The Potassium Fluoride-catalyzed Reaction. IV. The Michael Addition of Nitroalkanes to α, β-Unsaturated Compounds

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Wakamatsu and Shimo[1] recently reported liquid ammonia-catalyzed Michael additions of nitroalkanes to acrylonitrile and other acceptors, but such a catalyst has not generally been utilized in synthesis. In connection with previously-reported additions[2-4] of reactive methylene compounds to α, β-unsaturated compounds, using potassium fluoride as the catalyst, the present study deals with the additions of nitroalkanes to such Michael acceptors as acrylonitrile, methyl acrylate, methyl methacrylate, methyl crotonate, dimethyl fumarate and methyl cinnamate.

The addition of nitromethane to acrylonitrile in 95% ethanol containing potssium fluoride at the refluxing temperature of the solution gave crystalline tris(β-cyanoethyl)nitromethane (I) after one hour, even when a 1 : 1 molar proportion of the reactants was used. When dioxane-water (9 : 1) was employed as the solvent, the addition product I was obtained in a very low yield (0.2%); on the other hand, the starting materials were recovered unreacted in the case of a dioxane (anhydrous) solution under the same conditions. Adamcik et al.[5] have already observed that no cyanoethylation occurs in such nonhydroxylic solvents as dioxane and tetrahydrofuran.

In the cyanoethylation of nitromethane, it is noted that the yield of I is dependent upon the concentration of potassium fluoride used. The use of 0.01 mole of the fluoride per mole of nitromethane yielded 11% of I, but 0.1 mole of the catalyst gave a 63% yield. Furthermore, the nature of the solvent has a remarkable effect on the rate of the reaction and on the product yield. The yield increased with the solvating ability of the solvent in the following order;

$$(CH_3)_3COH < (CH_3)_2CHOH < 50\%\ \text{aqueous}\ C_2H_5OH \approx 95\%\ C_2H_5OH$$

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[1] S. Wakamatsu and K. Shimo, *J. Org. Chem.*, **27**, 1609 (1962).

[2] H. Yasuda, H. Midorikawa and S. Aoyama, *Sci. Papers, Inst. Phys. Chem. Res., Tokyo*, **53**, 19 (1959).

[3] S. Kambe, H. Yasuda and H. Midorikawa, ibid., **58**, 118 (1964).

[4] S. Kambe and H. Yasuda, ibid., **58**, 148 (1964).

[5] J. A. Adamcik and E. J. Miklasiewicz, *J. Org. Chem.*, **28**, 336 (1963).

Table I. Nitro compounds obtained from nitroalkanes

Compound	R_1	R_2	R_3	R_4	R_5	B. p. °C/mmHg	Lit. °C/mmHg	Reac. time hr.	Yield %
I	$(CH_2)_2CN$	$(CH_2)_2CN$	H	H	CN	a)		2	63
II	CH_3	H	H	H	CN	106—107/2	107—110/2[b]	2	67
III	C_2H_5	H	H	H	CN	112—113/2	110/1[e]	2	52
IV	CH_3	CH_3	H	H	CN	108—109/2	105—107/1[e]	2	53
V	H	H	H	H	$COOCH_3$	79— 80/1	82— 83/3[c]	5	34
IV	H	$(CH_2)_2COOCH_3$	H	H	$COOCH_3$	141—143/1		5	48
VII	CH_3	H	H	H	$COOCH_3$	89— 90/2	88— 89/2[c]	5	31
VIII	CH_3	$(CH_2)_2COOCH_3$	H	H	$COOCH_3$	154—155/2		5	40
IX	C_2H_5	H	H	H	$COOCH_3$	97— 98/2	97/2[c]	5	24
X	C_2H_5	$(CH_2)_2COOCH_3$	H	H	$COOCH_3$	164—165/2		5	53
XI	CH_3	CH_3	H	H	$COOCH_3$	77— 78/1	77—78.5/1.3[c]	5	80
XII	H	H	H	CH_3	$COOCH_3$	76— 77/2	82— 83/3[c]	10	29
XIII	CH_3	H	H	CH_3	$COOCH_3$	88— 89/2	88— 89/2[c]	10	31
XIV	C_2H_5	H	H	CH_3	$COOCH_3$	94— 95/4	90— 93/4[c]	10	34
XV	CH_3	CH_3	H	CH_3	$COOCH_3$	75— 76/2	72/1.3[d]	10	27
XVI	H	H	CH_3	H	$COOCH_3$	77— 79/1		20	24
XVII	CH_3	H	CH_3	H	$COOCH_3$	98— 99/2		20	6
XVIII	C_2H_5	H	CH_3	H	$COOCH_3$	92— 93/1		20	5
XIX	CH_3	CH_3	CH_3	H	$COOCH_3$	91— 92/1		20	4
XX	CH_3	CH_3	$COOCH_3$	H	$COOCH_3$	116—118/1	118—120/1[d]	7	54

a) M. p. 114—115°C. Lit., m. p. 114°C. H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **65**, 25 (1943).
b) G. D. Buckley, T. J. Elliott, F. G. Hunt and A. Lowe, *J. Chem. Soc.*, **1947**, 1505.
c) N. J. Leonard and G. L. Shoemaker, *J. Am. Chem. Soc.*, **71**, 1760 (1949).
d) M. C. Kloetzel, *J. Am. Chem. Soc.*, **70**, 3571 (1948).

In general, all primary and secondary alcohols react easily with acrylonitrile in the presence of alkaline catalysts to form the corresponding alkoxypropionitriles, but a negligible amount of ethoxypropionitrile is obtained, even in the presence of ethanol, when potassium fluoride is used.

Acrylonitrile also reacted with other nitroalkanes within two hours (see Table I). Prolonged heating (for more than two hours) did not increase the yield. No bis- or tris-cyanoethylated products were obtained in these reactions even in the presence of an excess of acrylonitrile.

Methyl acrylate readily condensed with nitroalkanes within five hours at about 80°C under the catalytic influence of potassium fluoride. The variation in adducts obtained may be attributed to the difference in the number of replaceable hydrogen atoms of the acidic nitro compounds. 2-Nitropropane, thus, gave only a 1 : 1-addition product, whereas the other nitroalkanes examined yielded 1 : 1- and 1 : 2-adducts in each case (see Table I).

In the addition of nitroalkanes to methyl methacrylate, methyl crotonate and methyl cinnamate in the presence of potassium fluoride, the yield decreased in the following order;

$$CH_2=C(CH_3)COOCH_3 > CH_3CH=CHCOOCH_3 > C_6H_5CH=CHOOCH_3$$

Methyl 2-methyl-4-nitrobutanoate (XII), for example, was obtained when methyl methacrylate was allowed to react with nitromethane at about 80°C for less than ten hours. Methyl crotonate gave the corresponding adduct XVI with nitromethane, but the relative yield was much lower than those obtained from the methacrylate, even after treatment had been continued for twenty hours. Methyl cinnamate, however, gave no evidence of reaction with the nitroalkanes examined, even after they had been refluxed for thirty hours, and it was recovered quantitatively.

This phenomenon[6] has also been observed in other Michael additions. This suggests that the substitution of the methyl or phenyl group at the β-position of the acceptor would offer a larger steric hindrance to nitroalkane addition than the substitution of the methyl group at the α-position.

The extension of these studies to dimethyl fumarate had disclosed an advantage of employing potassium fluoride as a catalyst; i. e., the fumarate yielded dimethyl 3-methyl-3-nitro-1, 2-butanedicarboxylate (XX) from 2-nitropropane, but the addition products from the other nitroalkanes examined could not be purified by means of distillation.

The results obtained are shown in Table I, along with the infrared data.

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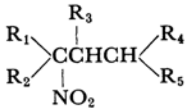
[6] R. Connor and Wm. R. McClellan, ibid., **3**, 570 (1939).

AND α, β-UNSATURATED MATERIALS



$R_1R_2\underset{NO_2}{\mathrm{C}}\overset{R_3}{\mathrm{C}}\mathrm{HCH}R_4R_5$

Forumula	C, %		H, %		N, %		C≡N str. cm^{-1}	C=O str. (ester) cm^{-1}	NO$_2$ str. asym. cm^{-1}	NO$_2$ str. sym. cm^{-1}
	Calcd.	Found	Calcd.	Found	Calcd.	Found				
							2250m		1542 s	1340m
							2240m		1540 s	1350m
							2250m		1550 s	1345m
							2240m		1540 s	1345m
$C_5H_9O_4N$	40.81	41.02	6.12	6.02	9.52	9.48		1730 s	1550 s	1345m
$C_9H_{15}O_6N$	46.35	46.35	6.43	6.26	6.00	5.89		1730 s	1545 s	1350sh
								1730 s	1543 s	1360m
$C_{10}H_{17}O_6N$	48.58	48.72	6.88	6.64	5.66	5.58		1730 s	1538 s	1360m
								1738 s	1550 s	1350m
$C_{11}H_{19}O_6N$	50.57	50.86	7.27	6.98	5.36	5.27		1730 s	1540 s	1320m
								1735 s	1538 s	1350m
								1725 s	1550 s	1340sh
								1730 s	1545 s	1358m
								1730 s	1550 s	1340m
								1738 s	1540 s	1348m
$C_6H_{11}O_4N$	51.89	51.29	5.94	5.90	7.56	7.67		1730 s	1550 s	1350sh
$C_7H_{13}O_4N$	47.99	48.01	7.48	7.66	8.00	7.80		1733 s	1548 s	1360m
$C_8H_{15}O_4N$	50.78	51.09	7.99	7.52	7.40	7.27		1730 s	1550 s	1360sh
$C_8H_{15}O_4N$	50.78	49.78	7.99	7.56	7.40	7.40		1735 s	1540 s	1350m
								1730 s	1542 s	1343m

e) U. S. Pat. 2361259 (1944); *Chem. Abstr.*, **39**, 2079 (1945).
Abbriviation; s, strong. m, medium, sh, shoulder. str., stretching. asym., asymmetric. sym., symmetric.
The infrared data were obtained by Shimazu IR-27C infrared spectrophotometer. Compound I was measured in KBr disk, and all other compounds were measured in liquid film.

Experimental*

The Addition of Nitroalkanes to Acrylonitrile. —A mixture of an appropriate nitroalkane (0.1 mole) and acrylonitrile (0.1 mole, 5.3 g.) in ethanol (50 ml.) containing potassium fluoride (0.01 mole, 0.58 g.) was heated to reflux on a water bath for a suitable number of hours (cf, Table I). After the catalyst had been removed by filtration, the reaction mixture was poured into water (20 ml.). The resulting oily matter was extracted with ether, and the ethereal extract was dried over anhydrous calcium chloride. After the solvent had then been removed, the residual oil was distilled fractionally under diminished pressure. The results obtained are summarized in Table I. In the case of nitromethane, the only product obtained was that of the tris-cyanoethylation; no mono- or bis-cyanoethylated product was detected.

The Addition of Nitroalkanes to *α*, *β*-Unsaturated Esters. — The procedure used was essentially the same as that described above. The yields are also listed in Table I.

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* All boiling and melting points are uncorrected.