duced more carbon dioxide than carbon monoxide, and more benzoic acid than benzaldehyde. At 500° the benzaldehyde predominated. Phenylpyruvic acid generated slightly more carbon monoxide than dioxide. It yielded also phenylacetic acid and a considerable quantity of intractable dehydration products. .

EVANSTON, ILLINOIS RECEIVED JANUARY 26, 1934

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

Keto Ethers. I. Methoxymethyl Ketones[1]

BY HENRY R. HENZE AND NEIL E. RIGLER

Continuing the investigation in this Laboratory on aliphatic compounds of bifunctional type,[2] attention has now been directed to the synthesis of keto ethers of the type $R-CO-CH_2-O-R'$. Of the several methods which have been utilized to prepare alkoxy ketones only those involving the acetoacetic ester synthesis[3] and the Grignard reaction[4] are of general application. By means of the former, James[3] claims to have prepared methoxymethyl *s*-butyl ketone. He treated the ethyl ester of diethylacetoacetic acid with phosphorus pentachloride, obtaining a mixture of mono- and di-chlorodiethylacetoacetic esters. The monochloro compound was converted into the methyl ester of a methoxy derivative which, on hydrolysis, yielded the compound formulated as methoxymethyl *s*-butyl ketone. For it he recorded a boiling point of 130–132° and density of 0.855 at 20°, and stated that it did not form a bisulfite addition product.[5] The Grignard reaction was used by Gauthier[4] to synthesize methyl, ethyl and *n*-propyl methoxymethyl ketones; however, for these keto ethers no physical data other than their boiling points were recorded.[6]

Ten methoxymethyl alkyl ketones, including the four already mentioned, have been synthesized by means of the Grignard reaction and adequately characterized. Secondary or tertiary alkyl had not previously been utilized in the preparation of alkoxyalkyl ketones from nitriles. A critical study of the physical properties of these interesting compounds, which possess valuable solvent properties, will be reported elsewhere.

TABLE I

METHOXYMETHYL ALKYL KETONES, CH_3-O-CH_2-CO-R

R	B. p. (corr.), °C.	Mm.	d^{20}_4	n^{20}_D	Yield, %
Methyl	114.6	746	0.9491	1.3980	48
Ethyl[a]	133–133.6	757	.9292	1.4063	48.5
n-Propyl[b]	152–153	745	.9139	1.4119	51
s-Propyl	143.5–145	748	.9097	1.4078	44
n-Butyl	167–169	744	.9031	1.4173	34
i-Butyl	163–164	751	.8982	1.4140	30
s-Butyl[c]	164	757	.9047	1.4162	32
t-Butyl	158–159	743	.9091	1.4193	19
n-Amyl	191–191.5	753	.8960	1.4220	46
i-Amyl	185–186	752	.8942	1.4210	71

R	Molecular refractivity Calcd.	Molecular refractivity Obs.	Analyses, % Carbon Calcd.	Analyses, % Carbon Found	Analyses, % Hydrogen Calcd.	Analyses, % Hydrogen Found
Methyl	22.21	22.41	54.51	54.73	9.16	9.06
Ethyl	26.83	27.00	58.78	59.19	9.87	10.08
n-Propyl	31.44	31.61	62.02	61.86	10.42	10.40
s-Propyl	31.44	31.47	62.02	62.19	10.42	10.37
n-Butyl	36.06	36.25	64.56	64.59	10.85	10.72
i-Butyl	36.06	36.20	64.56	64.40	10.85	10.72
s-Butyl	36.06	36.05	64.56	64.30	10.85	10.73
t-Butyl	36.06	36.18	64.56	64.51	10.85	10.78
n-Amyl	40.67	40.88	66.61	66.84	11.19	11.12
i-Amyl	40.67	40.88	66.61	66.46	11.19	11.29

[a] In 1933, Maruyama [*Sci. Papers Inst. Phys. Chem. Research* (Tokyo), **20,** 53 (1933)] reported the synthesis of the following ketones, recording the boiling points but no other physical or analytical data: methoxymethyl ethyl ketone, b. p. "about 130°"; methoxymethyl *n*-propyl ketone, b. p. 117° (175 mm.); methoxymethyl *n*-butyl ketone, b. p. 131–132° (173 mm.); methoxymethyl *i*-amyl ketone, b. p. 117° (87 mm.).

[b] Evidence that the b. p. of 142–150° recorded by Gauthier (Ref. 4) is seriously in error.

[c] Proof that James (Ref. 3) did not prepare *s*-butyl methoxymethyl ketone.

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[1] From the thesis of Neil E. Rigler for the M.A. degree, June, 1932. This paper was read in part at the Waco meeting of the Central Texas Section of the American Chemical Society on April 23, 1932.

[2] Henze and Murchison, THIS JOURNAL, **55,** 4255 (1933).

[3] James, *Ann.*, **231,** 240 (1885); Isbert, *ibid.*, **234,** 193 (1886); Fittig and Erlenbach, *Ber.*, **21,** 2138, 2647 (1888); Erlenbach, *Ann.*, **269,** 22 (1892).

[4] Béhal and Sommelet, *Compt. rend.*, **138,** 89 (1904); Sommelet, *Ann. chim. phys.*, [8] **9,** 484 (1906); Gauthier, *ibid.*, [8] **16,** 22 (1909).

[5] Although Sommelet [*Bull. soc. chim.*, [4] **1,** 380 (1907)], in commenting on the reaction as formulated by James, stated that, "The difficulty of interpreting simply this reaction suffices to place in doubt the announced constitution," the compound in question has not previously been resynthesized.

[6] The b. ps. recorded by Gauthier (Ref. 4) are: *n*-propyl methoxymethyl ketone 142–150° (730 mm.), ethyl ketone 130–131° (729 mm.), methyl ketone 114° (732 mm.). Henry [*Rec. trav. chim.*, **23,** 347 (1904)] had synthesized methoxyacetone by a different method and reported b. p. 118° and d^{20} 0.9570.

Experimental

Methoxyacetonitrile.—The method used by Gauthier[7] was found satisfactory for this preparation. One hundred and forty-one grams of monochloromethyl ether was added slowly with stirring to 141 g. of cuprous cyanide over a period of one hour. The mixture was warmed on a steam-bath for four hours longer and distilled, the yield being 74% of the theoretical; b. p. 120–121° (759 mm.)(corr.); d_4^{20} 0.9492; n_{D}^{20} 1.3831; M_R calcd., 17.34; M_R found, 17.46.

Preparation of Methoxymethyl Alkyl Ketones.—The ketones were obtained from methoxyacetonitrile by means of the Grignard reaction. The Grignard reagents were prepared in the usual manner, the cyano ether being added slowly with cooling and the reaction product allowed to stand for about eighteen hours before being hydrolyzed by hydrochloric acid. The ether layer was separated, washed with sodium carbonate solution and dried over anhydrous calcium chloride. The keto ethers were carefully fractionated at atmospheric pressure in all cases except that of the tertiary butyl derivative. Boiling points were taken with short, calibrated Anschütz thermometers and the properly corrected values are reported.

The ten alkoxy ketones synthesized are limpid, colorless liquids with slightly rancid, ester-like odors. Although miscible with the usual organic solvents, the solubility in water decreases rapidly with increasing molecular weight. The carbonyl group is fairly reactive as the ketones reduce Fehling's and Tollens' solutions when boiled with these reagents; addition products are formed with saturated sodium bisulfite solution and the magenta color is restored to Schiff's reagent after standing for several hours in the cold, the primary alkyl derivatives bringing about this change most rapidly and the tertiary least readily. All the ketones reacted to give liquid phenylhydrazones which were unstable and showed no tendency to crystallize. When the keto ethers were treated with aqueous solutions of sodium nitroprusside and sodium hydroxide, a dark red coloration resulted which rapidly faded to a light yellow color. The physical data concerning the ten ketones synthesized are collected in Table I.

Summary

1. The Grignard reaction has been utilized to prepare the ten simplest members of the methoxymethyl alkyl ketone series. The condensation, involving an alkoxynitrile and Grignard reagents derived from secondary and tertiary alkyl halides, has for the first time been accomplished.

AUSTIN, TEXAS RECEIVED FEBRUARY 9, 1934

[7] Gauthier, *Compt. rend.*, **143**, 831 (1906), reported b. p. 118–9° (731 mm.); d_4^{28} 0.9373; n_{D}^{28} 1.380; [M_R calcd., 17.34; M_R found, 17.56].

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF INDIANA UNIVERSITY]

Studies Concerning the Relationships of the Isomeric *d*-Glucoses and *d*-Glucose Phenylhydrazones[1]

BY GUIDO H. STEMPEL, JR.[2]

This investigation was undertaken to determine if any structural relationships could be shown to exist between the hydrazones of α- and β-*d*-glucose and the isomeric *d*-glucoses. Isbell and Pigman[3] have demonstrated that β-glucose is oxidized by bromine about thirty-five times as fast as α-glucose, a result which they explain as being due to the configuration of an intermediate molecular compound formed by bromine with glucose, rather than to any inherent difference between the *d*-glucose isomers themselves.

M. Frèrejacque,[4] in attempting to correlate the isomers of *d*-glucose phenylhydrazone with α- and β-*d*-glucose, reported that the hydrolysis of the α- and β-*d*-glucose phenylhydrazones described by Behrend and Lohr[5] leads in both cases to the formation of α-*d*-glucose. He drew this conclusion from the observation that upon completion of the hydrolysis the rotatory power of the solution decreased, which he explained by assuming that the α-*d*-glucose formed mutarotated. This would indicate a very close relationship to exist between α-*d*-glucose and *d*-glucose phenylhydrazones. Frèrejacque carried out the hydrolysis, which is catalyzed by acids, in the presence of oxalic and of picric acid, both of which form insoluble salts with phenylhydrazine, thus removing it from solution and causing the reaction to go practically to completion. Since Frèrejacque's paper is devoid of any quantitative data, the first part of this study was undertaken in an attempt to follow the reaction quantitatively with the hope of proving the presence of α-*d*-glucose in the hydrolysis products by its mutarotation rate, and thus show definitely that the hydrolysis results primarily in the formation of the α-isomer of *d*-glucose.

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[1] Extracted from a thesis for the Degree of Doctor of Philosophy at Indiana University.

[2] Present address: Carnegie Institute of Technology, Pittsburgh, Pa.

[3] H. S. Isbell and W. Pigman, *Bur. Standards J. Research*, **10**, 337–356 (1933).

[4] M. Frèrejacque, *Compt. rend.*, **180**, 1210 (1925).

[5] R. Behrend and Lohr, *Ann.*, **362**, 78 (1908).