tions, $[\alpha]^{27}D$ +10.83°. Thus although the percentage yields are comparable, the new method is less laborious and gives a much purer product.

Experimental

D(+)-2,3-Diacetoxybutane (II).—The glycol,[10] I, was distilled at 10 mm., b. p. 77.5–78°, $\alpha^{25}D$ −12.92°, $[\alpha]^{25}D$[11] −13.09°. To 180 g. (2 moles) of I were added 450 g. (4.4 moles) of freshly distilled acetic anhydride and 800 g. freshly distilled pyridine. After the mixture stood overnight, the volatile impurities were removed by distillation at 10 mm., followed by II; b. p. 82°, $\alpha^{25}D$ +13.87°, slightly lower than +14.10° of recrystallized product[2]; yield 319 g., 91.5%.

L(+)-erythro-3-Chloro-2-butanol (III).—Gaseous hydrogen chloride was passed into a solution of 315 g. (1.81 moles) of II in 460 g. concentrated hydrochloric acid at −18 to −20° in two 1-liter ampoules until 162 g. was absorbed by the two. The ampoules were sealed, and the solutions allowed to stand at room temperature for three weeks. The solutions were poured over one kilo of powdered technical sodium bicarbonate, the inorganic solids were removed by suction filtration, the organic liquid was separated, the salt cake was washed with isopropyl ether, and the aqueous phase was extracted with isopropyl ether. After the combined organic phase was washed with aqueous sodium bicarbonate, it was filtered through Dry Ice to remove water. Distillation gave 150 g. of crude III (yield 76.5%, over-all, 70%), b. p. (10 mm.) 56–62°, $\alpha^{25}D$ (obsd.) +9.77°. The boiling range and high rotation[12] can be ascribed to the presence of some chlorohydrin acetate, but this is no particular detriment because it is converted into IV at the next step.

D(+)-2,3-Epoxybutane (IV).—Into a 125-ml. flask containing a solution of 250 g. of potassium hydroxide pellets in 125 ml. of water maintained at 90 to 95° was slowly added 37.6 g. (0.348 mole) of III; IV distilled as formed. Finally the temperature was raised to boiling, to drive over all oxide. After drying the two-phase distillate (without separation) with potassium hydroxide, 22 g. of IV distilled at 53.5° at 746 mm., $\alpha^{25}D$ +46.75°, slightly lower than previous value[2] of +47.23°; yield 88%, over-all, 61.6%.

L(−)-2-Butanol (V).—To a solution of 5 g. (0.132 mole) of lithium aluminum hydride (Metal Hydrides, Inc.)[13] in 150 ml. of absolute ether, 22 g. (0.306 mole) of IV was added slowly with stirring over a period of 1 hour, at a rate to produce gentle boiling of the solvent. Refluxing was continued for another hour. After addition of 20 ml. water during cooling, the mixture was poured into 50 ml. of 10% aqueous potassium hydroxide, and the aqueous phase was extracted four times with ethyl ether. After drying with anhydrous potassium carbonate, fractional distillation gave 18.1 g. of V, b. p. (745 mm.) 97.5–98.0°, $\alpha^{25}D$ −10.67°, $[\alpha]^{25}D$ −13.51°; yield 80%, over-all, 49.3%.

Summary

The reduction of D(+)-2,3-epoxybutane to L-(−)-2-butanol with lithium aluminum hydride proceeds smoothly and gives a good yield of active alcohol having an optical purity of 99%. The over-all yield of alcohol from D(−)-2,3-butanediol is about 50%.

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[10] We are indebted to Dr. G. A. Ledingham, Director, and to Drs. A. C. Neish and J. A. Wheat of the Division of Applied Biology, National Research Council of Canada, for a supply of the active glycol, obtained by fermentation of starch with *Aerobacillus polymyxa*. We take this occasion to express our appreciation of this courtesy.

[11] Previous values,[6,8] −13.0°, −13.34° and −13.19°; also −12.85°.

[12] Previous value[2] for L(+)-*erythro*-3-chloro-2-butanol, $\alpha^{25}D$ (obsd.) +9.47°.

[13] An excess was taken to ensure a sufficient amount, because the container had been opened a number of times, with possible deterioration of the reagent.

PASADENA, CALIFORNIA RECEIVED MAY 22, 1950

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

Ketimines. III. ω-Cyclohexylalkyl Alkyl Type[1]

BY P. L. PICKARD AND C. W. YOUNG[2]

Previous reports[3,4] from this Laboratory have described a method for synthesis of ketimines under anhydrous conditions. The compounds reported were all prepared from aromatic nitriles and aryl or alkyl Grignard reagents. Since the catalytic methods of ketimine synthesis reported by Mignonac[5,6] had failed for dialkyl compounds, it seemed judicious to test the generality of the method used in this Laboratory by the synthesis of such ketimines.

The series of ω-cyclohexyl aliphatic acids obtained from Dow Chemical Company was selected as a source of nitriles. A study of the literature indicated that data on these acids and the corresponding acid halides, amides and nitriles were far from complete. The intermediate compounds were synthesized by non-ambiguous methods and purified before using them in further work.

TABLE I

ACID CHLORIDES

Acid chloride R = cyclohexyl	Yield, %	B. p., °C.	Mm.	d^{25}_4	$n^{25}D$	Chlorine, % Calcd.	Chlorine, % Exptl.
R—CH₂—CO—Cl[a]	87.0	64	4	1.0528	1.4698	22.07	22.16
R—(CH₂)₂—CO—Cl[b]	94.5	74	1	1.0345	1.4768	20.30	20.15
R—(CH₂)₃—CO—Cl	92.5	83	1	1.0175	1.4710	18.79	18.68
R-(CH₂)₄—CO—Cl[c]	93.5	94	1	1.0053	1.4710	17.49	17.31
R—(CH₂)₅—CO—Cl	96.0	106	1	0.9987	1.4714	16.35	16.49

[a] Darzens and Rost, *Compt. rend.*, **153**, 774 (1911), gives b. p. (23 mm.) as 98–100°. [b] Mastagli and Metayer, *ibid.*, **224**, 1779 (1948), lists the b. p. (35 mm.) as 124–126° and the b. p. (17 mm.) as 108°. [c] Katsnel'son and Dubinin, *Compt. rend. acad. sci.* (*U. R. S. S.*) (*N. S.*), **4**, 405 (1936), gives the b. p. (15 mm.) as 139°.

The nitriles were treated with a 25% excess of *s*-butylmagnesium bromide and the ketimines isolated

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[1] From a thesis presented in partial fulfillment of the requirements for the Master of Science Degree at The University of Oklahoma.

[2] William Earl Schlueter Fellow at The University of Oklahoma, 1949–1950.

[3] P. L. Pickard and D. J. Vaughan, THIS JOURNAL, **72**, 876 (1950).

[4] P. L. Pickard and D. J. Vaughan, *ibid.*, **72**, 5017 (1950).

[5] G. Mignonac, *Compt. rend.*, **169**, 237 (1919).

[6] G. Mignonac, *ibid.*, **170**, 936 (1920).

TABLE II

AMIDES

Amide R = cyclohexyl	M. p., °C.	Nitrogen, % Calcd.	 Exptl.
R—CH_2—CO—NH_2[a]	170		
R—$(CH_2)_2$—CO—NH_2[b]	120		
R—$(CH_2)_3$—CO—NH_2	111	8.28	8.36
R—$(CH_2)_4$—CO—NH_2[c]	124		
R—$(CH_2)_5$—CO—NH_2	117	7.10	7.37

[a] Wallach, *Ann.*, **353**, 297 (1907), gives the m. p. as 168°. [b] Sabatier and Murat, *Compt. rend.*, **156**, 753 (1913), give the m. p. as 123°. [c] Katsnel'son and Dubinin, *Compt. rend. acad. sci.* (*U. R. S. S.*) (*N. S.*), 4, 405 (1936), give the m. p. as 123°.

TABLE III

NITRILES

Nitrile R = cyclohexyl	Yield, %	B. p. °C.	 Mm.	d^{20}_4	$n^{20}D$	Chlorine, % Calcd.	 Exptl.
R—CH_2—CN[a]	70.0	57	1	0.9180	1.4575		
R—$(CH_2)_2$—CN	80.0	71	1	.9107	1.4602	10.20	10.42
R—$(CH_2)_3$—CN	83.0	82	1	.9056	1.4607	9.26	9.40
R—$(CH_2)_4$—CN	85.0	93	1	.8950	1.4618	8.48	8.76
R—$(CH_2)_5$—CN	86.0	112	1	.8979	1.4637	7.80	7.90

[a] Wallach, *Ann.*, **359**, 311 (1908), reports $n^{18}D$ 1.4575 and $n^{20}D$ 0.913.

TABLE IV

KETIMINES

Ketimine R = cyclohexyl, R_2 = *s*-butyl	Yield, %	B. p. °C.	 Mm.	d^{20}_4	$n^{20}D$	Nitrogen, % Calcd.	 Exptl.
R—$(CH_2)_2$—C(=NH)—R_2	56.0	101	2	0.8680	1.4689	7.17	7.00
R—$(CH_2)_3$—C(=NH)—R_2	43.0	107	1	.8611	1.4699	6.68	6.57
R—$(CH_2)_4$—C(=NH)—R_2	45.0	121	1	.8754	1.4700	6.11	6.00
R—$(CH_2)_5$—C(=NH)—R_2	60.0	130	1	.8808	1.4719	5.90	5.65

in the manner previously described.[3] The only product obtained with ω-cyclohexylacetonitrile was a tarry material which could not be purified. Similar tars were obtained in varying amounts from the other nitriles. It was assumed that these tars were iminonitriles of the type indicated by Hauser.[7]

Experimental

Acid Chlorides.—The acid chlorides were prepared by the method described in "Organic Syntheses."[8] Analyses were obtained by refluxing samples of the acid halides with standard sodium hydroxide and back-titrating the excess alkali with standard hydrochloric acid. The end-point arbitrarily set at *p*H 8.0, was determined by a Beckman *p*H meter. Physical constants and analyses are given in Table I.

Amides.—The acid chlorides were added slowly to well-stirred ice-cold ammonium hydroxide. The amides were filtered, washed with water and recrystallized from methanol-water. All yields were above 80%. Melting points and analytical data are given in Table II.

Nitriles.—The amides were dehydrated with an excess of phosphorus oxychloride and the nitriles purified by distillation. Yields, physical constants and analyses are given in Table III.

Ketimines.—The procedure of Pickard and Vaughan[1] was followed using 0.25 mole of *s*-butyl bromide and 0.20 mole of nitrile. The yields, physical properties and analyses are given in Table IV.

Summary

1. Five acid chlorides, two not previously described, have been prepared and characterized.

2. Five amides, two not previously reported, have been prepared.

3. Five nitriles, four not previously described, have been prepared and characterized.

4. Four new ketimines have been prepared and characterized.

(7) C. R. Hauser and W. J. Humphlett, *J. Org. Chem.*, **15**, 359 (1950).

(8) "Organic Syntheses," Collective Volume I, John Wiley and Sons, New York, N. Y., 1946, p. 147.

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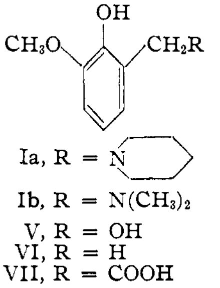
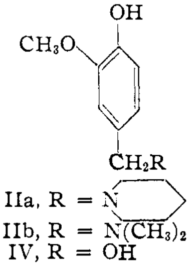
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

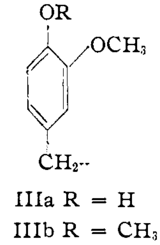
The Structure of the Guaiacol "Mannich Bases"

BY ERNEST L. ELIEL

The recent finding[1] that certain "Mannich Bases" derived from phenols[2] can be used as carbon alkylation agents suggested an investigation of corresponding reactions of dialkylaminomethylguaiacols (I or II), in view of the fact that the 3-methoxy-4-hydroxybenzyl (IIIa) and especially the 3,4-dimethoxybenzyl (IIIb) system are of frequent occurrence in products of natural origin. It seemed possible that guaiacol Mannich bases might be convenient intermediates in the synthesis of some of these natural products and that they might even play a part in their biosynthesis.







The product of the reaction of guaiacol with formaldehyde and piperidine was first described by Auwers and Dombrowski.[3] These authors assumed

(1) (a) Salzer and Andersag, U. S. Patent 2,315,661 (1943); *C. A.*, **37**, 5418 (1943). (b) J. H. Brewster, Ph.D. Dissertation, University of Illinois, Urbana, Ill., 1948.

(2) (a) Blicke in Adams, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303; (b) Carlin and Landerl, THIS JOURNAL, **72**, 2762 (1950).

(3) Auwers and Dombrowski, *Ann.*, **344**, 288 (1905). The name "Mannich Base" as applied to the dialkylaminoalkylphenols is obviously a misnomer but is used in this paper in agreement with established custom.