The oxime of the material produced in the anomalous reaction, melting at 138.5–139.5°, showed no depression in melting point when mixed with an authentic sample.[7]

1,2-Di-(2-furyl)-1,2-di-(4-methoxyphenyl)-ethane-1,2-diol.—A solution of 4-methoxyphenylmagnesium bromide (0.20 mole) was cooled to −7° and treated with 9.5 g. (0.05 mole) of 2,2′-furil.[8]

Hydrolysis was then effected by shaking with cracked ice. The precipitated salts were dissolved by adding concentrated ammonium chloride solution. The gray solid which remained undissolved was combined with a small amount of material obtained from the organic layer by evaporation. This crude pinacol was recrystallized from ethanol to give 8.2 g. (51%) of nearly pure 1,2-di-(2-furyl)-1,2-di-(4-methoxyphenyl)-ethane-1,2-diol melting at 144.0–145.0°. For analysis, the material was recrystallized once more from ethanol. The resulting white crystals melted at 144.5–145.5°.

Anal. Calcd. for $C_{24}H_{22}O_6$: C, 70.90; H, 5.47. Found: C, 71.06; H, 5.48.

When this pinacol was subjected to the conditions of rearrangement and degradation outlined previously under method 1 and method 2, the only product which could be isolated was anisic acid, which sublimed at 10 mm. and a bath temperature of 150° and melted at 179–181°. The material showed no depression in melting point when mixed with an authentic sample. The yields were 4.9 and 14%, respectively.

1,2-Di-(2-furyl)-1,2-di-(2-thienyl)-ethane-1,2-diol.—The method of preparation was the same as that for the pinacol containing the 4-methoxyphenyl and the 2-thienyl groups. Starting with 0.16 mole of 2-bromothiophene there resulted 15.1 g. of crude crystalline pinacol. This was treated with decolorizing charcoal in boiling benzene, filtered and treated with petroleum ether (b.p. 60–75°). After standing overnight there had deposited 5.5 g. (38%) of nearly pure crystals of 1,2-di-(2-furyl)-1,2-di-(2-thienyl)-ethane-1,2-diol melting at 115°. For analysis, a small sample of this material was recrystallized from benzene–petroleum ether mixture.

Anal. Calcd. for $C_{18}H_{14}O_4S_2$: C, 60.32; H, 3.95; S, 17.88. Found: C, 60.33, 60.38; H, 3.77, 3.77; S, 17.98.

After this pinacol had been subjected to the previously described conditions for rearrangement and degradation, the acid fraction was found to consist only of a low yield of what was evidently thenoic acid contaminated with some other material, perhaps furoic acid. The yields were 12 and 8.5%, respectively. The data are given in Table IV.

TABLE IV

	M.p., °C.	Analyses, % C	H	S
Lit. or calcd. for thenoic acid	126.5	46.84	3.15	25.01
Lit. or calcd. for furoic acid	133–134	53.57	3.80	0.00
Acid from method 1	112.5–122.0	48.50	3.89	23.15
Acid from method 2	113.0–122.5	48.73	3.81	23.20

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(7) L. Vargha and F. Gonszy, THIS JOURNAL, **72**, 2738 (1950).

(8) W. W. Hartman and J. B. Dickey, *ibid.*, **55**, 1228 (1933).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF NEW HAMPSHIRE]

Molecular Rearrangements. IV. The Pinacol Rearrangement of 1-Hydroxy-1-cyclohexylmethylphenylcarbinol[1]

BY GLORIA G. LYLE, RUPERT A. COVEY AND ROBERT E. LYLE

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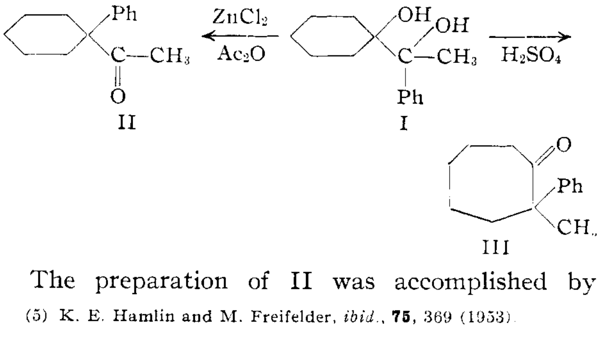
The pinacol rearrangement of 1-hydroxy-1-cyclohexylmethylphenylcarbinol (I) in sulfuric acid has been reinvestigated and the structure of the principal product shown to be 2-methyl-2-phenylcycloheptanone (III). The structure of the second product of the rearrangement has been confirmed by an alternate synthesis as 1-phenyl-1-cyclohexyl methyl ketone (II). A new method of preparation of hydroxy ketones is described.

The pinacol rearrangement of 1-hydroxy-1-cyclohexylmethylphenylcarbinol (I) has been mentioned in three recent publications.[2,3] The two earlier articles[2,3a] indicated that sulfuric acid caused rearrangement of I to form 1-phenyl-1-cyclohexyl methyl ketone (II) while rearrangement in zinc chloride in acetic anhydride resulted in the formation of 2-methyl-2-phenylcycloheptanone (III). Since these results were contradictory to those which would be predicted on the basis of the rearrangement of 1-hydroxy-1-cyclohexyldiphenylcarbinol[4] under similar conditions, a reinvestigation of the pinacol rearrangement of 1-hydroxy-1-cyclohexylmethylphenylcarbinol (I) was initiated in this Laboratory. During the course of this work an abstract of a report by Cauquil[3b] was published which partially corrected the earlier publications; however, there is no record of the isolation or characterization of the pure ketone obtained from the sulfuric acid rearrangement of I.

Rearrangement of I could produce II, III or 1-methyl-1-cyclohexyl phenyl ketone (IV). The synthesis of IV was reported by Russell[2] and by Hamlin and Freifelder,[5] and this ketone proved to be different from any product obtained by the rearrangement of I. Thus since either II or III could be the structure of the rearrangement product and the literature contained several discrepancies, an alternate, unequivocal synthesis of II was developed.



The preparation of II was accomplished by

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(1) This work was supported in part by a Frederick Gardner Cottrell Grant from the Research Corporation of New York.

(2) C. Russell, L. Stroup and J. English, THIS JOURNAL, **74**, 3882 (1952).

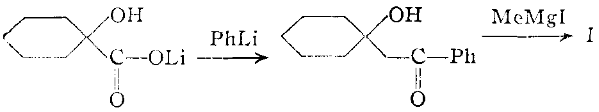
(3) G. Cauquil and J. Rouazud, Abstracts of papers presented to Montpellier Section, France, March 27, 1953, and May 22, 1953. (a) *Bull. soc. chim.*, 671 (1953); (b) *ibid.*, 795 (1953).

(4) R. E. Lyle and G. G. Lyle, THIS JOURNAL, **74**, 4059 (1952).

(5) K. E. Hamlin and M. Freifelder, *ibid.*, **75**, 369 (1953).

treating the acid chloride of 1-phenylcyclohexanecarboxylic acid[4] with dimethylcadmium according to the procedure of Cason.[6] This produced 1-phenyl-1-cyclohexyl methyl ketone (II) in 70% yield. The compound melted at 33–35° and yielded derivatives having properties in agreement with the compound produced by Cauquil[3a] as one of the products of the rearrangement of I in zinc chloride in acetic anhydride. This compound also seems to be identical with that obtained by Sackur[7] by treatment of either 1-chloro-1-cyclohexyl phenyl ketone with methylmagnesium iodide or 1-chloro-1-cyclohexyl methyl ketone with phenylmagnesium iodide. Russell, however, reported that the ketone obtained by the method of Sackur melted at 124.5° but failed to give analyses even though this value differed considerably from that reported by Sackur. Our synthesis of II appears to be unequivocal, however, and the physical constants agree with those given by Cauquil and Sackur, so that it seems evident that Russell's assignment was incorrect.

In order to investigate the rearrangement of I in sulfuric acid, this glycol was synthesized by a new method involving the reaction of phenyllithium with lithium 1-hydroxycyclohexanecarboxylate. By this process only one mole of the lithium reagent was added to the carboxyl function forming 1-hydroxy-1-cyclohexyl phenyl ketone[8] (V). Since the usual synthesis of a ketone from an acid requires the preparation of the acid chloride, the α-hydroxy group must be protected to avoid replacement with chlorine. Thus the above method of synthesis avoids both the protection of the hydroxyl group and the preparation of the acid chloride and seems to be a method worthy of investigation as a general procedure for the synthesis of α-hydroxy ketones. The reaction of the hydroxy ketone (V) and methylmagnesium iodide readily gave 1-hydroxy-1-cyclohexylmethylphenylcarbinol (I).



V

Since Russell[2] obtained only a 31% yield of the oxime from the oil produced by the rearrangement of I in sulfuric acid, it seemed likely that more than one product was formed in the reaction and that the material identified as 1-phenyl-1-cyclohexyl methyl ketone (II) was actually only the minor product. In addition, the prediction from our earlier work[4] would indicate that rearrangement in sulfuric acid should result primarily in ring enlargement to yield 2-methyl-2-phenylcycloheptanone (III). Cauquil[3b] also postulated the same reaction in her later communication but did not make any attempt to confirm this speculation.

Rearrangement of the glycol I in cold concentrated sulfuric acid gave a quantitative yield of a mixture of ketones. The separation of this mixture could not be effected by distillation but when the mixture was treated with semicarbazide hydrochloride only the semicarbazone of II was formed. The unreacted ketone was again subjected to the same treatment, but no additional semicarbazone could be detected. The yield of semicarbazone amounted to 28% of the original mixture. Distillation of the unreacted ketone gave a pure ketone in 62% yield whose physical constants were not in agreement with any product thus far obtained. This ketone formed an oxime in quantitative yield under stringent conditions[9] and also a 2,4-dinitrophenylhydrazone. The mixture melting points of these derivatives with those of derivatives of II showed significant depressions.

Allowing for material losses, largely in the separation of III, it seems that the rearrangement of I in sulfuric acid produces a mixture of ketones consisting of about 70% of III and 30% of II.

The ultraviolet spectrum of III shows many similarities to those of other α-phenyl ketones. A carbonyl band at 288 mμ with $\epsilon_{\max}$ 176 compares favorably with the carbonyl band of 2-phenylcyclohexanone[10] ($\lambda_{\max}$ 290 mμ, $\epsilon_{\max}$ 40). The intensity of the band is much greater in III than in 2-phenylcyclohexanone, but this is to be expected since the α-carbon atom carrying the aromatic substituent is quaternary rather than tertiary. The spectrum of 2-methyl-2-phenylcycloheptanone (III) also shows maxima in the region of 260 mμ characteristic of phenyl groups and observed in other aromatic compounds. From these data it appears that there can be little question that the structure of the ketone formed in the larger amount by the rearrangement of I in sulfuric acid is 2-methyl-2-phenylcycloheptanone (III).

In our previous studies of the pinacol rearrangement of unsymmetrical diaryldialkylethylene glycols of type VI where the R groups may be simple aliphatic groups or in an alicyclic structure, it has been observed that the initiation of this rearrangement in a protonic solvent is the formation of the diarylcarbonium ion (VIII, A = Ph), for the product is the result of alkyl migration.[4,11] It is thus evident that the primary product of the pinacol rearrangement of a monoaryltrialkylethylene glycol, such as VI (A = alkyl), in a protonic medium should result from the intermediate arylcarbonium ion (VIII, A = alkyl). The fact that both possible carbonium ions are intermediate in the pinacol rearrangement of I in sulfuric acid is not unexpected for the differential in stability of these two carbonium ions is less than the differential in stability of the carbonium ions formed from the unsymmetrical diaryldialkylethylene glycols due to the replacement of one of the aromatic groups by an alkyl group.

It has been further noted that these unsymmetrical diaryldialkylethylene glycols may be caused to undergo the pinacol rearrangement in a non-protonic medium by the catalytic effect of a Lewis acid.[4,9,11] Under these conditions, however, the primary product of the reaction indicates that the

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(6) J. Cason, THIS JOURNAL, **68**, 2078 (1946).

(7) O. Sackur, *Compt. rend.*, **208**, 1092 (1939).

(8) C. L. Stevens and E. Farkas, THIS JOURNAL, **74**, 618 (1952).

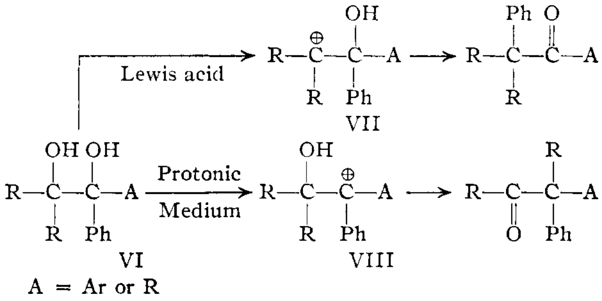
(9) R. E. Lyle and G. G. Lyle, *J. Org. Chem.*, **18**, 1058 (1953).

(10) E. Alpen, W. Kumler and L. Strait, THIS JOURNAL, **72**, 4558 (1950).

(11) For the rearrangement of VI (R = CH_3, A = Ph), see P. Ramart-Lucas, *Compt. rend.*, **188**, 1301 (1929). The rearrangement of an analogous heterocyclic compound was described in Paper No. 58 presented before the Organic Division of the American Chemical Society at Atlantic City, N. J., September 17, 1952.

rearrangement occurred through the intermediate dialkylcarbonium ion (VII, A = Ph). This condition appears to exist in the monoaryl series also, for Cauquil[3b] has indicated that the rearrangement of I in a non-protonic medium catalyzed by a Lewis acid produces II, which must be formed through the intermediate VII (A = Me).

Thus the reactions shown in the equation below would appear to represent a generality to be expected in the pinacol rearrangement of compounds of type VI.



Experimental

1-Phenyl-1-cyclohexyl Methyl Ketone (II).—A solution of dimethylcadmium in benzene was prepared from methylmagnesium bromide according to the method of Cason,[6] the quantity being based on 3.6 g. (0.15 gram-atom) of magnesium. A benzene solution of the acid chloride of 1-phenylcyclohexanecarboxylic acid,[4] formed by the action of thionyl chloride on 3.0 g. of the acid, was added to the dimethylcadmium solution. These quantities assured a tenfold excess of the cadmium alkyl. The mixture was refluxed for 1.5 hr. and allowed to stand overnight. After hydrolyzing the mixture with ice-water and dilute hydrochloric acid, the benzene layer was separated and washed with water, sodium hydroxide solution and again water and dried over calcium chloride. The solvent was removed leaving 2.08 g. (70% based on the acid) of 1-phenyl-1-cyclohexyl methyl ketone (II) which distilled at 125° at 6 mm. On cooling in an ice-bath, the oil crystallized and was recrystallized from petroleum ether; m.p. 33–35°, lit.[3b] m.p. 38°, lit.[7] m.p. 35°.

The 2,4-dinitrophenylhydrazone was prepared and melted at 136–137° after recrystallization from ethanol; lit.[3b] m.p. 137–138°. **The oxime**, after recrystallization from ethanol, melted at 137–138°, lit.[3b] m.p. 139°, lit.[7] 137–138°. **The semicarbazone** melted at 217–218° after recrystallization from ethanol; lit.[3b] m.p. 227–228°, lit.[7] m.p. 223–224°.[12]

1-Hydroxy-1-cyclohexyl Phenyl Ketone (V).—Lithium 1-hydroxycyclohexanecarboxylate was prepared by dissolving 1-hydroxy-1-cyclohexanecarboxylic acid in hot water and adding the theoretical amount of lithium carbonate. The water was removed under reduced pressure and the solid salt heated to constant weight. A quantitative yield of the salt was obtained.

A solution of 1.67 moles of phenyllithium in ether was prepared from 23.2 g. of lithium and 174 ml. of bromobenzene. To this solution was added 100 g. of lithium 1-hydroxycyclohexanecarboxylate and the mixture refluxed for 7 hr. The mixture was hydrolyzed with water and the ether layer separated and washed with water. After drying, the ether was removed and the remaining oil distilled. The fraction boiling at 112–165° at 2 mm. was collected and crystallized by the addition of seed crystals. After recrystallization from petroleum ether, 38.7 g. (28%) of 1-hydroxy-1-cyclohexyl phenyl ketone (V) was obtained, m.p. 46–48°, lit.[8] m.p. 48–49°.

1-Hydroxy-1-cyclohexylmethylphenylcarbinol (I).—The Grignard reagent was prepared from 14.3 g. (0.588 gram-atom) of magnesium and 36.6 ml. (0.588 mole) of methyl iodide in ether. To the solution 30 g. (0.147 mole) of 1-hydroxy-1-cyclohexyl phenyl ketone (V) in ether was added. The mixture was allowed to stand for 12 hr. and hydrolyzed with dilute hydrochloric acid. The ether layer was separated and washed with water. On removal of the ether, the theoretical yield of 1-hydroxy-1-cyclohexylmethylphenylcarbinol (I) was obtained. After recrystallization from ethanol, the product melted at 107.5–108°, lit.[13] m.p. 104°.

Sulfuric Acid Rearrangement of I.—In a 250-ml. erlenmeyer flask 40 ml. of concentrated sulfuric acid was cooled to 0° and 5.00 g. (0.023 mole) of the glycol I was added in portions. At the end of 45 minutes a clear red solution remained and was poured into ice. The colorless oil which separated was taken up in ether and the water solution extracted once with ether. The ethereal solution was dried over sodium sulfate and the ether removed. Distillation of the oil gave only one fraction boiling at 165–168° at 13 mm.

The sweet-smelling light yellow oil was dissolved in 30 ml. of ethanol and 10 ml. of water. Enough ethanol was added to remove the turbidity and 3 g. of semicarbazide hydrochloride and 4.5 g. of sodium acetate was added. The mixture was shaken until all of the solid was in solution and then the solution was placed in a boiling water-bath and allowed to cool to room temperature. The semicarbazone which crystallized was filtered off, recrystallized from ethanol and melted at 215–217°. It did not depress the melting point of the semicarbazone of II, prepared from 1-phenylcyclohexanecarboxylic acid.

The filtrate from the semicarbazone was extracted with petroleum ether and the ether washed with water. A small amount of semicarbazone appeared in the wash water and was filtered off. The total yield of semicarbazone was 1.47 g., representing 27.7% of the distilled product. The petroleum ether extract was dried over sodium sulfate and distilled yielding 2.58 g. of oil boiling at 163–165° at 12 mm.

All of the oil from the distillation was treated with semicarbazide hydrochloride as above, but no semicarbazone was detected in this preparation. The oil on distillation yielded 1.96 g. of 2-methyl-2-phenylcycloheptanone (III) boiling at 162–164° at 11 mm., n^{25}_{D} 1.5365. This fraction of the ketone was combined with a small amount of ketone of the same degree of purity from an earlier preparation and was treated with semicarbazide hydrochloride as above. No semicarbazone was obtained and the reaction mixture was worked up as above, the ketone distilling at 164° at 11 mm., n^{25}_{D} 1.5368, d^{25}_{4} 1.0294. The ketone III was a colorless oil with only a faintly sweet odor.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97; *MR*, 61.1. Found: C, 83.52; H, 9.20; *MR*, 61.4.

The 2,4-dinitrophenylhydrazone was prepared using Brady reagent[14] and crystallized after standing 12 hr. Recrystallization from ethanol gave an 80% yield of bright orange crystals, m.p. 134.6–136.0°. A mixture melting point with 2,4-dinitrophenylhydrazone of II melted 118–131°.

Anal. Calcd. for $C_{20}H_{22}N_4O_4$: C, 62.81; H, 5.80. Found: C, 63.20; H, 5.87.

The oxime was prepared using the pyridine method[9] but with a 6-hr. refluxing period. A theoretical yield of the derivative was obtained which melted crude, 160–162°, and after recrystallization from ethanol, melted 164.1–165.0°.

Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 76.62; H, 8.65.

Ultraviolet Absorption Spectrum.—The ultraviolet absorption spectrum of 2-methyl-2-phenylcycloheptanone was determined using a Beckman model DU quartz spectrophotometer equipped with a photomultiplier attachment. A solution in 95% ethanol was used having a concentration of 1.60×10^{-3} *M.*

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[12] These data do not agree entirely with the values of the physical constants of II and its derivatives reported by Russell and his collaborators (see ref. 2) prepared by the method of Sackur: II, m.p. 124.5°; 2,4-dinitrophenylhydrazone, m.p. 188°; oxime, m.p. 137°.

[13] I. Felkin and B. Tchoubar, *Bull. soc. chim.*, 551 (1952).

[14] O. L. Brady, *J. Chem. Soc.*, 756 (1931).