anisoles listed in Table I are based on the weight of 2-amino-4-chlorobenzoic acid used.

4-Chlorobenzenediazonium-2-carboxylate (2). 2-Amino-5-chlorobenzoic acid was diazotized with isopentyl nitrite in tetrahydrofuran solution containing a catalytic amount of trichloroacetic acid, after Logullo and Friedman.[6] The resulting precipitate was collected, washed twice with methanol, and then transferred into methanol for reaction.

The preparation and properties of **3a** and **4a** have been described by Bunnett and Happer.[8]

1-(2-Iodo-4-chlorophenyl)-2-benzenesulfonhydrazide (**3b**) was prepared from 2-iodo-4-chloroaniline[20] by the method of Bunnett and Happer,[8] and purified by crystallization from benzene containing a trace of methanol. White needles formed, mp 154.5–155°.

Anal. Calcd for $C_{12}H_{10}ClIN_2O_2S$: C, 35.25; H, 2.45; halogen, 39.78. Found: C, 35.43; H, 2.59; halogen, 39.58.

1-(2-Iodo-5-chlorophenyl)-2-benzenesulfonhydrazide (4b). 2-Iodo-5-chloronitrobenzene[21] was reduced to 2-iodo-5-chloroaniline which was characterized as its acetyl derivative, mp 180–180.5°.

Anal. Calcd for C_8H_7ClINO: C, 32.49; H, 2.37; halogen, 54.99. Found: C, 32.61; H, 2.39; halogen, 54.92.

The aniline was converted to **4b**, white crystals from ether–pentane, mp 149.5–150.5°, analogously to the above.

Anal. Calcd for $C_{12}H_{10}ClIN_2O_2S$: C, 35.25; H, 2.45; I, 31.06. Found: C, 35.83; 35.86; H, 2.62, 2.92; I, 30.64.

Diazonium fluoroborates **5** and **6** were made by diazotization of the corresponding anilines in 37–40% fluoroboric acid in water, at *ca.* −5 to 0°. The precipitated diazonium salts were collected, washed with small portions of the chilled fluoroboric acid solution and ice-cold water, dissolved in acetone, and precipitated by addition of ether. The reprecipitated salts were colorless; they were collected and dried.

Anal. Calcd for **5**, $C_6H_3BBrClF_4N_2$: C, 23.60; H, 0.99. Found: C, 23.83, 23.53; H, 1.27, 1.17.

Anal. Calcd for **6**, $C_6H_3BBrClF_4N_2$: C, 23.60; H, 0.99. Found: C, 23.90, 23.86; H, 1.29, 1.35.

Procedure for Reactions and Analysis of Products. In a small round-bottom flask, a weighed quantity of a 4-chlorobenzyne precursor (usually 0.001 mole), weighed quantities of suitable comparison standards for purposes of analysis by gas–liquid chromatography, and a measured volume of a standard methanolic solution of sodium methoxide were combined. In the reactions with 0.1 *M* sodium methoxide, approximately 1 equiv of $NaOCH_3$ was furnished per mole of precursor. The comparison standards used included bromobenzene (with **3b** and **4b**), *p*-bromochlorobenzene and *o*-chloroanisole (with **3a** and **5a**), *m*-bromochlorobenzene and *o*-chloroanisole (with **4a** and **6**), and *o*-chloroanisole (with **1**). A reflux condenser was fitted to the flask. In the cases of **5** and **6**, the reaction solution was prepared at *ca.* −20°. No gas evolution was evident at that temperature, but gas evolution commenced as the solutions warmed to the vicinity of room temperature. In the other cases, gas evolution was not evident until the reaction mixtures were heated as noted in Table I.

On completion of heating, the reaction solution was poured into cold water and the resulting mixture was extracted with pentane or benzene. In several cases, as indicated in Table I, the water layer was acidified with nitric acid and diluted to standard volume, and aliquots of the diluted solution were titrated potentiometrically with silver nitrate for determination of halide ion. The pentane or benzene layer was dried over magnesium sulfate and analyzed by gas–liquid partition chromatography (10% Carbowax 20M on Chromosorb P columns). Molar response ratios were determined and the observed areas were corrected as necessary. In the cases of **1**, **3a**, **4a**, **5**, and **6**, chloroanisole yields were determined *vs.* *o*-chloroanisole as standard and bromochlorobenzene yields against the added isomeric bromochlorobenzene as standard.

For the most part peaks were identified by retention time analysis. From one reaction of **3b** with 2 *M* sodium methoxide, the two chloroanisole products were condensed from the effluent of a gas–liquid chromatography column. Their infrared spectra were identical with those of authentic samples of the relevant isomers.

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[20] K. W. Breukink, L. H. Krol, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim.*, **76**, 401 (1957).

[21] *Jahresber.*, 328 (1875).

Stereochemistry of the Cycloaddition Reaction of 1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and Electron-Rich Alkenes[1]

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Contribution No. 1163 from the Central Research Department,
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Wilmington, Delaware 19898. *Received May 4, 1966*

Abstract: 1,2-Bis(trifluoromethyl)-1,2-dicyanocyclobutanes are formed at room temperature by the cycloaddition of *cis*- and *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene to electron-rich alkenes. Although the rate of cyclobutane formation is strongly influenced by solvent, comparative fluorine nmr studies establish that many of these cycloaddition reactions take place with high stereospecificity over a wide range of solvent polarity. The first examples of nonstereospecific cycloaddition reactions of this type are reported, and evidence is presented that these polar additions occur *via* an intermediate.

Cycloaddition reactions of alkene to alkene have generally been achieved either thermally or photochemically,[2] but it has been demonstrated that strongly electrophilic olefins may cycloadd to electron-rich alkenes under surprisingly mild conditions without the influence of light or heat. Thus, the strong π acid, tetracyanoethylene, forms 1,1,2,2-tetracyanocyclobutanes (I) exothermically with a variety of electron-rich alkenes at 0–30°.[3] In contrast, thermal cycloadditions undergone by simple alkenes, allenes, fluoroalkenes,

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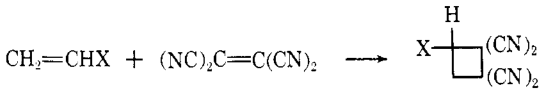
[1] For a preliminary communication, see S. Proskow, H. E. Simmons, and T. L. Cairns *J. Am. Chem. Soc.*, **85**, 2341 (1963).

[2] (a) J. D. Roberts and C. M. Sharts, *Org. Reactions.*, **12**, 1 (1962); (b) P. D. Bartlett and L. K. Montgomery, *J. Am. Chem. Soc.*, **86**, 628 (1964), and other papers in this series; (c) K. C. Brannock, A. Bell, R. D. Burpitt, and C. A. Kelly, *J. Org. Chem.*, **26**, 625 (1961); (d) J. C. Little, *J. Am. Chem. Soc.*, **87**, 4020 (1965).

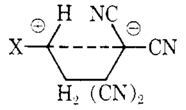
[3] J. K. Williams, D. W. Wiley, and B. C. McKusick, *ibid.*, **84**, 2210 (1962).



I

X = RO, RS, R(R'CO)N, p-ROC$_6$H$_4$

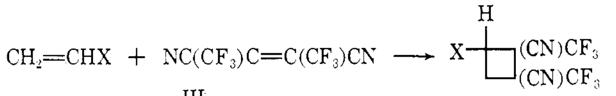
and ketenes usually require several hours heating at 100–225°. The rate of cyclobutane formation with tetracyanoethylene is strongly influenced by the polarity of the solvent,[3] which suggests that substantial charge separation is involved in the rate-limiting transition state.[4] The question of whether the over-all reaction proceeds *via* an intermediate, *e.g.*, II, has not been resolved.



II

Thermal cycloaddition reactions are generally considered to be radical processes,[2] and the present investigation was undertaken to obtain more information on the course of polar cycloaddition reactions. We report some stereochemical studies relating to the mechanism of the latter process.

1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (III), a strongly electrophilic molecule, has been found to react rapidly at room temperature with electron-rich alkenes to form 1,2-bis(trifluoromethyl)-1,2-dicyanocyclobutanes (IV), generally in high yields. The reactions are easily followed by observing the disappearance of the color of the transient charge-transfer complex.



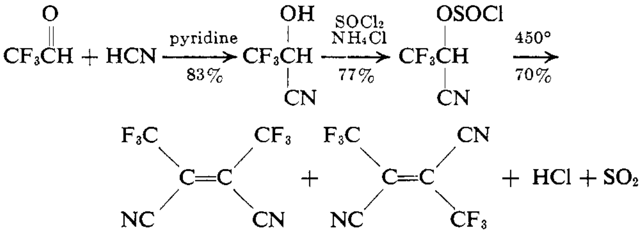
III IV

X = RO, RS, R(R'CO)N, p-ROC$_6$H$_4$

Early in this work which was conducted with the more stable, easily accessible, *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene, it became evident that the stereochemical relationship of the groups attached to the olefin was usually maintained in the product. This was readily deduced from the fluorine nmr spectra of the crude products that showed clearly only that number of diastereomeric cyclobutanes which would be predicted from a stereospecific cycloaddition reaction. We therefore undertook a study based on comparative fluorine nmr spectroscopy; it was of particular interest to determine the stereochemistry of the products derived from the less stable *cis* isomer and the stereochemical course of the reaction in solvents of varying polarity. Although the precise stereoisomeric structure of the many highly substituted cyclobutanes produced in this work could not be unequivocally assigned, this did not prevent the determination of the salient stereochemical features of the cycloaddition reactions, which will become evident in the discussion. It was found that the reactions show high stereospecificity in many cases as well as a large rate dependency on solvent, but that polar cycloadditions are not generally stereospecific.

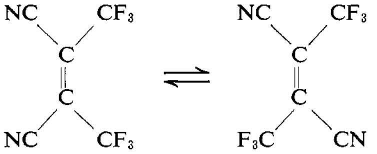
Results and Discussion

Synthesis, Characterization, and Isomerization of *cis*- and *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene. *cis*- and *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene were synthesized according to the following sequence. The preparations are given in the experimental section, but details of this chemistry will be given in a forthcoming publication. In the final pyrolytic step, IIIa and b are formed as a 1:1 mixture in 70% yield.



IIIa IIIb

The equilibrium between *cis*-IIIa and *trans*-IIIb is such that the less thermodynamically stable *cis* isomer is rapidly converted almost completely into the more stable *trans* isomer under the influence of anionic catalysts such as tetraethylammonium fluoride or basic catalysts such as triethylamine. Fluorine nmr spectra of the equilibrated mixture show that the position of equilibrium is greater than 95% in favor of the *trans* isomer.[5]



IIIa IIIb

trans-IIIb is a colorless, volatile solid, mp 61–61.5° (bp *ca.* 100°), whose F^{19} nmr resonance occurs at −4.25 ppm with respect to 1,2-difluoro-1,1,2,2-tetrachloroethane (Freon 112). The *cis* isomer IIIa, a colorless liquid at room temperature, melts at −8 to −5.5° (bp *ca.* 100°) and has its F^{19} nmr resonance at −7.25 ppm. A comparison of the infrared spectra of the pure isomers indicated that the assignment of configurations was correct.[6]

Other evidence supporting the assignment of configurations was found in the Diels–Alder reaction of the pure isomers with 1,3-cyclohexadiene. The method is based on the stereospecific nature of this reaction and a study of the fluorine nmr spectra of the products. The reaction of *trans*-IIIb with 1,3-cyclohexadiene gave a single bicyclooctene derivative V whose fluorine nmr spectrum exhibited two resonances of equal intensity due to the two chemically nonequivalent trifluoromethyl groups. The reaction of *cis*-IIIa with 1,3-cyclohexadiene, which would be predicted to form two bicyclooctene derivatives, VIa and VIb, gave only one product whose fluorine nmr spectrum consisted of a single

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(4) C. A. Stewart, Jr., *J. Am. Chem. Soc.*, **84**, 117 (1962), reported a similar observation in a study of the competitive formation of cyclobutane and cyclohexene adducts from tetracyanoethylene.

(5) The equilibrium composition at 74° in acetonitrile (N(C$_2$H$_5$)$_4$F catalyst) as determined by integration of the F^{19} nmr resonances of the two isomers was 1.3% *cis* and 98.7% *trans*. This equilibrium composition is not appreciably different at room temperature and was demonstrated by equilibration of either the *cis* or the *trans* isomer. When the liquid *cis* isomer is treated at room temperature with a trace of N(C$_2$H$_5$)$_4$F, it rapidly crystallizes to give almost pure solid *trans* isomer.

(6) The *cis* isomer has an absorption at 6.17 μ (C=C stretching), whereas the *trans* isomer shows essentially no absorption in this region.

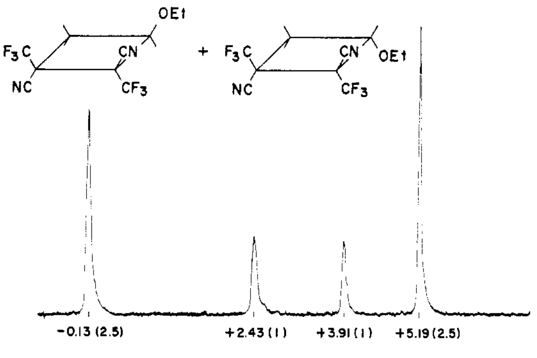
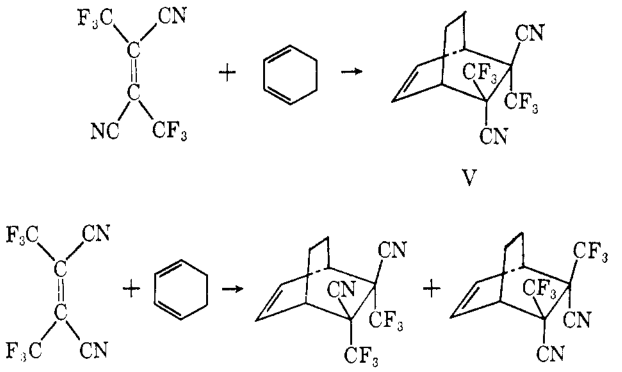


Figure 1. F^{19} nmr spectrum of cyclobutane diastereomers from reaction of *trans*-IIIb and ethyl vinyl ether, determined neat at 56.4 Mc/ecs and externally referenced in terms of displacement in ppm relative to 1,2-difluoro-1,1,2,2-tetrachloroethane ("Freon" 112). Relative areas are indicated in parentheses.

resonance twice the intensity of that of the product derived from the *trans* isomer. Apparently, only one of the expected isomers was formed. From the "Alder rule" and steric considerations based on molecular models, it was concluded that VIb is the preferred configuration for the product.



V

VIa VIb

Stereochemistry of the Cycloaddition Reaction. The fluorine-containing cyclobutanes are prepared easily by mixing molar quantities of the two reactants either neat or in a suitable solvent at room temperature. Unlike tetracyanoethylene, the isomeric 1,2-bis(trifluoromethyl)-1,2-dicyanoethylenes have a wide range of solubility in organic media. The course of the reaction is similar to that described for tetracyanoethylene; that is, the solution becomes colored, heat is evolved, and when the color disappears the reaction is complete. As indicated above, ethyl vinyl ether, *p*-methoxystyrene, *t*-butyl vinyl sulfide, and N-vinyl-2-pyrrolidone have been found to form cyclobutanes. Under comparable conditions, the rate of reaction of these olefins with IIIa,b was found to be somewhat less than with tetracyanoethylene. The cyclic structure of the products was confirmed by their composition and spectral analysis (see discussion below and Experimental Section).

A. Stereospecific Additions. If cyclobutane formation proceeds by a stereospecific mechanism, an unsubstituted vinyl compound, $CH_2{=}CHX$, would be predicted to give two diastereomeric cyclobutanes (VIIa,b) when treated with *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene.

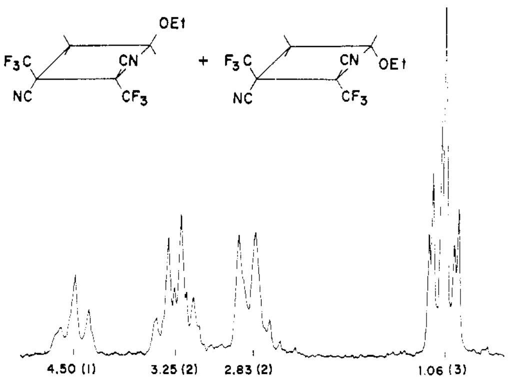
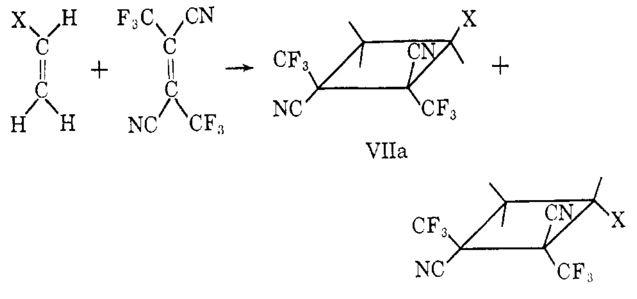


Figure 2. Proton nmr spectrum of cyclobutane diastereomers from reaction of *trans*-IIIb and ethyl vinyl ether, determined neat at 60 Mc/sec and referenced externally in terms of lower field displacement in ppm from the proton resonance of tetramethylsilane. Relative areas are indicated in parentheses.

Reaction of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene with excess ethyl vinyl ether at room temperature without solvent gave a 75% yield of a binary mixture of liquid cyclobutanes whose structures were established grossly from the elemental analysis and interpretation of the infrared spectrum. The fluorine nmr spectrum, which consisted of four singlet resonances appearing as two pairs whose components are of equal intensity, clearly demonstrates that only two diastereomers are formed (see Figure 1). From the areas under the two pairs of resonances the diastereomer ratio was 1:2.5.



VIIa

VIIb

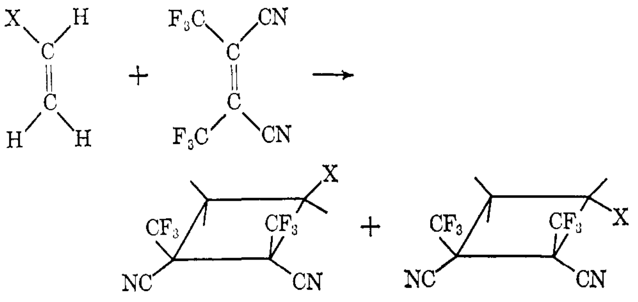
The proton nmr spectrum of the mixture (Figure 2) is consistent with the cyclic nature of the product, showing ring CH (4.50 ppm), ring CH_2 (2.83 ppm), and ethoxy protons (3.25 and 1.06 ppm). The presence of two diastereomers is apparent, but it is not possible to determine a precise isomer ratio. Vapor phase chromatography, which was carried out both analytically and preparatively, also showed only two components in approximate ratio 1:3. A clean separation of diastereomers was not possible, but the least abundant diastereomer was obtained in about 90% purity by careful collection of fractions. This diastereomer also exhibited infrared and nmr (fluorine and proton) spectra in complete accord with the cyclobutane structure.

The cyclobutane mixture formed from the reaction of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene and excess *t*-butyl vinyl sulfide at room temperature was similarly analyzed. In this case, the fluorine nmr spectrum also exhibited four resonances as two pairs of singlets whose components are of equal intensity;

the two diastereomers are produced in a ratio of 1:4.6. Proton nmr and vapor phase chromatography data further confirm the cyclobutane structures and composition of the mixture. Since the product is an oily solid composed largely of one cyclobutane, a pure crystalline diastereomer could readily be isolated in good yield by fractional recrystallization.

Binary mixtures of cyclobutane diastereomers were also formed from reactions at room temperature of *p*-methoxystyrene and N-vinyl-2-pyrrolidone with *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene. These reactions were complicated by accompanying polymerization of the electron-rich alkenes, but the polymers were free of fluorine and did not hinder interpretation of the fluorine nmr spectra of the crude mixtures. In both cases the spectra exhibited four singlet resonances as two equal-intensity pairs, and one diastereomer predominated to a large extent. The cycloadduct with *p*-methoxystyrene was isolated by distillation and analyzed as the mixture of diastereomers. A single, crystalline isomer of the adduct with N-vinyl-2-pyrrolidone was isolated by fractional crystallization.

Stereospecific cycloaddition reactions involving the less stable *cis*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene and an unsubstituted vinyl compound, $CH_2{=}CH{-}X$, would be predicted to give two different cyclobutane diastereomers (VIIIa,b).



VIIIa VIIIb

In reactions of the *cis* isomer with excess ethyl vinyl ether, *t*-butyl vinyl sulfide, and *p*-methoxystyrene at room temperature, it was found that in each case cyclobutane products were obtained that were different from those obtained in the corresponding reactions of the *trans* isomer, as determined by comparing the fluorine nmr spectra. In addition to different chemical shifts, the resonances of the diastereomers from the *cis* isomer appear as pairs of quadruplets rather than pairs of singlets.[7] The fluorine nmr spectra of the reaction mixtures obtained from the cycloaddition of *cis*- and *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene to *t*-butyl vinyl sulfide are given in Figure 3.

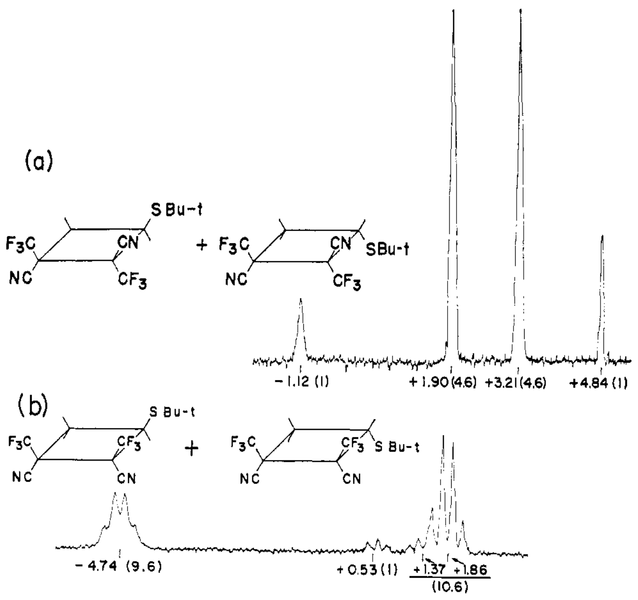


Figure 3. F^{19} nmr spectra of cyclobutane diastereomers from reaction of: *trans*-IIIb and *t*-butyl vinyl sulfide; *cis*-IIIa and *t*-butyl vinyl sulfide. Spectra determined in carbon tetrachloride at 56.4 Mc/sec and externally referenced in terms of displacement in ppm relative to 1,2-difluoro-1,1,2,2-tetrachloroethane ("Freon" 112). Relative areas are indicated in parentheses.

It is evident from Figure 3 (b) that there is virtually one product (VIIIa or VIIIb, X = $SC(CH_3)_3$) produced in the reaction of *cis*-IIIa with *t*-butyl vinyl sulfide, but it is difficult to ascertain whether the weak triplet-like resonances are due to the other diastereomer containing *cis* trifluoromethyl groups. Vapor phase chromatography showed the presence of two components in approximate ratio 1:20, but the preparative-scale separation was not complete because of the overlap of fractions. Apparently, one diastereomeric cyclobutane was formed preferentially, and it was furthermore shown that the reaction is stereospecific. A small sample of the least abundant component, obtained in *ca.* 95% purity, showed fluorine nmr resonances coinciding with the weak triplet-like resonances of the crude sample. These resonances, however, are evident as parts of two skewed quartets (equal areas), characteristic of an A_3B_3 system. Since the infrared spectrum of this component is consistent with a cyclobutane structure, it is clear that a second *cis* diastereomer is produced, albeit in very low amount. The *cis* diastereomer formed in larger amounts is easily obtained pure by fractional crystallization of the crude mixture. This product has the correct elemental analysis and shows infrared and nmr (proton and fluorine) spectra consistent with a cyclobutane structure.[8]

The crude product from the reaction of *cis*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene and ethyl vinyl ether had a fluorine nmr spectrum that is very similar to that obtained for the crude product from the *t*-butyl vinyl sulfide reaction. The weak pair of quartets from a second *cis* diastereomeric cyclobutane is partially

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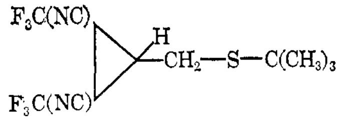
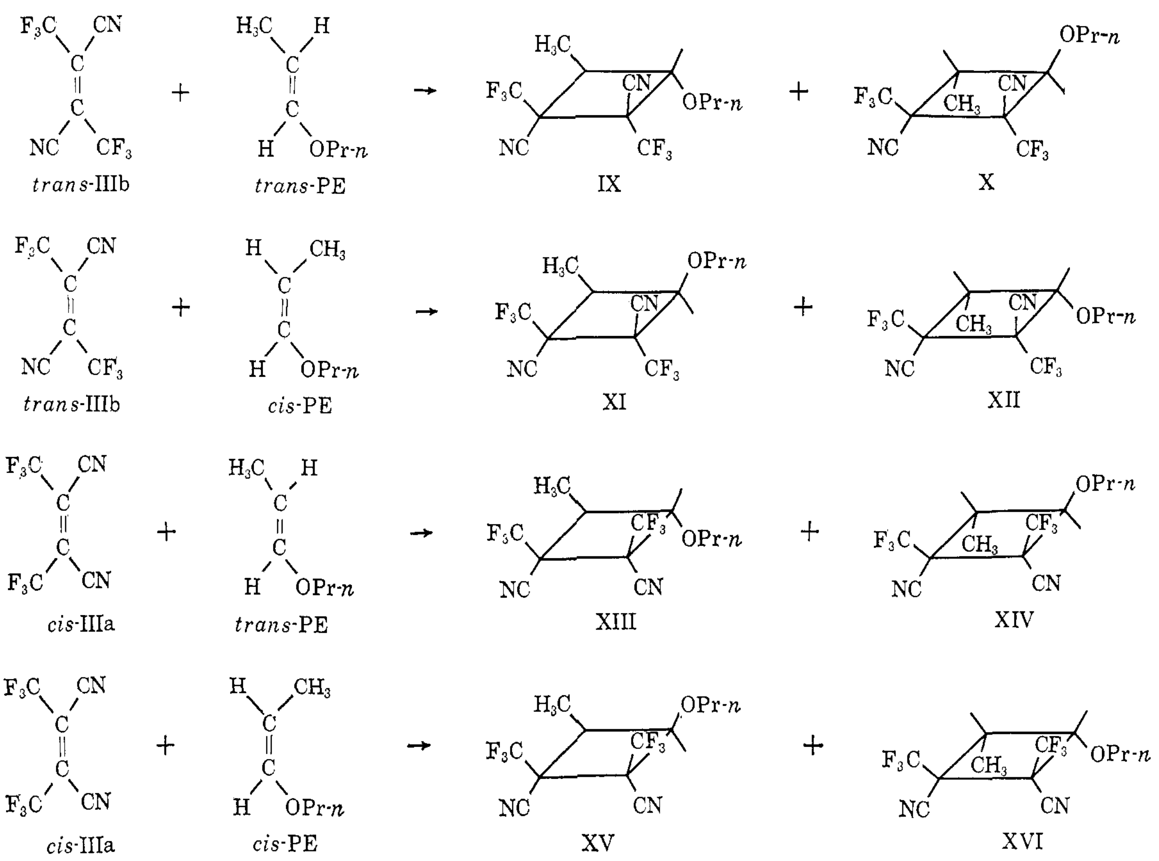
(7) The spin coupling of vicinal trifluoromethyl groups *cis*-oriented in these cyclobutanes has been attributed to the direct overlap of the electronic clouds of the fluorine atoms, *i.e.*, by the "through-space" mechanism. See S. Ng and C. H. Sederholm, *J. Chem. Phys.*, **40**, 2090 (1964).

(8) The spin coupling between the CH and CH_2 groups in the ring was that of a typical ABC system rather than that of an ABX system as might be expected.[9] In this respect the proton nmr spectrum of the product was different from those (ABX) generally encountered and suggested that a rearranged product, such as



might have been formed. The position of the CH multiplet at 4.42 ppm is inconsistent, however, with the cyclopropane structure. It is apparent that the protons on the methylene group in the cyclobutane structure have almost identical chemical shifts.

(9) Comparison with calculated spectra; *cf.* K. B. Wiberg and B. J. Nist, "The Interpretation of Nmr Spectra," W. A. Benjamin, Inc., New York, N. Y., 1962.



obscured by one of the quartets of the predominant isomer, and chromatography again established that a second isomer is formed. The resolution was not sufficient to provide a highly enriched sample of the least abundant product, but it was possible to ascertain that the triplet-like absorptions are actually skewed quartets of equal areas (A_3B_3 system).[10]

The reaction of *cis*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene with *p*-methoxystyrene produced two *cis*-cyclobutanes in the proportion 1:11.5.[11]

It is thus evident that unsubstituted vinyl compounds react with IIIa,b in a stereospecific manner, producing only those cyclobutanes in which the trifluoromethyl groups bear the same steric relationship as in the reactant.

B. Nonstereospecific Additions. All of the preceding cycloadditions employed electron-rich vinyl compounds which are unsubstituted, so that although the additions are stereospecific with respect to the electron-deficient olefin, no information was obtained on the stereospecificity with respect to the vinyl compound. It was reported in our preliminary communication[1] that the reactions of *trans*-IIIb with *cis*- and *trans*-propenyl *n*-propyl ether (*cis*- and *trans*-PE)[12] were stereospecific on the basis of studies not fully complete, but we have now found that certain additions of *cis*-IIIa and *trans*-IIIb to these vinyl ethers do not occur stereospecifically. These appear to be the first examples of nonstereospecific polar cycloaddition reactions.

Stereospecific reactions of IIIa and b with the *cis*- and *trans*-propenyl ethers could produce eight diastereomeric cyclobutanes (IX–XVI). Our original report[1] was based on reactions of *trans*-IIIb with the propenyl ethers in acetonitrile, ethyl acetate, and carbon tetrachloride.[13] The *trans*/*cis* combination, which should produce cyclobutanes XI and XII, gave a fluorine nmr spectrum with two singlet resonances of equal area (one isomer, $J = 0$) and two quartets of equal area (other isomer, $J = 12$ cps). The presence of a third diastereomer was indicated by a pair of weak, equal intensity singlets ($J = 0$), which previously were unassigned. The *trans*/*trans* combination gave two equal-area pairs of singlets ($J = 0$ for each isomer, assigned as IX and X), different from the pair of singlets obtained for the *trans*/*cis* combination.

Although the number of cyclobutanes formed in each reaction was thus thought to be in accord with prediction, it became evident after our communication and after the nmr analysis by Ng and Sederholm[7] that the major product in the *trans*/*cis* case had *cis*-oriented trifluoromethyl groups as shown by the "anomolous" quartet-splitting.

We have now carried out all combinations of the reactions of *cis*-IIIa and *trans*-IIIb with the *cis*- and *trans*-propenyl ethers in certain solvents and neat. The neat reactions occurred more rapidly and were complete in several hours, while the reactions in sol-

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(10) This was more evident by chromatography of certain samples of the crude product obtained with *trans*-IIIb in which relatively large amounts of the *cis* diastereomeric cyclobutanes were also present. The least abundant *cis*-cyclobutane was retained on the column with the most abundant *trans* diastereomeric cyclobutane. Since the resonances of *trans*-cyclobutanes are pairs of sharp singlets, they did not obscure the weak quartet absorptions of the *cis*-cyclobutane.

(11) This ratio of isomers was readily ascertained because the fluorine resonances are seen clearly as two sets of quadruplets.

(12) We are indebted to Dr. T. J. Prosser, Research Center, Hercules Powder Co., Wilmington, Del., for generous samples of these isomers; see T. J. Prosser, *J. Am. Chem. Soc.*, **83**, 1701 (1961).

(13) The observed reaction times in each solvent at 25° are 2.25 hr, 4 days, and 7 months, respectively, for the *trans*/*trans* combination and 1.5 hr, 2 days, and 3 months, respectively, for the *trans*/*cis* combination. Steric and polarizability considerations make it plausible that this vinyl ether reacts much slower with IIIa,b than does *t*-butyl vinyl sulfide.

vents such as methylene chloride were only complete after about 6 days. The product dependency on solvent is discussed in the next section, and Table I gives the results using ethyl acetate as solvent. The structures assigned in the table are not known unequivocally, but are made plausible by the following discussion. In all cases, no rearrangement of starting materials was detected. Unfortunately, analysis of the complicated proton spectra has not been possible, so that direct observation of loss of stereochemistry of the vinyl ethers in the products was not possible.

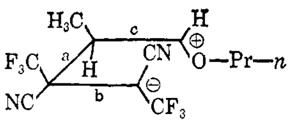
Table I. Reaction of *cis*-IIIa and *trans*-IIIb with *cis*- and *trans*-Propenyl *n*-Propyl Ether[a]

Reactants	Products, predicted if stereospecific	Products, found[b]
trans-IIIb + *trans*-PE	IX + X	IX (1.0) + X (2.1)
trans-IIIb + *cis*-PE	XI + XII	XI (1.0) + XII (7.0) + XVI (9.3)
cis-IIIa + *cis*-PE	XV + XVI	XI (2.2) + XII (1.0) + XVI (4.7)
cis-IIIa + *trans*-PE	XIII + XIV	XIV[c]

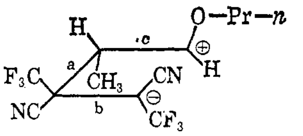
[a] The values in this table refer to ethyl acetate as solvent. The values in parentheses are relative weights. [b] The product assignments are based on the discussion in the text but have not been established unequivocally by chemical means. [c] Only a single cyclobutane was formed.

It is immediately seen that in the reactions *trans*-IIIb/*cis*-PE and *cis*-IIIa/*cis*-PE, cross-products are obtained that could only have been formed by loss of the relative stereochemistry of the trifluoromethyl groups. Since *cis*-IIIa is very easily isomerized almost completely to *trans*-IIIb by a variety of weak bases, it is particularly important to note that in the reaction *trans*-IIIb/*trans*-PE, *a major product (XVI) is formed whose trifluoromethyl groups are cis oriented.*

The structures IX–XVI were assigned on the basis of analyses, spectral data, and mechanistic arguments as follows. In the first place, loss of stereochemistry during cyclobutane formation occurs only in the reactions *trans*-IIIb/*cis*-PE and *cis*-IIIa/*cis*-PE, *i.e.*, in reactions of the *cis*-propenyl ethers where steric crowding in transition states, any intermediates, and in products is expected to be greatest. This suggests that intermediates of substantial lifetime may be involved, and the large solvent effect on rate and other arguments given below make it plausible to assume that a dipolar ion, such as II, is involved in such additions. At this point we will make this assumption and the further one that the structure of the dipolar ion places the positive charge on the carbon bearing the ether group since this must be the most stable carbonium ion. For example, the two possible ions in the reaction *trans*-IIIb/*trans*-PE are XVII and XVIII. Such structures are meant to imply that bond a is formed first and that the products of collapse of the ion to a cyclobutane are determined by the lifetime of the ion. Rotation around bonds b and/or c will result in loss of stereospecificity. Furthermore, in the transition state leading to the intermediate, it might be expected that steric effects associated with the groups on bond a will be important in fixing this junction. We anticipate that the rate of formation of XVIII will be greater than that of XVII, since the methyl and trifluoromethyl groups are oriented *trans* in the former.



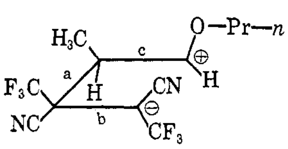
XVII



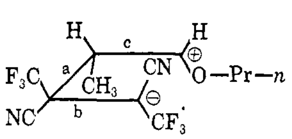
XVIII

With these considerations in mind, it is reasonable that the two products formed in the *trans*/*trans* reaction in Table I, whose nmr spectra show their trifluoromethyl groups are *trans* oriented, are simply the products expected from stereospecific collapse of XVII and XVIII. The product formed in largest amount can then be assigned structure X. This interpretation assumes no isomerization occurred about bonds c. This is reasonable since if both intermediate ions were formed and if such isomerization occurred, it would have to be complete in both XVII and XVIII, for only two products were observed in the reaction. It will be seen that this is unlikely based on the following finding.

In the *trans*/*cis* reaction, two products are again formed with *trans*-oriented trifluoromethyl groups, and these products are different from the two cyclobutanes formed in the *trans*/*trans* reaction. It is clear that both intermediates XIX and XX must occur and both must collapse directly in part to produce these two new diastereomers. Therefore, these two products can be assigned structures XI and XII, and the cyclobutane formed in largest amount is expected to be XII. The major product in the *trans*/*cis* reaction, however, has *cis*-oriented trifluoromethyl groups and must have arisen from isomerization of the intermediates XIX or XX. It was also shown that isomerization of *trans*-IIIb to *cis*-IIIa, perhaps by reversal of XIX or XX to starting materials *after* rotation around bond b, could not account for the products, since when the reaction in ethyl acetate was monitored throughout by F^{19} nmr no trace of *cis*-IIIa was detected. If appreciable *cis*-IIIa had formed, it would have been expected to accumulate, since the rates of the cycloaddition reaction with both isomers are comparable. Rotation must occur at least around bond b before collapse, and since complex mixtures of cyclobutanes were not formed in this and in the following case, it is reasonable to assume that stereochemistry is lost only at the carbanion portion of the intermediate. The results of all four cases in Table I cannot be easily made to accord with the view that stereochemistry is also lost around bond c. Now, it is evident that once bond a has been formed, steric crowding in the region of the dipolar ion is more serious in XX than in XIX, since in the former the large propoxy and trifluoromethyl groups are opposed. We anticipate then that the major product of the reaction has structure XVI, formed from ion XX after rotation around bond b. The less sterically crowded



XIX



XX

Table II. Isomerization of *cis*-IIIa by Solvent at 25°

Solvent	Approximate extent of isomerization, %, after 1 hr	2 hr	9 days
Acetic acid	None	. . .	. . .
Nitromethane	. . .	20	. . .
Acetonitrile	60	98[a]	. . .
Ethyl acetate	None	Trace	60
Carbon tetrachloride	None	None	None

[a] Equilibrium composition.

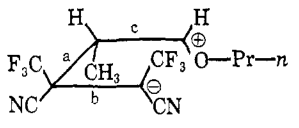
Table III. Effect of Solvent on Rate and Stereospecificity of the Reaction of *cis*-IIIa or *trans*-IIIb with *t*-Butyl Vinyl Sulfide at 25°

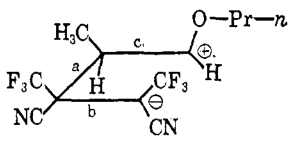
	cis-IIIa			*trans*-IIIb		
Solvent	Reaction time, min	Product stereochemistry[a]	Isomer ratio	Reaction time, min	Product stereochemistry[a]	Isomer ratio
CCl_4	4320	VIIIa + VIIIb	. . .	17,280	VIIa + VIIb	1:2.3
CH_2Cl_2	180	VIIIa + VIIIb	. . .	180	VIIa + VIIb	. . .
EtOAc	120	VIIIa + VIIIb	. . .	120	VIIa + VIIb	1:3
AcOH	6	VIIIa + VIIIb	. . .	30	VIIa + VIIb	1:2.9
CH_3CN	2	VIIIa + VIIIb	. . .	6	VIIa + VIIb	1:4.5
CH_3NO_2	<1	VIIIa + VIIIb	. . .	3	VIIa + VIIb	. . .
MeOH (H^+)[b]	<1	VIIIa + VIIIb	. . .	1.5	VIIa + VIIb	1:3.5

[a] $X = SC(CH_3)_3$. [b] One drop of concentrated hydrochloric acid was added.

ion XIX apparently collapses directly without suffering rotation of any bonds.

The products of the *cis*/*cis* reaction were the same diastereomers formed in the *trans*/*cis* reaction. Here, intermediate XXI would be expected to be formed in preference to XXII, and it is then clear that the observed products are the ones to be expected on the basis of previous arguments. Direct collapse of XXI gives the diastereomer XVI, the major product, and XII can only be formed by rotation around bond b before closure. It is interesting to note that stereospecific collapse of XXII to a cyclobutane would produce the most sterically crowded diastereomer of the full series of eight, *i.e.*, XV, in which all four of the bulky groups are on one side of the ring. It is understandable then that cyclobutane formation from XXII occurs only after the repulsions are relieved by rotation about bond b or c. The actual product XI can only be formed by rotation about b, in agreement with the *trans*/*cis* case where the products were also rationalized by loss of stereochemistry at the carbanion site only.


XXI


XXII

Finally, the *cis*/*trans* reaction produced only a single product whose trifluoromethyl groups are *cis* oriented. By analogous arguments, this diastereomer is assigned structure XIV, although XIII cannot be ruled out unequivocally. This case also demonstrates that no prior isomerization of the sensitive *cis*-IIIa occurs prior to cyclobutane formation.

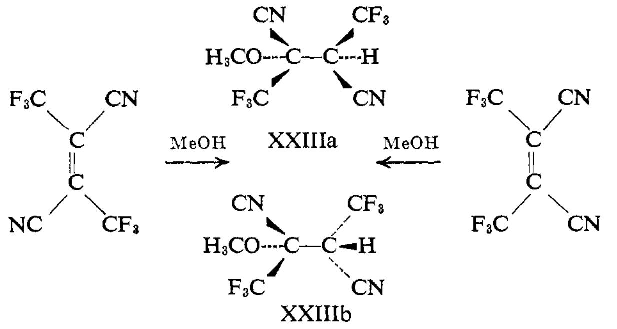
Effects of Solvent on the Cycloaddition Reaction. If some dipolar species is an intermediate in which strong resonance stabilization of both the positive and negative charges would be anticipated, then the stereospecificity of the over-all cycloaddition might be influenced by the nature and polarity of the solvent. Visual observation of the transient color due to the charge-transfer complex was the means employed to compare qualitatively the reaction times of these reactions in the different solvents. Since this color change may sometimes be obscured in reactions with ethyl vinyl ether or *p*-methoxystyrene because of polymerization, *t*-butyl vinyl sulfide was used exclusively for this study. To determine the stereochemistry, it was necessary only to examine the fluorine nmr spectra of the crude reaction mixtures.

It was found that certain solvents cause equilibration of the trifluoromethylcyano olefins (see Table II), and the observations of relative rates were made under conditions where the effect of this equilibration was eliminated or at a minimum. The experiments were performed in acid-washed equipment, and the *cis*- and *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylenes were added directly to the solution of *t*-butyl vinyl sulfide and solvent. The molar proportion of IIIa and IIIb to *t*-butyl vinyl sulfide was 1:2, respectively, with the reactants comprising 10% (w/v) of the solution. Reaction times were determined at the point the initial, deep-red color of the charge-transfer complex faded completely. The solvent and excess *t*-butyl vinyl sulfide were then removed *in vacuo*, and the residue was dissolved in a measured volume of either methylene chloride or carbon tetrachloride and examined spectroscopically to determine isomer distribution.

The results are given in Table III and show that the cycloaddition reactions of unsubstituted vinyl compounds are stereospecific throughout the range of solvent polarity tested. There is considerable difference in the rate of reaction depending on the polarity of the medium with the more polar solvents favoring the faster reactions. The rate in acetic acid was slower than in the acetonitrile, presumably because of protonation of the vinyl sulfide, causing decreased nucleophilic character. The *cis* isomer generally reacted faster than the *trans* isomer.

There is a trend of the least abundant *trans*-cyclobutane diastereomer to be formed in increasingly larger amounts in less polar media. The variation in the ratio of diastereomers with solvent polarity in the *cis*-cyclobutane mixtures was not determined because of the overlapping nature of the fluorine nmr resonances.

The cycloaddition reactions in methanol (H^+) (Table III) are accompanied by addition of the solvent to the double bond of the 1,2-bis(trifluoromethyl)-1,2-diyanoethylenes to give mixtures of the *threo* and *erythro* epimeric methyl ethers XXIIIa,b. The same *threo/erythro* product mixture is obtained when either *cis*- or *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene is caused to react with methanol alone.[14] The ratio of



the methyl ethers to cyclobutanes was greater from *trans*-IIIb than from *cis*-IIIa as expected, since the *cis* isomer was shown to react faster than the *trans* in cycloaddition.

The influence of solvent on the reactions of IIIa,b with the propyl propenyl ethers is shown in Table IV.

Table IV. Influence of Solvent on the Reactions of *cis*-IIIa and *trans*-IIIb with *cis*- and *trans*-*n*-Propyl Propenyl Ethers

Reaction	Products	Relative ratios of products in: Ethyl acetate	Acetonitrile	Methylene chloride	Neat[a]
trans-IIIb/*trans*-PE	IX	1.0	1.0		
	X	2.1	3.2		
trans-IIIb/*cis*-PE	XI	1.0	1.0		
	XII	7.0	6.0		
	XVI	9.3	5.4		
cis-IIIa/*cis*-PE	XI	1.0		1.0	1.0
	XII	0.45		0.16	0.21
	XVI	2.1		1.1	1.9
cis-IIIa/*trans*-PE	XIV			*b*	*b*

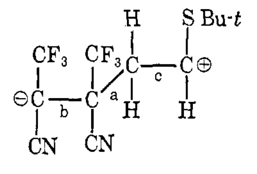
[a] Run in excess of the ether as solvent. [b] Only product formed.

The *trans/trans* reaction was stereospecific in the two solvents tried, ethyl acetate and acetonitrile. If an ionic intermediate is involved in this cycloaddition, it might be expected that tighter solvation would lead to more discrimination in product formation, and this is borne out since the product ratio is largest in the more polar acetonitrile. This was also quite generally the case in the solvent studies reported above employing *t*-butyl vinyl sulfide. In the *trans/cis* and *cis/cis* reactions which are not stereospecific, the product ratios are very sensitive to solvent; *e.g.*, in the *trans/cis* reaction, the rearranged product XVI predominates in ethyl acetate (D = 6.4) but not so in the more polar acetonitrile (D = 38.8). The specific effect of tighter solvation in this case cannot be predicted with certainty, but it may not be unlikely that rotation about bonds b and c in XX is more restricted in polar solvents where a tight solvent shell surrounds particularly the outer faces of the ions. A similar effect was observed in the *cis/cis* case where more rearrangement was observed in ethyl acetate (D = 6.4) than in methylene chloride (D = 9.1). This sensitivity of products to solvent polarity and specific solvent effects is not unexpected in the nonstereospecific cases if ionic intermediates intervene.

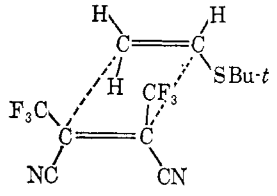
Furthermore, the reaction of *trans*-IIIb with the *cis*-propenyl ether in acetic acid and in methanol was studied to see if any intermediate could be trapped. In acetic acid, the reaction was stereospecific and stereoselective, giving a single cyclobutane XII. It was further shown that the product mixture from the *trans/cis* reaction run in ethyl acetate (see Table I) was stable by allowing it to stand in acetic acid for 1 week, where no change in the ratio of the three isomers was detected. In methanol, addition of solvent to IIIb occurred exclusively to give only XXIIIa and b, and cyclobutane formation was only barely evident. In neither case was any trace of an open-chain structure detected that would have arisen from trapping of an intermediate dipolar ion.

Conclusions. The findings that some polar cycloaddition reactions occur nonstereospecifically and that such additions show large rate accelerations in polar solvents are in accord with a mechanism in which a dipolar intermediate is involved. Bartlett and Montgomery[2b] have shown that a diradical is an intermediate in certain thermal cycloadditions of fluoroolefins that take place at elevated temperatures. Thus, both classes of cycloaddition reactions obey the selection rules of Hoffmann and Woodward[15] which predict that concerted cycloadditions (four-center, no intermediate) are disfavored thermal processes.

Our results suggest that many polar cycloadditions are stereospecific but that this is not an inherent aspect of these reactions since steric effects can control the ultimate stereochemistry. The stereospecificity observed in some cases makes a two-step reaction mechanism unlikely in a form characterized by an intermediate in which the reactant molecules approach each other largely endwise, *e.g.*, XXIV in the case of *t*-butyl vinyl sulfide. In this intermediate, free rotation about bonds b and c concurrent with rotation about a would certainly be likely in some solvents. The four-center reaction[16] in which the addition involves largely synchronous breaking and forming of bonds in a transition state such as XXV implies that no intermediate is involved. It should be pointed out that, when one or both of the reactants bears polar substituents, such a transition state may have a very large dipole moment, even in the case of symmetrical molecules like tetracyanoethylene. As transition state XXV is approached, all eight substituents would recede from the ring as their carbon centers become tetrahedral, and this will produce a large dipole moment in the direction of the



XXIV



XXV

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[14] This reaction will be described in detail in a subsequent publication.

(15) R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, **87**, 2046 (1965).

(16) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, Chapter 24.

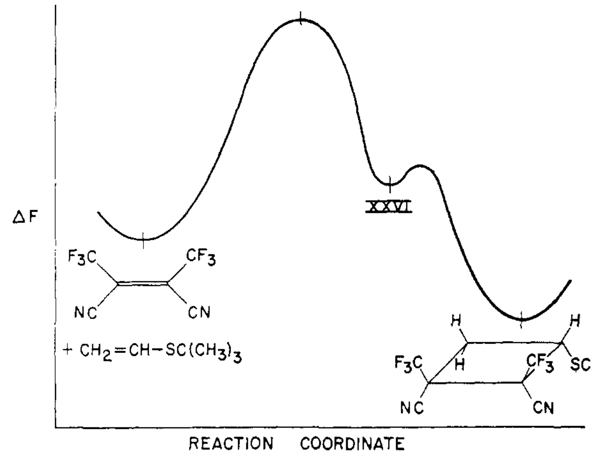
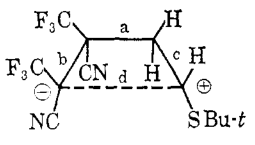


Figure 4. Possible energy profile for a typical polar cycloaddition reaction.

plane of the ring. It is anticipated that the associated rate would be accelerated by polar solvents, even if no ionic intermediate intervenes. The four-center mechanism cannot account, however, for nonstereospecific cycloadditions.

A mechanism compatible with our observations is one proceeding *via* an intermediate such as XXVI. The four centers align just prior to bonding and only a relatively small change in atomic positions would be necessary for the transformation to product. Bonding in the over-all process is then contemplated as proceeding in two distinct steps wherein the formation of bond a is first and rate limiting and that of bond d is a subsequent facile collapse of the internal ion pair. As noted above, the charge distribution after forming bond a would be appreciably more stable than that if bond d had formed first, since in the former charge is strongly delocalized by conjugation with *t*-butylthio groups. The solvent influence upon the reaction reflects the considerable charge separation that would be needed to form bond a. The proximity of the charged carbon atoms ensures that the stereochemistry of the reaction will not be disturbed unless steric crowding is severe. The reaction profile probably resembles the schematic one in Figure 4 where only a very small activation energy is needed to proceed from intermediate to product. This is in accord with the finding that no isomerization of the *reactants* is detected during these reactions, *i.e.*, the formation of the intermediate is essentially nonreversible.

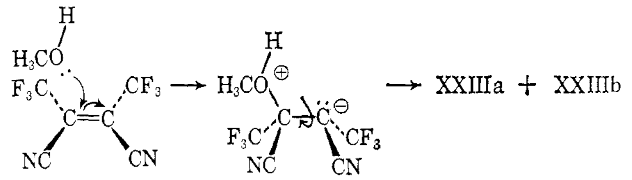


XXVI

The possibility that unsubstituted vinyl compounds react stereospecifically by a four-center mechanism involving no intermediate while steric crowding in *cis*-substituted vinyl compounds causes a *change in mechanism* to one involving a dipolar ion intermediate cannot be excluded by our results. We feel, however, that the single mechanism proposed better accounts for our observations with these structurally similar compounds.

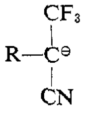
It can also be envisaged that in collisions in which the π overlap is not maximum, more or less extended forms such as XXIV occur in which bond a is not yet fully made. During the time of rotation about bond a to produce a cyclobutane, there is naturally sufficient time for rotation about bonds b or c. In such a case there would be no intermediate and the reaction mechanism could be called one step. In our view, it does not seem likely that such a mechanism can account for the large variation of rearranged product yield with solvent.[17]

It was hoped that the experiments involving competitive addition of methanol and *t*-butyl vinyl sulfide to IIIa,b would allow us to place some limits on the lifetime of the intermediate. The addition of methanol containing hydrochloric acid to, *e.g.*, IIIa most likely involves attack by the nucleophile methanol at the double bond. It could not be determined whether the addition occurred stereospecifically since it could be demonstrated that the products XXIIIa and b were rapidly interconverted under the reaction conditions. In fact, when the 1:1 mixture of XXIIIa,b was dissolved in pure methanol-*d*, the pair of quartets (due to both diastereomers) centered at 4.18 ppm in the proton nmr spectrum rapidly diminished in intensity. Proton exchange in neutral methanol-*d* was essentially over in less than 1 hr. This facile exchange makes unreliable any conclusions drawn on the stereochemical stability of an anion related to XXVII.



XXVII

Rotation barriers in tetra- and pentasubstituted ethanes containing bulky electronegative groups, such as cyano and trifluoromethyl, have been measured.[18] An order of magnitude estimate of the specific first-order rate constant for rotation may be taken to be $k_{\text{rot}} \simeq 10^9$ sec^{-1}. From the measured exchange rates of protons in molecules such as malononitrile[19] and 1,1,1,2,3,3,3-heptafluoropropane[20] under comparable conditions, it can be estimated that the pseudo-first-order rate constant for proton transfer from methanol to a carbanion like



$$\mathrm{R{-}\overset{\displaystyle CF_3}{\underset{\displaystyle CN}{C^{\ominus}}}}$$

is $k_{\text{H}} \simeq 10^{12}$ sec^{-1}. Hence, $k_{\text{H}}/k_{\text{rot}} \simeq 10^3$, and we might anticipate that capture of a dipolar ion like XXVI by protonation would be feasible, but unfortunately this was not realized. The collapse of XXVI to a single diastereomeric cyclobutane must have a specific first-order rate constant greater than that for rotation about bond b. If the geometry of XXVI is close to

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[17] We are grateful to Professor P. D. Bartlett for helpful discussion on this latter point.

[18] W. D. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 817 (1958).

[19] R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, **75**, 2439 (1953).

[20] S. Andreades, *ibid.*, **86**, 2003 (1964).

that depicted (to minimize charge separation), it would be expected that k_{rot} would be greatly depressed for both steric and electrical reasons. It can then be concluded that the rate of collapse (k_c) of XXVI to product must be $>10^{10}$ in those cases showing stereospecificity.

In the more pertinent case of *trans*-IIIb/*cis*-PE where stereochemistry of cyclobutane formation is lost, trapping experiments in methanol were unsuccessful because methanol added to IIIb so rapidly that cyclobutane formation did not compete (see previous section).

Finally, it can be seen from Table I that although the products are the same in the *trans*/*cis* and *cis*/*cis* cases, the ratios XII/XVI are not equal. This indicates that rotational equilibrium was not obtained, since the intermediates XX and XXI are equivalent if rotation is only restricted about bonds c. No evidence has been found, however, in any of our data that the stereochemistry is lost about the bond of the electron-rich olefin in polar cycloadditions.

Experimental Section[21]

Preparation of *cis*- and *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene. A. Trifluoroacetaldehyde Cyanohydrin. Commercial trifluoroacetaldehyde hydrate (100 g) was added dropwise to a stirred solution of 58 g of phosphorus pentoxide and 212 ml of concentrated sulfuric acid at 85–95°. The liberated trifluoroacetaldehyde was passed directly into a flask containing 50 ml of hydrogen cyanide, 150 ml of ether, and 0.5 ml of pyridine. The flask was equipped with a Dry Ice–acetone condenser to prevent loss of the aldehyde, and the reaction mixture was maintained at 0–5°. The solution was stirred 0.5 hr at 0° after the addition.

The solution was treated with 2 ml of concentrated sulfuric acid, and excess ether and hydrogen cyanide were removed by distillation. The crude residue was then distilled rapidly in a simple still at 2-mm pressure and the product collected in a receiver containing 0.5 ml of concentrated sulfuric acid. Pure cyanohydrin was obtained by fractional distillation of this material. A yield of 55 g of product, bp 97° (104 mm), $n^{27}D$ 1.3311, was obtained. Since the cyanohydrin of trifluoroacetaldehyde shows erratic stability on storage, it was stabilized immediately by addition of a drop of concentrated sulfuric acid. *Anal.* Calcd for $C_3H_2F_3NO$: N, 11.20. Found: N, 11.33.

The product was monomeric as judged from its experimental mol wt of 133 (calcd 125). The infrared and nmr spectra were consistent with the assigned structure.

B. 1-Cyano-2,2,2-trifluoroethyl Chlorosulfite. A mixture of 0.36 g of ammonium chloride and 72 ml of thionyl chloride was heated briefly at reflux, and then cooled to 0–10°. Trifluoroacetaldehyde cyanohydrin (36 g) was added, and the mixture was then refluxed for 10 hr.

The product was fractionally distilled at reduced pressure by means of an efficient distillation column. After removal of excess thionyl chloride at *ca.* 250-mm pressure, the pressure was reduced to 10 mm and a pale yellow liquid, bp 40–41°, was collected. The liquid weighed 45.5 g. It was identified as 1-cyano-2,2,2-trifluoroethyl chlorosulfite by elemental, infrared, and nmr analysis. *Anal.* Calcd for $C_3HClF_3NO_2S$: C, 17.36; H, 0.49; Cl, 17.08; F, 27.46; N, 6.75; S, 15.41. Found: C, 18.39; H, 0.81; Cl, 16.88; F, 27.62; N, 6.79; S, 15.08.

The fluorine nuclear magnetic resonance, which consisted of two peaks in the ratio of *ca.* 2:3, each peak being split into a doublet, further established that the product was a mixture of the two expected diastereomers.

C. 1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene.[22] The apparatus employed for this reaction was a 300-ml flask constructed with two vertical tubes about 30 cm long and 2.5 cm in diameter. One tube was equipped with a dropping funnel and nitrogen inlet. The other tube, the outlet tube, was attached in series to two traps by means of connecting tubes. A drying tube connected to the exit side of the second trap completed the assembly.

The flask was charged with about 200 g of sulfur, and a slow stream of nitrogen was flushed through the system while the flask was heated to 445° so that sulfur vapors were caused to reflux well up into the vertical outlet tube of the flask. The traps were then cooled with solid carbon dioxide–acetone, and the nitrogen flow rate was adjusted to *ca.* 100 cc/min. While maintaining these conditions, 45.5 g of 1-cyano-2,2,2-trifluoroethyl chlorosulfite was added dropwise from the funnel over a period of 1 hr. The volatile products were collected in the cooled traps, except for hydrogen chloride gas which escaped through the drying tube at the end of the system.

The trap contents were allowed to warm slowly to room temperature to remove the sulfur dioxide, and the residual liquid was evaporated at 1-mm pressure into a clean trap cooled to −80°. A near-colorless solid that liquefied on warming to room temperature was obtained. This product was fractionally distilled at atmospheric pressure to give 14.5 g (62%) of 1,2-bis(trifluoromethyl)-1,2-dicyanoethylene as a colorless liquid, bp 100–104°. *Anal.* Calcd for $C_6F_6N_2$: C, 33.66; F, 53.25; N, 13.09. Found: C, 33.91; F, 53.43; N, 12.81.

The product was a mixture consisting of approximately equal amounts of the *cis* and *trans* diastereomers. The structures of the components of the mixture were confirmed by infrared spectrographic analysis that indicated the presence of $C{\equiv}N$ (4.45 μ), conjugated $C{=}C$ (6.17 μ), and CF (8 μ region), and by two singlet fluorine nmr peaks at −7.25 ppm (*cis* isomer) and −4.25 ppm (*trans* isomer) relative to the fluorine resonance of "Freon" 112.

Separation of the *cis* and *trans* isomers was effected analytically by vapor phase chromatography at 53° with a column packing of 20% silicone fluid on 40–60 mesh calcined diatomaceous earth.

The *cis* isomer was converted to the *trans* isomer by treatment with such reagents as triethylamine, tetraethylammonium fluoride, and sodium fluoride. This conversion was essentially quantitative (see Discussion).

***trans*-2,3-Bis(trifluoromethyl)-2,3-dicyanobicyclo[2.2.2]oct-5-ene (V).** Pure *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene (2.0 g) was mixed with 1.5 ml of 1,3-cyclohexadiene. A red solution resulted. The solution became warm, and the color was discharged completely within about 15 min. The solid mass obtained on cooling was taken up in tetrahydrofuran, and the solution was evaporated at the water pump. Recrystallization of the residue from boiling cyclohexane gave 2.2 g (80%) of colorless crystals that sublimed at *ca.* 120–130°; mp 233° (sealed capillary). *Anal.* Calcd for $C_{12}H_8F_6N_2$: C, 48.99; H, 2.74; F, 38.76; N, 9.53. Found: C, 48.81; H, 3.42; F, 38.51; N, 9.46.

The infrared absorption spectrum of the product was consistent with the assigned structure, showing CH at 3.36 and 3.45 μ, $=$CH shoulder at 3.3 μ, weak CN at 4.43 μ, weak $C{=}C$ at 6.11 μ, and strong CF at 8–8.5 μ. The *trans* configuration of the cyano and trifluoromethyl groups was established from the fluorine nmr spectrum that exhibited two singlet resonances at −1.51 and −0.10 ppm of *equal* intensity (see Discussion).

***cis*-2,3-Bis(trifluoromethyl)-2,3-dicyanobicyclo[2.2.2]oct-5-ene (VIa or VIb).** *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (0.54 g) was mixed with 0.25 g of 1,3-cyclohexadiene. An exothermic reaction resulted, and the deep red solution decolorized within about 2 min. The solid that formed subsequently was recrystallized once from boiling cyclohexane to give 0.5 g (69%) of the pure adduct, mp 223–224° (sealed capillary). *Anal.* Calcd for $C_{12}H_8F_6N_2$: C, 48.99; H, 2.74; F, 38.76; N, 9.53. Found: C, 49.99; H, 2.89; F, 38.57; N, 9.26.

The infrared spectrum exhibited the general characteristic absorptions described above for the isomeric bicyclooctene V. The fluorine nmr spectrum was a singlet resonance at −4.38 ppm indicating that only one of the two possible stereoisomers (VIa or VIb) was formed (see Discussion).

1,2-Bis(trifluoromethyl)-1,2-dicyano-3-ethoxycyclobutanes. A. *trans* Mixture (VIIa + VIIb; X = OCH_2CH_3) from *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and Ethyl Vinyl Ether. A

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[21] Boiling and melting points are uncorrected. Fluorine nuclear magnetic resonance spectra were obtained with Varian Associates high-resolution nmr spectrometers and associate electromagnets operating at 40 and 56.4 mc/sec. Spectra were calibrated in terms of displacements in parts per million (ppm) from the F^{19} resonance of 1,2-difluoro-1,1,2,2-tetrachloroethane. Negative frequency displacements are for resonances occurring at lower field than the reference. The measurements are approximate and were obtained *via* a 152-cps scale set up between the reference standard and 1,1,1,2-tetrachloro-2,2-difluoroethane. Proton resonance spectra were obtained with a Varian Associates A-60 spectrometer. Spectra were calibrated in terms of lower field displacement in ppm from the proton resonance of tetramethylsilane used as an external reference.

[22] S. Proskow, U. S. Patent 3,133,115 (1964).

4.5-g sample of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene in a vial was treated with 2.5 ml of ethyl vinyl ether. In about 0.75 hr the yellow color of the solution faded completely. The crude product was then distilled *in vacuo* to give 4.5 g (75%) of a colorless, somewhat viscous liquid, bp 48° (0.2 mm), $n^{24.5}\text{D}$ 1.3806. *Anal.* Calcd for $C_{10}H_8F_6N_2O$: C, 41.96; H, 2.82; F, 39.83; N, 9.79. Found: C, 42.34; H, 2.81; F, 40.42; N, 9.52.

The infrared spectrum of the purified product (mixture) showed saturated CH (3.33, 3.40 μ), unconjugated CN (4.43 μ, w), strong CF (8-μ region) absorption, and no evidence of unsaturation in the double-bond stretching region. The proton nmr spectrum was consistent with the cyclobutane structures as determined from the resonances illustrated in Figure 2. Since the fluorine nmr spectrum of the distilled product was essentially like that of the crude product illustrated in Figure 1, the original isomer ratio of 1:2.5 was unaffected by the distillation.

Separation of the isomers by vapor phase chromatography was carried out analytically on a sample of the crude, undistilled mixture. A 1 × 0.25 in. o.d. stainless steel column packed with 20% by weight of bis(2-ethylhexyl) sebacate supported on 60–80 mesh Firebrick was operated at 165° oven temperature with preheater at 230° and helium flow rate at 45 cc/min (measured at the outlet). The isomers eluted at 7.0 and 8.3 min from injection, and no other peaks were found in the isomer region of the chromatogram. From the areas under the respective peaks, the isomer ratio was found to be *ca.* 1:3.

Similar conditions were used for the preparative vapor chromatography of the crude mixture. The fraction corresponding to the isomer having the above retention time of 7.0 min had two equal-intensity fluorine nmr bands coinciding with the bands at +2.43 and +3.91 ppm in the original mixture (*cf.* Figure 1), and only very weak bands due to the other isomer. The fraction corresponding to the isomer having the above retention time of 8.3 min had major fluorine bands at −0.13 and +5.19 ppm (*cf.* Figure 1), but appreciably strong bands due to the 7.0-min isomer were also evident. The infrared and proton nmr spectra of the individual fractions could be summed up in terms of the respective spectra of the original mixture.

B. *cis* Mixture (VIIIa + VIIIb; X = OCH_2CH_3) from *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and Ethyl Vinyl Ether. *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (4.23 g) was treated with 3 ml of ethyl vinyl ether by the same procedure (see above) used to prepare the *trans* mixture of cyclobutanes. The time of reaction was 3 min, and there was obtained on distillation *in vacuo* 4.45 g (79%) of colorless, slightly viscous liquid, bp 50–51° (0.6 mm), $n^{25.2}\text{D}$ 1.3788. *Anal.* Calcd for $C_{10}H_8F_6N_2O$: C, 41.96; H, 2.82; F, 39.83; N, 9.79. Found: C, 42.62; H, 3.10; F, 39.72; N, 9.92.

The infrared absorption spectrum of the distilled product was in agreement with the assigned structures. It had characteristic absorptions similar to those exhibited by the *trans* mixture above, and the over-all spectrum suggested an isomeric relationship. The fluorine nmr spectrum of the undistilled product displayed two strong quartets of equal areas centered at −3.74 and +2.76 ppm (J = 12 cps). This clearly established the presence of one cyclobutane isomer. The two quartets of the second isomer were weak and centered at about +1.30 and +2.12 ppm (J = 10 cps). Since one quartet was partially obscured by the strong quartet centered at +2.76 ppm and the other appeared somewhat like a triplet, chromatography was employed to establish this conclusively (see below). The approximate proportion of the two isomers as determined by integration of the peak areas centered at −3.74 and +1.30 ppm was 1:13. No marked differences were noted when the spectra of distilled and undistilled product were compared. The proton nmr spectrum was similar to that obtained for the *trans*-cyclobutane mixture with the exception that the spectrum appeared to be that of a single compound (*cf.* Figure 2).

Vapor chromatographic analysis was carried out on analytical and preparative stainless steel columns employing the same packing and conditions described above for the *trans* mixture. The data were obtained for crude reaction products that contained small amounts of the *trans* mixture of cyclobutanes. Two peaks appeared in the isomer region of the chromatogram. The small, first peak which eluted at 7.2 min contained the bulk of the *trans* mixture of cyclobutanes. This was verified by infrared and nmr (proton and fluorine) spectroscopy. The second peak, which comprised the bulk of the sample, eluted at 9.3 min and was found to contain both components of the *cis* mixture. However, by collecting fractions on the far side of the 9.3-min peak, it was possible to obtain samples where the isomer ratio was changed to approximately 1:1. The fluorine nmr spectrum in this case showed clearly that the multiplet centered at +1.30 ppm was truly a quadruplet and that its partner (quadruplet centered at +2.12 ppm) was semisuperimposed on one of the quadruplets (centered at +2.76 ppm) belonging to the other isomer. The infrared and proton nmr spectra were similar to those obtained for the starting material.

1,2-Bis(trifluoromethyl)-1,2-dicyano-3-(*t*-butylthio)cyclobutanes. A. *trans* Mixture (VIIa + VIIb; X = $SCMe_3$) from *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *t*-Butyl Vinyl Sulfide. A solution of 1.16 g of *t*-butyl vinyl sulfide in 5 ml of methylene chloride was treated, at 25°, with 2.14 g of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene. About 1 hr later, when the red-orange color had faded completely, the solution was evaporated to dryness *in vacuo* at the water pump.

The residual, oily solid exhibited two strong fluorine bands of equal intensity and two weak bands of equal intensity as illustrated in Figure 3a. The isomer ratio of 1:4.6 was obtained by integration of the areas under the four resonances. The proton nmr spectrum did not indicate the presence of two components, but was like that (see below) obtained for one of the pure isomers.

For purification, the crude product was dissolved in a minimum volume of pentane at room temperature, and the solution was then filtered and cooled gradually to −80°. The crystals that were collected by filtration were submitted to a second, similar recrystallization. There was obtained 2.0 g (61%) of material melting at 53–54°. The melting behavior remained unchanged after further recrystallization. *Anal.* Calcd for $C_{12}H_{12}F_6N_2S$: C, 43.63; H, 3.66; F, 34.51; N, 8.84; S, 9.71. Found: C, 44.09; H, 3.85; F, 34.68; N, 8.95; S, 9.59.

The purified product was identified, by fluorine nmr spectroscopy, as that single isomer (VIIa *or* VIIb; X = $SCMe_3$) which exhibits two equal-area bands at +1.90 and +3.21 ppm (*cf.* Figure 3a). Its infrared spectrum exhibited saturated CH (3.35, 3.45, and 3.5 μ), unconjugated CN (w, 4.45 μ), and strong CF (8-μ region) absorption. The proton nmr spectrum showed a singlet for the *t*-butylthio group at 1.38 ppm (area 9) as well as the spin–spin coupling pattern for an ABX system. The X part of the pattern appeared as three lines of total area 1 centered at 4.13 ppm ($J_{AX} + J_{BX}$ = 20 cps) and the AB part as eight lines (two quartets) of total area 2 centered at 2.92 ppm (J_{AB} = 13 cps).[23]

Analytical and preparative vapor chromatography of the crude reaction product was carried out using the same columns and conditions reported above for the separation of the 3-ethoxycyclobutanes. Analytically, the least abundant isomer eluted at 20.0 min and the most abundant isomer at 25.4 min; isomer ratio from peak areas was 1:4.8. The preparative scale work gave samples of the individual isomers having about 5–10% of the "other" isomer. This was readily established from the fluorine nmr spectra which gave, in each case, two equal-area singlets (predominantly) coinciding with the respective pairs in the original mixture. The proton nmr and infrared spectra of the individual fractions were in accord with the cyclobutane structure.

B. *cis* Mixture (VIIIa + VIIIb; X = $SCMe_3$) from *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *t*-Butyl Vinyl Sulfide. *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (2.12 g) was added to a solution of 2.3 g of *t*-butyl vinyl sulfide in 40 ml of methylene chloride. The initial red-orange color of the solution faded completely after 3 hr at room temperature. Evaporation of the solution to dryness *in vacuo* gave the crude product as a colorless, crystalline residue.

This residue was shown, by fluorine nmr spectroscopy, to consist of a mixture of two cyclobutane isomers in the proportion 1:9.6. The spectrum is illustrated by Figure 3b. One isomer is defined by the two strong quartets of equal area centered at −4.74 and +1.86 ppm (J = 11 cps); the other by very weak quartets centered at +0.53 and +1.37 ppm (J = 11 cps). As can be seen from the illustration, the pair of weak quartets are not clearly visible. The true nature of this absorption as two quartets of equal area was established after vapor chromatography of the mixture (see below). The above isomer proportion was determined by comparing the areas under the isolated quartets centered at −4.74 and +0.53 ppm.

The gross proton nmr spectrum of the mixture, which was

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[23] (a) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 6; (b) J. D. Roberts, "An Introduction to the Analysis of Spin–Spin Splitting in High-Resolution Nuclear Magnetic Resonance," W. A. Benjamin, Inc., New York, N. Y., 1961, Chapter 3.

essentially like that of the purified abundant isomer (see below), consisted of multiplet resonances centered at 4.42 (area 1, CH) and 2.92 ppm (area 2, CH_2), and a singlet resonance at 1.45 ppm (area 9, $SCMe_3$). However, the spin–spin splitting pattern between the CH and CH_2 groups was that of a typical AB_2 system ($J/\Delta\nu_{AB}$ ~0.33)[8] rather than an ABX system as might be expected. This spectrum, nevertheless, would be consistent with the cyclobutane structure if it so happened that the protons on the methylene group had identical chemical shifts (see Discussion). A very weak singlet peak at 1.38 ppm was assigned to the $SCMe_3$ group of the least abundant isomer.

Purification of the abundant isomer was readily accomplished by fractional crystallization of the mixture from pentane (cool to −80°). The pure crystals that were collected after one recrystallization weighed 2.0 g (61%) and had mp 84–86°. The melting behavior remained unchanged after another recrystallization. *Anal.* Calcd for $C_{12}H_{12}F_6N_2S$: C, 43.63; H, 3.66; F, 34.51; N, 8.48; S, 9.72. Found: C, 44.27; H, 3.72; F, 34.47; N, 8.45; S, 10.21.

The proton and fluorine nmr spectra of this purified isomer (VIIIa *or* VIIIb; X = $SCMe_3$) were similar to those described above for the mixture, but the spectra lacked the resonances attributable to the other least abundant isomer. The infrared spectrum had characteristic absorptions at 3.35, 3.43, and 3.46 (saturated CH), 4.43 (unconjugated CN), and 8 μ (CF). A sample of the purified product which had been sublimed at 60° (1 mm) had mp 84–86° and an infrared spectrum identical with that of the starting, recrystallized material.

The crude reaction mixture was vapor chromatographed using the same columns and procedure (see above) described for the other separations. The analytical column gave the abundant isomer at an elution time of 20.8 min and the least abundant isomer at an elution time of 26.2 min. From the areas under the peaks, the isomer ratio was 1:7.2. The preparative scale work gave the abundant product with nmr (fluorine and proton) and infrared spectra like those of the purified crystalline product above. In the case of the least abundant isomer, which was obtained essentially free from isomer contamination, the fluorine nmr spectrum clearly exhibited two quartets of equal area that are typical of an A_3B_3 type pattern. These quartets coincided with the partially obscured, weak resonances centered at +0.53 and +1.37 ppm in the original mixture. The infrared spectrum was consistent with the cyclobutane structure, and the proton nmr spectrum was similar to that obtained for the purified, *trans*-derived cyclobutane of mp 53–54°. The least abundant isomer thus displays an ABX splitting pattern for the CH and CH_2 groups in contrast to the AB_2 type pattern observed for the same groups of the abundant isomer.

1,2-Bis(trifluoromethyl)-1,2-dicyano-3-*p*-anisylcyclobutanes. A. *trans* Mixture (VIIa + VIIb; X = *p*-$CH_3OC_6H_4$) from *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *p*-Methoxystyrene. When the preparation of this adduct mixture is conducted in solvents having low polarity, there is obtained chiefly poly(*p*-methoxystyrene) because the rate of polymerization of the *p*-methoxystyrene exceeds the rate of adduct formation. Good yields of the adduct mixture are obtained, however, if the rate of adduct formation is enhanced by employing nitromethane as the solvent. A solution of 3.0 g of *p*-methoxystyrene in 10 ml of nitromethane was mixed at room temperature with a solution of 4.28 g of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene in 10 ml of nitromethane. The resulting solution became deep red, and the color gradually faded to a faint orange after about 1 hr. The solvent was then removed by vacuum evaporation. Distillation of the residual viscous liquid through a short path at 1-mm pressure gave 4.3 g (62%) of product, bp *ca.* 150°, $n^{25}D$ 1.4683. *Anal.* Calcd for $C_{15}H_{10}F_6N_2O$: C, 51.74; H, 2.89; F, 32.73; N, 8.04. Found: C, 51.97; H, 3.09; F, 32.75; N, 8.74.

The distilled product has a fluorine nmr spectrum consistent with a mixture of two cyclobutane diastereomers. The abundant isomer is identified by two equal-area singlets at +1.78 and +2.80 ppm; the other by two equal-area singlets at −0.95 and +4.78 ppm. The proportion of isomers as determined by integration of the fluorine nmr spectrum of a sample of the crude, undistilled material was 1:3.2.

The proton nmr spectrum shows aromatic H (multiplet of area 4 centered at 7.08 ppm), CH_3O (singlet of area 3 at 3.72 ppm), CH (multiplet of area 1 centered at 4.38 ppm), and CH_2 (multiplet of area 2 centered at 3.04 ppm). Although the spin–spin splitting between the CH and CH_2 groups is not well defined, it appears grossly like that of an ABX-type pattern. Infrared absorptions at 3.31 (=CH), 3.39 and 3.51 (saturated CH), 4.44 (CN), 6.17, 6.30, and 6.58 (aromatic C=C), and 8-μ region (CF) are as expected for the assigned cyclobutane structures.

B. *cis* Mixture (VIIIa + VIIIb; X = *p*-$CH_3OC_6H_4$) from *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *p*-Methoxystyrene. *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (1.07 g) was treated with 0.75 g of *p*-methoxystyrene by the same procedure (see above) used for the *trans* isomer. Distillation of the crude product through a short path at 1-mm pressure gave 1.1 g (63%) of the *cis* mixture of cyclobutanes as a colorless, viscous liquid, bp *ca.* 150°, $n^{24.5}D$ 1.4680. *Anal.* Calcd for $C_{15}H_{10}F_6N_2O$: C, 51.74; H, 2.89; F, 32.73; N, 8.04. Found: C, 51.78; H, 2.94; F, 32.73; N, 8.17.

The infrared and proton nmr spectra of the distilled product were closely similar to those obtained above for the *trans* mixture of isomers. However, the fluorine nmr spectrum exhibited two equal-area pairs of quadruplets. The quadruplets of the abundant isomer are centered at −4.26 and +2.33 ppm (J = 12 cps); those of ppm the other at −5.33 and −1.35 ppm (J = 10 cps). An isomer ratio of 1:11.5 was obtained by integration of the spectrum of a sample of the crude, undistilled material.

1,2-Bis(trifluoromethyl)-1,2-dicyano-3-(2′-oxopyrrolidinyl)cyclobutane. N-Vinyl-2-pyrrolidone (1.11 g) was added to a solution of 2.14 g of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene in 5 ml of methylene chloride, and the resulting yellow solution was allowed to stand at room temperature overnight. The oily crude product, which was obtained by evaporation of the solvent, exhibited two strong singlet bands of equal intensity and two weak bands of equal intensity in the fluorine nmr spectrum. This is consistent with the formation of two cyclobutane diastereomers (VIIa + VIIb; X = C_4H_6NO) by a stereospecific cycloaddition process.

Purification of the crude product by recrystallization was difficult because of the presence of polymeric impurities. After repeated recrystallization from boiling cyclohexane, a product, mp 92–95°, was obtained. This had the expected infrared absorption bands for CH (3.35, 3.45 μ), CN (4.45 μ), lactam CO (5.9 μ), and CF (8-μ region). From the analysis, the product appeared still to contain impurities. The yield was poor. *Anal.* Calcd for $C_{12}H_9F_6N_3O$: C, 44.31; H, 2.79; F, 35.05; N, 12.92. Found: C, 45.06; H, 2.93; F, 34.01; N, 12.96.

1,2-Bis(trifluoromethyl)-1,2-dicyano-3-propoxy-4-methylcyclobutanes. A. Cyclobutane Mixture (IX + X) from *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *trans*-Propenyl *n*-Propyl Ether. *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene (3.64 g) was added at room temperature to a solution of 1.7 g of *trans*-propenyl *n*-propyl ether in 10 ml of acetonitrile. When the yellow solution decolorized, the solvent was evaporated. Distillation of the residual liquid *in vacuo* gave 3.6 g (67%) of colorless product, bp 70–72° (0.6 mm), $n^{24.5}D$ 1.3885. *Anal.* Calcd for $C_{12}H_{12}F_6N_2O$: C, 45.86; H, 3.85; F, 36.28; N, 8.92. Found: C, 46.17; H, 3.96; F, 35.98; N, 9.20.

A sample of the distilled product gave an infrared spectrum showing CH at 3.35, 3.4, and 3.45 μ, CN at 4.42 μ, and strong CF at 8 μ. The proton nmr spectrum, which had much overlapping of resonances, was not well enough defined to be useful diagnostically. However, the general regions of absorptions were in predictable locations.

The fluorine nmr spectrum was consistent with the formation of two diastereomeric cyclobutanes. It had two equal-area singlets at −1.12 and −0.67 ppm (abundant isomer X) and two equal-area singlets at +1.16 and +2.27 ppm (isomer IX). Integration of these resonances for a sample of the crude, undistilled mixture gave an isomer ratio of 1:2.1.

B. Cyclobutane Mixture (XI + XII + XVI) from *trans*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *cis*-Propenyl *n*-Propyl Ether. A 2.0-g portion of *cis*-propenyl *n*-propyl ether in 10 ml of acetonitrile was treated with 4.28 g of *trans*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene. After decolorization, the solvent was removed, and the residual liquid was distilled through a short path at reduced pressure. There was obtained 4.4 g (70%) of colorless liquid, bp 73–76° (0.7 mm), $n^{25}D$ 1.3890. *Anal.* Calcd for $C_{12}H_{12}F_6N_2O$: C, 45.86; H, 3.85; F, 36.28; N, 8.92. Found: C, 45.93; H, 4.30; F, 36.41; N, 9.25.

The distilled product had infrared and proton nmr spectra closely similar to the spectra obtained for the *trans/trans*-derived cyclobutanes (see A above). The fluorine nmr spectrum exhibited a pair of singlet resonances at −2.06 and +5.04 ppm (equal areas; isomer XII), a pair of skewed quadruplets centered at +1.10 and +2.17 ppm (equal areas, J = 12 cps; isomer XVI), and a weak pair of singlet resonances at −1.71 and +3.80 ppm (equal areas; isomer XI). The proportion of the three isomers formed in the reaction was found to be 7:9:1, respectively, by integrating the resonances for a sample of the crude, undistilled product.

C. Cyclobutane Mixture (XI + XII + XVI) from *cis*-1,2-Bis-(trifluoromethyl)-1,2-dicyanoethylene and *cis*-Propenyl *n*-Propyl Ether. A 0.21-g sample of *cis*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene was treated with 0.23 g of *cis*-propenyl *n*-propyl ether in 2 ml of methylene chloride. The solvent and excess reactant were removed *in vacuo* when the pale orange solution decolorized completely (*ca.* 6 days). The residual oily product was redissolved in fresh solvent to examine the fluorine nmr spectrum of the cyclobutane mixture.

The spectrum showed the same cyclobutane products (XI + XII + XVI) that were formed in the reaction of *trans*-fluorocyano olefin and *cis*-propenyl ether (see B above). The ratio of the isomers in this case was found to be XI:XII:XVI = 2.1:1.0:2.5. Similar results were obtained when the reaction was run neat and in ethyl acetate.

D. Cyclobutanes XIII or XIV from *cis*-1,2-Bis(trifluoromethyl)-1,2-dicyanoethylene and *trans*-Propenyl *n*-Propyl Ether. A solution of 0.23 g of *trans*-propenyl *n*-propyl ether in 2 ml of methylene chloride was mixed with 0.21 g of *cis*-1,2-bis(trifluoromethyl)-1,2-dicyanoethylene. After about 6 days, the product was isolated and analyzed by fluorine nmr spectroscopy as described previously (see C above). The spectrum exhibited a pair of quadruplets (equal area, $J = 12$ cps) at −4.36 and +1.14 ppm, establishing that only a single cyclobutane isomer, XIII or XIV, was formed.

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The Hydroxylation of Anisole by Hydrogen Peroxide in the Presence of Catalytic Amounts of Ferric Ion and Catechol. Scope, Requirements, and Kinetic Studies[1,2]

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Abstract: Anisole is hydroxylated by aqueous H_2O_2 when catalytic amounts of Fe(III) and an enediol catalyst, such as catechol, are present in solution. The scope and requirements for this reaction and its kinetics have been investigated in some detail and the results are reported here. It has been found that: Fe(III) cannot be replaced by Cr(III), Co(III), Zn(II), Mn(II), Al(III), or Mg(II), but Cu(II) may act as an inefficient catalyst; 1,2-dihydroxy or 1,4-dihydroxy aromatic compounds are catalysts, whereas monohydroxy or 1,3-dihydroxy aromatic compounds are not catalysts; the rate appears to depend on the concentration of H_2O_2 to the first power and the concentration of Fe(III) to the first power, but the reaction is inhibited by high concentrations of the enediol catalyst; the reaction rate is also decreased by high concentrations of the buffer and by the presence of organic solvents such as ether or acetone. The kinetic results do not seem consistent with any of a number of free-radical chain mechanisms. The results suggest that the hydroxylating agent is a complex of Fe(III), the enediol, and H_2O_2.

In 1954, Udenfriend and co-workers[4] reported that aromatic compounds are hydroxylated by O_2 or H_2O_2 when Fe(II), ascorbic acid, and ethylenediaminetetracetic acid (EDTA) are present in a buffered solution around neutral pH. Since this system (Udenfriend system) bears some resemblance to enzymic hydroxylations of aromatic compounds by O_2 or H_2O_2, it has been the subject of several investigations.[5–7] Although most of the early investigators concluded that the hydroxylated products obtained with this system are the same when either O_2 or H_2O_2 is used as the oxidant, it is now quite clear that different products are obtained with these two oxidants.[2,6,7] There is now strong evidence that the hydroxyl radical (HO·) is the actual hydroxylating agent when H_2O_2 is the oxidizing agent in the Udenfriend system.[2,6] It has recently been proposed that the hydroxylating agent, when O_2 is present in the Udenfriend system, is a complex of O_2, ascorbic acid, and Fe(II), and this complex is capable of transferring an oxygen atom to the aromatic substrate.[8]

When we began our investigation of the mechanism of the Udenfriend oxidations the above conclusions were not evident. In an attempt to find a version of the Udenfriend system better suited to a study of the mechanism, we replaced ascorbic acid by other enediols and looked for hydroxylation of anisole by H_2O_2. Preliminary studies indicated that, with catechol or hydroquinone as catalyst, a hydroxylating agent different from that in either of the Udenfriend reactions (O_2 or H_2O_2) was involved.[2] Since the system bears a resemblance to some enzyme reactions we have looked at its characteristics more thoroughly. This paper presents results on the scope and kinetics of the reaction and the following paper reports product studies.[9]

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(2) A preliminary communication of part of this work has appeared: G. A. Hamilton and J. P. Friedman, *J. Am. Chem. Soc.*, **85**, 1008 (1963).

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