Solvent-Catalyzed Michael Reaction of Nitroparaffins with Acrylic Acid Derivatives in Liquid Ammonia

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Received October 16, 1961

Michael-type condensation of nitroparaffins with acrylonitrile, acrylic ester, or acrylamide can take place without the use of catalyst in liquid ammonia to give an excellent yield of a variety of products depending upon proportions of the reactants. The reaction is characteristic of an effective catalytic action of the solvent. Eight new compounds have been prepared in the present investigation.

Michael-type condensation of nitroparaffins with acrylonitrile,[1,2] acrylic ester,[3,4] or acrylamide[5] has usually been achieved under the influence of a strong alkaline catalyst such as potassium hydroxide, sodium ethoxide, or benzyltrimethylammonium hydroxide (Triton B). Triethylamine[6] or certain anion exchange resins[7] were also used effectively as catalyst in the carbalkoxyethylation reaction of nitroparaffins. Recently we reported[8,9] a new modification of the Michael reaction wherein derivatives of malonic and cyanoacetic acids could each be condensed with acrylonitrile, acrylic ester, or acrylamide without the use of catalyst in liquid ammonia to yield the corresponding condensation products. It has now

TABLE I

MICHAEL REACTION OF NITROPARAFFINS WITH ACRYLIC ACID DERIVATIVES IN LIQUID AMMONIA

RNO_2 R	$CH_2{=}CH{-}X$ X	Mole Ratio $RNO_2{:}CH_2{=}CH{-}X$	Method[a]	Product	Yield, %[b]
CH_3	CN	1:1	B	$O_2NCH(CH_2CH_2CN)_2$	68[c]
CH_3	CN	1:3	A	$O_2NC(CH_2CH_2CN)_3$	94[d]
CH_3	$CO_2C_2H_5$	1:1	B	$O_2NCH_2CH_2CH_2CO_2C_2H_5$	28[c]
				$O_2NCH(CH_2CH_2CO_2C_2H_5)_2$	55[c]
CH_3	$CO_2C_2H_5$	1:3	B	$O_2NCH(CH_2CH_2CO_2C_2H_5)_2$	56
				$O_2NC(CH_2CH_2CO_2C_2H_5)_3$	34
CH_3	$CONH_2$	1:1	A	$O_2NCH(CH_2CH_2CONH_2)_2$	12[c,e,f]
C_2H_5	CN	1:2	B[g]	$CH_3CH(NO_2)CH_2CH_2CN$	11
				$CH_3C(NO_2)(CH_2CH_2CN)_2$	77
C_2H_5	$CO_2C_2H_5$	1:2	B[h]	$CH_3CH(NO_2)CH_2CH_2CO_2C_2H_5$	12
				$CH_3C(NO_2)(CH_2CH_2CO_2C_2H_5)_2$	77
C_2H_5	$CONH_2$	1:2	A	$CH_3C(NO_2)(CH_2CH_2CONH_2)_2$	57[f]
C_3H_7	CN	1:1	B	$C_2H_5CH(NO_2)CH_2CH_2CN$	71[c]
				$C_2H_5C(NO_2)(CH_2CH_2CN)_2$	26[c]
C_3H_7	CN	1:2	B	$C_2H_5C(NO_2)(CH_2CH_2CN)_2$	76
C_3H_7	$CO_2C_2H_5$	1:1	B[i]	$C_2H_5CH(NO_2)CH_2CH_2CO_2C_2H_5$	76[c]
				$C_2H_5C(NO_2)(CH_2CH_2CO_2C_2H_5)_2$	14[c]
C_3H_7	$CO_2C_2H_5$	1:2	B	$C_2H_5CH(NO_2)CH_2CH_2CO_2C_2H_5$	44
				$C_2H_5C(NO_2)(CH_2CH_2CO_2C_2H_5)_2$	52
C_3H_7	$CONH_2$	1:1	A[j]	$C_2H_5CH(NO_2)CH_2CH_2CONH_2$	71[f]
i-C_3H_7	CN	1:1	B	$(CH_3)_2C(NO_2)CH_2CH_2CN$	68
i-C_3H_7	$CO_2C_2H_5$	1:1	B	$(CH_3)_2C(NO_2)CH_2CH_2CO_2C_2H_5$	38
i-C_3H_7	$CONH_2$	1:1	A	$(CH_3)_2C(NO_2)CH_2CH_2CONH_2$	51[f]

[a] See Experimental. [b] Based on RNO_2. [c] Based on $CH_2{=}CH{-}X$. [d] Under method B, the yield was 97%. [e] When the reaction was carried out as in B with three molar equivalents of acrylamide none of the condensation product could be obtained and starting materials were recovered quantitatively. [f] For identification, the product was also prepared in the course of the present work by ammonolysis of the condensation product from the nitroparaffin and ethyl acrylate with liquid ammonia. [g] From equimolar quantities of the reactants, primarily the dicyanoethylation product was formed. The yield was 79% (based on acrylonitrile) accompanied by a 9% of monocyanoethylation product. [h] The reactants in equimolecular proportions gave chiefly disubstitution product. The yield was 61% (based on ethyl acrylate) accompanying a 25% of monosubstitution product. [i] When the reaction was carried out with two moles of 1-nitropropane and one mole of ethyl acrylate, the monocarbethoxyethylation product was obtained exclusively; yield 83% (based on ethyl acrylate). [j] Even with two molar equivalents of acrylamide in A, the monosubstitution product was produced exclusively. The yield was 78%.

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(1) O. Wulff, H. Hopff, and G. Wiest, German Patent 728,531 (October 29, 1942).

(2) H. A. Bruson, U. S. Patent 2,361,259 (October 24, 1944).

(3) H. A. Bruson, U. S. Patent 2,342,119 (February 22, 1944).

(4) H. A. Bruson, U. S. Patent 2,390,918 (December 11, 1945).

(5) H. A. Bruson, U. S. Patent 2,370,142 (February 27, 1945).

(6) M. C. Kloetzel, U. S. Patent 2,554,831 (May 29, 1951).

(7) C. J. Schmidle and R. C. Mansfield, U. S. Patent 2,658,070 (November 3, 1953).

(8) K. Shimo and S. Wakamatsu, *J. Org. Chem.*, **26**, 3788 (1961).

(9) S. Wakamatsu, *J. Org. Chem.*, **27**, 1285 (1962).

TABLE II

PHYSICAL PROPERTIES OF MICHAEL REACTION PRODUCTS, $O_2NCR_1R_2R_3$

R_1	R_2	R_3	M.P. or B.P. (mm.)	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
H	CH_2CH_2CN	CH_2CH_2CN	66–67[a,o]	$C_7H_9N_3O_2$	50.29	50.42	5.43	5.48	25.14	24.85
CH_2CH_2CN	CH_2CH_2CN	CH_2CH_2CN	112.5–114[b,p]	$C_{10}H_{12}N_4O_2$					25.44	24.97
H	H	$CH_2CH_2CO_2C_2H_5$	96 (2)[c]	$C_6H_{11}NO_4$	44.71	44.72	6.88	6.72	8.69	8.60
H	$CH_2CH_2CO_2C_2H_5$	$CH_2CH_2CO_2C_2H_5$	160–161 (2)[d]	$C_{11}H_{19}NO_6$	50.57	50.54	7.33	7.10	5.36	5.39
$CH_2CH_2CO_2C_2H_5$	$CH_2CH_2CO_2C_2H_5$	$CH_2CH_2CO_2C_2H_5$	212–216 (2–3)[d]	$C_{16}H_{27}NO_8$	53.18	53.69	7.53	7.49	3.88	3.52
H	H	$CH_2CH_2CONH_2$	88–89.5[d,o,r]	$C_4H_8N_2O_3$	36.36	36.47	6.10	6.07	21.20	20.97
H	$CH_2CH_2CONH_2$	$CH_2CH_2CONH_2$	141–142.5[e,p]	$C_7H_{13}N_3O_4$	41.38	41.43	6.45	6.31	20.68	20.61
CH_3	CH_2CH_2CN	CH_2CH_2CN	210–212 (1)[d,f]	$C_8H_{11}N_3O_2$	53.03	52.69	6.12	5.81	23.19	22.50
CH_3	H	$CH_2CH_2CO_2C_2H_5$	94–95 (1)[d]	$C_7H_{13}NO_4$	47.99	48.12	7.48	7.31	8.00	7.55
CH_3	$CH_2CH_2CO_2C_2H_5$	$CH_2CH_2CO_2C_2H_5$	152 (1–2)[g]	$C_{12}H_{21}NO_6$	52.35	52.13	7.69	7.81	5.09	5.11
CH_3	$CH_2CH_2CONH_2$	$CH_2CH_2CONH_2$	129.5–131[d,q]	$C_8H_{15}N_3O_4$	44.23	44.29	6.90	6.79	19.35	19.18
C_2H_5	H	CH_2CH_2CN	115 (3)[h]	$C_6H_{10}N_2O_2$	50.69	50.69	7.09	6.78	19.71	19.21
C_2H_5	CH_2CH_2CN	CH_2CH_2CN	216 (2.5–3)[d,i]	$C_9H_{13}N_3O_2$	55.37	55.66	6.71	6.16	21.53	21.23
C_2H_5	H	$CH_2CH_2CO_2C_2H_5$	103–104 (3–4)[j]	$C_8H_{15}NO_4$	50.78	50.52	7.99	7.87	7.40	7.38
C_2H_5	$CH_2CH_2CO_2C_2H_5$	$CH_2CH_2CO_2C_2H_5$	172–174 (2–3)[k]	$C_{13}H_{23}NO_6$	53.97	53.85	8.01	7.91	4.84	4.83
C_2H_5	H	$CH_2CH_2CONH_2$	84–85.5[d,q]	$C_6H_{12}N_2O_3$	44.99	45.10	7.55	7.44	17.49	17.20
CH_3	CH_3	CH_2CH_2CN	120–121 (4)[l]	$C_6H_{10}N_2O_2$	50.69	50.34	7.09	6.97	19.71	19.32
CH_3	CH_3	$CH_2CH_2CO_2C_2H_5$	108–110 (3)[m]	$C_8H_{15}NO_4$	50.78	50.56	7.99	7.84	7.40	7.04
CH_3	CH_3	$CH_2CH_2CONH_2$	77–81[n,q]	$C_6H_{12}N_2O_3$	44.99	45.03	7.55	7.60	17.49	17.43

[a] Ref. 1, m.p. 60–63°. [b] Ref. 2, m.p. 114°. [c] Lit.[10] reported b.p. 115° (2 mm.). [d] New compound or product whose properties have not been reported in literature. [e] Ref. 10, m.p. 146°. [f] Decomposed to some extent upon distillation. Ref. 1, ref. 2 reported that this product could not be distilled without decomposition. [g] Ref. 3, b.p. 154–155° (1 mm.). [h] Ref. 2, b.p. 110° (1 mm.). [i] Decomposed to some extent upon distillation. Ref. 2 reported that this product was nondistillable. [j] Ref. 3, b.p. 90–91° (1 mm.). [k] Ref. 3, b.p. 160–164° (1 mm.). [l] Ref. 2, b.p. 105–107° (1 mm.). [m] Ref. 3, b.p. 89–90° (1 mm.). [n] Ref. 5, m.p. 81°. [o] Recrystallized from benzene. [p] Recrystallized from ethanol–water. [q] Recrystallized from water. [r] Obtained by ammonolysis of the corresponding ethyl ester in liquid ammonia. See Experimental.

been found that nitroparaffins possessing a methinyl, methylene, or methyl group adjacent to the nitro group condense successfully in liquid ammonia with acrylonitrile, acrylic ester, or acrylamide to give excellent yields of a variety of products, depending upon proportions of the reactants. For example, nitromethane and acrylonitrile in equimolecular quantities give a good yield of the dicyanoethylation product. With three moles of acrylonitrile the product is tris(β-cyanoethyl)-nitromethane exclusively. In neither case can the monocyanoethylation product be isolated. When a molar equivalent of acrylic ester is employed as an acceptor, nitromethane yields a mixture of mono- and dicarbethoxyethylation products. On the other hand, from the reaction between one mole of nitromethane and three moles of acrylic ester a mixture of di- and trisubstitution products is obtained. Nitroethane reacts with acrylonitrile, acrylic ester, and acrylamide to form primarily the respective disubstitution products, regardless of the relative amounts of the reactants. Analogous reactions of less reactive 1-nitropropane with acrylonitrile or acrylic ester in equimolar proportions give chiefly monosubstitution products. With two moles each of acceptors, however, disubstitution predominates. Acrylamide reacts more slowly with 1-nitropropane to form exclusively the monocarbamoylethyl product even with the use of two molar equivalents of the former. 2-Nitropropane gives relatively small yields of the expected condensation products with acrylic acid derivatives. The results of these reactions are summarized in Table I. Table II shows physical properties of the products.

Experimental[11]

The nitroparaffins and acrylic acid derivatives used in this work were commercially available. Two different methods of the reaction were employed; (A) the use of a pressure vessel at room temperature and (B) the reaction at atmospheric pressure below the boiling point of liquid ammonia(−50°). These are illustrated by typical examples as follows.

Tris(β-cyanoethyl)nitromethane (Method A).—A mixture of 3.05 g. (0.05 mole) of nitromethane and 7.95 g. (0.15 moles) of acrylonitrile in a glass pressure vessel[12] was treated with 30 cc. of liquid ammonia while cooling with ice water until the exothermic reaction ceased, then allowed to stand at room temperature for about 0.5 hr. The solids remaining when the ammonia was evaporated were washed with ethanol to yield 10.3 g. of tris(β-cyanoethyl)nitromethane.

Ethyl 4-Nitrobutyrate and Ethyl 4-Nitropimelate (Method B).—A mixture of 6.1 g. (0.1 mole) of nitromethane and 10.0 g. (0.1 mole) of ethyl acrylate was added dropwise to a well stirred 100 cc. of liquid ammonia during the course of 25 min. while maintaining the reaction temperature at −50°. After the addition was complete, the mixture was stirred for 1 hr. and then the ammonia was evaporated. The residual oil was fractionated in vacuum to give the products described in Tables I and II. The corresponding amides of both products, *4-nitrobutyramide* (m.p. 88–89.5° from benzene) and *4-nitropimelamide* (m.p. 141–142.5° from ethanol–water), were prepared by ammonolysis of the esters in liquid ammonia in the presence of ammonium chloride as catalyst.

4-Methyl-4-nitropimelamide (Method A).—Nitroethane (3.75 g., 0.05 mole) was added to a well agitated solution of 7.1 g. (0.1 mole) of acrylamide in 50 cc. of liquid ammonia in a glass pressure vessel and the mixture was then allowed to stand at room temperature for 1 hr. Evaporation of the ammonia yielded the product as a pale green oil which rapidly solidified. Upon one recrystallization from water it melted at 126–129.5°; yield 6.2 g. (57%). After an additional recrystallization the melting point was raised to 129.5–131°.

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[10] Badische Aniline und Soda-Fabrik A.-G., German Patent 857,362 (November 27, 1952).

[11] Melting points and boiling points are uncorrected. Microanalyses were by the Institute of Physical and Chemical Research, Tokyo, Japan.

[12] K. Shimo and S. Wakamatsu, *J. Org. Chem.*, **24**, 19 (1959).