

prior to hydrolysis; only a trace of benzilic acid was formed. Other pinacols were converted to hydrols by 40% sodium amalgam in the same manner.

When a solution of 0.50 g. of benzophenone and 0.51 g. of benzohydrol was shaken with 2.5 g. of 40% sodium amalgam in a mixture of ether and benzene, no hydrogen was evolved; the solution became dark blue and later violet-red in color. Hydrolysis after fifteen minutes gave a 95% yield of benzohydrol.

The formation of the violet-red color was an indication that benzophenone is converted to benzophenone-disodium by 40% sodium amalgam. This was surprising in view of the work of Schlenk and Bergmann,³ who showed that mercury removes one sodium from benzophenone-disodium and gives sodium ketyl. We find that a small amount of mercury removes little or no sodium and consequently 40% sodium amalgam can be used to prepare disodium derivatives of ketones. We have prepared a number of disodium derivatives by this method; in one instance, fluorenone, the disodium derivative is formed when 1% amalgam is used. The amalgam has certain advantages over the free metal and the method promises to be a convenient way of making these derivatives. Details of these experiments will be published in a future communication.

Summary

Benzopinacol and substituted benzopinacols are converted by a small amount of sodium alcoholate into a mixture of equivalent parts of ketone and hydrol. Free ketyl radicals are formed as intermediate products; these radicals are then converted by unreacted pinacol into the ketone and hydrol.

The pinacols are reduced quantitatively to hydrols by sodium amalgam in anhydrous ether-benzene solutions. This reaction, likewise, takes place through the intermediate formation of free ketyl radicals.

³ Schlenk and Bergmann, *Ann.*, **463**, 1 (1928).

ANN ARBOR, MICHIGAN

RECEIVED JULY 22, 1932
PUBLISHED JANUARY 11, 1933

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Tertiary Aliphatic Alcohols and Chlorides Containing Normal Butyl Groups

BY FRANK C. WHITMORE AND H. MILTON WOODBURN¹

While most alcohols are capable of rearrangement,² those which show this tendency to the greatest degree contain the grouping, $R_3\overset{|}{C}COH$.

Tertiary alcohols and their halides are needed for the preparation of these substances. To make such tertiary alcohols available for this work and to gain experience in handling them, this research was undertaken. The alcohols studied contain only normal aliphatic groups, including in each case at least one *n*-butyl group but no groups higher than butyl. All ten alcohols of this type were made and their boiling points, densities and

¹ Presented in partial fulfilment of the requirements for the Ph.D. degree. This study was completed in July, 1930.

² Whitmore, *THIS JOURNAL*, **54**, 3274, 3431 (1932).

refractive indices were determined under comparable conditions. Of the ten alcohols, seven have been mentioned in the literature but no adequate studies have been made with most of them. Of the ten chlorides only one, 2-chloro-2-methylhexane, has been described.³ It was made from the carbinol by the action of hydrogen chloride or acetyl chloride.

In a few cases olefins were obtained from the carbinols or their chlorides. Preliminary studies were made on the action of bromine with some of the alcohols and on the hydrolysis of the resulting dibromides.⁴

Experimental

Preparation of the Alcohols.—All of the alcohols were made by the action of suitable Grignard reagents and carbonyl compounds.⁵ These methods are summarized in Table I. The alcohols were fractionated through effective columns.⁶ The higher ones were distilled under reduced pressure.

TABLE I

Carbinol	Literature preparation	Yield, %	Present method	Yield	
				%	g.
Me ₂ Bu	BuCO ₂ Et + MeMgBr				
	Me ₂ CO + BuMgBr	92	Me ₂ CO + BuMgBr ^a	40	560
MeEtBu	MeBuCO + EtMgI				
	MeEtCO + BuMgBr	62	MeEtCO + BuMgBr ^b	71	480
MePrBu	MeBuCO + PrMgI		MePrCO + BuMgBr ^c	68	340
MeBu ₂	Ph ₂ CHOAc + BuMgI		AcOEt + BuMgBr	65	950
Et ₂ Bu	Et ₂ CO + BuMgBr		BuCO ₂ Et + EtMgCl	30	30
EtPrBu			EtPrCO + BuMgBr ^d	52	130
EtBu ₂			EtCO ₂ Me + BuMgBr	33	110
Pr ₂ Bu			BuCO ₂ Me + PrMgBr	37	90
PrBu ₂			PrCO ₂ Me + BuMgBr	70	250
Bu ₃	Bu ₂ CO + BuMgBr		Et ₂ CO ₂ + BuMgBr ^e	80	280

^a A large by-product, b. p. 100–125°, was obtained.

^b By-products of b. p. 105–108° and 119–121°.

^c The methyl propyl ketone was first made from acetoacetic ester ("Organic Syntheses," 1928, Vol. VIII, p. 36). As only a 20% yield was obtained, the ketone was then made by dehydrogenating (brass catalyst at 375°) methylpropylcarbinol made from methylmagnesium chloride and *n*-butyraldehyde (from commercial "Butalyde" supplied by the Commercial Solvents Corporation). The boiling points (at 740 mm.) of the carbinol and ketone used were 118–119° and 100.0–101.5°.

^d Ethyl propyl ketone, b. p. 122–123° (730 mm.), was prepared in 70% yield by dehydrogenating ethylpropylcarbinol, b. p. 132–134° (730 mm.), prepared in 58% yield from ethylmagnesium chloride and butyraldehyde.

^e During the addition of the ethyl carbonate to the Grignard solution, the latter was kept at about 30°. If cooling was used, the ethyl carbonate accumulated in the solution and later reacted violently.

³ Muset, *Bull. acad. roy. Belg.*, 775–789 (1906); Henry and de Wael, *Rec. trav. chim.*, 28, 448 (1909); *Chem. Zentr.*, I, 1854 (1909).

⁴ These results have been supplemented by W. L. Evers of this Laboratory and will be published by him.

⁵ Cf. Edgar and co-workers, *THIS JOURNAL*, 51, 1483 (1929).

⁶ Whitmore and Lux, *ibid.*, 54, 3451, 3453 (1932).

Properties of the Alcohols.—In determining the physical constants of the alcohols, the same apparatus and method were used throughout. All constants for a given alcohol were determined on the same sample. The boiling points were determined by actually distilling a large amount of each alcohol and taking the boiling range of the main fraction. When reduced pressure was used a barostat was employed to maintain constant pressure. The densities were determined at 20 and 25° with a bottle type pycnometer. Refractive indices were determined with an Abbé refractometer with its prism controlled by water from an automatic thermostat held at $20.0 \pm 0.2^\circ$. The alcohols were all colorless. In one case, methyl dibutylcarbinol, the sample became slightly yellow on standing for several weeks. The odors were pleasant. In viscosity they ranged from limpid liquids (dimethylbutylcarbinol) to thin syrups (tributylcarbinol). Table II gives the physical properties of the alcohols.

With one exception, the refractive indices increase in a fairly regular way with increasing molecular weight. Such is not the case with the densities. The properties of methyl dibutylcarbinol seem to be peculiar.

TABLE II

C atoms	Carbinol	Boiling point, °C. (mm.)		Density			Refractive index	
		Literature	Determined	Literature	Determined d_4^{20}	d_4^{25}	Literature n_D^{20}	Detd., n_D^{25}
7	Me ₂ Bu	141-142 (755) 58-60 (20)	139.4-140.4 (735) 53-53.5 (15)	d_4^{20} 0.815 d .8155	0.8119	0.8094	n_D 1.41592 n_D^{25} 1.4187	1.4175
8	MeEtBu	153-160 (745) 161-162 (763) 163.5 corr.	160 (732) 65.2-65.8 (15)	d_4^{19} .8273 d_4^0 .8446 d_4^{15} .8325	.8282	.8249	n_D^{25} 1.42735 n_D^{15} 1.4279	1.4279
9	MePrBu	178-183	178-9 (732) 78.5-79.5 (15) 56.2-56.4 (4)		.8267	.8237		1.4327
9	Et ₂ Bu	119-121 (110) 116-118 (105)	180-180.5 (733) 76.5-77.5 (15)	d_4^{20} 0.8409	.8399	.8365	n_D^{25} 1.4360	1.4362
10	MeBu ₂	84-85 (10)	91.4-92.4 (15)		.8290	.8253		1.4341
10	EtPrBu		88.8-89.6 (15)		.8369	.8337		1.4378
11	Pr ₂ Bu		101.4-102.4 (15)		.8351	.8319		1.4390
11	EtBu ₂		102.6-103.6 (15.5)		.8376	.8345		1.4400
12	PrBu ₂		113.6-114.2 (15)		.8370	.8340		1.4419
13	Bu ₃	120 (10) 177-178 (15) 230-235 dec.	125.0 (15) 99.8-100.0 (4)	d_4^{18} 0.844	.8408	.8368	n_D^{18} 1.4448	1.4434

Preparation and Properties of the Chlorides.—The method of Halse⁷ was used. The carbinol, cooled to -10° , was saturated with dry hydrogen chloride. The halide layer was dried and freed from hydrogen chloride by standing in a vacuum desiccator over sodium hydroxide. It was also found possible to wash the chlorides with cold 5% sodium carbonate solution. In distilling the chlorides it was necessary to use a much lower pressure than with the carbinols as they are much more sensitive to heat. The decomposition appeared to be catalyzed by traces of hydrogen chloride. In such cases it was necessary to wash the chloride again with cold 5%

⁷ Halse, *J. prakt. Chem.*, [2] **89**, 451 (1913).

sodium carbonate solution and dry it before redistilling at a lower pressure. In preparing the chlorides, deep colors often developed. These ranged from purple to black and were most noticeable with the chlorides from dimethylbutyl, methylethylbutyl and methylpropylbutylcarbinols.

The pure chlorides were colorless liquids. The odor was fainter and slightly less pleasant than that of the carbinols. There was no odor of hydrogen chloride. The pure chlorides were remarkably stable on standing. Impure samples of the chlorides darkened rapidly and gave considerable amounts of hydrogen chloride. The physical properties of the chlorides were determined as with the alcohols.

The samples were purified by distillation at reduced pressures (McLeod gage for pressures below 5 mm.) through a 30×1 cm. indented insulated column with complete condenser and variable take-off.⁶ This arrangement was far superior to an ordinary vacuum distillation because it allowed the use of a high reflux ratio. The yields of purified products were 65-75%. The properties of the chlorides are given in Table III. Again the properties of the methyldibutyl derivative were irregular.

TABLE III

C atoms	Chloride	Boiling point, °C. (mm.)	Density		Refractive index, n_D^{20}	Stability ^b		
			d_4^{20}	d_4^{25}		Analysis, % Cl Calcd. Found		
7	Me ₂ BuCCl	35.0-35.5 (15.5)	0.8698	0.8661	1.4205	3, 4, 5	26.37	26.2, 26.1
8	MeEtBuCCl	55.0 (15)	.8764	.8729	1.4315	3, 7, 8	23.88	24.2, 23.6, 23.7
9	MePrBuCCl	70.8-71.4 (14.5)	.8723	.8690	1.4349	6, 7, 8	21.82	21.7, 21.7, 22.2
9	Et ₂ BuCCl	46.0 (3)	.8856	.8822	1.4400		21.82	21.6, 21.5, 21.5
10	MeBu ₂ CCl	60.5 (3.5)	.8707	.8676	1.4382	4, 6, 8	20.09	19.8, 19.9
10	EtPrBuCCl	53-54 (2)	.8804	.8773	1.4421	4, 6, 8	20.09	20.0, 20.0
11	Pr ₂ BuCCl	66.5-67.5 (2.5)	.8743	.8715	1.4430	3, 4, 5	18.62	18.4, 18.4
11	EtBu ₂ CCl	69.5-70.0 (2.75)	.8784	.8756	1.4442	4, 6, 8	18.62	18.6, 18.6
12	PrBu ₂ CCl	78.8-79.2 (3)	.8736	.8715	1.4461	3, 7, 8	17.34	16.9, 17.0
13	Bu ₃ CCl ^a	91.5-92.5 (2.5)	.8701	.8673	1.4480	3, 4, 8	16.24	16.0, 16.0

^a This chloride was most difficult to distil unless all traces of hydrogen chloride had been removed by long standing in the vacuum desiccator over alkali.

^b These are the changes in the chlorides on standing for 26 months in the laboratory in ordinary bottles. 3. Slight yellow color developed. 4. No odor of hydrogen chloride. 5. Change in refractive index of about +0.001. 6. Still colorless. 7. Odor of hydrogen chloride. 8. Change in refractive index of less than +0.0004.

Preparation of Various Olefins.—In one preparation of methylethylbutylcarbinol partial dehydration took place. Five fractionations of the low boiling material gave 20 cc. with b. p. 105-108° and 125 cc. with b. p. 119-121° at 734 mm. Both reacted with bromine water to give dibromides but were not further identified.

Dehydration of 240 g. of crude methyldibutylcarbinol gave on fractionation 107 g. of olefin of b. p. 162-164° (739 mm.). The distillation of tributylcarbinyl chloride at 20 mm. gave 5-butylnonene-4,⁸ b. p. 212.5-213° (735 mm.) and 60° (1.2 mm.), d_4^{20} 0.7724, n_D^{20} 1.4392.

⁸ Ivanoff, *Bull. soc. chim.*, [4] 37, 287 (1925).

Summary

1. Ten aliphatic tertiary alcohols containing *n*-butyl groups have been prepared and some of their properties have been determined.
2. Ethylpropylbutyl, ethyldibutyl, dipropylbutyl and propyldibutyl carbinols have been prepared for the first time.
3. The ten corresponding tertiary chlorides have been prepared and studied. All except one of these are new.

STATE COLLEGE, PENNSYLVANIA

RECEIVED JULY 22, 1932
PUBLISHED JANUARY 11, 1933

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF MIAMI UNIVERSITY]

Alkamine Esters: Novocaine Analogs. III

BY MARLIN T. LEFFLER¹ AND HARVEY C. BRILL

In accord with the statement in a previous communication:² "In the absence of any considerable number of trustworthy generalizations that relate chemical structure and physiological activity, the only means of learning of the effects of such relationships are to prepare compounds of slight structural differences and study the effects of such changes," the data herewith accumulated from further studies of anesthetic compounds are presented.

The anesthetic properties of the compounds that have been prepared and are herein described were determined by the use of goldfish as detailed by Adams and co-workers³ with this slight modification, that the water used in the tests was in all cases aerated to avoid any possible effect on the fish from lack of oxygen in the water in which they were submerged.

The compounds synthesized and studied are listed below. The hydrochlorides of the esters formed by esterification of β -4-morpholinoethanol with benzoic acid, phenylacetic acid, β -phenylpropionic acid, cinnamic acid and tetrahydropyran-4-carboxylic acid, respectively; a second series of these same acids with β -N-piperidinoethanol; and a third series of esters from β -menthylethylaminoethanol with benzoic acid and tetrahydropyran-4-carboxylic acid.

Experimental

Preparation of the Alkaminioethanols.—Menthylamine was synthesized by means of the following series of reactions: menthol (U. S. P.) \longrightarrow menthone \longrightarrow menthone oxime \longrightarrow menthylamine. Reduction of the oxime and its recovery were carried out in accordance with the procedure detailed by Wallach and others.⁴ The amine, distilled in an

¹ Honors Student in Chemistry at Miami University, 1932.

² Brill, *THIS JOURNAL*, **54**, 2484 (1932).

³ Adams, Ridea, Burnett, Jenkins and Dreger, *ibid.*, **48**, 1758 (1926).

⁴ Wallach, *Ann.*, **276**, 293 (1893); Read and Story, *J. Chem. Soc.*, 2221 (1926); Read and Robertson, *ibid.*, 2209 (1926); Mailhe, *Bull. soc. chim.*, **33**, 83 (1923).