[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Hydrogenation of Optically Active Compounds over Nickel and Copper–Chromium Oxide

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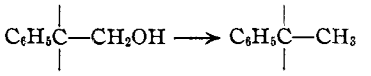
This paper is a report of the experimental results obtained in seeking an answer to the question as to whether optically active compounds may be prepared by the hydrogenation of esters to alcohols, over copper–chromium oxide and of phenyl substituted alcohols to the corresponding cyclohexyl compounds over nickel at 200 to 250°. The data are summarized in Table I.

Optically active alcohols were obtained except in the case of the lactate. The optical activities of the alcohols from α-phenylpropionate, α-phenylbutyrate and α-methylbutyrate were relatively low as compared with those of the original esters. In contrast with this were the high optical activities of the *d*- and *l*-3-phenylbutanol-1. The optical activities of the alcohols from β-methylvalerate, α-ethylpelargonate and α-ethyl-δ-phenylvalerate were low but of the same order of magnitude as the original esters, so that apparently in these cases also little, if any, racemization occurred during hydrogenation. Unquestionably the temperature, rate and extent of hydrogenation and probably other variables determine the extent to which racemization occurs but from the data available no definite conclusions can be drawn with regard to these factors.

The hydrogenation of α-phenyl esters is complicated by the fact that the reaction



$$C_6H_5\overset{|}{\underset{|}{C}}—CH_2OH \longrightarrow C_6H_5\overset{|}{\underset{|}{C}}—CH_3$$

occurs under the same conditions as does the hydrogenation of esters to alcohols.[1] Therefore the alcohols from α-phenylpropionate and α-phenylbutyrate were accompanied by considerable amounts of hydrocarbons. In one case the hydrocarbon so produced had a low optical activity so that apparently the reaction indicated above may occur over copper–chromium oxide at 250° without complete racemization.

Quite a different type of reaction from those referred to above is the hydrogenation of the benzenoid ring over nickel. Optically active 2- and 3-cyclohexylbutanols were obtained by the hydrogenation of the corresponding phenylbutanols. The optical activities of the former were considerably lower than the phenyl compounds submitted to hydrogenation, but this is not evidence of racemization since the phenyl group is much more potent than the cyclohexyl group in enhancing optical activity.

Still another type of reaction involving the preparation of an optically active compound by hydrogenation was the conversion of camphor to active borneol over copper–chromium oxide. Active borneols were so produced but the proportion of the isomers was apparently a function of the temperature of hydrogenation.

Experimental Part

The optically active esters were prepared as follows: α-ethyl-δ-phenylvaleric acid, b. p. 141–143° (6 mm.), was resolved as the cinchonidine salt by crystallization from 85% acetone. α-Ethylpelargonic acid, b. p. 117–118° (6 mm.), was similarly resolved except that 75% acetone was used for crystallization. The acids were prepared: (1) by the reaction of an aldehyde ($C_6H_5CH=CHCHO$ or $C_6H_{13}CHO$) with malonic ester followed (2) by hydrogenation of the alkene linkages, (3) alkylation with ethyl bromide, (4) hydrolysis of the malonic ester, (5) decarboxylation of the malonic acid. The acids were esterified with ethanol in the presence of sulfuric acid. α-Phenylbutyric acid supplied by Dr. V. H. Wallingford of the Mallinckrodt Chemical Co. was resolved by crystallizing the menthyl esters from methanol. α-Phenylpropionic, β-phenylbutyric, β-methylvaleric and α-methylbutyric acids were resolved as previously described[2] and esterified through the formation of the acid chlorides.

The hydrogenations were in general carried out at 250° under a pressure of 150 to 200 atmospheres over various samples (a, b and c) of copper–chromium oxide in a copper liner as described elsewhere.[3] The following exceptions to these conditions may be noted: butyl lactate was hydrogenated at 225° and the first hydrogenation of camphor was made at 150° and the second at 120°. Raney nickel (d) was catalyst for the hydrogenation of phenylbutanols at 200°. The experiments marked (e) were made at 200 to 275 atmospheres in the bomb described as "B" in a recent paper.[4] The following matters should also be noted in connection with the presentation of the experimental results. The "menthol" recovered from the hydrogenation of the menthyl esters was not identical with the original compound. It did not have the characteristic

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[1] *Cf.* Adkins, Wojcik and Covert, THIS JOURNAL, **55**, 1669 (1933).

[2] Raper, *J. Chem. Soc.*, **123**, 2557 (1923); Rupe, *Ann.*, **369**, 323 (1909); *Helv. Chim. Acta*, **13**, 373 (1930); Levene and Marker, *J. Biol. Chem.*, **91**, 84 (1931); Marckwald, *Ber.*, **29**, 53 (1896).

[3] Adkins, *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).

[4] Adkins, THIS JOURNAL, **55**, 4272 (1933).

TABLE I

HYDROGENATION OF VARIOUS OPTICALLY ACTIVE COMPOUNDS (COPPER–CHROMIUM OXIDE (a, b, c) OR RANEY NICKEL (d))

Name and g. of compound	(α)D	Catalyst, g.	Time, hrs.	%	Yield of products	(α)D
Et α-Ph-propionate (16)	−22.9	2a	3.0	17	Ester	− 2.4
				33	Isopropylbenzene	...
				16	2-Ph-propanol-1	+ 2.5
Et α-Ph-propionate (12)	+65.1	6a	2.3	4	Ester	+ 1.8
				80	Isopropylbenzene	...
Bu lactate (50)	+ 4.9		2.0	9	Ester	+ 3.0
				81	Propanediol-1,2	0
Menthyl β-Ph-butyrate (45)	−90.3	7c	2.6	9	Ester	−89.7
				73	3-Ph-butanol-1	−26.0
Menthyl β-Ph-butyrate (25)	−90.3	5c	2.5	20	Ester	−84.8
				61	3-Ph-butanol-1	−31.4
Menthyl β-Ph-butyrate (43)	−40.5	6c	1.8	21	Ester	−25.1
				60	3-Ph-butanol-1	+12.2
Menthyl β-Ph-butyrate (47)	−40.9	7b	5.8	26	Ester	−26.0
				61	3-Ph-butanol-1	+15.7
Menthyl β-Ph-butyrate (50)	−40.9	6b	2.8	64	Ester	−40.0
				33	3-Ph-butanol-1	+15.7
Menthyl α-Ph-butyrate (42)	−82.0	6a	3.0	23	Ester	−66.1
				17	2-Ph-butanol-1	− 3.7
				26	*sec*-Butylbenzene	+ 0.4
Et α-Ph-butyrate (14)	− 6.0	2a	2.5	3.5	Ester	...
				50	2-Ph-butanol-1	<− 0.50
				24	*sec*-Butylbenzene	0
Et α-Ph-butyrate (22)	− 2.3	3a	1.3e	5	Ester	0
				61	2-Ph-butanol-1	− 0.10
Et α-Me-butyrate (15)	+ 3.04	5a	3.0	80	2-Me-butanol-1	0
Et α-Me-butyrate (15)	− 8.3	3a	1.8e	97	2-Me-butanol-1	+ 1.2
Et β-Me-valerate (14)	+ 1.79	3a	1.5e	10	Ester	
				90	3-Me-pentanol-1	+ 1.8
Et α-Et-pelargonate (15)	− 0.65	3a	0.8e	50	Recov. acid	− 0.6
				50	2-Et-nonanol-1	− 0.2
Et α-Et-δ-Ph-valerate (11)	+ 0.26	2a	0.9e	53	Recov. acid	
				47	2-Et-5-Ph-pentanol-1	+ 0.26
3-Ph-butanol-1 (30)	+14.0	4d	2.0e	91	3-Cyclohexylbutanol-1	+ 4.02
2-Ph-butanol-1 (33)	− 2.4	4d	2.8e	68	2-Cyclohexylbutanol-1	− 1.22
Camphor (76)	+46.5	6b	1.3	100	"Borneol" (m. p. 197°)	− 9.2
Camphor (76)	+46.5	6b	1.0	100	"α-Isoborneol" (m. p. 208–209°)	−22.3

TABLE II

ANALYSES

Compound	B. p., °C. (mm.)	Formula	*d*	(α)D	Calcd. C	Calcd. H	Found C	Found H
Menthyl α-Ph-butyrate	M. p., 58	$C_{20}H_{30}O_2$	...	−41.2[a]	79.47	9.93	79.50	9.88
α-Ethylpelargonic acid	117–118 (5–6)	$C_{11}H_{22}O_2$	...	.....	70.97	12.36	70.88	12.33
l-Et-α-Et-pelargonate	131 (23)	$C_{13}H_{26}O_2$	0.879	− 0.65	72.90	12.15	73.10	12.23
α-Et-δ-Ph-valeric acid	141–143 (5–6)	$C_{13}H_{18}O_2$	...	.....	75.73	8.74	75.66	8.66
d-Et-α-Et-δ-Ph-valerate	162–165 (23–25)	$C_{15}H_{22}O_2$	1.000	+ .26	76.92	9.40	76.12	9.22
l-2-Et-nonanol-1	126 (19–20)	$C_{11}H_{24}O$	0.860	− .20	76.74	13.95	76.59	14.19
d-2-Et-5-Ph-pentanol-1	150–153 (18–20)	$C_{13}H_{20}O$	.984	+ .26	81.25	10.42	81.30	10.27
d-3-Cyclohexylbutanol-1	130 (18–20)	$C_{10}H_{20}O$	.946	+ 4.02	76.91	12.82	76.80	12.79
l,2-Cyclohexylbutanol-1	119–121 (18)	$C_{10}H_{20}O$	.948	− 1.22	76.91	12.82	76.89	12.87

[a] Rotation determined in a 2-dm. tube in a methanol solution containing 4.2462 g. of ester per 100 ml. of solution. All other rotations were determined on the liquids in a 0.5-dm. tube.

odor and was apparently an isomeric compound or a mixture of isomers. The recovered "menthol" had the following constants: $(\alpha)_D$ −17°, d_{20}^{25} 0.927, and n_D^{25} 1.4610. A hydrocarbon fraction boiling lower than *sec*-butylbenzene was obtained in the hydrogenation of the esters of α-phenylbutyric acid. This appeared to be isopropylbenzene but the amount available was too small to be identified with certainty. The 2-phenylpropanol-1 was present in the reaction mixture from ethyl α-phenylpropionate as 2-phenylpropyl-α-phenylpropionate (186–188° (13 mm.)). The rotation of the alcohol (100°, 13 mm.) was determined in pyridine and it was characterized as the benzoate (201–202° (20 mm.)). The (α) of the latter was +0.50°. The yields recorded in Table I for ethyl β-methylvalerate, ethyl α-ethylpelargonate and ethyl δ-phenylvalerate are calculated on the basis of the weight of material obtained after filtration of the catalyst.

Summary

The preparation of various optically active alcohols by the hydrogenation of optically active esters, alcohols and ketones over copper–chromium oxide and nickel has been described.

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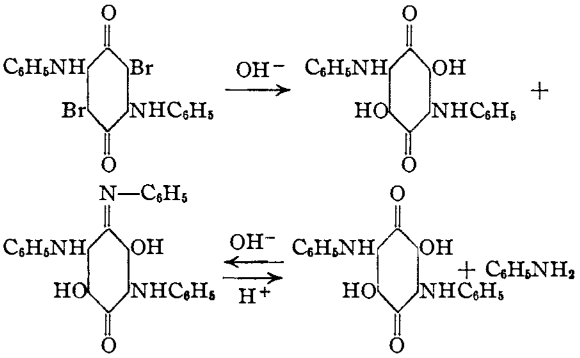
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Action of Alkali on Dianilinodibromobenzoquinone

BY MURRAY M. SPRUNG[1]

During a study of the reactions of tetrabromomethylquinol and bromanil, dianilinodibromoquinone was obtained. This substance was prepared as early as 1872 by Stenhouse,[2] who analyzed it, but gave no melting point or further description. In order to establish that the bromines had been replaced symmetrically, as in similar reactions of this type, two reactions were carried out: 2,5-diphenoxy-3,6-dibromoquinone was treated with aniline, in the hope that the dianilinodibromoquinone would be formed; and the dianilinodibromoquinone, itself, was treated with alkali, in the expectation that bromoanilic acid (2,5-dihydroxy-3,6-dibromoquinone) would be obtained.

The first reaction went quantitatively as expected,[3] and therefore established the symmetrical nature of the compound; it is 2,5-dianilino-3,6-dibromo-*p*-benzoquinone. The second reaction, however, gave no trace of bromoanilic acid. Instead, two new quinone derivatives were obtained. The first, a pale yellow substance, was identified as 2,5-dianilino-3,6-dihydroxybenzoquinone, formed by replacement of the second pair of bromine atoms by hydroxyl groups. The second, a chocolate brown substance, proved to be the mono-anil of the dianilinodihydroxyquinone. The structure of the anil was established by its synthesis from the latter compound and aniline in alkaline solution, and by its hydrolysis to dianilinodihydroxyquinone and aniline in acid solution.



By-products of the reaction between dianilinodibromoquinone and alkali are hydrogen bromide, aniline and small amounts of impure materials formed by replacement of both bromine and anilino groups. It is from the latter type of replacement that the aniline necessary for the formation of the anil comes. However, no *pure* compound containing less than two nitrogen atoms could be isolated.

Both dianilinodihydroxyquinone and its mono-anil are acidic substances, but the former is a considerably stronger acid than the latter. Advantage was taken of this fact in effecting a separation of the two.

It was observed that bromoanilic acid was unaffected when heated with aniline or when boiled with excess alkali. This is of interest in view of the fact that alkali readily replaces the bromine atoms of dianilinodibromoquinone, and that the phenoxy groups in dibromodiphenoxyquinone are easily replaced either by hydroxyl or by anilino groups. Hydroxyl groups thus markedly decrease the ease of replacement of other substituents in such symmetrically substituted quinones. The ease of replacement under compara-

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[1] The work to be described was done while the author was a National Research Council Fellow.

[2] Stenhouse, *Ann.*, *Sup.*, **8**, 22 (1872).

[3] *Cf.* Jackson and Grindley, *Am. Chem. J.*, **17**, 597 (1895), who studied the reaction between dichlorodiphenoxy quinone and aniline.