[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Keto Ethers. X. 1-Methoxyethyl Alkyl Ketones

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In connection with two other problems being investigated in this Laboratory, namely, the extension of the Pfitzinger procedure to the synthesis of alkoxyalkylquinolines[2,3] and to the preparation of hydantoin derivatives[4] possessing therapeutic activity, a number of alkyl 1-methoxyethyl ketones were needed. Methyl and ethyl members of this series had previously been prepared by Gauthier[5] who reported, however, no data other than boiling points for their physical properties. These two keto ethers, together with eight additional examples of this type, have now been prepared.

Experimental

1-Chloroethyl Methyl Ether.[6]—Henry's[7] method was utilized through condensation of methyl alcohol (10 moles) with an equivalent amount of paraldehyde by means of dry hydrogen chloride. A yield of 810 g. (95% of the theoretical) of crude material was obtained; by fractionation 485 g. was collected; b. p. 70–72° (746 mm.); d^{20}_4 0.9909; $n^{20}D$ 1.3969; *MR* calcd. 22.56; *MR* found 22.96.

α-Methoxypropionitrile.[8]—In resynthesizing this compound, because of unsatisfactory yields, various diluents were used; dry ether proved best, but with it only a 36% yield was obtained; b. p. 117–119° (740 mm.); d^{20}_4 0.8928; $n^{20}D$ 1.3818; *MR* calcd. 22.13; *MR* found 22.17.

Alkyl 1-Methoxyethyl Ketones.—After preparing the necessary alkylmagnesium bromide in the usual way, the ether solution of α-methoxypropionitrile was added slowly at such a rate that there was rapid refluxing of the solvent. Usually the reaction product stood for twelve to eighteen hours before being decomposed by addition of ice-cold dilute hydrochloric acid. The ether layer was separated and combined with the ether extract of the neutralized acidic layer. After washing with sodium bicarbonate solution and with water, the ether extract was dried over anhydrous calcium chloride and fractionally distilled; the first three members were fractionated at atmospheric pressure and the remainder under reduced pressure. The keto ethers are mobile liquids which frequently required repeated distillation in order to be obtained water white and of pleasant ester-like odor.

The data determined for physical properties of the keto ethers, together with results obtained from their analysis, are reported in Table I. Although excellent agreement between the calculated and found values for molecular refraction was obtained, and despite the fact that in all cases save one combustion analyses yielded satisfactory values for hydrogen content, the values found for percentage of carbon were uniformly high. Only a poor yield of *t*-butyl ketone was obtained using *t*-butylmagnesium chloride; no yield resulted from attempted use of the corresponding bromide or iodide.

In order to further characterize the keto ethers, they were converted into semicarbazones which could be recrystallized from benzene to sharp melting points. The data for these derivatives are recorded in Table I.

TABLE I

ALKYL 1-METHOXYETHYL KETONES, R—CO—CH(CH₃)—O—CH₃

	Ketones											Semicarbazones		
	B. p.,					Mol. refract.		Carbon, %		Hydrogen, %		M. p.,	Nitrogen, %	
—R	°C. (cor.)	mm.	Yield, %	d^{20}_4	$n^{20}D$	Calcd.	Found	Calcd.	Found	Calcd.	Found	°C. (cor.)	Calcd.	Found
Methyl[a]	115–116	739	37	0.9014	1.3936	26.94	27.08					141	26.40	26.55
Ethyl[b]	135–136	750	22	.8965	1.4019	31.56	31.54					120.5	24.26	24.11
n-Propyl	154–155	746	33	.8913	1.4091	36.18	36.12	64.58	66.3	10.84	10.50	169	22.44	22.35
Isopropyl	57–58	31	13	.8890	1.4092	36.18	36.22	64.58	65.9	10.84	10.31	146	22.42	22.48
n-Butyl	81–82	36	63	.8862	1.4160	40.80	40.82	66.63	67.5	11.18	10.88	154	20.88	20.75
Isobutyl	51–52	9	21	.8795	1.4128	40.80	40.85	66.63	67.5	11.18	10.83	145	20.88	20.76
s-Butyl	76–77	36	43	.8872	1.4158	40.80	40.75	66.63	67.3	11.18	10.95	127	20.88	20.67
t-Butyl	54–64	34	14	.8895	1.4130	40.80	40.41	66.63	68.8	11.18	9.74	121	20.88	23.59
n-Amyl	60–61	3	36	.8828	1.4207	45.42	45.40	68.31	68.9	11.47	11.17	144	19.52	19.50
Isoamyl	64–65	6	29	.8795	1.4191	45.42	45.41	68.31	68.2	11.47	11.16	154.5	19.52	19.65

[a] Gauthier, ref. 5, reported b. p. 114° (727 mm.); Diels and Pflaumer [*Ber.*, 48, 230 (1915)] recorded b. p. 113° (759 mm.). [b] Gauthier, *ibid.*, reported b. p. 133° (729 mm.).

Summary

1. The series of alkyl 1-methoxymethyl ketones has been extended, by the synthesis of eight additional members, to include branched as well as normal groupings. The methyl and ethyl members have been resynthesized and characterized more fully.

2. Semicarbazones, useful in identification of these keto ethers, have been prepared for each member.

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(1) From the M. A. thesis of W. P. Wallace.

(2) Lesesne with Henze, THIS JOURNAL, **64**, 1897 (1942).

(3) A. F. Isbell, M. A. Thesis, August, 1941; E. J. Smith, unpublished research.

(4) Rigler with Henze, THIS JOURNAL, **58**, 474 (1936); Speer and Henze, *ibid.*, **61**, 3376 (1939).

(5) Gauthier, *Ann. chim. phys.*, [8] **16**, 289 (1909).

(6) Henze and Murchison, THIS JOURNAL, **53**, 4077 (1931).

(7) Henry, *Bull. soc. chim.*, [2] **44**, 458 (1885).

(8) Gauthier, ref. 5, reported b. p. 118° (729 mm.); d^{20}_4 0.893; $n^{20}D$ 1.382.