nitrogen. The solid was filtered and addition of petroleum ether (bp 30–60°) gave a second crop. The solid was recrystallized twice from methanol to remove tin salts, giving 3.8 g of biuret as a white solid, mp 175.5–179°. *Anal.* Calcd for $C_{20}H_{14}F_3N_3O_2$: C, 62.4; H, 3.7; N, 11.2. Found: C, 62.1; H, 3.6; N, 10.9. Ir 2.96, 3.16 (NH), 3.25 (=CH), 5.85, 6.02 (C=O), 6.23, 6.45, 6.58, 6.65 (C=C and amide II), ~8 (CF), 11.93, 12.08, 12.36, 12.43 μ (para-disubstituted aromatic); ^{19}F nmr (CH_3CN) −112.8 (1 F), −117.7 (2 F).

7-Fluoro-1-(4-fluorophenyl)-3-(4-fluorophenylcarbamoyl)-2-benzimidazolinone (3a), had mp 201.5–203° (CH_3CN). *Anal.* Calcd for $C_{20}H_{12}F_3N_3O_2$: C, 62.6; H, 3.1; N, 10.9. Found: C, 62.5; H, 3.3; N, 11.1. Uv max (THF) 242 nm (ε 32,800), sh 283 (6570), 288 (5620); ir (KBr) 3.12 (NH), 3.23 (CH), 5.70, 5.86 (C=O), 6.16, 6.35, 6.60, 6.75 (C=C and amide II), 12.07 μ (para aromatic); pmr (DMSO) δ 6.79 (d, d, 1, J = 9, 2 Hz), 6.97 (d, t, 1, J = 2, 9 Hz), 7.12 (t, 2, J = 9 Hz), 7.35 (t, 2, J = 9 Hz), 7.57 (m, 4), 8.21 (d, d, 1, J = 9.5 Hz), 10.73 (broad s, NH); ^{19}F nmr (CH_3CN) δ −112.2 (t, t, 1, J = 5, 9 Hz,) −117.1 (d, t, 1, J = 5, 9 Hz), −118.1 (t, t, 1, J = 5, 9 Hz); mass spectrum (calcd for $C_{20}H_{12}F_3N_3O_2$, 383.0881) 383.0885, (calcd for $C_{13}H_8F_2N_2O$, 246.0604) 246.0608, 217.0556 ($C_{12}H_7F_2N_2$), 137 (C_7H_4FNO).

Pyrolysis of Imidazolinone 3a.—A solution of 200 mg of imidazolinone **3a** and 3 ml of a 10% potassium hydroxide solution was refluxed under nitrogen for 2 hr. On cooling a yellow solid formed and was extracted into ether and dried, the ether was removed on a rotary evaporator, and the product was recrystallized from acetonitrile to give 50 mg of white needles, mp 224–225°. *Anal.* (HRMS). Calcd for $C_{13}H_8F_2N_2O$: mol wt, 246. Found: mol wt, 246 (mass spectrum). Ir 3.13, 3.23, 5.83, 6.18, 6.25, 6.60, 6.69, 8–9, 12.04, 12.51 μ; uv (THF) 293 nm (ε 7960), 250 (6030); pmr (CH_3CN) δ 6.80 (d, d, 1, J = 9, 2 Hz), 6.85 (d, t, 1, J = 2, 9 Hz), 7.08 (d, 1, J = 9 Hz), 7.32 (t, 2, J = 9 Hz), 7.57 (d, d, 2, J = 9, 5 Hz), 8.8 (broad, 1, NH); ^{19}F nmr (CH_3CN) δ −114.3 (1 F), −121.6 (1 F).

1-Phenyl-2-benzimidazolinone was prepared by the reaction of phosgene with *N*-phenyl-*o*-phenylenediamine.[11]

2-Anilinocarbanilide was prepared by the reaction of phenyl isocyanate with *N*-phenyl-*o*-phenylenediamine.[12]

(11) M. L. Oftedahl, R. W. Rädue, and M. W. Dietrich, *J. Org. Chem.*, **28**, 578 (1963).

(12) M. C. Kloetzel, S. J. Davis, U. Pandit, C. R. Smith, and H. Nishihara, *J. Med. Pharm. Chem.*, **1**, 197 (1959).

1,3-Diphenyl-1*H*,3*H*,5*H*-1,3,5-benzotriazepine-2,4-dione (1b).—To 100 ml of phosgene-saturated *o*-dichlorobenzene at 10° was added dropwise a solution of 5 g of 2-anilinocarbanilide in 30 ml of THF. After the addition was complete, the solution was warmed to room temperature, and excess phosgene was allowed to escape. Solvent was removed at reduced pressure, leaving a residue which was recrystallized from DMSO–H_2O, giving 1.3 g of triazepinedione as a white solid, mp 197–200°. *Anal.* Calcd for $C_{20}H_{15}N_3O_2$: C, 72.9; H, 4.6; N, 12.8. Found: C, 73.0; H, 4.7; N, 12.9. Ir 5.88, 6.21, 6.26, 6.66, 6.74 μ; nmr (DMSO-d_6–TMS) δ 11.05 (s, NH), 7.52 (s, 8 H), 7.05 (m, 6 H).

1-Phenyl-3-phenylcarbamoyl-2-benzimidazolinone (3b).—A slurry of 4 g of benzimidazolinone **2b**, 2.5 g of phenyl isocyanate, and 5 g of stannic chloride was heated in a test tube under N_2. The initially formed homogeneous melt deposited a solid. The solid was cooled to room temperature, slurried with CH_3OH, and filtered. Chromatography over neutral SilicAR and elution with 1:1 benzene–pentane gave 1 g of imidazolinone, which was recrystallized from CH_3CN, mp 166–168°. *Anal.* Found: C, 72.95; H, 4.60; N, 12.64. Nmr δ 10.6 (s, NH), 8.20 (m, 1 H), 7.62–7.51 (m, 7 H), 7.36 (t, J = 8 Hz, 2 H), 7.26–7.18 (m, 2 H), 7.13 (t, J = 7 Hz, 1 H), 6.99 (m, 1 H); ir 3.11, 3.16, 3.22, 5.75, 5.86, 6.22, 6.37, 6.64, 6.75, 13.20, 14.17 μ.

Reaction of Pentadeuterionitrobenzene with CO.—A solution of 0.7 ml of $C_6D_5NO_2$, 5 mg of $PdCl_2$, and 1 ml of CH_3CN was pressured with 100 atm of CO and heated at 275° for 2 hr. Volatile products were removed by distillation and the residue was sublimed using a Dowtherm bath at 0.05 Torr. The ir spectrum showed significant absorptions at 2495, 2455, and 2390 cm^{-1} (N–D stretch).

Registry No.—**1b**, 38456-60-9; **2a**, 38456-61-0; **2b**, 14813-85-5; **3a**, 38456-63-2; **3b**, 38456-64-3; 4-fluorophenyl azide, 3296-02-4; carbon monoxide, 630-08-0; 4-fluorophenyl isocyanate, 1195-45-5; 4-fluoronitrobenzene, 350-46-9; 1,3,5-tris(4-fluorophenyl)biuret, 38456-65-4; 4-chloronitrobenzene, 100-00-5; 4-chlorophenyl isocyanate, 104-12-1; phenyl isocyanate, 103-71-9.

Acknowledgment.—The author thanks Professor B. L. Trost for valuable discussions.

Reactions of Isocyanides with Activated Acetylenes in Protic Solvents[1]

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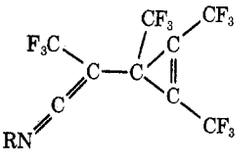
The reaction of isocyanides with activated acetylenes in alcoholic solvents has been shown to produce a mixture of two different 1:1:1 adducts (isocyanide:acetylene:alcohol), an unsaturated imino ester, and a ketenimine. The configurations of the imino esters have been determined and the initial product is always that which results from trans addition. In some cases (methyl propiolate) the initial product is easily isomerized to the more stable isomer. The relative amounts of ketenimine and imino ester that form are dependent on the structures of the acetylene and the isocyanide and to some extent on the nature of the alcohol. In one case, the reaction of *p*-nitrophenyl isocyanide with dimethyl acetylenedicarboxylate in methanol, an ortho ester is obtained. In all cases the results are best interpreted by assuming the initial formation of a 1:1 intermediate (isocyanide:acetylene) with net trans addition to the acetylenic bond.

Previously we demonstrated that isocyanides would react with hexafluorobutyne-2 in aprotic solvents to produce 1:2 adducts of structure **1**.[2]

A few years prior to this work, Meinwald and Aue[3] had produced a similar type of product from the reaction of a nitrene with a normal acetylene. They postulated that their 1:2 product might be produced from an initially formed 1:1 intermediate that could possibly possess predominate carbene or carbonium ion character.



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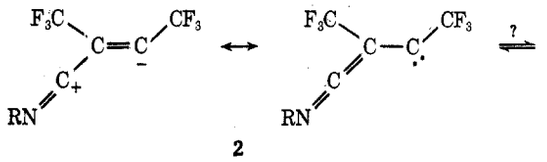
(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Presented in part at the 161st National Meeting of the American Chemical Society, Los Angeles, Calif., March 1971, Abstract ORGN-106.

(2) T. R. Oakes, H. G. David, and F. J. Nagel, *J. Amer. Chem. Soc.*, **91**, 4761 (1969).

(3) J. Meinwald and D. H. Aue, *ibid.*, **88**, 2849 (1966).

In our analogous situation we postulated that our 1:2 adduct was being formed from a 1:1 intermediate (2) that might possess predominate carbene or carban-



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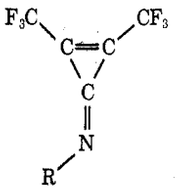
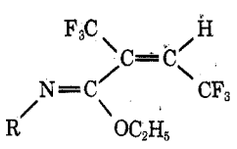


ion character or perhaps even resemble a cyclopropenone imine.

Others[4-6] have postulated similar 1:1 intermediates for the reaction of isocyanides with different activated acetylenes.

In aprotic solvents the products obtained may be 1:2 adducts[2,6] (isocyanide:acetylene), 2:1 adducts,[7] 3:1 adducts,[7] or 2:3 adducts.[4] In all cases it seems reasonable to assume the prior information of a 1:1 intermediate. Previously[2] we had indicated the existence of a 1:1 intermediate by treating isocyanides with hexafluorobutyne-2 in the presence of a protic solvent (ethanol) to form two different 1:1:1 adducts (isocyanide:acetylene:ethanol), an imino ester (3),



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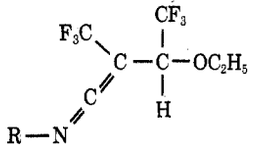

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and a ketenimine (4). Thus, in protic solvents, the 1:1 intermediate could be trapped.

In this work, we have investigated this reaction more fully; we have continued the trapping experiments; we have determined the stereochemistry of the imino esters (3), we have studied the effect of changes of substituents in para-substituted phenyl isocyanides on the composition of the trapped products, and we have also studied the reaction of isocyanides with some other activated acetylenes.

Results and Discussion

To date, the 1:1 intermediate has not been trapped by typical carbene trapping agents other than alcohols. We have attempted to trap the 1:1 intermediate by employing solvent concentrations of various olefins (cyclohexene, dimethyl fumarate, and dimethyl maleate), but the only product obtained in these nonprotic solvents was the original 1:2 adduct **1**. Even under conditions of high-dilution addition of hexafluorobutyne-2 to isocyanides in olefin solvents, the only product obtained was **1**. The high-dilution reactions generally proceed with much more polymer formation than is obtained by mixing equivalent amounts of isocyanide and hexafluorobutyne-2 in a Parr bottle and the yield of **1** is generally lower, but we have not been able to detect any new low molecular weight compounds. This would argue that the 1:1 intermediate possesses little carbene character. However, others[8] have experienced similar difficulty in trapping oxacarbene intermediates with anything other than alcohols.

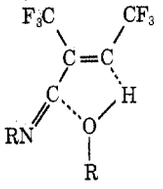
In order to examine the nature of the 1:1 intermediate more fully, we have conducted a substituent study of the reaction of para-substituted phenyl isocyanides with hexafluorobutyne-2 using various alcohols as solvents. Using a variety of substituents we have determined the product ratios of **3** to **4**. In alcohol solutions these are the only two products obtained and generally in overall yields of 80–90%.

The relative amounts of the two compounds were determined by integration of the ^{19}F nmr spectrum of the reaction mixture after removal of the solvent. The wide separation of the ^{19}F peaks enabled us to obtain good relative yield data. After the nmr spectrum had been obtained, the mixture was subjected to fractional distillation and spectra and analyses were obtained on the pure compounds. The relative yields are summarized in Table I.

TABLE I
YIELDS OF IMINO ESTERS (3) AND KETENIMINES (4)

Alcohol	Isocyanide	Total yield, %	Ratio of 3:4
Methyl	*p*-$NO_2C_6H_4$	80	100:0
Methyl	*p*-ClC_6H_4	73	81:19
Methyl	C_6H_5	94	70:30
Methyl	*p*-$CH_3C_6H_4$	89	72:28
Methyl	*p*-$CH_3OC_6H_4$	94	71:29
Ethyl	C_6H_5	80	65:35
Isopropyl	C_6H_5	80	54:46

The data in Table I demonstrate that the reaction is somewhat affected by changes of substituents in the isocyanides. It is interesting to note that electron-withdrawing substituents have a marked effect while electron-donating substituents appear to have no effect on the course of the reaction. The fact that the imino ester possess a trans configuration (*vide infra*), that electron-withdrawing groups favor the formation of the imino ester, and that other normal carbene trapping agents are ineffective in this reaction is consistent with the formation a 1:1 intermediate which is predominantly polar with little or no carbene or cyclopropenone imine character. A single mechanism that accounts for all of the observations is given in Scheme I. The fact that the configuration of the imino ester is exclusively trans would indicate that the addition of alcohol to the intermediate is stepwise or involves more than 1 mol of alcohol. It would exclude a concerted cisoid intermediate of the following type.



(4) Y. Suzuki, N. Obata, and T. Takizawa, *Tetrahedron Lett.*, 2667 (1970).

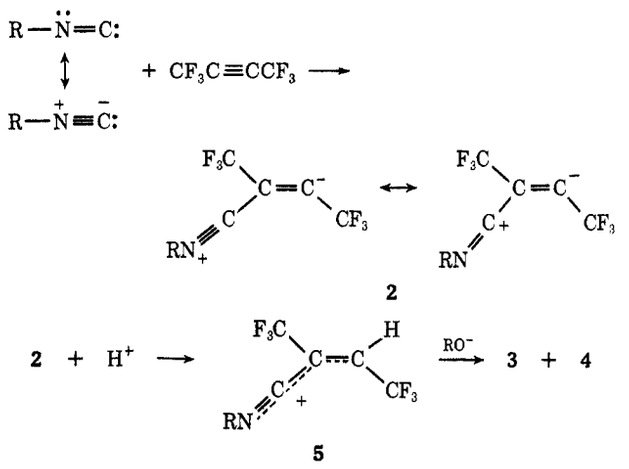
(5) F. Johnson, A. H. Gulbenkian, and W. A. Nasutavicus, *Chem. Commun.*, 608 (1970).

(6) E. Winterfeldt, D. Schumann, and H. J. Dillinger, *Chem. Ber.*, **102**, 1656 (1969).

(7) T. Takizawz, N. Obata, Y. Suzuki, and T. Yanagida, *Tetrahedron Lett.*, 3407 (1969).

(8) D. R. Morton, E. Lee-Ruff, R. M. Southam, and N. J. Turro, *J. Amer. Chem. Soc.*, **92**, 4349 (1970).

SCHEME I



It would also cast some doubt on the cisoid structure proposed for the 1:1 intermediates,[2,4,5] and upon the intermediacy of a cyclopropenone imine. However, the fact that the imino esters are *exclusively* trans does give us some insight to the stereochemistry of nucleophilic additions to triple bonds in general. These types of additions have been carefully studied by a number of authors. Thus, Truce[9] has developed a "Rule of Trans Nucleophilic Addition." An exception to the rule was noted in the base-catalyzed addition of *p*-toluenethiol to sodium propiolate.[10] Others[11,12] have shown that the reaction of amines with activated acetylenes also involves an exception to the rule. In this last case, the incoming amine is a neutral species and the nitrogen atom begins to develop positive charge in the transition state. It is therefore not unreasonable to expect that the developing negative charge takes a cisoid course. A similar intermediate may be postulated for the reaction of an isocyanide with hexafluorobutyne-2.

It should be stressed that, in any of the above cases where a carbonyl group exists on the acetylene, the vinyl anion may be configurationally unstable or perhaps even linear owing to resonance interaction of the carbonyl group.[13] In the present case, where the electron-withdrawing groups are trifluoromethyl groups, this complication would not be at hand, since such a resonance effect is largely inoperative.

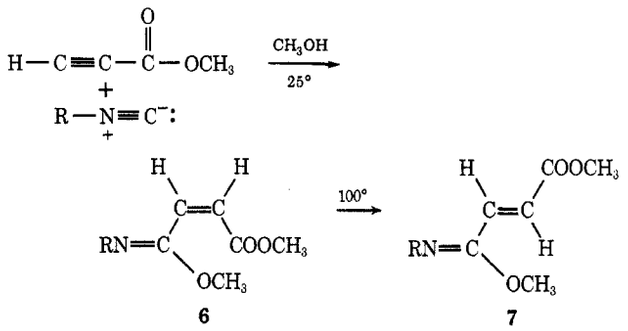
In comparing the attack of an amine to that of an isocyanide on an activated acetylene, it should be noted that both are neutral species and that both incoming groups begin to develop positive charge in the transition state. Thus, a cisoid type intermediate might be anticipated in both cases. However, in the case of the amine a proton is immediately available for concerted transfer while in the case of isocyanide, protonation occurs from the solvent. Thus, the mere development of positive charge on the incoming group does not appear to be sufficient reason for cis addition.

It is possible, of course, that the initial addition does take a cisoid course but that isomerization occurs in some subsequent intermediate or perhaps that the initially formed cis addition product (the imino ester) rearranges to the trans addition product. We have not been able to obtain the imino ester resulting from cis addition either by direct reaction or by attempts at rearranging the obtained imino ester. We have attempted both thermal- and ultraviolet-initiated rearrangement of the trans imino ester but with no success. Thus, we cannot be certain that an initially formed cis addition product does not rearrange to the trans addition product. We do have good indications that this is not the case, however.

We have been able to obtain both the cis and trans addition compounds of methanol and ethanol to hexafluorobutyne-2. As demonstrated by Raunio and Frey,[14] the product that forms is greater than 95% trans when methanol is added to hexafluorobutyne-2, using sodium methoxide as the catalyst. We have shown that this trans compound can then be rearranged to the cis compound by irradiation with ultraviolet light in the presence of acetophenone as the sensitizer. Both cis and trans compounds are quite stable with regard to thermal cis–trans rearrangement. Heating in a sealed tube for 2 hr at 110° caused no rearrangement. Thus compounds similar to the imino esters are thermally stable.

In addition, Saegusa and coworkers[15] have recently reported on the reaction of isocyanides with methyl propiolate in methanol as solvent. By running the reaction in a sealed tube for 24 hr at 110° they obtained the trans imino ester (**7**) exclusively. This would infer a cis addition. We have repeated their work and we have confirmed their results. However, we have discovered that the same reaction will occur at room temperature if the reaction time is extended (4 to 5 days). Under these conditions, we obtain the cis imino ester **6**, which infers a trans addition. Furthermore, the cis imino ester obtained at room temperature can be rearranged to the trans compound by heating at 100° for 24 hr (see Scheme II). Thus,

SCHEME II



it seems likely that the trans imino ester **7** obtained by Saegusa results from an initial trans addition followed by rearrangement.

Even though the cis imino ester **6** will undergo rearrangement when heated at 100° for 24 hr, it is stable enough to be distilled at 70° and only about 50% has rearranged after 10 hr at 100°. Thus, in the reactions of hexafluorobutyne-2, performed at room temperature, it also seems likely that the product obtained

(9) W. E. Truce and J. A. Simms, *J. Amer. Chem. Soc.*, **78**, 2756 (1956).
(10) W. E. Truce and R. F. Heine, *ibid.*, **79**, 5311 (1957).
(11) J. E. Dolfini, *J. Org. Chem.*, **30**, 1298 (1965).
(12) E. Winterfeldt and H. Preuss, *Chem. Ber.*, **99**, 450 (1966).
(13) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962, p 234.
(14) E. K. Raunio and T. G. Frey, *J. Org. Chem.*, **36**, 345 (1971).
(15) T. Saegusa, Y. Ito, S. Tomita, H. Kinoshita, and N. Taka-Ishi, *Tetrahedron*, **27**, 27 (1971).

(the imino ester **3**) is the kinetically controlled product and that it did not result from rearrangement of an initially formed cis addition product. With regard to the geometry of the postulated intermediates, there appears to be no reason to invoke a cisoid or cyclopropenone imine type intermediate. Sterically such intermediates appear more stable, but in order to explain the trans addition products either transoid intermediates or a concerted mechanism must be invoked. It may be, of course, that no discrete 1:1 intermediate exists in protic solvents but rather that the reaction between the isocyanide, acetylene, and alcohol is a concerted process and that the steric effect of the two incoming groups is the determining factor. This would be analogous to the mechanism proposed by Winterfeldt[12] for the tertiary amine catalyzed addition of alcohols to activated acetylenes.

The configurational assignments of the cis and trans imino esters from methyl propiolate were made on the basis of their coupling constants. The cis imino ester **6**, formed at room temperature, possesses an AB quartet (assigned to the vinyl protons) centered at $\delta_{TMS}^{CCl_4}$ 6.22 with a coupling constant of 12 Hz, while the product formed by thermal rearrangement or by using Saegusa's conditions has an AB quartet centered at $\delta_{TMS}^{CCl_4}$ 6.84 with a coupling constant of 16 Hz. These coupling constants are consistent with other similar types of alkenes.[16]

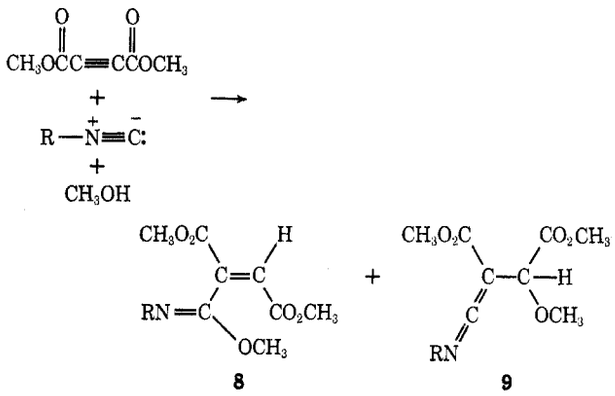
The trans configuration of the imino esters obtained from hexafluorobutyne-2, isocyanides, and alcohols was assigned on the basis of ^{19}F coupling constants.

Raunio and Frey[14] have assigned the configurations to the cis and trans addition products of methanol to hexafluorobutyne-2. For the trans addition product they report no coupling between the two CF_3 groups, while for the cis addition product they report an F_1F_4 coupling constant of 11 Hz. This is consistent with our results. We have also obtained the cis and trans ethanol adducts of hexafluorobutyne-2. In this case, for the trans isomer the F_1F_4 coupling constant is 1.8 Hz while for the cis isomer it is 10 Hz. Others[17] have also reported F_1F_4 coupling constants for similar type compounds and their results agree with ours and with Raunio and Frey. The F_1F_4 coupling constants in the hexafluoroimino esters obtained in this work are 1.5–2.0 Hz. Thus the configuration of the two CF_3 groups is trans.

We have also examined the reaction of isocyanides with dimethyl acetylenedicarboxylate in both the absence and presence of alcohols. In both cases a reaction takes place at room temperature. In the absence of protic solvents (in CH_2Cl_2) the only product isolated is a 2:3 adduct (isocyanide:acetylene) similar to that reported by others.[4] In the presence of methanol a similar reaction takes place as in the case of hexafluorobutyne-2. Again, both imino esters (**8**) and ketenimines (**9**) are obtained (Scheme III).

When R is an aryl group (phenyl, *o*-tolyl, or *p*-nitrophenyl) the only product obtained is the imino ester **8** whereas when R is alkyl (cyclohexyl or *tert*-butyl) both the imino ester **8** and the ketenimine **9** are obtained. In the case of cyclohexyl the ratio of **8**:**9** is about 1:1, whereas in the case of *tert*-butyl isocyanide the ratio is about 1:9. Thus the attack by methoxide may be governed by the steric effect of R in an intermediate similar to **5**. It should be pointed out that the overall yields in this reaction were generally less than in the case of hexafluorobutyne-2. This is partially due to difficulties in distilling these higher boiling materials and partially due to the apparent greater tendency of dimethyl acetylenedicarboxylate to simply undergo an addition reaction with the methanol under these reaction conditions. It is interesting to note that the addition product of methanol to dimethyl acetylenedicarboxylate, which is apparently catalyzed by the isocyanide acting as a base, is predominantly (90%) of the trans configuration, as determined by comparison of the chemical shifts of this compound to that reported by Winterfeldt and Preuss.[12]

SCHEME III



It is assumed that the imino esters obtained from the reaction of isocyanides with dimethyl acetylenedicarboxylate in methanol are trans addition products (**8**). This assumption is based on the formation of the analogous imino esters, formed *via* trans addition, from hexafluorobutyne-2 and from the room-temperature reaction of methylpropiolate. In addition, an interesting product, thought to be an ortho ester, obtained in the case of *p*-nitrophenyl isocyanide helps substantiate the assumed mode of addition to dimethyl acetylenedicarboxylate.

When *p*-nitrophenyl isocyanide is allowed to react with dimethyl acetylenedicarboxylate in methanol for 2 or 3 weeks at room temperature, the product obtained (in 20% yield) after evaporation of the methanol and recrystallization from benzene is a 1:1:2 adduct (isocyanide:acetylene:methanol). The nmr spectrum displays four absorptions of relative area 4:1:3:9. The quartet representing four protons at δ 8.1 is due to the *p*-nitrophenyl protons, the singlet in the vinyl region at 6.70 accounts for one proton, the singlet at 3.80 representing three protons is assigned to a carbomethoxy group, and a singlet at 3.25 representing nine protons is assigned to the ortho ester grouping. A very broad absorption at δ 9.6 accounting for one proton is assigned to a hydrogen-bonded NH proton.

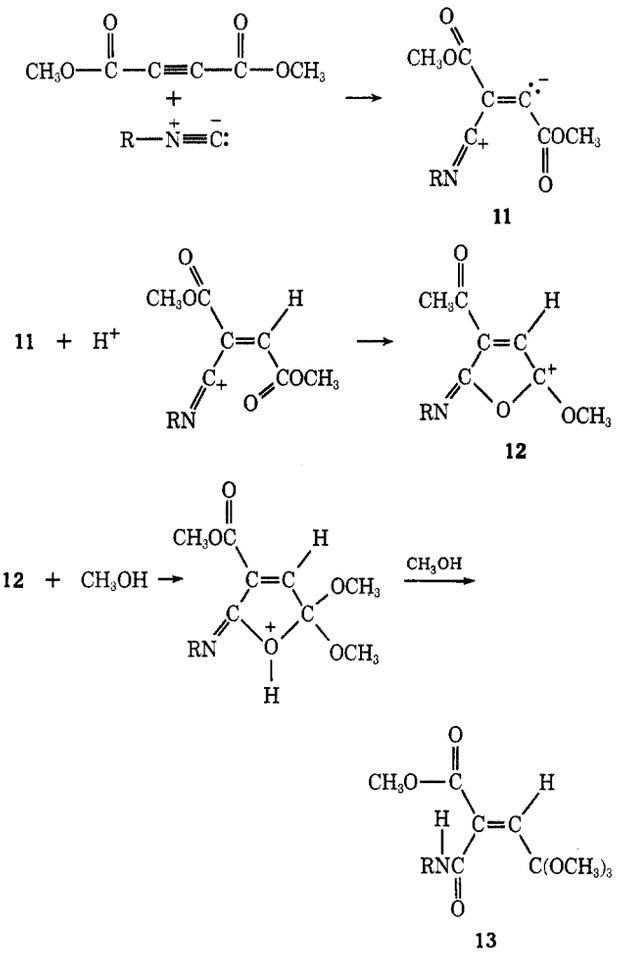
The infrared spectrum displays an NH peak at 3335 cm^{-1} and carbonyl peaks at 1725, 1650, and 1550 cm^{-1}.

A mechanism that accounts for the formation of this compound is given in Scheme IV.

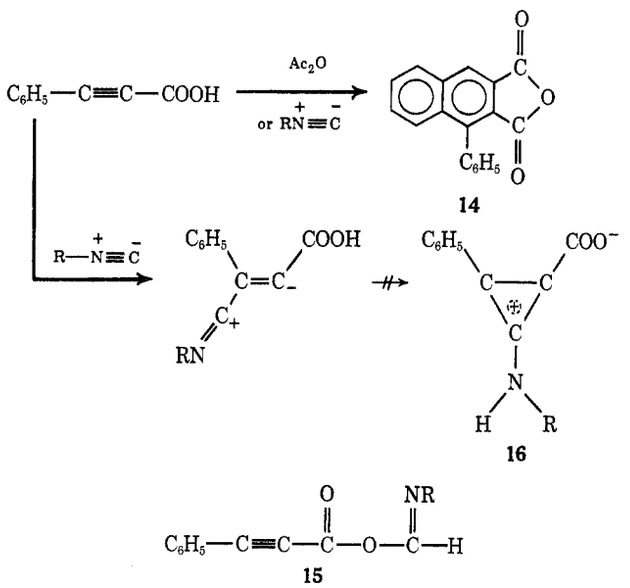
(16) J. W. Emsley, J. Feeney, and L. H. Stucliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, Oxford, 1966, p 739.

(17) Reference 16, p 912.

SCHEME IV



SCHEME V



The formation of naphthoic anhydride derivatives from phenylpropiolic acid and acetic anhydride has been studied extensively.[19] It appears essential that an anhydride be formed first in order that cyclization may occur. The surprising thing in the reaction mediated by isocyanides is that it takes place under such mild conditions.

In order to invoke this mechanism, the intermediates involved must result from trans addition.

From all of the above data we feel that the reaction of isocyanides with activated acetylenes in protic solvents involves a trans addition and no evidence exists for the intermediacy of a cisoid intermediate with or without cyclopropenone imine character. Initially we[2] and others[4,5,18] felt that cyclopropenone imines might be formed in these reactions. Apparently the presence of the strong electron-withdrawing groups, that are required to cause the isocyanide to react with the acetylene, sufficiently destabilize the three-membered aromatic system (the cyclopropenone) so as to preclude its formation.

In a final attempt to isolate a cyclopropenone imine type derivative we treated phenylpropiolic acid with various isocyanides, hoping that the isocyanide would react faster with the acetylene function than with the carboxylic acid group, and that proton transfer would result in a stable system (**16**). This was not the case; rather, a naphthoic anhydride derivative resulted (**14**). This same product has been obtained by treating phenylpropiolic acid with acetic anhydride.[19] Thus it is likely that the isocyanide undergoes an α,α addition with the carboxylic acid to form an anhydride-like intermediate (**15**) which then cyclizes to the naphthoic anhydride (Scheme V).

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Experimental Section

The infrared spectra were determined using a Beckman IR-8 spectrophotometer; the nmr spectra were determined with a Varian T-60 equipped with an auxiliary ^{19}F probe or with a Varian 56/60 spectrophotometer; TMS was used as the internal standard for the ^1H spectra while CCl_3F was used for the ^{19}F spectra. The isocyanides were all carefully purified and shown to be free of amines by their nmr spectrum.

Reaction of Isocyanides with Hexafluorobutyne-2 in Methanol.—A 500-ml Parr bottle, with inlet and outlet tubes equipped with $CaCl_2$ drying tubes, in a Dry Ice–acetone bath was charged with 200 ml of alcohol, 0.025 mol of isocyanide, and 10.0 g (0.062 mol) of hexafluorobutyne-2. The bottle was then stoppered and shaken on a Parr apparatus for 2 hr at room temperature. The pressure rapidly rose to 25 psi, but after 2 hr it usually had decreased to about 15 psi. At the end of this time the isocyanide had completely disappeared, as evidenced by ir spectra and lack of odor. The solvent was removed using a rotary evaporator and the crude reaction mixture was analyzed using ir, ^1H nmr, and ^{19}F nmr spectroscopy. Integration of the ^{19}F nmr spectra gave the relative amounts of imino ester and ketenimine. Each reaction was run and analyzed two times or more. At least three integrations of the ^{19}F spectrum were determined for each reaction mixture. The relative yields thus determined are summarized in Table I.

The crude reaction mixture was then fractionally distilled under vacuum to obtain the pure imino ester and ketenimine. These were further examined spectroscopically to conclusively assign the absorptions in the ^{19}F nmr spectra of the mixtures.

The lower boiling fraction, the imino esters, possessed a strong peak in the ir near 1666 cm^{-1} while the high-boiling fraction, the ketenimines, possessed a strong characteristic absorption near 2083 cm^{-1}. The ^1H and ^{19}F chemical shifts are given in Table II. Typical coupling constants are HF_1 = 7.2 Hz for the geminal hydrogen and CF_3 group, HF_4 = 1.8 Hz for the hydrogen cis to the other CF_3 group, and F_1F_4 = 1.8 Hz for the two trans CF_3 groups.

A middle cut of each compound was sent out for analysis. The data are summarized in Table II.

The reaction of phenyl isocyanide with hexafluorobutyne-2 in ethanol and 2-propanol was also examined but analytical samples

TABLE II

PROPERTIES AND ANALYSIS OF IMINO ESTERS (3) AND KETENIMINES (4)

Compd type (registry no.)	Alcohol (registry no.)	Isocyanide (registry no.)	Bp, °C (mm)		Analysis % C	% H	% N	% F	Proton nmr[a]	^{19}F nmr[b]
3	Methyl	C_6H_5	30–33	Calcd	48.50	3.05	4.71	38.35	3.90 (s, 3), 6.20 (q of	64.4 (d of q, 3)
(38308-64-4)	(67-56-1)	(931-54-4)	(0.25)	Found	48.34	3.18	4.93	38.11	q, 1), 7.0 (m, 5)	65.6 (p, 3)
4	Methyl	C_6H_5	40	Calcd	48.50	3.05	4.71	38.35	3.53 (s, 3), 4.13 (q, 1),	57.9 (s, 3)
(38308-65-5)			(0.25)	Found	49.32	3.52	4.92	38.68	7.30 (s, 5)	79.4 (d, 3)
3	Methyl	p-$CH_3OC_6H_4$	55–58	Calcd	47.72	3.39	4.28	34.83	3.66 (s, 3), 3.86 (s, 3),	65.0 (d of q, 3)
(38308-66-6)		(10349-38-9)	(0.15)	Found	48.42	3.46	4.42	35.42	6.21 (q of q, 1), 6.70 (s, 4)	66.1 (p, 3)
4	Methyl	p-$CH_3OC_6H_4$	76	Calcd	47.72	3.39	4.28	34.83	3.53 (s, 3), 3.75 (s, 3),	58.2 (s, 3)
(38308-67-7)			(0.15)	Found	47.02	3.34	4.73	33.36	4.13 (q, 1), 7.04 (q, 4)	79.6 (d, 3)
3	Methyl	p-$CH_3C_6H_4$	35–36.5	Calcd	50.17	3.56	4.50	36.63	3.25 (s, 3), 3.86 (s, 3),	64.7 (d of q, 3)
(38308-68-8)		(7175-47-5)	(0.15)	Found	50.39	3.82	4.44	35.94	6.16 (q of q, 1), 6.80 (s, 4)	65.8 (p, 3)
4	Methyl	p-$CH_3C_6H_4$	53	Calcd	50.17	3.56	4.50	36.63	3.40 (s, 3), 3.56 (s, 3),	57.9 (s, 3)
(38308-69-9)			(0.15)	Found	50.99	3.91	4.48	34.62	4.13 (q, 1), 7.15 (s, 4)	79.5 (d, 3)
3[c]	Methyl	p-ClC_6H_4	48	Calcd	43.46	2.43	4.22	34.37	3.95 (s, 3), 6.27 (q of	64.7 (d of q, 3)
(38308-70-2)		(1885-81-0)	(0.20)	Found	44.31	2.36	4.35	34.47	q, 1), 7.0 (q, 4)	65.7 (p, 3)
3	Methyl	p-$NO_2C_6H_4$	99–102	Calcd	42.12	2.36	8.19	33.31	4.00 (s, 3), 6.20 (q of	64.7 (d of q, 3)
(38308-71-3)		(1984-23-2)	(mp)	Found	42.40	2.05	8.21	33.73	q, 1), 7.53 (q, 4)	66.1 (p, 3)

[a] The data are given in parts per million (δ) relative to TMS as an internal standard in CCl_4; s = singlet, q = quartet, m = multiplet; the number in parentheses represents the number of protons obtained from integration. [b] The data are given in parts per million relative to CCl_3F as an internal standard in CCl_4; s = singlet, d = doublet, q = quartet, p = pentet. [c] We were not able to obtain an analytical sample of the corresponding ketenimine; however, ir and nmr spectra demonstrated its presence in the original reaction mixture.

were not obtained. The spectral properties of these imino esters and ketenimines are consistent with the assigned structures.

Attempts to isomerize the imino esters, either thermally or with a 450-W Hanovia high-pressure quartz mercury-vapor lamp, were unsuccessful. In contrast, the simple methanol and ethanol adducts of hexafluorobutyne-2, prepared by the method of Haszeldine[20] and shown to be greater than 95% trans by Raunio and Frey,[14] were easily isomerized in the presence of acetophenone to the cis isomer using a 450-W Hanovia lamp. Both of these cis and trans isomers were unaffected upon heating in a sealed tube at 110° for 2 hr.

Methyl *cis*-γ-(*N*-Cyclohexylimino)-γ-methoxycrotonate (6).—To 8.4 g (0.1 mol) of methyl propiolate in 50 ml of methanol was added 10.9 g (0.1 mol) of cyclohexyl isocyanide. The stoppered reaction flask was allowed to stand at 25° for 5 days. The methanol was removed without heating using a rotary evaporator. Distillation of the residue produced a low-boiling fraction, bp 25–35° (0.1 mm), consisting of the cis and trans adducts of methanol to methyl propiolate, and a higher boiling fraction, bp 75–77° (0.1 mm), yield 5.2 g (23%) of **6**. The nmr spectrum displayed two doublets ($\delta^{TMS}_{CCl_4}$) for two vinyl protons at 6.0 and 6.42, two singlets at 3.56 and 3.62 for the two methoxy groups, and a broad cyclohexyl absorption centered at 1.4. The infrared spectrum displayed significant peaks at 2930, 2860, 1735, 1685, and 1615 cm^{-1}.

Anal. Calcd for $C_{12}H_{19}NO_3$: C, 63.97; H, 8.50; N, 6.22. Found: C, 63.16; H, 8.59; N, 6.88.

Methyl *trans*-γ-(*N*-Cyclohexylimino)-γ-methoxycrotonate (7).—This compound could be prepared either by the method of Saegusa[15] or by heating the cis compound (**6**) in a sealed tube at 110° for 20 hr. The two vinyl doublets now appeared at δ 6.46 and 7.22, the two methoxy singlets at 3.58 and 3.70, and the broad cyclohexyl peak at 1.5. The infrared spectrum displayed significant peaks at 2925, 2850, 1725, 1660, 1615, and 970 cm^{-1}. This last peak was absent in the spectrum of the cis compound.

Reactions of Isocyanides with Dimethyl Acetylenedicarboxylate in Methanol.—To 0.1 mol of the isocyanide in 200 ml of methanol was added 14.2 g (0.1 mol) of dimethyl acetylenedicarboxylate. The alkyl isocyanides were let stand for 2–3 days, while aryl isocyanides required 2–3 weeks for any significant reaction to occur. The methanol was removed using a rotary evaporator and the thick oil was distilled at reduced pressure.

A. Cyclohexyl Isocyanide.—An infrared spectrum of the crude material indicated the presence of both the ketenimine (2050 cm^{-1}) and the imino ester (1675 cm^{-1}). Distillation of the thick oil gave two major cuts. The first cut, bp 95–110° (0.5 mm), possessed a very weak absorption at 2050 cm^{-1} and a medium absorption at 1625 cm^{-1}. For the second cut, bp 115–125° (0.2 mm), the former peak was very strong while the latter was absent. The total yield of both isomers was 50%, each present in about equal amounts as determined by the nmr spectrum of the crude mixture.

Each of the two cuts was redistilled and a center cut was sent out for analysis. The infrared spectrum of the low-boiling distillate (the imino ester **8**) displayed significant peaks at 2940, 2860, 1720, 1675, 1625, and 1225 cm^{-1}. The nmr spectrum ($\delta^{TMS}_{CCl_4}$) displayed a singlet (1 H) at 6.90 (vinyl proton), three singlets (9 H) at 3.66, 3.70, and 3.78 (methoxy protons), a broad multiplet (1 H) at 2.9 (C_1 cyclohexyl proton), and a broad multiplet (10 H) at 1.4 (cyclohexyl protons). *Anal.* Calcd for $C_{14}H_{21}NO_5$: C, 59.40; H, 7.43; N, 4.95. Found: C, 59.80; H, 7.38; N, 5.17.

The high-boiling cut, the ketenimine **9**, displayed significant peaks in the ir at 2940, 2860, 2050, 1725, 1675, and 1240 cm^{-1}. The nmr spectrum ($\delta^{TMS}_{CCl_4}$) displayed a singlet (1 H) at 4.62 (methine proton), two closely spaced singlets (6 H) at 3.66 and 3.68 (carbomethoxy protons), a singlet (3 H) at 3.33 (methoxy protons), and a broad, diffuse peak (11 H) centered at 1.6 (cyclohexyl protons). *Anal.* Calcd for $C_{14}H_{21}NO_5$: C, 59.40; H, 7.43; N, 4.95. Found: C, 59.39; H, 7.61; N, 5.28.

B. *tert*-Butyl Isocyanide.—The oil was distilled; a large forerun consisting of the addition product of methanol to dimethyl acetylenedicarboxylate (17 g, 65%) and a high-boiling fraction, bp 115–120° (0.3 mm) (5.0 g, 25%), was obtained. The high-boiling fraction possessed a strong ir peak in the ketenimine region (2050 cm^{-1}) and only a small shoulder in the imino ester region (1615 cm^{-1}). The nmr spectrum indicated the presence of about 10% imino ester.

Redistillation produced a pure sample of ketenimine **9**. The ir spectrum possessed significant peaks at 2980, 2050, 1725, 1675, and 1250 cm^{-1}. The nmr spectrum ($\delta^{TMS}_{CCl_4}$) displayed a singlet (1 H) at 4.60 (methine proton), a broadened singlet (6 H) at 3.70 (carbomethoxy protons), a singlet (3 H) at 3.33 (methoxy protons), and a singlet (9 H) at 1.40 (*tert*-butyl protons). *Anal.* Calcd for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.45. Found: C, 55.46; H, 7.73; N, 4.98.

C. Phenyl Isocyanide.—The thick oil after removal of the methanol showed no absorption in the ketenimine region (2050

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cm^{-1}). Distillation gave 5 g (19%) of a thick yellow oil, bp 132–138° (0.25 mm). The ir spectrum displayed significant peaks at 3050 (shoulder), 3000, 2940, 1700, 1650, 1610, 1370, and 1240 cm^{-1}. The nmr spectrum indicated the presence of the imino ester and some impurity (*ca.* 15%) that could not be removed by repeated distillation. The good chemical analysis indicates that the impurity is an isomer of the imino ester (but it is not the ketenimine). The nmr displayed peaks ($\delta^{TMS}_{CCl_4}$) at 7.0 (broad multiplet, 5 H) for the phenyl protons, 6.72 (singlet, 1 H) for the vinyl proton which was superimposed on the phenyl protons, and three singlets at 3.90, 3.70, and 3.64, each representing three protons for the three methoxy groups. *Anal.* Calcd for $C_{14}H_{15}NO_5$: C, 60.60; H, 5.40; N, 5.05. Found: C, 60.12; H, 6.02; N, 5.36.

D. *o*-Tolyl Isocyanide.—After removal of the methanol, the thick oil, which showed no ir absorption in the ketenimine region, was distilled, giving a 60% yield of the imino ester **8**, bp 126–127° (0.25 mm). The ir spectrum displayed significant peaks at 3050 (shoulder), 3000, 2950, 1700, 1650, 1610, 1575, and 1250 cm^{-1}. The nmr spectrum displayed peaks ($\delta^{TMS}_{CCl_4}$) at 6.9 (broad multiplet, 4 H) for the phenyl protons, 6.80 (singlet, 1 H) for the vinyl proton superimposed on the phenyl protons, 3.95, 3.37, and 3.55, all singlets, each representing three protons for the three methoxy groups, and 2.12, a singlet (3 H) for the *o*-methyl group. *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.25; H, 5.50; N, 5.15. Found: C, 61.05; H, 5.75; N, 5.22.

E. *p*-Nitrophenyl Isocyanide. Ortho Ester Formation (13).—To 4.7 g (0.032 mol) of *p*-nitrophenyl isocyanide in 200 ml of methanol was added 4.5 g (0.032 mol) of dimethyl acetylenedicarboxylate. The solution was let stand for 2 weeks and the methanol was removed using a rotary evaporator. The viscous oil was dissolved in 50 ml of benzene and the benzene solution was allowed to evaporate at room temperature. After 2 days crystals had formed; they were collected and recrystallized from benzene, yield 2.2 g (20%), mp 155–159°. The ir spectrum (KBr) displayed significant peaks at 3340, 1725, 1650, 1550, and 1500 cm^{-1}. The nmr spectrum, in deuterioacetone, displayed a quartet at δ 8.10 (4 H, *p*-nitrophenyl protons), a singlet at 6.70 (1 H, vinyl proton), a singlet at 3.80 (3 H, carbomethoxy protons), and a singlet at 3.25 (9 H, methyl ortho ester protons). In addition, a very broad, ill-defined absorption centered at 9.66 integrating for one proton was also present (hydrogen bonded NH). *Anal.* Calcd for $C_{15}H_{18}N_2O_8$: C, 50.84; H, 5.08: N, 7.91; mol wt, 354. Found: C, 50.95; H, 5.10; N, 7.87; mol wt, 343.

F. *p*-Nitrophenyl Isocyanide. Imino Ester Formation (8).—If the above reaction mixture was let stand for only 1 week and the same work-up procedure was used, a small amount (*ca.* 1–2%) of the imino ester **8** could be isolated, mp 94–97°. The ir displayed significant peaks at 2950, 1700, 1670, and 1250 cm^{-1}. The nmr spectrum ($\delta^{TMS}_{CCl_4}$) displayed two doublets (4 H) for the *p*-nitrophenyl protons at 8.10 and 6.84, a singlet (1 H) at 6.75 for the vinyl proton, and three singlets, each representing three protons, at 3.91, 3.80, and 3.75 for the three methoxy groups. *Anal.* Calcd for $C_{14}H_{14}N_2O_7$: C, 52.20; H, 4.35; N, 8.70. Found: C, 52.19; H, 4.47; N, 8.70.

Reaction of Isocyanides with Phenylpropiolic Acid.—Phenylpropiolic acid (1 g) was dissolved in 35 ml of dry benzene and an equimolar amount of an isocyanide (cyclohexyl, *tert*-butyl, benzyl, or *p*-methoxyphenyl) was added. The solution was allowed to stand overnight. (If the benzene was moist, a small amount of the amine salt of phenylpropiolic acid would form owing to hydrolysis of the isocyanide.) Removal of the benzene using a rotary evaporator gave 0.4–0.6 g of pale yellow crystals, mp 255–257°. The ir spectrum displayed two strong peaks at 1820 and 1760 cm^{-1}, the former being weaker than the latter (a cyclic anhydride). A mixture melting point with an authentic sample[21] of 1-phenyl-2,3-naphthoic anhydride gave no depression. The ir spectrum of the product was identical with that of an authentic sample of 1-phenyl-2,3-naphthoic anhydride obtained by refluxing phenylpropiolic acid with acetic anhydride.

Registry No.—**6** (R = cyclohexyl), 38355-41-8; **7** (R = cyclohexyl), 31849-65-7; **8** (R = cyclohexyl), 38308-75-7; **8** (R = phenyl), 38308-76-8; **8** (R = *o*-tolyl), 38308-77-9; **8** (R = *p*-$NO_2C_6H_4$), 38308-78-0; **9** (R = cyclohexyl), 38308-79-1; **9** (R = *t*-Bu), 38308-80-4; **13** (R = *p*-$NO_2C_6H_4$), 38308-81-5; methyl propiolate, 922-67-8; cyclohexyl isocyanide, 931-53-3; dimethyl acetylenedicarboxylate, 762-42-5; *tert*-butyl isocyanide, 7188-38-7; *o*-tolyl isocyanide, 10468-64-1; phenylpropiolic acid, 637-44-5; 1-phenyl-2,3-naphthoic anhydride, 1985-37-1.

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Methyl- and Ethylnitrosocyanamide. Some Properties and Reactions[1]

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Methylnitrosocyanamide (**3**) and ethylnitrosocyanamide (**4**) were synthesized by aqueous nitrosation of the cyanamides. The ir spectra showed C≡N and N=O bands. The uv spectra indicated resonance structures similar to those of nitrosoureas and nitrosamines. The pmr of **3** and **4** (like those of dialkylnitrosamines) showed N-alkyl nonequivalence attributed to restricted rotation about the N–NO bond. In contrast, the pmr of alkylnitrosoureas showed NH_2 nonequivalence. The mass spectra of **3** and **4** had prominent peaks due to NO^+ and loss of N_2. Compound **4** was more stable to alkali and less stable to acid than ethylnitrosourea. In acid, **3** and **4** gave HNO_2 and the corresponding nitrosoureas (30–61%), perhaps because they are denitrosated to alkylcyanamides, hydrolyzed to alkylureas, and renitrosated. In alkali, **4** gave diazoethane (25%) and cyanate (79%). Nitrosation of methylguanidine proceeded slowly to give **3** (2%), methylnitrosourea (up to 35%), and a third unidentified uv-absorbing product.

Most *N*-nitroso compounds are powerful carcinogens in experimental animals and hence could be involved in the etiology of certain types of human cancer, if they were present in food or were synthesized by acid-catalyzed nitrosation in the stomach.[2] In support of the latter possibility, kinetic studies[3] showed that the acid-catalyzed N-nitrosation of some secondary amines, *N*-alkylureas, and *N*-alkylcarbamates proceeds very readily.

We reported[3d] that nitrosation of methylguanidine (**1**) gave methylnitrosourea (**2**), the new compound methylnitrosocyanamide (**3**), and an unidentified

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