF_3]^+$), 225 (27, $[M-HF-CF_3]^+$), 195 (14), 188 (10), 145 (13), 138 (8), 69 (100, $[CF_3]^+$), 59 (65, $[MeO_2C]^+$). Anal. calc. for $C_9H_4F_6N_4O_2$ (314.15): C 34.41, H 1.28, N 17.84; found: C 34.71, H 1.32, N 17.73.

2.2. *Methyl* cis-*4,5-Dicyano-4,5-dihydro-4,5-bis(trifluoromethyl)-1*H-*pyrazole 3-carboxylate* (*cis*-**13**). *Methyl diazoacetate* (**12**, 560 mg, 5.60 mmol) and (*Z*)-**BTE** (1.00 g, 4.67 mmol; contained 2.2% (*E*)-**BTE**) were reacted in $CDCl_3$ (10 ml), as described above. After removal of the solvent, the residue crystallized from CH_2Cl_2 (0.5 ml) and hexane (4 ml) at −18°: *cis*-**13** (1.03 g, 70%). M.p. 62–66°. The ^{19}F-NMR spectrum shows an admixture of *trans*-**13** (2.6%). *cis*-**13** is distillable at 40°/0.03 Torr, and the crystallization requires some patience. IR (film): 766*m*, 960*m*, 1045*s*; 1150*s*, 1215v*s* (br.), 1278*s*, 1345*s* (CF_3 stretch), 1448*s*; 1583*s* (C=N), 1738v*s* (C=O), 2250*w* (C≡N), 3290*s* (br., N–H). ^{1}H-NMR (80 MHz): 4.00 (*s*, MeO); 8.40 (br. *s*, NH). ^{13}C-NMR (20.2 MHz): 54.1 (*q*, MeO); 58.9 (*q*, ^2J(C,F) = 34.8, C(4)); 74.4 (*q*, 2 signals visible, ^2J(C,F) = 36.6, C(5)); 108.2 (*q*, ^3J(C,F) = 1.8, CN); 110.5 (*s*, CN); 119.6 (*q*, ^1J(C,F) = 285.0, CF_3); 119.9 (*q*, ^1J(C,F) = 290.5, CF_3); 134.8 (*s*, C(3)); 157.7 (*s*, C=O). ^{19}F-NMR (376 MHz): −66.63, −68.81 (2*q*, ^5J(F,F) = 12.3, 2 CF_3). Anal. calc. for $C_9H_4F_6N_4O_2$ (314.15): C 34.41, H 1.28, N 17.84; found: C 34.71, H 1.41, N 17.87.

3. *Rate Measurements of Cycloadditions.* 3.1. *Analytical Methods.* The quant. ^{1}H-NMR analysis (80 MHz) was based on the decrease of the CH *s* of **12** at δ 4.75 as well as on the increase of the MeO *s* of *trans*-**13** (δ 3.98) and *cis*-**13** (δ 4.00), resp. This double rate measurement enhances the precision since the single concentration measurement by ^{1}H-NMR is not better than ±5% relative. Solns. of **12** (distilled at 0.7 Torr), (*E*)-**BTE** or (*Z*)-**BTE** (purified by prep. GC), and 1,1,2,2-tetrachloroethane as weight standard (δ 5.92) were prepared with $CDCl_3$ in 1-ml volumetric flasks. Aliquots were combined (*Hamilton* syringe) in an NMR tube, which remained in the instrument at the constant temp. of 36° (glycol thermometer) for 35 min (formation of *trans*-**13** up to 91% reaction) or 70 min (formation of *cis*-**13** up to 81%). For each kinetic run, 8–22 concentration measurements were carried out; each machine integral was compared with that of the weight standard. The rate constants were evaluated graphically and by linear regression, based on the second-order law (*Eqn. 1*) with A = (*E*)-**BTE** or (*Z*)-**BTE**, B = **12**, and C = *trans*-**13** or *cis*-**13**. For the decrease of **12**, $A_t = A_0 - B_t + B_0$, and for the increase of **13**, $B_t = (B_0 - C_t)$ and $A_t = (A_0 - C_t)$ were used. The ^{1}H-NMR spectra showed virtually no other products than *trans*-**13** and *cis*-**13** besides the excess of **12**. The sample of (*Z*)-**BTE** contained *ca.* 2% of (*E*)-**BTE**.

3.2. *Example and Results.* A_0 (0.420M (*E*)-**BTE**) and B_0 (0.704M **12**) were reacted in $CDCl_3$ (500 µl soln.) at 36°; 15 concentration data of B_t up to 91% of *trans*-**13** gave on linear regression $k_2 = 2.51 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$] with correlation coefficient $r = 0.99$. The corresponding data for the decrease of **12** provided $k_2 = 2.40 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$] with $r = 0.99$. After two further runs, the six rate constants afforded an average $k_2 = 2.50 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$] for the cycloaddition to (*E*)-**BTE**. An analogous six k_2 values for the reaction of (*Z*)-**BTE** furnished $1.16 \cdot 10^{-3}$ [$M^{-1}\,s^{-1}$].

$$k_2 t = \frac{1}{B_0 - A_0} \ln \frac{A_0\, B_t}{B_0\, A_t} \tag{1}$$

4. *Stereospecificity of Cycloadditions.* 4.1. *(*E*)-***BTE**. The equilibration of (*E*)-**BTE** ⇌ (*Z*)-**BTE** (95 : 5 in $CDCl_3$ at 25°) is slow at r.t., but is subject to nucleophilic catalysis [8]. The reaction of (*E*)-**BTE** (0.470M) with **12** (0.578M) in the presence of trifluoroanisole (0.249M) as weight and frequency standard in $CDCl_3$ at 25° was monitored by ^{19}F-NMR spectroscopy (376 MHz). The acquisition of the spectrum (64

pulses) required 8 min, half of which was added to the reaction time. The integrals of the two *s* of *trans*-**13** at δ −68.94 and −75.71 as well as the sharp *s* of (*E*)-**BTE** were compared with the *s* of $PhOCF_3$ at −58.38 and showed 50, 73, and 80% reaction after 29, 84, and 134 min, respectively. The material balance, *i.e.*, (*E*)-**BTE** + *trans*-**13**, was at 97–98%.

The spectrum after 134 min revealed a tiny *s* at −59.38 for (*Z*)-**BTE**, the isomerization product. Due to the excess of **12**, the dipolarophile **BTE** was consumed after several days, and the machine integral at high amplification disclosed the downfield *q* of *cis*-**13** at −66.66 (0.07%); the identity was established by the signal increase after adding a trace of authentic *cis*-**13**. Thus, the *trans*-cycloadduct prevails to the extent of 99.93%.

4.2. (*Z*)-**BTE**. By a similar procedure, the steric course in the cycloaddition of **12** was tested with a sample of liquid (*Z*)-**BTE** (m.p. −5° to −3.5° [5]) that contained 2.04% of (*E*)-**BTE**; the sharp *s* of (*Z*)-**BTE** (−59.38) and (*E*)-**BTE** (−62.68) allowed a rather precise integration. Since (*E*)-**BTE** reacts faster with **12** than (*Z*)-**BTE**, the percentage of the (*E*)-form in **BTE** continuously decreased from 2.04% to 0.58% in the first 66% of the reaction (*Table 3*). The CF_3 balance remained constant at 98–99%. There is a slight increase of the *trans*-share, *i.e.*, (*E*)-**BTE** + *trans*-**13** from 9.78 to 10.37 μmol (last column of *Table 3*) in the course of the reaction. This rise by *ca.* 0.6 μmol diminishes the retention in the overall cycloaddition of (*Z*)-**BTE** + **12** to 99.8% (*i.e.*, 0.6/299.5 μmol corresponds to 0.2%). It is more probable to ascribe the extra 0.6 μmol of *trans*-**13** to the thermal isomerization of (*Z*)-**BTE** to (*E*)-**BTE** and subsequent addition of **12** with retention.

$$\frac{k_E}{k_Z} = \frac{\log[(E) - \mathbf{BTE}]_0 - \log[(E) - \mathbf{BTE}]_t}{\log[(Z) - \mathbf{BTE}]_0 - \log[(Z) - \mathbf{BTE}]_t} \quad (2)$$

Table 3. *Cycloaddition of Methyl Diazoacetate* (**12**) *with (Z)*-**BTE** (2.04% (*E*) content) *in* $CDCl_3$ (1.0 ml soln.) *at 25°*. Monitoring with ^{19}F-NMR spectroscopy (376 MHz). Decimals not rounded.

Reaction time [min]	Percent reaction	**BTE** [μmol]		% (*E*) in **BTE**	**13** [μmol]		*trans*-**13** + (*E*)-**BTE** [μmol]
		(*Z*)	(*E*)		cis	trans	
0	0	470.4	9.78	2.04	0	0	9.78
47	40	281.2	2.81	1.00	180.9	7.0	9.81
94	57	202.5	1.34	0.66	261.4	8.5	9.84
134	66	164.9	0.97	0.58	299.5	9.4	10.37

(*Z*)-**BTE** and (*E*)-**BTE** are competing for **12**, and k_E/k_Z was calculated from the decrease of the (*E*)- and (*Z*)-isomers on the basis of *Eqn. 2*. The three analyses of *Table 1* afforded $\kappa = 2.4, 2.4$, and 2.2, closely related to the value obtained from direct rate measurements (*Sect. 3.2*). These three ^{19}F-NMR analyses also offer access to the rate constants of cycloaddition. The results for (*E*)-**BTE**, $k_2 = 7.5 \cdot 10^{-4}$ [M^{-1} s^{-1}], and for (*Z*)-**BTE**, $k_2 = 3.5 \cdot 10^{-4}$ [$M^{-1}s^{-1}$], in $CDCl_3$ at 25°, are based only on three concentration measurements each and are less reliable than the 36° values in *Sect. 3.2*.

5. cis/trans-*Isomerization of Cycloadducts.* 5.1. *Observations on Thermal Reactions.* When cycloadduct *cis*-**13** was subjected to bulb-to-bulb distillation (120°/12 Torr), the ^{19}F-NMR spectrum indicated a *trans*-**13**/*cis*-**13** ratio of 63:37. The soln. of *cis*-**13** in C_6D_6 in a closed NMR tube was heated in a 80°-bath. The isomerization to *trans*-**13** was monitored by ^{19}F-NMR, but the kinetic evaluation was flawed. In benzonitrile at 80°, a *trans* ⇌ *cis* equilibrium of 89:11 was measured, but a subsequent reaction of **13** thwarted the rate evaluation.

5.2. *Base Catalysis of Isomerization*. After 1 week at 25°, the 0.143M soln. of *cis*-**13** in C_6D_6 in an acid-rinsed NMR tube showed no change in the ^{19}F-NMR spectrum. When 7 mol-% of triethylenediamine (DABCO) was added, the stereoisomerization set in and furnished the equilibrium with $t_{1/2}$ *ca.* 5 min. In a further test, 0.143M *cis*-**13** in C_6D_6 was treated with 11 mol-% of 1,8-bis(dimethylamino)naphthalene ('proton sponge') at r.t., the first ^{19}F-NMR analysis after *ca*. 2 min indicated the established equilibrium.

Interestingly, methyl diazoacetate (**12**; 2.7 equiv.) turned out to be a weak catalyst (C_6D_6, r.t.); after 8 h, 40% of *cis*-**13** was isomerized to *trans*-**13**. In dioxane, a *trans*-**13**/*cis*-**13** ratio of 90 : 10 was established at r.t. either with DABCO (8 mol-%) or with DBU (=1,8-diazabicyclo[5.4.0]undec-7-ene, 6 mol-%).

6. N-*Methylation of* trans-**13** *and* cis-**13**. Dihydropyrazoles **13** did not react when treated with 3 equiv. of MeI in C_6D_6 (or (D_6)acetone) for 16 h at 40° in the absence of base. *trans*-**13** (50 mg) was dissolved in methyl fluorosulfonate (0.5 ml); workup after 2 h at r.t. rendered unchanged *trans*-**13**.

6.1. *Methyl* trans-*4,5-Dicyano-4,5-dihydro-1-methyl-4,5-bis(trifluoromethyl)-1*H-*pyrazole-3-carboxylate* (*trans*-**15**). Into the yellow soln. of *trans*-**13** (115.4 mg, 0.37 mmol) and proton sponge (80 mg, 0.37 mmol) in $CDCl_3$ (1 ml), methyl fluorosulfonate (55 mg, 0.48 mmol), dissolved in little $CDCl_3$,was injected. The colorless fluorosulfonate of the protonated base precipitated immediately. After filtering and washing with $CDCl_3$, *trans*-**13** was no longer detectable in the reaction soln. After washing with aq. $NaHCO_3$ and evaporation of $CDCl_3$, *trans*-**15** (91 mg, 75%) remained as a colorless oil; bulb-to-bulb distillation at 60°/0.3 Torr furnished the anal. sample. In another experiment, MeI was used, and the crystallization of the hydroiodide of proton sponge required 8 h. IR ($CDCl_3$): 844*s*; 1130–1280v*s* (br., C–F), 1444*s*; 1555*s* (C=N), 1725*s* (C=O). ^{1}H-NMR (80 MHz): 3.45 (*s*, MeN); 3.93 (*s*, MeO). ^{19}F-NMR (94 MHz): −68.6 (*s*, CF_3–C(4)); −72.3 (*s*, CF_3–C(5)). MS: 328 (50, M^+), 309 (3, $[M-F]^+$), 297 (50, $[M-MeO]^+$), 259 (100, $[M-CF_3]^+$), 202 (17), 193 (22), 159 (33), 69 (66, CF_3^+), 59 (33, $[MeO-C{\equiv}O]^+$). Anal. calc. for $C_{10}H_6F_6N_4O_2$ (328.18): C 36.60, H 1.84, N 17.07; found: C 36.93, H 1.91, N 16.91.

6.2. *Methyl* cis-*4,5-Dicyano-4,5-dihydro-1-methyl-4,5-bis(trifluoromethyl)-1*H-*pyrazole-3-carboxylate* (*cis*-**15**). The procedure described above was applied to (*Z*)-**BTE** and afforded a crude product that contained *trans*-**11**/*cis*-**11** 65 : 35, and 9% of an unknown *trans*-compound (2*s* in ^{19}F-NMR spectrum). To reduce the extent of a preceding isomerization, *cis*-**14** → *trans*-**14**, the deprotonation took place in the presence of the methylating agent. *cis*-**13** (325 mg, 1.04 mmol) and methyl fluorosulfonate (510 mg, 4.47 mmol) were dissolved in CH_2Cl_2 (1 ml), and proton sponge (222 mg, 1.04 mmol) in CH_2Cl_2 (1 ml) was added. After 10 min at r.t., the salt was filtered, and the ^{19}F-NMR analysis of the soln. exhibited *trans*-**15**/*cis*-**15** 40 : 60. Washing with 2N HCl, H_2O, and $NaHCO_3$, followed by repeated PLC on silica gel (pentane/ether 10 : 1), an enrichment with a *trans*/*cis* ratio of 25 : 75 was achieved. ^{1}H-NMR (80 MHz): 3.35 (*q*, ^5J(H,F)≈1, MeN); 3.95 (*s*, MeO). ^{19}F-NMR (94 MHz): −66.41, −66.82 (2 br. *q*, 2 CF_3). When the soln. was treated with DABCO (3 equiv.) for 4 h at r.t., the *trans*/*cis* ratio remained unchanged.

7. *The Role of Dihydropyrazolide Anions.* 7.1. *UV and IR Spectra.* The colorless soln. of *trans*-**9** in $CDCl_3$ (λ_{max}=261 nm, log ε=3.90) turned yellow upon addition of base. After adding proton sponge (1.0 equiv.) to *trans*-**13** (2.73 mM) in $CDCl_3$, a new maximum at 320 nm and a weak and broad one at *ca.* 400 nm appeared, the latter being responsible for the color. When the spectrum was measured again after 30 and 60 min, the absorbance of both bands had sunk due to a subsequent reaction of the dihydropyrazolide.

Solns. of *trans*-**13** (0.687 mmol), and 1 or 3 equiv. of proton sponge in $CHCl_3$ (0.6 ml) showed no diazo IR absorbance in the region of *ca.* 2100 cm^{-1}.

7.2. *^{19}F-NMR Spectra.* 7.2.1. *^{19}F-NMR Signals of Neutral and Anionic Species.* When solns. of *trans*-**13** or *cis*-**13** in $CDCl_3$ at 25° were successively treated with 0.5–2.0 equiv. of DABCO, the *cis* ⇌ *trans* equilibrium was established after 10 min. The proton exchange between dihydropyrazole and dihydropyrazolide led to line broadening of the ^{19}F signals. The sharpness of the two *s* of *trans*-**13** (0.70M, $CDCl_3$, 25°) – measured by the signal heights – went through a minimum, when DABCO was added, as shown in *Table 4* for the *s* of CF_3–C(4).

Table 4. *Signal Sharpness in Dependence of the Amount of DABCO Added.*

Equiv. of DABCO	Signal sharpness [mm/μmol]
0	4.84
0.5	1.75
1.0	1.43
2.0	3.05

7.2.2. cis⇌trans *Equilibrium of Dihydropyrazolide Anions.* Adduct *cis*-**13** (0.372M, $CDCl_3$, 25°) and DABCO (0.727M, 1.95 equiv.) gave rise to *trans*-**14**/*cis*-**14** 97:3, and a similar experiment with *trans*-**13** produced the same ratio of *trans*- and *cis*-anion. ^{19}F-NMR Spectra recorded at lower temperatures (every 10° from −40° to 0°) showed signal broadening by coalescence, the reason of which has not been clarified: hindered rotation about the C−CF_3 bond, incomplete equilibration of neutral species and anion, or other dynamic processes. Inconsistencies in the temp. dependence of the *cis*-content were noticed in the spectra recorded from −60° to 25°. Although the integration of 'soft' signals is problematic, our impression was that, in the solns. with high base content, secondary reactions take place on storing; more experimental insight is desirable.

7.2.3. *Competition of* cis/trans *Isomerization and Formation of Product* **22**. Dihydropyrazole *cis*-**13** (225.4 mg, 0.72 mmol, 2.3% *trans*-**13** as impurity) and $PhOCF_3$ (64.4 mg) as weight and frequency standard were dissolved in $CDCl_3$ in a 1-ml volumetric flask and transferred to a NMR tube; 200 µmol of a soln. of DABCO (22.52 µmol, 3.1 mol-%) in $CDCl_3$ was added by *Hamilton* syringe. Signals of ^{19}F-NMR analysis (376 MHz): δ −66.65 (*q*, *cis*-**13**), −75.72 (*s*, *trans*-**13**), −73.1 (2*d*, **22A**+**22B**), −68.24 (*s*, **22A**), −68.41 (*s*, **22B**), −58.38 (*s*, $PhOCF_3$). In each spectrum, the machine integrals of reactants and products were calibrated by that of trifluoroanisole, the weight standard. ^{19}F-NMR Monitoring showed an increase of percentage of *trans*-**13** in the *cis*/*trans*-mixture: min (% *trans*-**13**)=0 (2.3), 8 (22), 18 (34), 28 (41), 38 (45), 241 (71). The pseudo-first-order rate constant was not time-independent; 10^5 $k_{\psi 1}$ [s^{-1}] sank from 53 after 8 min to 9.7 after 241 min, due to deactivation of the base by salt formation with HF. After 241 min, the sum (*trans*-**13**+*cis*-**13**) was reduced to 86% of (*cis*-**13**)$_0$, and the C_{18} compound **22** (2.6%) was formed. Another 16 mol-% of DABCO was added, and 10 d later the material balance amounted to 3% of **13** (*trans*/*cis* 94:6) and 71% of **22A**+**22B**. A corresponding experiment with *trans*-**13** as starting material is described in *Table 2*.

8. *The Bis(dehydrofluoro) Dimer* **22**. 8.1. *Conversion of* trans-**13** *Catalyzed by Silica Gel*. Silica gel *60* (*Merck*, 10% H_2O content, pH 6.5–7.5, 50 g) was filled into a 20-cm column. *trans*-**13** (500 mg, 1.59 mmol) in CH_2Cl_2 (1 ml) was adsorbed and developed a yellow zone within 1 h. On elution with CH_2Cl_2 – no separation of zones – a light-yellow viscous oil (330 mg) was obtained. When the soln. in Et_2O (3 ml) was kept at −18° für 20 h, **22** in light-yellow crystals (247 mg, **A**/**B** 67:33) precipitated, m.p. 95–97° (turbid melt); the mother liquor afforded further 80 mg (together 73% yield), m.p. 85–96°. Two recrystallizations from (i-Pr)$_2$O gave the anal. sample, m.p. 97–99°.

The ^{1}H- and ^{19}F-NMR spectra of **22A** and **22B** confirmed the identity with the product of the DABCO-catalyzed conversion described above. From the soln. of **22** (crude crystals, 150 mg) in MeOH (4 ml) crystallized at −18° light-yellow material (32 mg), m.p. 101–104°; the ^{1}H- and ^{19}F-NMR spectra disclosed an enrichment to **22A**/**22B** 88:12; the larger part of **22** had reacted with MeOH. Attempts to achieve a separation by fractional crystallization or chromatography failed.

7.2. *Methyl 4,5-Dicyano-1-[2,3-dicyano-4-diazo-4-(methoxycarbonyl)-3-(trifluoromethyl)but-1-enyl]-4,5-dihydro-4,5-bis(trifluoromethyl)-1*H*-pyrazole-3-carboxylate* (**22**, **A** and **B**). IR (film on KBr plate): 1221v*s*, 1321*s* (br., C−F); 1404*m*, 1441*m*; 1610*m*, 1664*s*; 1716*s*, 1745*s* (C=O), 2121*s* (NN stretch., 'diazo band'); 2240v*w*, 2265v*w* (C≡N). ^{1}H-NMR ($CDCl_3$, 400 MHz): 3.916, 3.923 (2*s*, MeO of **22A**/**22B** 63:37); 4.06 (*s*, slightly broadened, MeO of **A**+**B**). ^{1}H-NMR (C_6D_6, 400 MHz): 3.039, 3.044 (2*s*, partially separated, MeO of **A**+**B**); 3.12, 3.14 (2*s*, MeO, **A**/**B** 62:38). ^{13}C-NMR (100.6 MHz, 32768 pulses, ^{1}H-decoupled, C_6D_6, *J*(C,F) values are listed, ratios **22A**/**22B** from signal-heights average 63:37): 46.95 (*dq*, ^2J=32.5, ^5J=4.2, C(3′) of **A**); 47.13 (*dq*, ^2J=32.3, ^5J=4.2, C(3′) of **B**); 52.93, 52.95 (2*s*, 2 MeO, **B**/**A** 38:62); 53.96, 53.99 (2*s*, 2 MeO, **A**/**B** 65:35); 56.26 (*m*, probably 2 overlapping *q*, low intensity, C(4′) of **A**+**B**); 60.70 (*q*, ^2J=33.5, C(4) of **A**); 60.81 (*q*, ^2J=33.2, C(4) of **B**); 69.81 (*dq*, ^2J=34.7, ^5J=4.2, C(5) of **B**); 70.00 (*dq*, ^2J=33.6, ^5J=4.2, C(5) of **A**); 86.85 (*d*, ^2J=29.8, C(2′) of **A**+**B**); 105.20 (*s*, partial split, CN, **A**+**B**); 105.35, 105.46 (2*s*, 2 CN, **B**/**A** 31:69); 109.60, 109.70 (2 slightly br. *s*, 2 CN, **A**/**B** 64:36); 109.85, 109.94 (2*d*, ^3J=5.7, *C*N−C(3′), **A**/**B** 66:34); 119.74 (*dq*, ^1J=292.8, ^5J=1.2, CF_3) and 120.02 (*dq*, ^1J=292.1, ^5J=1.2, CF_3, **B**/**A** 33:67); 120.43 (*q*, ^1J=291.5, *C*F_3−C(4) of **A**); 120.47 (*q*, ^1J=291.3, *C*F_3−C(4) of **B**); 122.07 (*dq*, ^1J=288.1, ^5J=3.3, *C*F_3−C(3′) of **B**), 122.14 (*dq*, ^1J=288.1, ^5J=2.6, *C*F_3−C(3′) of **A**); 136.73 (*d*, ^3J=1.9, C(3) of **A**); 137.17 (*d*, ^3J=2.3, C(3) of **B**); 155.80 (*s*, MeO*C*O−C(3) of **A**+**B**); 157.43 (*d*, ^1J=283.5, C(1′) of **B**); 157.58 (*d*, ^1J=283.9, C(1′) of **A**); 162.28, 162.40 (2*s*, MeO*C*O−C(4′) of **A** and **B**). ^{19}F-NMR (376.3 MHz, *J*(F,F) parameters, $PhOCF_3$ with δ

– 58.38 as secondary frequency standard, $CDCl_3$): – 68.23, – 68.40 (2*s*, CF_3–C(4), **A**/**B** 69 : 31); – 70.77 (asym. *m*, 3 lines in expanded signal, CF_3–C(3′) of **A** and **B**, sits on flat, unresolved signal of F–C(1′), integrates for 3.8 F); – 73.09, – 73.11 (2*d* with overlap, $^5J \approx 10-11$, CF_3–C(5), **B** + **A**); more informative is ^{19}F-NMR in C_6D_6 (Cl_3CF as chemical shift standard; *Fig.*): – 68.34, – 68.62 (2*s*, CF_3–C(4), **A** and **B**); – 69.6 (br. structured *m*, F–C(1′) of **B**); – 70.4 (br. unstructured *m*, F–C(1′) of **A**); – 71.04 (*d*, $^5J = 7.4$, CF_3–C(3′) of **A**); – 71.12 (*d*, $^5J = 9.5$, CF_3–C(3′) of **B**, **A**/**B** 66 : 34); – 73.35, – 73.39 (2*d*, partial overlap in the middle, $^5J \approx 9.4$ and 14.2, CF_3–C(5), **A** + **B**). MS (80°): 588 (15, M^+, ^{13}C calc. 3.0, found 3.1), 560 (50, $[M - N_2]^+$, ^{13}C 10.0/10.6), 491 (8.5, $[M - N_2 - CF_3]^+$; ^{13}C 1.61/1.65), 447 (7.8), 406 (12, $[491 - CO_2\text{-Me} - CN]^+$, $C_{14}H_3F_7N_5O_2^+$, ^{13}C 1.9/2.1), 247 (42, $[M - \mathbf{13} - N_2 + H]^+$, $C_9H_3F_4N_2O_2^+$; ^{13}C 4.2/4.6), 219 (51, $[560 - \mathbf{13} - HCN]^+$, ^{13}C 4.5/4.7), 214 (5, $[\mathbf{BTE}]^+$), 148 (12), 69 (61, $[CF_3]^+$), 59 (100, $[MeOC{\equiv}O]^+$). Anal. calc. for $C_{18}H_6F_{10}N_8O_4$ (588.29): C 36.75, H 1.03, N 19.05; found: C 36.50, H 1.20, N 19.01.

8.3. *Conversion of* cis-**13** *to* **22** *on Silica Gel.* Compound *cis*-**13** (310 mg, 0.99 mmol) in pentane was adsorbed on silica gel (40 g, column); here the yellow ring was developed after some min. Elution with CH_2Cl_2 and evaporation of the solvent left a thick light-yellow oil (150 mg). The ^{19}F-NMR analysis in $CDCl_3$ with $PhOCF_3$ as weight standard showed the three signal groups of **22** as main product (62% of the eluted material, 32% based on *cis*-**13**). The 2*s* at – 68.23 and – 68.40 corresponded to **A**/**B** 66 : 34. Many smaller signals suggested a less smooth reaction than in the case of *trans*-**13**. The isolated crystals of **22** (120 mg, 21%), m.p. 94–97°, gave the same IR spectrum as the sample obtained from *trans*-**13**.

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