Chemistry of Cyclobutene-1,2-dicarbonitrile. 1. Solvolytic and Michael Processes

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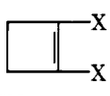
Quenching sulfuric acid solutions of cyclobutene-1,2-dicarbonitrile (1) with water or with methanol yields the diamide 2 and the dimethyl ester 3, respectively, in excellent yields. Prolonged treatment of 1 with dilute sulfuric acid yields the diacid 4. Treatment of 1 with 2-methyl-2-butene in the presence of sulfuric acid gives the Ritter reaction product 5. The dinitrile 1 reacts with secondary amines to give the usual Michael addition products; these undergo facile thermal elimination of hydrogen cyanide to give cyanoenamines, 2-aminocyclobutenecarbonitriles 9 and 10. The latter, upon hydrolysis, give 2-cyanocyclobutanone (12). With basic methanol, 1 yields the expected ethers as minor products, with the major products being imidate esters. The dinitrile 1 undergoes double-bond addition reactions with chlorine and hydrogen chloride; the latter reagent yields secondary products via reaction at the nitrile groups.

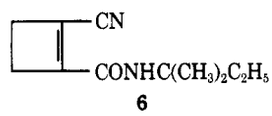
Although the synthesis of cyclobutene-1,2-dicarbonitrile (1) was first reported several years ago,[1] its chemistry has remained virtually unknown. With the recent development of a more convenient synthesis,[2,3] reports concerning the reactions of 1 and related materials have begun to appear.[2,4] For some time we have been investigating the often unique chemistry of this cyclic dinitrile, and wish to report here some of our findings, viz., those concerning solvolysis reactions, ionic additions to the double bond, and processes which involve reactions at both the double bond and nitrile groups.

Dinitrile 1 dissolves immediately in 95% sulfuric acid, giving a colorless solution. On a small scale, this occurs with a modest exotherm; however, on a larger scale (with more than 200 mmol or so of 1), the process may be controlled only by the rather unusual sequence of slow addition of 1 to excess acid with provision for some cooling. Under "normal" conditions (i.e., addition of acid to 1, even slowly and over a prolonged period) on a large scale, after an induction period a strongly exothermic reaction invariably occurred that could not be controlled. Addition of sulfuric acid solutions of 1 to ice water or to methanol afforded excellent yields of cyclobutene-1,2-dicarboxamide (2) and dimethyl cyclobutene-1,2-dicarboxylate (3), respectively. Complete hydrolysis of 1 occurred slowly with hot, dilute (12 N) sulfuric acid, giving cyclobutene-1,2-dicarboxylic acid (4).

It might have been anticipated that the imide would have been formed rather than the diamide 2 in this sequence, and, indeed the imide is formed by a similar treatment of cyclohexene-1,2-dicarbonitrile and *cis,cis*-1,5-cyclooctadiene-1,2,5,6-tetracarbonitrile.[3] However, the imide in this system, a bicyclo[3.2.0]hept-$1^{1,5}$-ene, is apparently too strained for normal existence.[5] On the other hand, solvolysis of derivatives of *cis*-cyclobutane-1,2-dicarbonitrile does result in the formation of imides.[3] Since the dinitrile 1 is thus incapable of forming an imide, it was possible for a normal Ritter process to occur. Thus, reaction of 1 with 2-methyl-2-butene in 96% sulfuric acid gave *N,N'*-bis(1,1-dimethylpropyl)cyclobutene-1,2-dicarboxamide (5), as well as a little of the cyano amide 6.



1, X = CN
2, X = $CONH_2$
3, X = CO_2CH_3
4, X = CO_2H
5, X = $CONHC(CH_3)_2C_2H_5$



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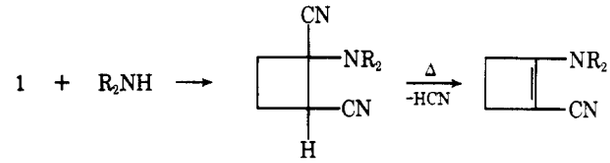
A number of nucleophilic reagents readily add to the double bond system of 1. Since it was found that, e.g., cyclohexene-1,2-dicarbonitrile undergoes no comparable reactions,[3] the reactivity of 1 may be ascribed both to the strong activation of the double bond by the cyano groups and the modest strain present in the cyclobutene system which is relieved upon going to the saturated derivatives. A facile reaction occurred with the secondary amines piperidine and dimethylamine to give the simple adducts 7 and, though not isolated, by analogy, 8, 1-substituted aminocyclobutane-1,2-dicarbonitrile. With piperidine, ^1H NMR monitoring demonstrated that the reaction to 7 was complete within a few hours at room temperature. While the simple adduct 7 (and presumably 8) was reasonably stable at room temperature (vide infra), facile elimination of hydrogen cyanide occurred upon distillation to yield the cyano enamine 9 (and 10), 2-(1-piperidino)cyclobutene-1-carbonitrile. Formation of 9 and 10 was demonstrated by development of an intense enamine absorption in the infrared region at about 1630 cm^{-1} (arising from the strongly polarized double bond) with a concurrent shift of the nitrile absorption to about 2180 cm^{-1}.



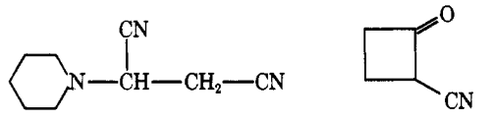
7, R = $-(CH_2)_5-$ 9, R = $-(CH_2)_5-$
8, R = CH_3 10, R = CH_3

In a related system, 3 reportedly underwent smooth addition of diethylamine to give a thermally stable ester analogue of 8.[6] On the other hand, facile elimination processes leading to cyclobutenes related to 9 and 10 have been noted in other work.[7] It is probable that the major determinants in these systems are the presence of a good leaving group (cyanide in the present case, mercaptan in the previous work[7]) and the establishment of a resonance-stabilized, highly dipolar cyano enamine, thus overcoming any reluctance to reestablish the strained cyclobutene system.

To gain further insight into the present elimination process, the relative thermal stability of the acyclic analogue of 7, 2-(1-piperidino)succinonitrile[8] (11), was noted qualitatively. It began to lose hydrogen cyanide at a perceptible rate at about 140–150 °C.[9] In contrast, formation of 9 (or 10) from 7 (or 8) proceeded at 100 °C or less; indeed, 7 exhibited some instability even at room temperature, since stored samples liquefied and developed the odor of hydrogen cyanide.

Although cyano enamines related to 9 and 10 have been available for a number of years,[7,10] the facile preparation described here represents probably the most convenient synthesis for the otherwise unsubstituted cyclobutene cyano

enamines. Very little of the chemistry of **9** or **10** was noted. However, it was found that hydrolysis of **9** under mild conditions gave the elusive[11] 2-cyanocyclobutanone (**12**) (of limited stability), in excellent yields.

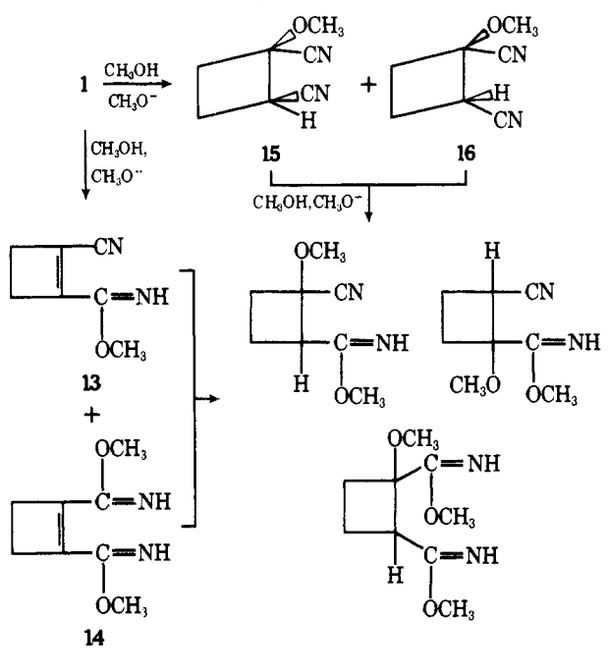


11 **12**

In contrast to the straightforward reaction of **1** with secondary amines, condensation with primary amines was more complex.[12] Aniline itself was unreactive. However, *tert*-butylamine and 1,1-dimethylhydrazine did undergo very slow reaction (NMR and VPC monitoring showed that reaction was only 50–60% complete in several weeks), but we were unable to isolate discrete reaction products.

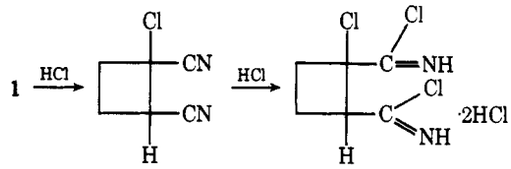
The reaction of **1** with methanol in the presence of sodium methylate or a quaternary ammonium hydroxide was also complex. Products arising from reaction at several positions were observed, i.e., the double bond, one or both of the cyano groups, and all of these positions. The major products were the mono- and diimidate esters **13** and **14**, with small amounts of the simple addition products (*E*)- and (*Z*)-1-methoxycyclobutane-1,2-dicarbonitrile (**15** and **16**) being isolated (earlier workers noted that the ester **3** is inert toward alkoxide[14]). Other products isolated included imidate esters (from spectral data) arising from **15** and **16**, but of otherwise undetermined structure (see Scheme I). Under identical conditions, **1** failed to undergo reaction with *tert*-butyl alcohol.

Scheme I



13 + **14**

Cyclobutene **1** underwent slow reaction with chlorine at room temperature to give a 90:10 mixture of *trans*- and *cis*-1,2-dichlorocyclobutane-1,2-dicarbonitrile.[15] Monitoring the process by VPC demonstrated that this ratio remained constant throughout the reaction period. The addition of hydrogen chloride to **1**, although somewhat faster than chlorine (VPC and NMR indicated complete reaction in a few hours), was complicated by a secondary reaction involving both cyano groups. While no attempt was made to distinguish between them, the (VPC) ratio of the two simple adducts, *cis*- and *trans*-1-chlorocyclobutane-1,2-dicarbonitrile, was about 2:1. As a by-product, an appreciable amount (30–35 wt % yield) of an organic salt (containing no cyano groups) was formed. Analyses of this moisture-sensitive salt were ambiguous, but suggested that formation of imidoyl chlorides such as **17** or **18**



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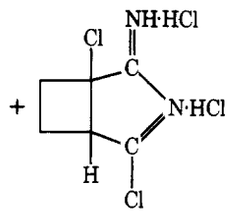

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might be involved. The product was very soluble (with a strong exotherm) in water, yielding copious amounts of hydrogen chloride and ammonium chloride (about 25 wt %) as the inorganic products.

Experimental Section[16]

Cyclobutene-1,2-dicarboxamide (2). Sulfuric acid (96%, 75 mL) was stirred in a water bath at ca. 25 °C, maintaining this temperature by the addition of a few pieces of ice as necessary, while 30 g of cyclobutene-1,2-dicarbonitrile (**1**) was added dropwise over a period of 4 h. The pale yellow solution, after being stored at room temperature for a day or so, was poured over 50 g of crushed ice. The resulting white solid was filtered, washed well with cold water, and recrystallized from 1500 mL of boiling water (Norit) to give 26.0 g (65%) of **2**: mp 238 °C dec (ammonia liberated) (lit.[2] mp 250–252 °C); IR (KBr) 3420, 3220, 1680, 1640 cm^{-1}. Anal. Calcd for $C_6H_8N_2O_2$: C, 51.43; H, 5.75; N, 19.99. Found: C, 51.19; H, 5.74; N, 19.80.

Dimethyl Cyclobutene-1,2-dicarboxylate (3). A sulfuric acid solution of **1** (30 g), prepared as in the preparation of **2**, was poured slowly into 1 L of methanol. The solution was heated under reflux for 48 h, and the methanol then removed under aspirator pressure. The residual oil, taken up in ice water, was extracted three times with ether. The combined extracts were washed three times with water, dried over magnesium sulfate, and stripped to give 30 g of a solid. Recrystallization from ether (100 mL) afforded 13.9 g (first crop) of **3** as snow-white crystals: mp 42–43 °C (lit.[2] mp 43.5–44 °C) (further crops of **3** were obtained from the ether filtrate, and by further extraction of the water solution with chloroform, giving a total yield of crystallized **3**, of varying purity, of about 35 g); IR (KBr) 1730 (C=O), 1640 (C=C), 1220 cm^{-1}. Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 55.98; H, 5.66.[17]

Cyclobutene-1,2-dicarboxylic Acid (4). A mixture of 20 g of **1**, 100 mL of water, and 50 mL of 96% sulfuric acid was stirred on a steam bath for 20 h. The resulting hot solution, after treating with Norit, was cooled to give the acid **4** as a white, crystalline solid. The aqueous solution was extracted with methylene chloride. Removal of the solvent from the extracts gave more of the acid **4** (total yield of 8 g). Recrystallization from ether gave **4** as white crystals: mp 176–178 °C (gaseous dec) (lit.[2] mp 183–185 °C); IR (KBr) 2500–3000, 1710, 1590, 1265, 1235 cm^{-1}; ^1H NMR (CF_3COCF_3·D_2O) δ 5.63 (s, CO_2H), 2.82 (CH_2). Anal. Calcd for $C_6H_8O_4$: C, 50.71; H, 4.26. Found: C, 50.65; H, 4.08.

***N,N'*-Bis(1,1-dimethylpropyl)cyclobutene-1,2-dicarboxamide (5).** A solution of 5.2 g (0.05 mol) of **1** in 25 mL of acetic acid and 10 mL of 96% sulfuric acid, after being allowed to stand at room temperature for 30 min, was stirred with cooling in a water bath (25–30 °C) while 7.0 g (0.10 mol) of 2-methyl-2-butene was slowly added. After being allowed to stand at room temperature overnight, the solution was poured into ice. The resulting semisolid was extracted into ether, and the ether solution was washed with water, aqueous bicarbonate, and again with water. Removal of the ether gave ca. 8 g of an oil. Recrystallization from hexane gave 5.85 g of a low-melting solid. This was taken up in ether, removing 0.33 g of insoluble **2-cyano-*N*-(1,1-dimethylpropyl)cyclobutene-1-carboxamide (6)**: mp 134–136 °C (from ether); IR (KBr) 3340 (NH), 2230 (CN), 1635, 1540 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.6 (broad s, NH, 1), 2.74 (s, ring CH_2, 4),

Table I. Spectral Properties of Methanol Adducts of 1

Adduct	IR, cm^{-1} [a]	NMR, δ [b] ^1H	NMR, δ [b] ^{13}C	Mass spectrum, m/e [c] (rel abundance)
13	3285 (=NH)	3.84 (CH_3, s, 3)	164 (C=N)	136 (100)
	2230 (CN)	2.75 (CH_2, s, 4)	114 (C≡N)	121 (55)
	1650 (C=C)		53.2 (OCH_3)	105 (52)
	1595 (C=N)		28.7 (CH_2)	78 (83)
	1093 (C-O-C)		28.2 (CH_2)	58 (40)
14	3220, 3305 (=NH) [d]	8.18 (NH, 2)	163 (C=N)	Like 13
	1630 (C=C)	3.82 (CH_3, s, 6)	138.1 (C=C)	
	1595, 1600 (C=N)	2.55 (CH_2, s, 4)	52.8 (OCH_3)	
	1095 (C-O-C)		26.2 (CH_2)	
15	2280 (CN)	3.65 (CH, m, 1)		136 (0.4)
	1150 (ether)	3.54 (CH_3, s, 3)		108 (72)
		2.54 (CH_2, m, 4)		83 (100)
16	2280 (CN)	3.47 (CH_3, s, 3)		Like 15
	1150 (ether)	3.3 (CH, m, 1)		
		2.4 (CH_2, m, 4)		

[a] KBr pellet. [b] $CDCl_3$, Me_4Si as internal standard. [c] Major fragmentations only. [d] Became a single peak in CCl_4, 3320 cm^{-1}.

1.80 (quartet, chain CH_2, 2), 1.36 (s, CH_3, 6), 0.86 ppm (t, CH_3, 3). Anal. Calcd for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.58; H, 7.93; N, 13.92.[17]

After removal of insoluble **6**, the ether solution was diluted with hexane and chilled at −70 °C to give 4.80 g of **5**. Recrystallization once from ether and once from a mixture of ether and hexane afforded **5** as off-white crystals: mp 99–101 °C; IR (KBr) 3300 (NH), 1670, 1630, 1590, 1540, 1210 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55 (s, NH, 2), 2.54 (s, ring CH_2, 4), 1.83 (quartet, chain CH_2, 4), 1.37 (s, CH_3, 12), 0.90 (t, CH_3, 6). Anal. Calcd for $C_{16}H_{28}N_2O_2$: C, 68.54; H, 10.06; N, 9.99. Found: C, 68.22; H, 9.56; N, 10.14.

1-(1-Piperidino)cyclobutane-1,2-dicarbonitrile (7). A solution of 10.4 g (0.1 mol) of **1** and 8.5 g (0.1 mol) of piperidine in 10 mL of carbon tetrachloride was allowed to stand under nitrogen in a refrigerator for 3 weeks. The solvent was removed in vacuo, and the residue was taken up in 50 mL of ether, discarding a small amount of insoluble material. Chilling of the ether solution for several days at −70 °C gave **7**, 3.0 g after two recrystallizations from ether in the same manner, as hard, ivory-colored crystals: mp 40–42 °C; IR (KBr) 2270 (CN), 1470, 805 cm^{-1}; ^{1}NMR ($CDCl_3$) δ 3.19 (m, CH, 1), 2.36 (m, CH_2N and ring CH_2, 8), 1.58 (m, CH_2, 6); mass spectrum m/e (rel intensity) 162 (46, M − HCN), 161 (44), 136 (64), 135 (48), 133 (16), 53 (>100), 52 (100) (many others). Anal. Calcd for $C_{11}H_{15}N_3$: C, 69.80; H, 7.99; N, 22.21. Found: C, 69.94; H, 7.47; N, 21.62.[17]

2-(1-Piperidino)cyclobutene-1-carbonitrile (9). A solution of 52 g (0.5 mol) of **1** in 300 mL of chloroform was stirred under nitrogen at 20 °C (water bath) while 42.5 g (0.5 mol) of piperidine in 100 mL of ether was added during 1 h. After the solution was allowed to stand at room temperature overnight and the solvent was removed, the product was distilled in vacuo through a 15-in. Vigreux column to give 4.0 g of unreacted **1** and then 65 g of **9**: bp 125 °C (0.4 mm); IR (neat) 2200 (CN), 1640 (C=C), 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (m, CH_2N, 4), 2.47 (s, ring CH_2, 4), 1.62 (m, CH_2, 6); mass spectrum m/e (rel intensity) 162 (78, M^+), 161 (100), 147 (19), 133 (30), 120 (31), 119 (48) (many others). Anal. Calcd for $C_{10}H_{14}N_2$: C, 74.04; H, 8.70; N, 17.26. Found: C, 73.59; H, 9.02; N, 17.08.[17]

2-Dimethylaminocyclobutene-1-carbonitrile (10). A solution of 52.0 g (0.5 mol) of **1** in 300 mL of ether was stirred while 25 g of dimethylamine was added through a gas dispersion tube over a 2–3-h period. The temperature quickly rose to 34 °C, remaining there throughout the remainder of the addition, and the solution rapidly darkened. Analysis (VPC) showed that the reaction was 83% complete when addition of amine was terminated. After the solution was allowed to stand at room temperature overnight, the ether was removed. The residual oil was distilled in vacuo through a 6-in. Vigreux column to give 75 g of a mixture of **8** (CN absorption at 2300 cm^{-1}) and **10**, bp 102 °C (1.5 mm) [lit.[7a] bp 105 °C (4 mm)]; this was redistilled at 10 mm to give **10**. Storage in the refrigerator caused solidification: mp ca. 8 °C; IR (neat) 2180 (CN), 1660 (C=C), 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.88 (s, CH_3, 6), 2.45 (m, CH_2, 4).

2-(1-Piperidino)succinonitrile (11) was prepared by the mixing of ethereal solutions of fumaronitrile and piperidine: mp 83–84 °C (lit.[8] mp 86–87 °C); IR (KBr) 2270 (CN), 1465, 1430, 1110, 895 cm^{-1}.

2-Cyanocyclobutanone (12). A solution of 17.5 g (0.108 mol) of the piperidino cyanoenamine **9** in 50 mL of chloroform was stirred vigorously at room temperature with 50 mL of 6 N hydrochloric acid. The reaction was monitored by VPC and was found to be essentially complete in 1 h. After 3 h, the organic layer was separated, washed twice with water (evaporation of the water solution gave piperidine hydrochloride), and then stripped under aspirator pressure. The residue, 12 g, was taken up in ether, removing 2.0 g of what was probably the hydrochloride of **9**:[18] mp 168–170 °C (from chloroform); IR (KBr) 2130 cm^{-1} (broad, strong, amine HCl). After removal of this insoluble salt, the ether solution was distilled in vacuo through a 6-in. Vigreux column to give 6.0 g of **12** as a colorless oil: bp 67 °C (0.5 mm); IR (neat) 2240 (CN), 1805 (C=O), 1070 cm^{-1}; ^1H NMR (neat) δ 4.32 (complex t, CH, 1), 1.8–3.5 (m, CH_2, 4). Anal. Calcd for C_5H_5NO: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.87; H, 5.39; N, 14.35. This cyano ketone **12** became viscous upon storage, and spectral analyses indicated the presence of nitrile, ketone, and acid groups (at 2240, 1805, and 3400 and 1730 cm^{-1}, respectively). Hydrolysis of the piperidino cyano enamine **9** (16.2 g) in ether (100 mL) with 6 N hydrochloric acid (50 mL) for an extended period showed (by VPC) rapid formation of **12** (100% in ~1 h), and then gradual conversion of this to (probably) cyanobutyric acid and glutaric acid; after 140 h, **12** and these other products were present in 14, 16, and 66% yields, respectively. Workup of the reaction mixture after 140 h afforded about 3.0 g of glutaric acid from each of the two phases: mp 89–99 °C (from ether and pentane); IR (KBr) 2500–3120 (strong, broad), 1730, 915 cm^{-1}; ^1H NMR (acetone-d_6) δ 9.21 (s, CO_2H, 2), 2.2–2.6 (m, CH_2, 4), 1.7–2.0 (m, CH_2, 2).

Reaction of Cyclobutene-1,2-dicarbonitrile with Methanol. A solution of 26 g of **1** in 250 mL of methanol was stirred at 25 °C while a 10% solution of sodium methylate in methanol was added at the rate of ca. 2–3 mL/h for 6 h; VPC monitoring showed that reaction was rapid. After addition of carbon dioxide to "neutralize" the base and filtration of the resultant solid, the methanol solution was stripped under reduced pressure. The residue was taken up in ether, removing an insoluble solid [5.9 g, not investigated further; IR (KBr) 1640, 1470, 1370, 1100, 825 cm^{-1}]. The ether solution was washed several times with saturated salt solution, dried ($MgSO_4$), and distilled through a 6-in. Vigreux column in vacuo to give 26 g of an oil, bp 75–85 °C (0.3 mm). This was redistilled through a spinning band column, giving, as a first cut (reflux ratio of 50:1), an oil, bp 70 °C (0.3 mm), which solidified. Recrystallization twice from ether gave **15** as white crystals, mp 58–59 °C (see Table I for spectral data). Anal. Calcd for $C_7H_8N_2O$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.19; H, 5.90; N, 19.45.[17] Last fractions from this distillation, bp 77–81 °C (0.4 mm) (about half of the material), were combined and redistilled in the same apparatus at a reflux ratio of 100:1. The first cut was rich in **15** (VPC), while the latter cuts became successively richer in two other major components. These were separated by VPC trapping to give **16** as a pure component (see Table I). Anal. Found: C, 61.36; H, 5.95; N, 20.03. The other component was apparently a mixture of products obtained by addition of 2 equiv of methanol to **1** (see Scheme I); IR (neat) 3340 (NH), 2250 (CN), 1655 (C=O), 1590 (C=N), 1350, 1130 (ether), 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.6 (broad s, NH), 3.90 (s, CH_3O), 3.82 (s, CH_3O), 3.56 (s, CH_3O), 3.48 (s, CH_3O), 3.46 (s, CH_3O), 3.33 (s, CH_3O), 3.25 (s, CH_3O), 2.38 (s, CH_2) (in an H ratio of 1:2:3:1:2:1:4:2:13, respectively); mass spectrum m/e (rel intensity) 168 (1.4), 153 (100), 140 (24), 114 (51), 110 (37), 108 (42), 100 (40), 84 (56), 83 (59). Anal. Calcd for

$C_8H_{12}N_2O_2$: C, 57.12; H, 7.19; N, 16.66. Found: C, 56.74; H, 7.08; N, 17.05.

In another similar run, the oil obtained after washing the initial ether solution of the product with water was recrystallized from ether at −70 °C to give 4.7 g of white crystals, mp 63–75 °C. Fractional crystallization of this from ether gave **13**, mp 62–63 °C (impure, see below), and **14**, mp 119–119.5 °C, as the more and less soluble components, respectively (see Table I). **14**: Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.12; H, 7.19; N, 16.66. Found: C, 56.4; H, 7.1; N, 16.5. **13**: NMR, mass, and IR spectra suggested that the sample contained (about 20%) **14** as an impurity.

1,2-Dichlorocyclobutane-1,2-dicarbonitrile. A solution of 7.1 g (0.1 mol) of chlorine in 150 mL of carbon tetrachloride was stirred at room temperature while 10.4 g of **1** was added slowly. After 16 h, reaction was only ca. 50% complete (VPC); another 10 g of chlorine was added. After another 18 h (VPC showed that reaction was 91% complete), the reaction solution was evaporated. The residual colorless oil, 20 g, was recrystallized from ethanol at −70 °C to give *trans*-1,2-dichlorocyclobutane-1,2-dicarbonitrile, mp 73–75 °C.[19]

Addition of Hydrogen Chloride to Cyclobutene-1,2-dicarbonitrile. A solution of 50 g of **1** in 250 mL of chloroform was stirred under nitrogen with water-bath cooling while hydrogen chloride was introduced slowly. Monitoring by VPC and NMR showed that the reaction was complete in a few hours. After a short time, a white solid began appearing. After 45 h, the mixture was filtered under nitrogen, and the solid was washed well with chloroform and ether (yield 16.7 g): IR (KBr) 3320 (NH), 2670 (~N·HCl?), 1785, 1700 (C=O), 1590 cm^{-1} (C=N). A small sample was recrystallized from a mixture of chloroform and ether at −70 °C (under nitrogen) to give white crystals: mp 200–205 °C; IR (KBr) 2800–3300 (broad, strong, acid?), 1785 and 1700 (imide or anhydride C=O?), ca. 1640, 1168 cm^{-1}. Anal. Found: C, 36.12; H, 3.69; Cl, 35.9; N, 4.13.[21] A small sample of the (unrecrystallized) solid, 2.9 g, dissolved immediately in 3 mL of water, accompanied by a copious evolution of hydrogen chloride and a strong exotherm. After heating for 1 h at 100 °C, cooling gave 0.13 g of ammonium chloride; another 0.60 g of the salt was recovered by addition of isopropyl alcohol and ether to the aqueous filtrate.

After removal of the solid reaction product, the chloroform solution was washed four times with water, dried ($MgSO_4$), and distilled in vacuo through a Claisen head to give 42 g of 1-chlorocyclobutane-1,2-dicarbonitrile, bp 100 °C (0.7 mm).[22]

Registry No.—**1**, 3716-97-0; **2**, 23335-15-1; **3**, 1128-10-5; **4**, 16508-05-7; **5**, 61812-58-6; **6**, 61812-59-7; **7**, 61812-60-0; **9**, 61812-61-1; **9** HCl, 61812-62-2; **10**, 18329-03-8; **11**, 6652-02-4; **12**, 52903-54-5; **13**, 61812-63-3; **14**, 61812-64-4; **15**, 61812-65-5; **16**, 61812-66-6; piperidine, 110-89-4; dimethylamine, 124-40-3; glutaric acid, 110-94-1; methanol, 67-56-1; *trans*-1,2-dichlorocyclobutane-1,2-dicarbonitrile, 52477-39-1; chlorine, 22537-15-1; HCl, 7647-01-0; *cis*-1-chlorocyclobutane-1,2-dicarbonitrile, 61812-67-7; *trans*-1-chlorocyclobutane-1,2-dicarbonitrile, 61812-68-8; *cis*-1,2-dichlorocyclobutane-1,2-dicarbonitrile, 52477-38-0.

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(17) While elemental analyses were not entirely satisfactory, these with supporting spectral data clearly established the assigned structure.
(18) Elemental analyses agreed as well as would be expected for the dihydrate of such a moisture-sensitive material. Anal. Calcd for $C_{10}H_{14}N_2 \cdot HCl \cdot 2H_2O$; C, 51.17; H, 8.16; N, 11.93; Cl, 15.10. Found: C, 51.6; H, 7.0; N, 13.7; Cl, 16.2.
(19) This material was identical with authentic *trans*-1,2-cyclobutane-1,2-dicarbonitrile prepared by chlorination of cyclobutane-1,2-dicarbonitrile.[2,3,20]
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(21) These results correspond to an empirical formula of $C_6H_7Cl_2N_{0.5}O_{2.5}$. Anal. Calcd: C, 36.58; H, 3.58; Cl, 35.99; N, 3.55. Partial hydrolysis of the moisture-sensitive salt, perhaps **17** or **18**, introduced oxygen-containing derivatives as impurities.
(22) Identical (by VPC) with material prepared by chlorination of cyclobutane-1,2-dicarbonitrile.[2,3,20]

A Rationalization on the Relative Thermodynamic Stabilities of Fused Five-Membered Tetrahydrofurans with Epimerizable Substitutents. An Anomeric Effect in Furanoses

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A rationalization on the fact that the thermodynamically more stable isomers of fused five-membered tetrahydrofuran derivatives with epimerizable substituents are generally not the expected exo isomers but the endo isomers is proposed. The fact that 2,3-*O*-isopropylidene or benzylidene furanoses exist mainly in the trans-C_1,C_2 configuration should not be explained based on the generally accepted concept that the bicyclo[3.3.0]octane system tends to exist with the fewest possible large endo substituents but should be explained in terms of the anomeric effect.

In this paper, we would like to propose a rationalization on the unexpected fact that the thermodynamically more stable isomers of the fused five-membered tetrahydrofuran derivatives with epimerizable substituents are generally not the exo isomers but the endo isomers.[1] Although the fact was first observed by Ohrui et al.[1] in the field of carbohydrate chemistry, the fact and the rationalization proposed in this paper are believed to be general in organic chemistry.