[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DIVISION, TENNESSEE EASTMAN CORPORATION]

Preparation of γ-Alkoxy-*n*-propylamines

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The reaction of acrylonitrile with a number of monohydric alcohols to give β-alkoxy propionitriles has been recently described.[2] Huber[3a] and Whitmore, *et al.*,[3b] have discussed the reduction of basically substituted nitriles to the corresponding primary and secondary amines, using Raney nickel catalyst and molecular hydrogen. French Patent 796,001[2d] disclosed the preparation of γ-*n*-butoxy-*n*-propylamine by hydrogenation of the corresponding nitrile in the presence of a supported nickel catalyst. Hydrogenation of the products from acrylonitrile and a number of commercially available alcohols has now led to a group of γ-alkoxy-*n*-propylamines, of value in other work of this Laboratory, according to the series of reactions

$$\mathrm{ROH + CH_2{=}CH{-}CN \longrightarrow RO{-}CH_2{-}CH_2{-}CN} \quad (1)$$

$$\mathrm{ROCH_2CH_2CN + H_2 \longrightarrow ROCH_2CH_2CH{=}NH} \quad (2)$$

$$\mathrm{ROCH_2CH_2CH{=}NH + H_2 \longrightarrow ROCH_2CH_2CH_2NH_2} \quad (3)$$

Reaction (1) was effected by a strong alkali catalyst such as sodium methoxide or aqueous 40% trimethylbenzylammonium hydroxide ("Triton B"). Reactions (2) and (3) were preferably accomplished with Raney nickel catalyst and hydrogen under high pressure.

The addition products from acrylonitrile and alcohols were formed rapidly and generally in high conversion and yield when the above alkaline catalysts were used. These reactions appeared to come to an equilibrium state, as portions of the relatively low-boiling reactants could always be isolated in fractionation of the neutralized reaction mixtures. The location of the equilibrium position apparently is a function of the type of alcohol used, as isopropanol gave a distinctly lower yield of addition product than did primary alcohols, and *t*-butanol has been shown to be inert toward acrylonitrile.[4] The alcohols did not react with acrylonitrile in the absence of a basic catalyst. No products were formed which boiled higher than the alkoxy nitriles. The latter materials were colorless liquids, some of which possessed heavily sweet, unpleasant odors. They were stable to vacuum distillation and to storage at ordinary temperatures.

The reduction of the alkoxy nitriles to alkoxy amines was accomplished with Raney nickel catalyst at temperatures of 90–100° and hydrogen pressures of 50 to 250 atmospheres. Whereas nitriles usually have a threshold catalytic hydrogenation temperature of about 100° and a preferred hydrogenation temperature of 125–150°,[5] these alkoxy propionitriles had the corresponding temperature levels at about 75 and 90–100°, respectively. Trial runs made at 125° led to more cleavage and lower yields of the primary amine than did the runs made at 90 to 100°. The catalytic reduction of these nitriles, as with many other nitriles previously studied,[3,6] produced a mixture of primary and secondary amine. The latter was probably formed by a reaction of part of the primary amine which had been produced with the intermediate imine (equations 4 and 5, $\mathrm{R = R'OCH_2CH_2{-}}$)

$$\mathrm{RCH{=}NH + RCH_2NH_2 \longrightarrow RCH(NH_2)NHCH_2R} \quad (4)$$

$$\mathrm{RCH(NH_2)NHCH_2R + H_2 \longrightarrow RCH_2NHCH_2R + NH_3} \quad (5)$$

The secondary amine was usually produced in only small quantity in these reductions, this desirable result being obtained by carrying out the reduction in the presence of ammonia,[3,7] thus tending to suppress reactions (4) and (5) which produced the secondary amine. Of the various alkoxy nitriles hydrogenated, only the lowest member of the series, β-methoxypropionitrile, gave secondary amine in isolable amounts larger than a few per cent. Yields of purified primary amine ranged from 50 to 78%, except in the case of the hydrogenation of benzyloxypropionitrile, where much cleavage at the oxygen atom occurred, and from which benzyloxy-*n*-propylamine was produced in only 25% yield. These primary amines were colorless liquids with typical strong odors. It is believed that maximum yields of the primary amines can be obtained by using hydrogen pressures as high as reasonably possible and temperatures near 100°, and by adding ammonia in rather large quantities (several moles of ammonia per mole of nitrile). No added solvents were used in the addition reaction, and none except liquid ammonia in the hydrogenation reactions.

Tables I and II give the nitriles and amines which were prepared, together with corrected boiling points, indices, specific gravities, conversions or yields, and observed and calculated analyses or neutralization equivalents. Compared with

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[2] (a) Bruson, U. S. Patents 2,280,790, 2,280,791, 2,280,792; (b) Clifford and Lichty, Canadian Patent 415,525; (c) Koelsch, THIS JOURNAL, **65**, 437 (1943); (d) I. G. Farbenindustrie, French Patent 796,001.

[3] (a) Huber, THIS JOURNAL, **66**, 876 (1944); (b) Whitmore, *et al.*, *ibid.*, **66**, 725 (1944).

[4] Bruson, *ibid.*, **64**, 2457 (1942); Bruson and Riener, *ibid.*, **64**, 2850 (1942); **65**, 18 (1943).

[5] Adkins, "Reactions of Hydrogen with Organic Compounds Over Chromium Oxide and Nickel Catalysts," University of Wisconsin Press, Madison, Wis., 1937.

[6] Winans and Adkins, THIS JOURNAL, **55**, 4167 (1933).

[7] Schwoeger and Adkins, *ibid.*, **61**, 3499 (1939).

TABLE I

ALKOXY NITRILES

-oxy-propionitrile	B. p., °C.	B. p., mm.	n^{20}_D	d^{20}_{20}	Nitrogen, %[a] Calcd.	Nitrogen, %[a] Found	Conversion, %[e]
Methyl	85.5	49	1.4032	0.9420	16.47	16.37	89
Ethyl[b]	77– 78	25	1.4068	.9062			78
Isopropyl	82.5	25	1.4089	.8969	12.38	12.24	69
Butyl[c]	98	20	1.4180	.8863	11.02	10.76	86
2-Ethylhexyl	89– 91	1.5	1.4342	.8785	7.64	7.51	77
Benzyl	114–116	0.5	1.5111	1.0457	8.69	8.50	94
Methoxyethyl[d]	98–100	9					87
Tetrahydrofurfuryl[d]	100	1.5					80
3,5-Dimethylcyclohexyl	95– 96	0.5	1.4549	0.9430	7.73	7.84	51

[a] These analyses and the neutralization equivalent titrations and analyses in Table II were carried out under the direction of Mr. D. C. Sievers. [b] Previously prepared by Koelsch, ref. 2c. [c] Previously reported, ref. 2d. [d] Previously described by Bruson, U. S. Patent 2,280,792. [e] Yields somewhat higher, if recovery of unreacted starting materials is considered.

TABLE II

ALKOXY AMINES

-oxy-*n*-propylamine	B. p., °C.	B. p., mm.	n^{20}_D	d^{20}_{20}	Neut. equiv. Calcd.	Neut. equiv. Found	N, % Calcd.	N, % Found	Yield, %
Methyl	117–118	733	1.4182	0.8737	89.0	88.8	15.73	15.27	50[a]
Ethyl	134–136	732	1.4201	0.8613	103.0	106.2	13.59	13.15	50
Isopropyl	85– 86	102	1.4195	0.8450	117.0	117.6	11.97	11.62	66
Butyl[b]	75– 76	21	1.4273	0.8514	131.0	131.5	10.68	10.54	71
2-Ethylhexyl	78	1.0	1.4398	0.8493	187.0	188.7	7.48	7.30	73
Benzyl	93.5	0.75	1.5170	1.0032	165.0	165.9	8.48	8.29	25
Methoxyethyl	77– 78	11	1.4350	0.9487	133.0	132.5	10.52	10.43	61
Tetrahydrofurfuryl	74– 75	1.5	1.4608	1.0010	159.0	160.0	8.80	8.65	55
3,5-Dimethylcyclohexyl	81– 82	0.5	1.4602	0.9077	185.0	183.9	7.56	7.55	78

[a] Di-(γ-methoxy-*n*-propyl)-amine was also formed, and isolated in 10% yield. [b] Previously reported, ref. 2d.

corresponding alkyl nitriles and amines possessing the same number of atoms in the chain (*e.g.*, γ-ethoxy-*n*-propylamine compared with *n*-hexylamine), these alkoxy nitriles and amines had higher boiling points, specific gravities, and solubilities in water, the differences in these values diminishing as the alkoxy group increased in size.

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Experimental

β-*n*-Butoxypropionitrile.—*n*-Butanol (148 g., 2 moles) was stirred under reflux with aqueous 40% trimethylbenzylammonium hydroxide ("Triton B," 2 g.), and acrylonitrile (106 g., 2 moles) was added at a rate such that the temperature did not rise above 45°. The mixture was stirred an hour after all of the acrylonitrile had been added, made acidic with acetic acid, and fractionated in vacuo through a jacketed Vigreux column equipped with a total condensation, variable take-off still-head. The product (219 g., 86% conversion) boiled at 98° (20 mm.).

β-2-Ethylhexyloxypropionitrile.—In a similar fashion, acrylonitrile (3 moles) was added to a mixture of 2-ethylhexanol (3 moles) and sodium methoxide (3 g.) maintained at 75°, to yield 425 g. of the addition product boiling at 89–91° (1.5 mm.). This represented a conversion of 77%, and, as 50 g. of 2-ethylhexanol was recovered, a yield of 89%. The other alkoxy nitriles of this group were made by the above methods.

γ-*n*-Butoxypropylamine.—β-*n*-Butoxypropionitrile (210 g., 1.65 moles) was hydrogenated at 100° in a rocking American Instrument bomb, in the presence of ammonia (approximately 100 ml. of liquid ammonia) and Raney nickel catalyst (10–15 g.), using hydrogen at an initial pressure of about 100 atmospheres. No further absorption of hydrogen was noted after about two hours of rocking. The reaction mixture and bomb rinsings (methanol) were filtered and fractionated *in vacuo* through the Vigreux column. γ-*n*-Butoxypropylamine was obtained as a colorless liquid with a faint odor, b. p. 75–76° (21 mm.), in 71% yield (154 g.).

The other amines of the group were prepared in a similar fashion. The three lowest molecular weight nitriles hydrogenated satisfactorily at 90°. The methoxy- and ethoxy-propylamines required normal pressure distillation through a modified spiral-wire Podbielniak type column to attain a satisfactory state of purity.

Summary

The reaction of acrylonitrile with a number of alcohols and the reduction of the resultant β-alkoxypropionitriles to the useful γ-alkoxy-*n*-propylamines has been studied. Nine of these compounds are described.

The reduction of these nitriles also gives small quantities of the alkoxy-substituted secondary amines. This reaction may be partially suppressed by carrying out the hydrogenation in the presence of ammonia.

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