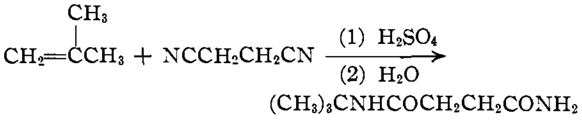
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

A New Reaction of Nitriles. III. Amides from Dinitriles[1]

BY FREDERIC R. BENSON[2] WITH JOHN J. RITTER

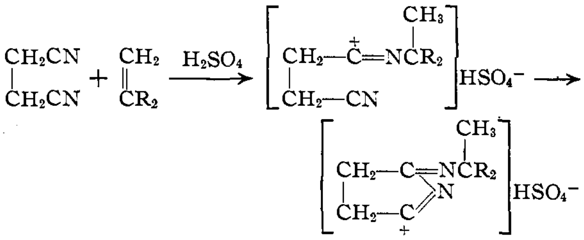
The previous publications in this series have described the interaction of mononitriles and olefins to form N-substituted amides,[3] and the application of this reaction to the synthesis of *t*-carbinamines.[4] The use of dinitriles in this substituted amide synthesis, as well as a description of a variation of the reaction in which alcohols are used in place of olefins, form the subject matter of the present report.

Reaction of one mole of malononitrile, succinonitrile or glutaronitrile with two moles of an olefin such as isobutene, 2-methylbutene-2, camphene or diisobutene was carried out according to the previously described procedure.[3] In most instances the anticipated N,N′-disubstituted diamides were obtained (Table I). The reaction of succinonitrile with isobutene, diisobutene or camphene, however, under the same conditions resulted in the formation of N-monosubstituted succinamides, the second cyanide group of the dinitrile hydrolyzing in the usual manner. This anomalous behavior of succinonitrile



$$CH_2{=}\overset{\overset{CH_3}{|}}{C}CH_3 + NCCH_2CH_2CN \xrightarrow[(2)\ H_2O]{(1)\ H_2SO_4} (CH_3)_3CNHCOCH_2CH_2CONH_2$$

possibly involves a cyclic mechanism according to the scheme



Subsequent hydrolytic reactions of the above intermediate would give rise to the monosubstituted amide. There is no immediately obvious explanation for the fact that 2-methylbutene-2-reacts with succinonitrile to yield the N,N′-diamide.

In view of the requirement of a strongly acid medium for the conduct of the reaction, it seems probable that a carbonium ion is an essential intermediate. Consideration of other possible sources of carbonium ions, besides the alkene–acid combination, led to the idea that alcohols might also function in this synthesis.[5] Accordingly, succinonitrile and *t*-butanol were subjected to reaction in the acetic acid–sulfuric acid solvent found suitable for use with olefins. The product isolated was found to be N-mono-*t*-butyl succinamide, identical with that obtained using isobutene. By means of this modification, it was found possible to utilize cyanogen in the synthesis of a diamide. Although preliminary work had failed to develop a means of effecting reaction between cyanogen and diisobutene, when *t*-butanol was employed, N,N′-di-*t*-butyloxamide was obtained, having the same properties described by Brander.[6]

The use of a secondary alcohol was investigated next. While reaction of secondary alcohols and nitriles in the acetic acid–sulfuric acid solvent could not be effected, concentrated sulfuric acid alone proved to be satisfactory for this purpose. Isopropyl alcohol and malononitrile produced N,N′-diisopropylmalonamide which has previously been prepared by conventional means.[7] Efforts to utilize a primary alcohol in the reaction proved fruitless; expedients such as the use of elevated temperatures, prolonged heating or the employment of fuming sulfuric acid were unsuccessful in the production of N-primary alkyl amides.

Comparison of the yields (Table I) of the products from dinitriles and olefins or alcohols, reveals that fumaronitrile is appreciably more active than any of the saturated dinitriles in the formation of substituted amides. It is evident that the reactivity of the cyanide groups is enhanced by the presence of the double bond.

Experimental

The following specific directions will serve to illustrate the methods followed in the preparation of the N-alkyl diamides. Recrystallizations of most of the succinamides and glutaramides were performed using benzene to which a small quantity of alcohol had been added. N,N′-Diisopropyl and *t*-butyl malonamides were recrystallized from hexane, while for N,N′-di-*t*-octylmalonamide, di-*t*-butyloxamide, and di-*t*-butylfumaramide an alcohol-water mixture was used. Glacial acetic acid was required for N,N′-dicyclohexylfumaramide.

The carbon, hydrogen and Kjeldahl nitrogen determinations were performed in the Laboratory of Microchemistry at New York University.

N,N′-Di-*t*-amylglutaramide.—A mixture of 50 ml. of glacial acetic acid, 10.2 g. (0.1 mole) of concentrated sulfuric acid and 4.7 g. (0.05 mole) of glutaronitrile was prepared at room temperature. To this solution was added 7.0 g. of 2-methylbutene-2 which dissolved immediately. The temperature of the reaction rose to 50° and was kept below this point by periodic cooling with water. After remaining overnight, the reaction mixture was poured into 250 ml. of water; white crystals separated quickly from

---

[1] Based upon the thesis submitted by Frederic R. Benson in February, 1947, to the Graduate School of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Present address: Remington Rand, Inc., South Norwalk, Conn.

[3] J. J. Ritter and P. P. Minieri, THIS JOURNAL, **70**, 4045 (1948).

[4] J. J. Ritter and J. Kalish, *ibid.*, **70**, 4048 (1948).

[5] The use of alcohols was developed with the collaboration of Robert M. Lusskin, Ph.D. research in progress.

[6] M. Brander, *Rec. trav. chim.*, **37**, 67 (1917).

[7] R. W. West, *J. Chem. Soc.*, **127**, 750 (1925).

TABLE I

N-ALKYL DIAMIDES

RNHCOYCONHR′; from NCYCN + alkenes or alcohols

Alkene or alcohol	R, R′[a]	Y	M. p., °C.	Yield, %	Formula	Nitrogen, %	
						Calcd.	Found
t-Butanol	$(CH_3)_3C$—	....	176	20	$C_{10}H_{20}O_2N_2$	..	..
Isopropanol	$(CH_3)_2CH$—	—CH_2—	115	40	$C_9H_{18}O_2N_2$	15.0	15.1
Isobutene	$(CH_3)_3C$—	—CH_2—	115	50	$C_{11}H_{22}O_2N_2$	13.1	12.9
Diisobutene	C_8H_{17}-(*t*-octyl)	—CH_2—	108	30	$C_{19}H_{38}O_2N_2$	8.6	8.6
t-Butanol[e]	R=$(CH_3)_3C$— R′=H	—$(CH_2)_2$—	149	25	$C_8H_{16}O_2N_2$	16.3	16.2
2-Methylbutene-2	$C_2H_5(CH_3)_2C$—	—$(CH_2)_2$—	164	40	$C_{14}H_{28}O_2N_2$	10.9	10.8
Diisobutene	R=C_8H_{17}-(*t*-octyl) R′=H	—$(CH_2)_2$—	150	50	$C_{12}H_{24}O_2N_2$	12.3	12.8
Camphene	R=$C_{10}H_{17}$-(isobornyl) R′=H	—$(CH_2)_2$—	130	24	$C_{14}H_{24}O_2N_2$	11.1	11.0
Isopropanol	$(CH_3)_2CH$—	—CH=CH—	320d	80	$C_{10}H_{18}O_2N_2$	14.1	14.2[b]
t-Butanol	$(CH_3)_3C$—	—CH=CH—	310d	88	$C_{12}H_{22}O_2N_2$	..	..[c]
Cyclohexanol	C_6H_{11}—	—CH=CH—	320d	87	$C_{16}H_{26}O_2N_2$	10.1	9.8[d]
Isobutene	$(CH_3)_3C$—	—$(CH_2)_3$—	196	25	$C_{13}H_{26}O_2N_2$	11.5	11.4
2-Methylbutene-2	$C_2H_5(CH_3)_2C$—	—$(CH_2)_3$—	147	35	$C_{15}H_{30}O_2N_2$	10.3	10.4

[a] R = R′ except where otherwise noted. [b] Calcd.: C, 60.6; H, 9.1. Found: C, 60.9; H, 8.9. [c] Calcd.: C, 63.7; H, 9.8. Found: C, 63.6; H, 9.3. [d] Calcd.: C, 69.0; H, 9.4. Found: C, 68.9; H, 9.2. [e] Or isobutene.

the solution. These were filtered, slurried with 50 ml. of dilute sodium carbonate solution, washed with 50 ml. of water and recrystallized from water. A further crop of crystals was obtained by neutralizing the acid filtrate with sodium carbonate. This batch of crystals was also recrystallized from water. On twice recrystallizing the combined yield from a mixture of benzene and hexane, 5.0 g. of the compound with a constant melting point of 147° was obtained.

N-Mono-*t*-butylsuccinamide: (1) From Isobutene.—Isobutene was passed for two and one-half hours into a solution of 16 g. (0.2 mole) of succinonitrile in 100 ml. of glacial acetic acid and 40.8 g. of concentrated sulfuric acid until 25 g. (0.45 mole) was absorbed. The mixture was allowed to stand overnight and was worked up as described above.

(2) **From *t*-Butanol.**—To a mixture of 10.2 g. of concentrated sulfuric acid, 50 ml. of glacial acetic acid and 4.0 g. of succinonitrile was added 7.4 g. (0.1 mole) of *t*-butanol. The temperature of the reaction mixture rose spontaneously to 50°, and was maintained below this point by occasional cooling. After standing overnight, the product was separated and worked up as described above. Its melting point, alone and mixed with the product from isobutene, was 149°.

N,N′-Di-*t*-butyloxamide.—Cyanogen, generated from 40 g. of sodium cyanide, was passed into a mixture of 40 ml. of glacial acetic acid, 10.2 g. of concentrated sulfuric acid and 7.5 g. of *t*-butanol. The temperature rose from 20 to 26°. Isolation and purification of the product was accomplished as indicated above immediately after stopping the flow of cyanogen.

N,N′-Diisopropylfumaramide.—To 3.9 g. of fumaronitrile dissolved at room temperature in 20 ml. of concentrated sulfuric acid, was added, over a period of twenty minutes, 6.0 g. (0.1 mole) of isopropyl alcohol, the temperature being kept below 45° by means of an ice-bath. After two hours the reaction mixture was treated as described to separate and purify the product. Both the recrystallized and unrecrystallized material melted with decomposition at 320°, after beginning to darken at 225°. The substance decolorizes aqueous potassium permanganate in the cold. The following qualitative solubilities were noted: insoluble in water, benzene, acetone, ethyl acetate; soluble in ethanol and hot methanol.

Summary

A series of dinitriles have been converted to N-substituted diamides by means of the reaction with olefins. Use of tertiary and secondary alcohols instead of alkenes in this reaction also leads to N-substituted amides.

WASHINGTON SQUARE
NEW YORK, N. Y.

RECEIVED JUNE 30, 1949