[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Preparation of α-Alkylacrylonitriles

BY C. S. MARVEL, WILLIAM R. MILLER AND LINDY C. CHOU

Some syntheses of α-alkylacrylonitriles have been described[1] but these involve the dehydration of the cyanohydrins of methyl ketones and thus lead to products which may not have the unsaturation in the desired position and are undoubtedly mixtures of isomers. An apparently unequivocal method of preparing α-alkylacrylonitriles was presented by the availability of α-alkylacroleins.[2] The preparation and dehydration of the oximes of these acroleins should give the desired α-alkylacrylonitriles without question as to the location of the double bond. Mowry and Morner[3] have successfully applied these reactions to the preparation of methacrylonitrile from methacrolein.

The oximes have now been prepared from the three α-alkylacroleins previously described,[2] the α-ethyl-, α-isopropyl- and α-*n*-amylacroleins, as well as of α-*n*-hexyl- and α-*n*-octylacroleins which have been obtained by the extension of the Mannich[4] reaction to octanal and decanal. These oximes are viscous oils which may be purified by distillation. With the ethyl and isopropyl homologs the distillation proceeds smoothly but with the *n*-amyl, *n*-hexyl and *n*-octyl compounds the conditions for successful distillation become more critical because some decomposition and polymerization occur on heating. Addition of a little hydroquinone facilitates the distillation and, in the case of the oxime of α-isopropylacrolein, prevents a violent reaction which has been observed to take place after bleeding air into the distillation system. In no case was the "explosive decomposition" which was noted by Mowry and Morner[3] in the distillation of the methacrolein oxime observed, although when the distillation of the α-ethylacrolein oxime was carried out by others in another investigation[5] an explosion did take place.

The oximes were dehydrated by refluxing with acetic anhydride. In the case of the ethyl homolog the procedure used in working up the nitrile was essentially that of Mowry and Morner.[3] The other nitriles were isolated by steam distillation of the neutralized reaction mixture. The two lower homologs tended to form azeotropes with acetic acid and/or anhydride which were resistant even to saturated potassium carbonate solution, but this difficulty was not encountered with the higher homologs. Only in the case of the α-*n*-octylacrolein oxime was the dehydration unsuccessful. This product, although of constant refractive index after several distillations, gave a very poor analysis.

Direct dehydration of the crude undistilled oximes was not successful as the products invariably had high refractive indices and were usually colored green or yellow.

The α-ethylacrylonitrile made by this procedure showed essentially the same absorption bands in the infrared as did α-methylacrylonitrile which indicates that the double bond had not rearranged to the ethyl group.

Experimental

The various α-alkylacroleins, their oximes, and the α-alkylacrylonitriles were prepared by essentially identical methods; hence only general directions are given and the yields, physical constants and analytical data for the new compounds are presented in Table I.

α-Alkylacroleins.—The preparations of α-ethyl-, α-isopropyl- and α-*n*-amylacroleins were carried out according to directions given by Marvel, Myers and Saunders.[2] α-*n*-Hexylacrolein was prepared in the same manner from 1-octanal; the Mannich reaction was carried on for 20 hours. A 2,4-dinitrophenylhydrazone was prepared by the standard procedure.[6] After one recrystallization from 95% alcohol to which a little ethyl acetate had been added, it melted at 127–128°.

Anal. Calcd. for $C_{15}H_{20}N_4O_4$: C, 56.24; H, 6.29; N, 17.49. Found: C, 56.30; H, 6.47; N, 17.33.

A semicarbazone prepared according to directions given by Shriner and Fuson[7] melted at 154–155° after two recrystallizations. Sommelet[8] reported a melting point of 156°.

α-*n*-Octylacrolein was prepared by the Mannich reaction with 1-decanal and the reaction time was 24 hours. A 2,4-dinitrophenylhydrazone melted at 125–126° after two recrystallizations.

Anal. Calcd. for $C_{17}H_{24}N_4O_4$: C, 58.60; H, 6.94; N, 16.09. Found: C, 58.74; H, 6.86; N, 15.88.

After two recrystallizations a semicarbazone melted at 152–153°. The melting point given by Sommelet[8] is 147.5°.

α-Alkylacrolein Oximes.—The oximes were prepared by placing the acrolein and a solution of 0.1 mole excess of hydroxylamine hydrochloride in water in a flask fitted with a reflux condenser, stirrer, thermometer and dropping funnel. A solution of sodium carbonate (equivalent to the hydroxylamine hydrochloride) in water was added rapidly, usually over a period of about two minutes, and the reaction mixture stirred for approximately twice the time it required for the temperature of the mixture to rise to a maximum, usually about 35°. This time was one-half hour for the ethyl and isopropyl homologs and two hours for the other members of the series. The oximes were then separated and washed (the semi-solid nature of the *n*-octyl homolog made washing impractical for this compound).

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[1] Bruylants, Ernould and Dekoker, *Bull. sci. acad. roy. Belg.*, [5] **16**, 721 (1930) [*C. A.*, **25**, 2116 (1931)]; Vermeulen and Adriaens, *Bull. soc. chim. Belg.*, **38**, 301 (1929); Vossen, *ibid.*, **41**, 331 (1932); Verhulst and Glorieux, *ibid.*, **41**, 501 (1932); Craen, *ibid.*, **42**, 410 (1933); Ceuterick, *ibid.*, **44**, 89 (1935).

[2] Marvel, Myers and Saunders, THIS JOURNAL, **70**, 1694 (1948).

[3] Mowry and Morner, *ibid.*, **69**, 1831 (1947).

[4] Mannich, Lesser and Silten, *Ber.*, **65**, 378 (1932).

[5] R. M. Ross and R. Rolih, private communication.

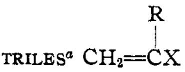
[6] Shriner and Fuson, "The Systematic Identification of Organic Compounds," Ed. 3, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

[7] Ref. 6, p. 170.

[8] Sommelet, *Ann. chim.*, [8] **9**, 560 (1906); *Bull. soc. chim.*, [4] **1**, 409 (1907).

TABLE I

α-ALKYLACROLEINS, α-ALKYLACROLEIN OXIMES AND α-ALKYLACRYLONITRILES[a]



$CH_2{=}\overset{\overset{R}{|}}{C}X$

X	R	Size run, moles	Yield, %	B. p., °C.	B. p., Mm.	$n^{20}D$	d^{20}_4	Analyses,[b] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
CHO	n-C_6H_{13}	2.0	70.3	69	41	1.4416	0.8407	77.10	77.15	11.49	11.47	...	...
	n-C_8H_{17}	0.85	70.7	69–70	2	1.4462	0.8412	78.50	78.28	11.99	11.84	...	...
CH=NOH	C_2H_5	1.5	81.7	78	30	1.4820[c]	....	60.58	60.60	9.15	9.18	14.13	14.16
	iso-C_3H_7	0.49	52.7	63	3.5	1.4744	....	63.67	63.48	9.80	9.79	12.38	12.75
	n-C_5H_{11}	.2	71.4	66	0.15	1.4770	....	68.04	68.17	10.71	10.55	9.92	10.11
	n-C_6H_{13}	.2	42.0	97	0.5	1.4750	....	69.63	69.60	11.03	11.05	9.03	9.05
	n-C_8H_{17}	.2	46.5	84	0.1	1.4754	....	72.07	72.12	11.55	11.68	7.64	7.67
CN	C_2H_5	1.4	30.2	111		1.4132	0.8075	74.03	74.20	8.70	8.71	17.27	17.24
	iso-C_3H_7	0.8	30.1	125–126		1.4128	.8038	75.74	75.13	9.53	9.76	14.73	15.06
	n-C_5H_{11}	.6	43.2	77–78	25	1.4310	.8213	78.00	78.28	10.63	10.46	11.37	11.31
	n-C_6H_{13}	.18	46.0	112	48	1.4350	.8242	78.77	78.73	11.02	10.92	10.21	10.19

[a] All constants reported were determined on analytical samples. [b] Analyses by Clark Microanalytical Laboratories. [c] $n^{21}D$ in this case.

A trace of hydroquinone was added and the mixture was distilled under reduced pressure. Best results for the higher members of the series were obtained by distilling from a 50-ml. standard taper flask attached directly to a cold-finger still-head, using carborundum chips for ebullition and a bath temperature of about 50° above the boiling point of the oxime.

α-Alkylacrylonitriles.—α-Ethylacrolein oxime was dehydrated by mixing with an equivalent amount of acetic anhydride, adding a crystal of *p*-*t*-butylcatechol and distilling the mixture through a 6-in. Vigreux column. The distillate was washed with 0.1 mole excess of sodium carbonate in water solution, the aqueous layer extracted with ether and the organic material dried and distilled, another crystal of inhibitor being added before distillation, through a small electrically-heated column packed with Berl saddles.

The other oximes were dehydrated by refluxing with acetic anhydride (fifteen minutes for the isopropyl homolog, thirty minutes for the others), treating the cooled reaction mixture with a solution containing 0.1 mole excess of sodium carbonate and steam-distilling this basic mixture. The nitrile was separated from the distillate, the aqueous layer extracted with ether and the organic material dried and distilled as above. In the case of the α-isopropylacrylonitrile some acetic acid and/or anhydride survived this treatment and it was necessary to wash the product with 10% sodium carbonate solution and redistil. As can be seen in Table I, the α-isopropylacrylonitrile was the least stable of the nitriles prepared, giving a poor analysis. This is in accord with the observations of Marvel, Myers and Saunders[2] on the parent acrolein. The oxime of α-*n*-octylacrolein could not be successfully dehydrated, the product apparently being a mixture from which the nitrile could not be separated by the fractionation procedures utilized.

Summary

Four new α-alkylacrylonitriles, which have as the alkyl substituents ethyl, isopropyl, *n*-amyl and *n*-hexyl groups, have been prepared by the dehydration of the oximes of the corresponding α-alkylacroleins and these nitriles have been characterized.

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Amine and Enol Derivatives of 1,1,1-Trifluoropropane[1]

BY W. R. NES[2] AND ALFRED BURGER

The chemical literature lists only very few compounds containing the trifluoromethyl group which have been studied pharmacologically. Since this radical manifests interesting chemical properties, it was considered worthwhile to prepare trifluoromethyl analogs of known pharmacologically active compounds, and in particular to prepare potential pressor amines in order to determine the effect of the fluorine atoms on the activity of such compounds.

We have synthesized 1,1,1-trifluoro-2-amino-3-phenylpropane (I) and 1,1,1-trifluoro-2-amino-3-cyclohexylpropane (II), and these have been compared with the corresponding non-fluorinated analogs, amphetamine and its hexahydro derivative, respectively. An interesting difference has been found for the amine II, which produces central depression in rats in a dose range of 25–150 mg./kg. In contrast, 1-cyclohexyl-2-aminopropane causes central stimulation at a dose of 25 mg./kg. The amine II does not exhibit anticonvulsant activity in doses up to 150 mg./kg. The amphetamine analog I is devoid of central stimulating activity after doses up to 30 mg./kg. intraperitoneally; in cats anesthetized with pentobarbital sodium, doses of 5 or 10 mg./kg. intravenously produce slight depressor effects. No inhibition or potentiation of acetylcholine

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(2) Smith, Kline & French Fellow, 1948–1949; du Pont Research Fellow, 1949; present address: Mayo Clinic, Rochester, Minnesota.