N-(Alkoxymethyl)acrylamides

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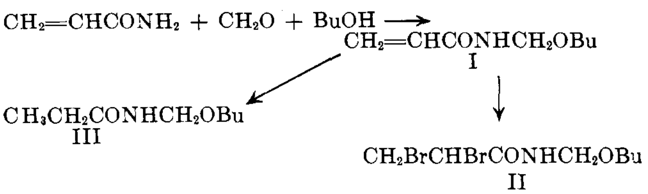
Preparation of a series of *N*-(alkoxymethyl)acrylamides, $CH_2{=}CHCONHCH_2OR$, is described. One of the by-products in the preparation was shown to be *N,N'*-oxydimethylenediacrylamide (IV), whose structure was proved by synthesis. The reactions and properties of *N*-(alkoxymethyl)acrylamides are discussed.

As part of a program directed at the synthesis of new polymerizable compounds, we investigated the methods of formation and chemistry of *N*-(alkoxymethyl)-acrylamides. Although N-alkoxymethyl derivatives of amides of saturated fatty acids are known,[1] the derivatives of acrylamide were unknown at the time we started our investigations. When our work was well under way it came to our attention, however, that a patent[2] disclosed preparation of *N*-(methoxymethyl)-methacrylamide and -acrylamide from the corresponding *N*-hydroxymethylamides and acidified methanol at 40–45°. In addition to this report, a mention of *N*-(alkoxymethyl)methacrylamides was made in a critical review[3] and the results which had been disclosed in a patent[4] were generalized in this review to include the reaction of alcohols with methacrylamide and formaldehyde to form *N*-(alkoxymethyl)methacrylamides. This article will show, however, that the reaction product[4] obtained from methacrylamide, formaldehyde, and butanol is not *N*-(butoxymethyl)methacrylamide, as was assumed previously.[4]

When acrylamide and a butanol solution of formaldehyde (about 40%) were refluxed in the presence of a polymerization inhibitor such as hydroquinone, there was obtained, in addition to dibutyl formal and a solid water-soluble by-product, approximately 70% yield of a viscous oil which proved to be *N*-(butoxymethyl)-acrylamide (I) on the basis of its analysis, infrared spectrum, molar refraction, and chemical behavior.

N-(Butoxymethyl)acrylamide is a high-boiling colorless oil, insoluble in water, which can be distilled in small samples at pressures of 0.01 to 0.1 mm. Distillation of larger samples causes its polymerization and decomposition with evolution of butanol and formaldehyde. In the presence of free-radical initiators, such as benzoyl peroxide, it can be polymerized and copolymerized with other monomers to high molecular weight polymers. When pure it can be kept at room temperature for several months without any visible change.



$$CH_2{=}CHCONH_2 + CH_2O + BuOH \longrightarrow \underset{\text{I}}{CH_2{=}CHCONHCH_2OBu}$$

$$\text{I} \longrightarrow \underset{\text{III}}{CH_3CH_2CONHCH_2OBu}$$

$$\text{I} \longrightarrow \underset{\text{II}}{CH_2BrCHBrCONHCH_2OBu}$$

Although I polymerized on attempted hydrogenation over palladium on charcoal, it could be hydrogenated over Raney nickel to obtain the propionamide derivative III. Addition of bromine to I proceeded smoothly to give a good yield of the dibromo compound II. Hydrolysis of III gave propionic acid, formaldehyde, and butanol.

After substantiating the structure of I, we turned our attention next to the water-soluble by-product from the preparation of I. By a suitable choice of solvents we succeeded in separating unchanged acrylamide and *N*-(hydroxymethyl)acrylamide, and isolated a compound, m.p. 133.5° (IV). Compound IV, $C_8H_{12}N_2O_3$, showed an infrared spectrum which appeared to be that of a substituted acrylamide. It reacted with bromine to give a tetrabromide V and, on heating with ammonium persulfate, gave an insoluble, cross-linked polymer. The structure of IV as *N*-acrylamidomethyl ether was finally confirmed by its synthesis from *N*-(hydroxymethyl)acrylamide.

$$CH_2{=}CHCONHCH_2OH \longrightarrow \underset{\text{IV}}{(CH_2{=}CHCONHCH_2)_2O} \longrightarrow \underset{\text{V}}{(CH_2BrCHBrCONHCH_2)_2O}$$

Contrary to a recent statement in the literature,[5] compounds of type IV have been reported[6] and a compound derived from methacrylamide has been described by Arbuzova, *et al.*[7]

After having prepared and characterized *N*-(butoxymethyl)acrylamide (I) we wished to extend this preparation to other alcohols in order to obtain *N*-(alkoxymethyl)acrylamides needed for another investigation. The application of this method to other alcohols, however, particularly to those of the lower boiling point, was more difficult. Although some of the desired compounds could be obtained by this method, yields were low and the products were difficult to purify. Similarly, application of the method described in a patent[2] to alcohols other than methanol failed, although *N*-(methoxymethyl)acrylamide could be obtained in a good yield.

Finally, we have succeeded in developing a convenient and simple method of obtaining *N*-(alkoxymethyl)-acrylamides by starting from acrylamide, paraformaldehyde, and an alcohol. The method could be applied to acrylamide or methacrylamide and an alcohol and consisted of reaction of the amide with paraformaldehyde[8] at pH 9–10 as a first step, and reaction of the

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[1] (a) J. W. Weaver, H. A. Schuyten, J. G. Frick, Jr., and J. D. Reid, *J. Org. Chem.*, **16**, 1111 (1951); (b) R. D. Haworth, R. MacGillivray, and D. H. Peacock, *J. Chem. Soc.*, 1493 (1950).

[2] Farbenfabriken Bayer Aktiengesellschaft, British Patent 780,284. This work has now appeared as an article, E. Müller, K. Dinges, and W. Graulich, *Makromol. Chem.*, **57**, 27 (1962).

[3] C. E. Schildknecht, "Vinyl and Related Polymers," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 321.

[4] D. E. Strain, U. S. Patent 2,173,005 (September 12, 1939).

[5] R. C. Petterson and H. R. Brownell, *J. Org. Chem.*, **25**, 843 (1960).

[6] G. Zigeuner, K. Voglar, E. Wiesenberger, and M. Sobotka, *Monatsh.*, **82**, 847 (1951); *cf.* also ref. 1b.

[7] I. A. Arbuzova, S. N. Ushakov, S. A. Plotkina, V. N. Efremova, and I. K. Ulezlo, *Zh. Obshch. Khim.*, **28**, 1266 (1958). After the present manuscript had been completed, compound IV was described by I. A. Arbuzova and I. K. Mosevich, *ibid.*, **31**, 3023 (1961).

TABLE I

N-(ALKOXYMETHYL)ACRYLAMIDES

$CH_2{=}CHCONHCH_2OR$

	Yield,[a] %	B.p., °C. (mm.)	M.p.,[b] °C.	$n^{25}D$	d^{25}	Molar refraction		Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
						Calcd.	Found		Calcd.	Found	Calcd.	Found	Calcd.	Found
Methyl	90–98	91–92 (0.1)	−3 to 1	1.4714	1.0538	30.08	30.58	$C_5H_9NO_2$	52.16	52.22	7.88	7.98	12.17	12.42
Ethyl	94	94–96 (0.1)	6–9	1.4673	1.0192	34.70	35.18	$C_6H_{11}NO_2$	55.79	56.28	8.59	8.88	10.85	11.40
Propyl	75	87–88 (0.01)	8–11	1.4649	0.9915	39.32	39.91	$C_7H_{13}NO_2$	58.72	59.01	9.15	9.25	9.79	9.69
Isopropyl	70	82–83.5 (0.01)	15–18	1.4621	0.9867	39.32	39.91	$C_7H_{13}NO_2$	58.72	58.87	9.15	9.23	9.79	9.88
Butyl	90	110–112 (0.03)	−9 to −6	1.4613	0.9693	43.93	44.54	$C_8H_{15}NO_2$	61.12	61.42	9.62	9.84	8.91	8.75
Isobutyl	48–76	99–100 (0.03)		1.4588	0.9654	43.93	44.51	$C_8H_{15}NO_2$	61.12	61.13	9.62	9.60	8.91	8.73
Allyl	69	105–109 (0.02)	−1 to 1	1.4821	1.0303	38.85	39.06	$C_7H_{11}NO_2$	59.55	58.41	7.86	7.99	9.92	10.16
Butyl[d]	57–70	83–87 (0.08)	2–4	1.4619	0.9649	48.55	48.79	$C_9H_{17}NO_2$	63.12	63.21	10.01	10.09	8.18	8.15

[a] The yields given are those after one flash distillation and are based on numerous runs, some of which involved minor variations in the procedure. [b] Melting points were determined by freezing a 20–25-g. sample and allowing it to warm slowly to the temperature of melting while being stirred with a thermometer. [c] Remaining liquid at *ca.* −35°, but solidifying to a glass at *ca.* −65°. [d] The compound is *N*-(butoxymethyl)methacrylamide which is included here for convenience.

resulting product, apparently *N*-(hydroxymethyl)acrylamide, which was not isolated, with an excess of the alcohol under acidic conditions (pH 3.5–4.5). The initial reaction was fast, as judged by the disappearance of formaldehyde, the equilibrium concentration of formaldehyde being reached in less than 1 hr., while in the second step the reaction was essentially complete for most alcohols after about 7 hr. at 85°. Good to excellent yields were obtained and the production of undesirable by-products was at a minimum. Thus, in a larger scale preparation of I by this method, no IV could be found and only an insignificant amount of dibutyl formal was isolated.

The *N*-(alkoxymethyl)acrylamides were water-soluble viscous oils, except for the *N*-butoxy compound. *N*-(Isobutoxymethyl)acrylamide and *N*-(butoxymethyl)methacrylamide were insoluble in water. In view of this, the water-soluble product described in a patent could not have been *N*-(butoxymethyl)methacrylamide. Some other properties and analyses of these compounds are listed in Table I. While some analyses, especially those of the compounds with R = lower alkyl, differ from the calculated values, this is probably the result of instability of these compounds on distillation, so that flash distillation had to be used first before final redistillation for analysis. Unchanged acrylamide could not be removed by washing because of water solubility of lower *N*-(alkoxymethyl)acrylamides and in part it codistilled with the products. Like *N*-(butoxymethyl)acrylamide, these homologs are sensitive to heat with resulting polymerization and decomposition, especially on distillation of larger samples or fractionation.

Molar refractions[9] shown by these compounds are in good agreement with those calculated, and a definite exaltation in this series is evident. The average exaltation is about 0.55, excluding *N*-(allyloxymethyl)acrylamide and *N*-(butoxymethyl)methacrylamide, and probably represents the effect of the double bond conjugated with the carbonyl group of the amide.

Experimental[10]

Preparation of *N*-(Butoxymethyl)acrylamide (I).—A mixture of 355 g. (5.0 mole) of acrylamide, 825 g. (about 12 moles of formaldehyde) of a 40% formaldehyde solution in 1-butanol (butyl Formcel of Celanese Chemical Company), 8 g. of hydroquinone, and 1500 g. of 1-butanol was refluxed for 3 hr. The resulting mixture was washed well with water and the organic layer was distilled at 7–9 mm. to obtain, beside excess of butanol and water, 619 g. of dibutyl formal. The residue, amounting to about 70%, was distilled in several portions. Thus, 150 g. of the crude reaction product, a dark orange liquid, was distilled with 1 g. of hydroquinone to obtain 127 g. of a nearly colorless liquid, b.p. 90° (0.1 mm.) to 135° (0.15 mm.). This was redistilled to obtain 89 g. of a colorless liquid, b.p. 121–124° (0.1 mm.), $n^{20}D$ 1.4620, showing strong bands at 3.10, 6.03, 6.17 and 9.2 μ in the infrared.

Anal. Calcd. for $C_8H_{15}NO_2$: N, 8.91. Found: N, 8.44.

Distillation of reaction products from acrylamide, formaldehyde, and corresponding alcohols gave *N*-isobutoxy-, *N*-propoxy- and *N*-(ethoxymethyl)acrylamides, which, although obtained in progressively lower yields, had correct analyses and showed the same constants as those compounds prepared later by a "two-step" method and listed in Table I.

Hydrogenation of *N*-(Butoxymethyl)acrylamide.—A mixture of 31.4 g. (0.20 mole) of I, 150 ml. of ethyl acetate, and 1 ml. of Raney nickel was shaken with hydrogen at an initial pressure of 45 p.s.i., whereupon an amount of hydrogen corresponding to 104% of that calculated was absorbed in 18 min. Distillation gave 30.8 g. (97%) of a colorless liquid, b.p. 92° (0.04 mm.) to 96° (0.06 mm.), which showed bands at 3.07 and 6.0 μ in the infrared. For analysis the liquid was redistilled and a fraction, b.p. 82° (0.01 mm.), $n^{27}D$ 1.4399, was collected.

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.44; H, 10.75; N, 8.81.

In another experiment, to estimate the purity of the crude I (prepared as described previously), a 200-g. sample of this material was hydrogenated to obtain 164 g. (81%) of colorless III, b.p. mostly at 94° (0.15 mm.), $n^{22}D$ 1.4411.

An attempted hydrogenation of I in ethyl acetate in the presence of 5% palladium on charcoal resulted in polymerization of the substrate. Thus, from 47.2 g. (0.30 mole) of I there was ob-

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(8) H. P. Wohnsiedler and P. Adams, U. S. Patent 2,864,861 (December 16, 1958).

(9) N. Bauer and K. Fajans, "Physical Methods of Organic Chemistry," Vol. I, Part II, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1949, p. 1141.

(10) The melting and boiling points were uncorrected. Carbon and hydrogen determinations were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. We are indebted to Dr. James B. Lear and his staff for nitrogen analyses and infrared spectra.

tained 49 g. of a clear, very viscous oil while only 55% of the theoretical uptake of hydrogen occurred.

Addition of Bromine to I. *N*-Butoxymethyl-2,3-dibromopropionamide (II).—To a stirred solution of 17.8 g. (0.114 mole) of I in 100 ml. of carbon tetrachloride and 10 ml. of acetic acid there was added dropwise a solution of 18.1 g. (0.114 mole) of bromine in 100 ml. of carbon tetrachloride. The orange solution was left overnight whereupon it became nearly colorless. Solvent was evaporated *in vacuo* and the residue was dissolved in benzene. The solution was filtered, diluted with hexane, and allowed to crystallize. Filtration gave 30.5 g. (85%) of a nearly white solid, m.p. 60–65°. Several recrystallizations from a mixture of warm benzene and petroleum hexane gave the analytical sample of II as a white solid, m.p. 77–79°, showing bands at 3.09 and 6.03 μ in the infrared.

Anal. Calcd. for $C_8H_{15}Br_2NO_2$: C, 30.30; H, 4.77; N, 4.42; Br, 50.41. Found: C, 30.53; H, 4.91; N, 4.69; Br, 52.11.

Isolation of *N*,*N'*-Oxydimethylenediacrylamide (IV).—A 40-g. sample of the crude by-product (obtained from evaporation of the aqueous extracts in the preparation of I) was dissolved in the smallest amount of warm methanol, the resulting solution treated with charcoal, filtered, and diluted with ethyl acetate. A small amount of gummy solid which separated was discarded. The solution was concentrated *in vacuo* until crystallization occurred. Filtration gave 19.5 g. of impure IV, m.p. 105–120°. Repeated recrystallizations from a mixture of methanol and ethyl acetate at Dry Ice temperatures gave IV as a white solid, m.p. 133.5–134.5°, showing bands at 3.13, 6.02, 6.17 and 9.7 μ in the infrared. The compound was identical in all respects with the authentic sample of IV prepared from *N*-(hydroxymethyl)acrylamide.

Anal. Calcd. for $C_8H_{12}N_2O_3$: C, 52.16; H, 6.59; N, 15.21. Found: C, 52.23; H, 6.73; N, 14.92.

The mother liquors contained acrylamide and *N*-(hydroxymethyl)acrylamide.

The crude by-product (6.21 g.) could also be sublimed at 65–70° (0.01 mm.) to obtain 0.63 g. (10.1%) of acrylamide. The residue, 5.56 g. of a light-brown solid, gave on recrystallization 2.90 g. (47%) of nearly white, impure IV, m.p. 115–120°, and a brown viscous oil, chiefly composed of *N*-(methylol)acrylamide.

Synthesis of IV.—A mixture of 20 g. of *N*-(hydroxymethyl)-acrylamide, 0.1 g. of hydroquinone, 1 drop of concentrated hydrochloric acid, and 100 ml. of carbon tetrachloride was stirred and heated at 45° for 70 min. and then allowed to stand at room temperature overnight. Filtration and drying gave 19.5 g. of a white solid, m.p. 101–110°, which was recrystallized from a mixture of methanol and ethyl acetate to give 8 g. of a white solid, m.p. 124–127°. Two additional recrystallizations from methanol with cooling in Dry Ice gave 5.3 g. (30%) of the compound IV, m.p. 132–134°. Its infrared spectrum was identical with that of the compound isolated from preparation of I and its melting point was unchanged on admixture of the latter compound.

Addition of Bromine to IV. *N*,*N'*-Oxydimethylenebis(2,3-dibromopropionamide) (V).—To a warm suspension of 6.20 g. (0.034 mole) of IV in 80 ml. of chloroform there was added in small portions a solution of 10.8 g. (0.068 mole) of bromine in 30 ml. of chloroform. The orange mixture which crystallized was left at room temperature overnight, then was filtered to give 16 g. (95%) of V as a white solid, m.p. 153–156° (bubbling). The analytical sample was prepared by several recrystallizations from a mixture of ethyl acetate and hexane and was obtained as a fluffy white solid, m.p. 168–169° (bubbling). Its infrared spectrum showed bands at 3.11 and 6.03 μ, but no unsaturation.

Anal. Calcd. for $C_8H_{12}Br_4N_2O_3$: C, 19.09; H, 2.40; Br, 63.44; N, 5.56. Found: C, 19.26; H, 2.31; Br, 64.14; N, 5.75.

Polymerization of IV.—A solution of 2.90 g. of IV, m.p. 128–133°, and 0.030 g. of ammonium persulfate in 40 ml. of water was heated on a steam bath whereupon, after about 10 min., the mixture became nearly solid and formed a gel. After 30 min. the mixture was cooled, filtered and the polymer washed with water and alcohol. On drying there was obtained a pure white powder not melting below 250° and not dissolving in hot water or boiling benzene.

Reaction of Acrylamide with Formaldehyde.—A mixture of 71 g. (1.0 mole) of acrylamide, 31.6 g. (1.0 mole) of 95% paraformaldehyde and 25 g. of butanol was heated to 50°. Several drops of 50% aqueous sodium hydroxide was added and samples were taken out for determination of formaldehyde. The results were as follows (time in min., % CH_2O): 0, 24.6; 12, 6.34; 32, 3.94; 52, 3.80; 72, 3.80; 132, 3.74.

A General Method of Preparation of *N*-(Alkoxymethyl)acrylamides.—A mixture of 71 g. (1.0 mole) of acrylamide, 1.0 mole of paraformaldehyde (31.6 g. or 33 g. of 95% or 91% material, respectively), and 25–35 g. of the required alcohol was heated to 50°. Five to fifteen drops of 50% aqueous sodium hydroxide was added to adjust the pH to 9–10. A slight exothermic reaction occurred and the mixture became homogeneous and transparent. Heating was interrupted to keep the temperature at 45–55°, but, after the initial exothermic reaction subsided, the mixture was heated again at 50° for a total of 2–4 hr. (usually 2.5 hr.). Four to five hundred grams of the appropriate alcohol was added, the pH adjusted to 3.5–4.5 by means of a 30% sulfuric acid solution in the same alcohol, 1 g. of hydroquinone was added, and the mixture was refluxed (with the lower alcohols) or heated at 85° (with the butyl alcohols) for 7 hr. To lower the reflux temperature of the butyl alcohols, benzene (100 g.) was added if reflux was desirable instead of heating at 85°. The mixture was then cooled and stirred for 0.5–1.0 hr. with 10–15 g. of solid sodium bicarbonate to adjust the pH to 7–7.5. The mixture was then filtered with suction through a pad of Celite, an additional 1 g. of hydroquinone was added, and the resulting filtrate concentrated *in vacuo* below 70°. The residue, usually a dark-brown to black oil, was distilled with 1 g. of hydroquinone. Distillation was carried out by adding the oil dropwise into a distilling flask which was heated to a suitable temperature by an oil bath and which was evacuated to 0.1–0.01 mm. and provided with a vacuum take-off and a receiver cooled in ice-water. The rate of addition was such that the vaporization was nearly instantaneous. The distilland in the flask never exceeded 5–10 ml. The *N*-(alkoxymethyl)acrylamides thus obtained were colorless to light yellow viscous oils. Analytical samples were prepared by several redistillations in the presence of hydroquinone in a short-path distillation apparatus and the middle fractions were used (Table I).

More important bands in the infrared spectra (neat liquids) of some representative compounds are given as follows (w, m, s referring to per cent transmittance and numbers in which hundredths of μ are omitted signifying that the band is broad).

N-(Methoxymethyl)acrylamide: 3.07 s, 3.32 w, 3.43 m, 3.58 w, 6.0 s, 6.16 s, 6.52 s, 6.9 m, 7.22 m, 7.68 m, 7.90 w, 8.13 s, 8.32 m, 8.86 s, 9.3 s, 10.2 m, 10.45 m, 10.93 m, 12.37 m.

N-(Ethoxymethyl)acrylamide: 3.06 s, 3.31 w, 3.39 m, 3.43 m, 3.51 m, 6.0 s, 6.15 s, 6.5 s, 6.94 m, 7.1 m, 7.70 m, 8.13 s, 8.96 m, 9.2 s, 9.89 m, 10.18 m, 11.45 w, 11.9 w, 12.37 m.

N-(Butoxymethyl)acrylamide: 3.10 s, 3.34 w, 3.45 s, 3.55 s, 6.03 s, 6.17 s, 6.5 s, 6.9 m, 7.19 m, 7.30 m, 7.72 m, 8.15 s, 9.2 s, 10.18 m, 10.52 m, 11.2 w, 11.5 w, 12.38 m.

N-(Butoxymethyl)methacrylamide: 3.02 s, 3.41 s, 3.51 m, 6.02 s, 6.15 s, 6.56 s, 6.92 m, 7.30 w, 7.65, m, 8.30 m, 9.00 m, 9.22 s, 9.90 w, 10.80 m, 12.0 w, 12.35 w.

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