

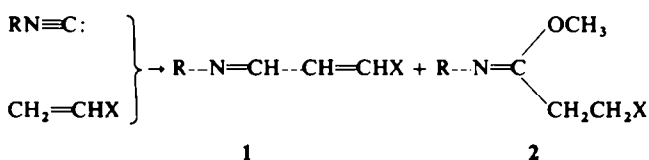
REACTION OF ISOCYANIDE WITH α,β -UNSATURATED CARBONYL AND NITRILE COMPOUNDS

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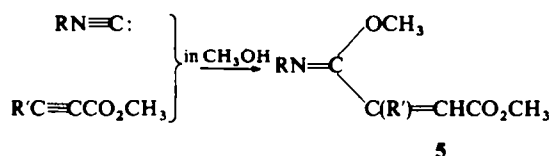
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Abstract—This paper reports new reactions of isocyanide with α,β -unsaturated carbonyl and nitrile compounds and with acetylene monocarboxylates. The reaction of isocyanide with α,β -unsaturated compound gives two types of products, (1 and 2). The product 2 is formed when the reaction is carried out in methanol. In *t*-butanol, 1 is produced exclusively.

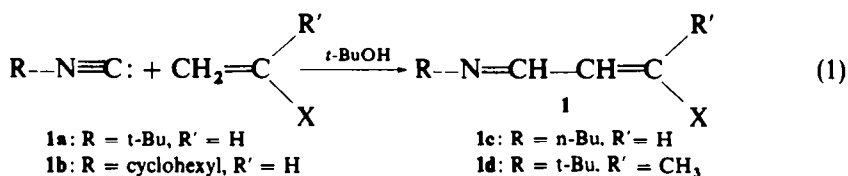


The reaction of isocyanide with acetylene monocarboxylate proceeds as follows:



Mechanisms of these reactions are discussed.

THIS paper describes an interesting new reaction of isocyanide with α,β -unsaturated nitrile and carbonyl compounds. Isocyanide is characterized by its nucleophilic nature due to the lone pair of electrons at the terminal C atom. We found that isocyanide reacts with electrophilic olefins such as acrylate in *t*-butanol according to Eq 1.



The structure of the product (1) may well be formulated as being produced by the α -addition of the β -C—H bond of acrylate to isocyanide. The results of the reactions of several isocyanides with methyl acrylate are shown in Table 1.

The reaction of Eq 1 in *t*-butanol seems to be specific for acrylate. Methacrylate and acrylonitrile do not react with isocyanide in *t*-butanol. In the reactions carried out in methanol, the results are somewhat different from those carried out in *t*-butanol. The methacrylate-isocyanide reaction takes place according to the mode of α -addition

(Eq 1), whereas the acrylonitrile-isocyanide reaction gives a product (**2a**) of different type.

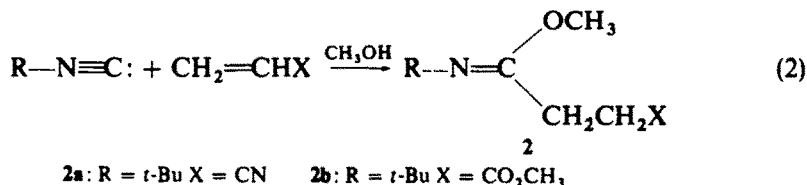


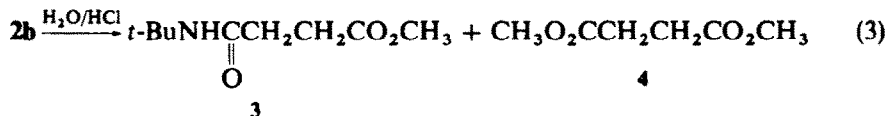
TABLE I. REACTION OF ISOCYANIDE WITH POLAR OLEFIN

R-NC (10 mmol)	Olefin (10 mmol)	Solvent (3-5 ml)	1 (%)	2 (%)
<i>t</i> -C ₄ H ₉ NC	CH ₂ =CHCO ₂ CH ₃	<i>t</i> -butanol ^a	44	
<i>c</i> -C ₆ H ₁₁ NC	CH ₂ =CHCO ₂ CH ₃	<i>t</i> -butanol ^a	43	
<i>n</i> -C ₄ H ₉ NC	CH ₂ =CHCO ₂ CH ₃	<i>t</i> -butanol ^a	13	
<i>t</i> -C ₄ H ₉ NC	CH ₂ =CHCO ₂ CH ₃	methanol ^b	11	35
<i>t</i> -C ₄ H ₉ NC	CH ₂ =CHCN	methanol ^b	--	9
<i>t</i> -C ₄ H ₉ NC	CH ₂ =C(CH ₃)CO ₂ CH ₃	methanol ^b	5	--

^a Reaction at 80° for 20 hr.

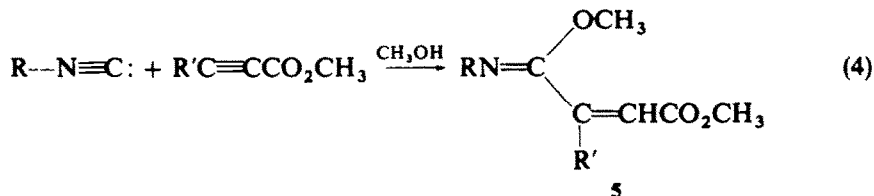
^b Reaction at 110° for 20 hr.

The acrylate-isocyanide reaction carried out in methanol gives the two products of **1** and **2b**. The structures of **2a** and **2b** were examined by IR and NMR spectra. In addition, they were confirmed on the basis of identification of the hydrolysis product of **2b**. In the acid hydrolysis of **2b**, the corresponding ester amide of succinic acid (**3**) and a small amount of dimethyl succinate (**4**) were formed (Eq 3).



Other olefins of electrophilic character, eg., crotonate, methacrylonitrile and methylenemalonate did not react with isocyanide in *t*-butanol and in methanol.

Acetylenemonocarboxylate reacts with isocyanide in methanol to give the product **5** (Eq 4). No reaction occurred between these components in *t*-butanol.



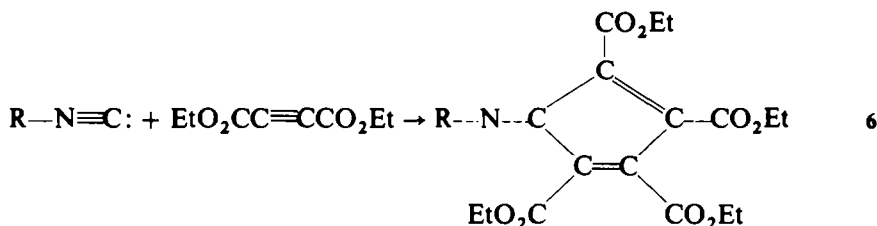
Some illustrative results of the reaction of isocyanide with acetylenemonocarboxylate are shown in Table 2.

The reaction of isocyanide with acetylenemonocarboxylate is related to the reaction of isocyanide with acetylene-dicarboxylate in which the cyclic 1:2 oligomer (**6**) is produced.¹

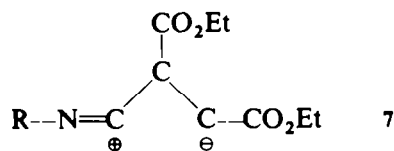
TABLE 2. REACTION OF ISOCYANIDE WITH ACETYLENEMONOCARBOXYLATE IN METHANOL^a

R-NC (10 mmol)	R'C \equiv CCO ₂ CH ₃ (10 mmol)	5 (%)
t-C ₄ H ₉ NC ^b	HC \equiv CCO ₂ CH ₃	12
c-C ₆ H ₁₁ NC ^b	HC \equiv CCO ₂ CH ₃	45
t-C ₄ H ₉ NC ^b	CH ₃ C \equiv CCO ₂ CH ₃	17

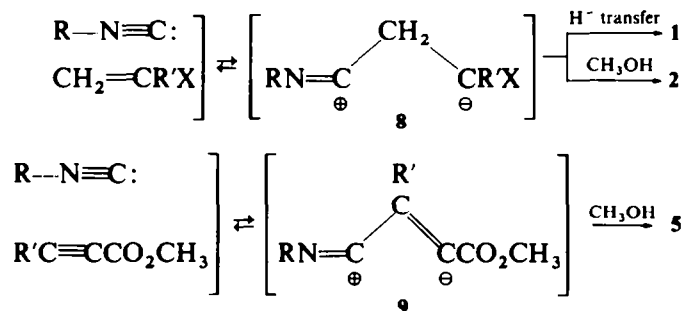
^a Methanol 3.5 ml. ^b Reaction at 110° for 20 hr.



The formation of 6 has been explained by a betain type intermediate (7). Two reactions of the present study, the isocyanide-olefin and isocyanide-acetylene reactions, may also be schematised by assuming the betain intermediate 8 and 9 respectively (Scheme 1).



Scheme 1

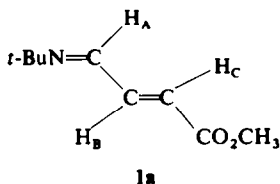


EXPERIMENTAL

Reagents. Methyl acrylate, methyl methacrylate, acrylonitrile and methacrylonitrile were all commercial reagents, which were purified by appropriate methods and distilled under N₂. Methyl propiolate² and methyl tetrolate³ were prepared from dibromosuccinate and β -dichloropropionate, respectively. Cyclohexyl, n-butyl and t-butylisocyanides were prepared by Ugi's procedure.⁴

Reaction of t-butyl isocyanide with methyl acrylate in t-butanol. A mixture of 0.83 g (10 mmol) t-butyl isocyanide and 0.86 g (10 mmol) methyl acrylate in 3.5 ml t-butanol was heated in a sealed tube at 80° for 20 hr. The mixture was fractionally distilled. The distillate boiling at 108–109°/45 mm was shown to

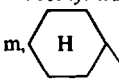
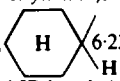
be the *trans* isomer of methyl γ -(*N*-*t*-butylimino)crotonate (**1a**), yield 44%; NMR (in CDCl_3): τ 8.73 (s, *t*-Bu), 6.20 (s, CO_2CH_3), 3.73 (d, H_C), 2.65 (q, H_B) and 1.99 (d, H_A), $J_{AB} = 8.5$ cs and $J_{BC} = 15.5$ cs;

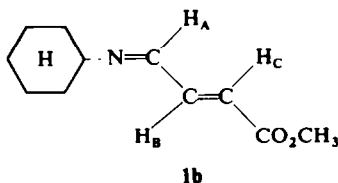


Principal IR bands (neat): 1712 (s), 1632 (w) and 1610 (s) cm^{-1} .

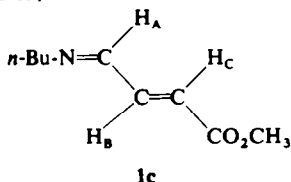
The treatment of **1a** with 2,4-dinitrophenylhydrazine gave the corresponding hydrazone, 2,4-(NO_2)₂C₆H₃NHN=CH—CH=CHCO₂CH₃, m.p. 191–193°. (Found: C, 44.40; H, 3.42; N, 19.16%. Calcd for C₁₁H₁₀O₆N₄, C, 44.91; H, 3.40; N, 19.05%).

Cyclohexyl isocyanide-methyl acrylate reaction and *n*-butyl isocyanide-methyl acrylate reaction in *t*-butanol were similarly performed.

Methyl *trans* γ -(*N*-cyclohexylimino)crotonate (**1b**), b.p. 94–95°/4 mm. NMR (in CDCl_3): τ 8.0–9.9 (broad, m,  6.9 (broad, m,  6.23 (s, CO_2CH_3), 3.78 (d, H_C), 2.70 (q, H_B) and 1.98 (d, H_A); $J_{BC} = 16$ cs and $J_{AB} = 9$ cs; principal IR bands (neat): 1720 (s), 1652 (m) and 1618 (m) cm^{-1} .



Methyl *trans* γ -(*N*-*n*-butylimino)crotonate (**1c**), b.p. 94–96°/7 mm; NMR (in CDCl_3): τ 9.2–7.5 (m, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{-N=}$), 6.42 (t, $-\text{CH}_2\text{-N=C}$), 6.20 (s, $-\text{CO}_2\text{CH}_3$), 3.76 (d, H_C), 2.70 (q, H_B) and 2.01 (d, H_A); $J_{AB} = 9$ cs and $J_{BC} = 15$ cs;



principal IR bands (neat): 1730 (s), 1650 (w) and 1625 (s) cm^{-1} .

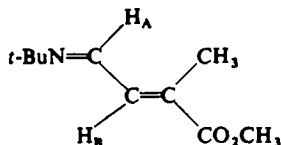
Reaction of *t*-butyl isocyanide with methyl acrylate in methanol. A mixture of 0.83 g (10 mmol) *t*-butyl isocyanide and 0.86 g (10 mmol) methyl acrylate in 3.5 ml MeOH was heated in a sealed tube at 110° for 20 hr. The fraction boiling at 103–112°/19 mm was collected and shown by GLPC analysis to contain two components. By comparison of its GLPC retention time and IR spectrum with the authentic sample, one component was identified as **1a**, yield 11%. The other component was isolated by preparative GLPC and shown to be **2b** by its NMR and IR spectrum as well as the hydrolysis product (see the following section). The yield of **2b** was 35%; NMR of **2b** (in CDCl_3): τ 8.70 (s, *t*-Bu), 7.40 (s, $-\text{CH}_2\text{CH}_2-$), 6.50 (s, $\text{CH}_3\text{O}-$) and 6.31 (s, CO_2CH_3); principal IR bands (neat): 1753 (s) and 1695 (m) cm^{-1} .

2b was treated with 10% HCl aq at room temp for 1 hr. The mixture was then extracted with ether. After removal of ether, the residue was analyzed by GLPC. By preparative GLPC, the main product was isolated and was identified as **3**; NMR (in CDCl_3): τ 8.65 (s, *t*-Bu), 7.47 (q, $-\text{CH}_2\text{CH}_2-$) and 6.30 (s, CO_2CH_3); principal IR bands (neat): 1740 (s), 1645 (s) and 1560 (s) cm^{-1} . The second product of the acid hydrolysis of **2b** was **4** (small amount), which was identified by comparison of the GLPC retention time with the authentic sample.

In a similar way, *t*-butyl isocyanide-acrylonitrile reaction and *t*-butyl isocyanide-methyl methacrylate reaction in MeOH were performed.

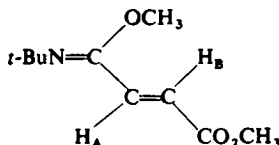
γ -(*N*-*t*-butylimino)- γ -methoxybutyronitrile (**2a**, R = *t*-Bu, X = CN). This was isolated by preparative GLPC; NMR of **2a** (in CDCl₃): τ 8.74 (s, *t*-Bu), 7.35 (s, —CH₂CH₂—) and 6.45 (s, OCH₃); principal IR bands (neat): 2270 (w) and 1690 cm⁻¹.

Methyl α -methyl- γ -(*N*-*t*-butylimino)crotonate (**1d**). This was isolated by preparative GLPC; NMR (in CDCl₃): τ 8.72 (s, *t*-Bu), 7.85 (s, —CH₃), 6.23 (s, —CO₂CH₃), 2.80 (d, H_B), 1.71 (d, H_A) and J_{A-B} = 8.5 cs;

**1d**

principal IR bands (neat); 1720 (s), 1636 (w) and 1610 (s) cm⁻¹.

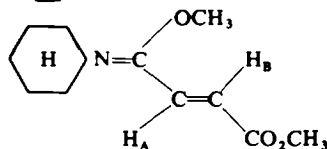
Reaction of *t*-butyl isocyanide with methyl propiolate in methanol. A mixture of 0.83 g (10 mmol) *t*-butyl isocyanide and 0.84 g (10 mmol) methyl propiolate in 3.5 ml MeOH was heated in a sealed tube at 110° for 20 hr. The product of **5** (R = *t*-Bu, R' = H, *trans* isomer) was isolated in 14% yield by fractional distillation, b.p. 70–73°/1 mmHg; NMR (in CDCl₃): τ 8.65 (s, *t*-Bu), 6.38 (s, —OCH₃), 6.20 (s, CO₂CH₃), 3.58 (d, H_A) and 2.70 (d, H_B);



principal IR bands (neat): 1738 (s), 1675 (m) and 1621 (m) cm⁻¹.

Cyclohexyl isocyanide—methyl propiolate reaction and *t*-butyl isocyanide—methyl tetrolate reaction in MeOH were similarly performed.

Methyl *trans*- γ -(*N*-cyclohexylimino)- γ -methoxycrotonate (**5**, R = *c*-C₆H₁₁, R' = H), b.p. 70–73°/1 mm; NMR (in CDCl₃): τ 9.00–8.50 (m,) , 6.38 (s, —OCH₃), 6.20 (s, CO₂CH₃), 3.58 (d, H_B) and 2.70 (d, H_A);



principal IR bands (neat): 1738 (s), 1675 (m) and 1621 (m) cm⁻¹.

Methyl *cis* and *trans*- γ -(*N*-*t*-butylimino)- γ -methoxy- β -methylcrotonate (**5**, R = *t*-Bu, R' = CH₃), b.p. 66–72°/0.6 mm, yield 17%; NMR (in CDCl₃): τ 8.72 (s, *t*-Bu), 7.92, 7.68 (2d, CH₃), 6.41, 6.37 (2s, OCH₃), 6.30, 6.26 (2s, CO₂CH₃) and 4.12 (d, =CH—); Principal IR bands (neat): 1730 (s), 1695 (m) and 1645 (m) cm⁻¹.

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