

Anal. Calcd. for $C_{20}H_{22}N_4O_4$: C, 62.8; H, 5.8; N, 14.6. Found: C, 62.5; H, 5.5; N, 14.2.

2-Methyl-2-(*p*-isopropylphenyl)-cyclohexanone.⁶—This ketone was prepared in 87% yield by methylation of 2-(*p*-isopropylphenyl)-cyclohexanone⁷ by the procedure described for a similar case⁴; b. p. 133–136° at 0.2 mm.

Anal. Calcd. for $C_{16}H_{22}O$: C, 83.4; H, 9.6. Found: C, 83.4; H, 9.5.

The **oxime**, prepared in absolute alcohol and pyridine, crystallized from absolute alcohol in colorless prisms; m. p. 136–137°. By warming a solution of 1 g. of the oxime in 10 ml. of concentrated hydrochloric acid on a steam-bath for eight hours a 95% yield of distilled regenerated ketone was obtained.

Anal. Calcd. for $C_{16}H_{23}NO$: C, 78.3; H, 9.4; N, 5.7. Found: C, 78.4; H, 9.3; N, 5.5.

The **semicarbazone** crystallized from alcohol in colorless prisms; m. p. 171–173°.

Anal. Calcd. for $C_{17}H_{25}N_3O$: C, 71.0; H, 8.8; N, 14.6. Found: C, 70.9; H, 8.6; N, 14.5.

2,6-Dimethyl-2-(*p*-isopropylphenyl)-6-carbomethoxycyclohexanone (III, R = CH(CH₃)₂, R' = H).—The reaction between 3 g. of 2-methyl-2-(*p*-isopropylphenyl)-cyclohexanone and 3 g. of dimethyl oxalate in the presence of sodium methoxide from 0.6 g. of sodium, conducted as described for a similar case,⁸ gave 4 g. (97%) of the glyoxa-

late as a liquid (presumably a mixture of stereoisomers), which gave an immediate deep maroon color with an alcoholic solution of ferric chloride. Without further purification the glyoxalate was heated with 1 g. of powdered glass at 160–165° for seven minutes. Distillation of the product at 180–185° and 0.2 mm. gave 2.54 g. of the keto ester as a viscous colorless liquid, which slowly gave a deep purple color with alcoholic ferric chloride. Methylation of 4.7 g. of the keto ester with 13 ml. of methyl iodide in the presence of sodium methoxide from 1.8 g. of sodium in the manner described⁸ yielded 4 g. of III (R = CH(CH₃)₂, R' = H) after distillation at 162–164° and 0.2 mm. Complete methylation was indicated by the absence of color with alcoholic ferric chloride. For analysis a sample was treated with hydroxylamine hydrochloride in pyridine and absolute alcohol; this treatment converted some contaminating ketone present in traces into the oxime, which was readily extracted from the methyl keto ester (which remained unaffected) by cold concentrated hydrochloric acid.

Anal. Calcd. for $C_{19}H_{25}O_2$: C, 75.5; H, 8.6. Found: C, 75.8; H, 8.7.

Summary

2,6-Dimethyl-2-phenyl-6-carbomethoxycyclohexanone and 2,6-dimethyl-2-(*p*-isopropylphenyl)-6-carbomethoxycyclohexanone were prepared as intermediates in proposed syntheses of resin acids.

ANN ARBOR, MICHIGAN RECEIVED NOVEMBER 7, 1949

(6) Prepared by G. I. Fujimoto in this laboratory.

(7) Bachmann, Fujimoto and Wick, *THIS JOURNAL*, **72**, 1995 (1950).

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

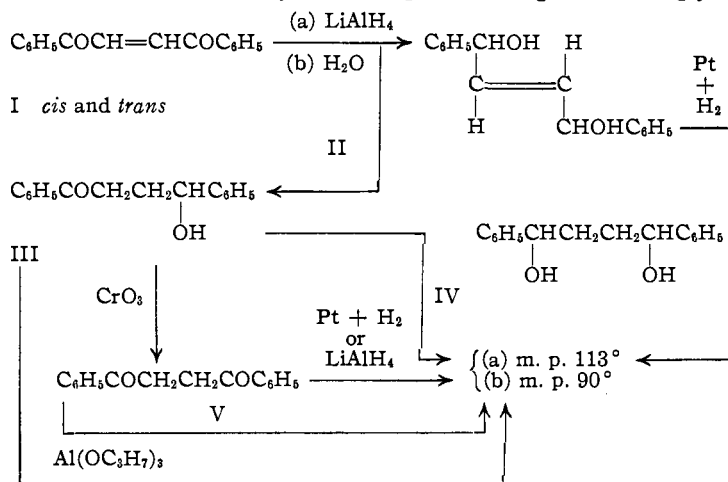
1,4-Reduction of Unsaturated 1,4-Diketones by Lithium Aluminum Hydride^{1a}

BY ROBERT E. LUTZ AND J. S. GILLESPIE, JR.^{1b}

The use of lithium aluminum hydride seemed of particular interest in this field because, in contrast with aluminum isopropoxide,² this reagent should not only be more powerful, but it also should theoretically be able to bring about 1,4-reductions analogous to 1,4-additions of the Grignard reagent with which it is to be compared.^{3a} Up to this time no such 1,4-reduction by this reagent has been demonstrated although a few systems capable of undergoing it have been studied.³

When *cis*- and *trans*-dibenzoyl-ethylenes (I) were reduced with an amount of lithium aluminum hydride in excess of that calculated for complete reduction, in ether at 35°, the same two products were obtained in identical yield ratios in each case. One of these, the minor product, was the *trans* unsaturated glycol (II) which under-

went subsequent platinum-hydrogen reduction exclusively to the higher-melting saturated glycol



(1)(a) Taken from a Doctorate Dissertation, University of Virginia, May, 1949. This work was reported at the Atlantic City Meeting of the American Chemical Society, September 12, 1949. (b) Present location, University of Richmond, Richmond, Va.

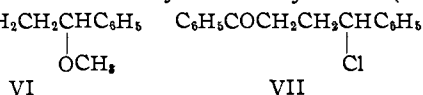
(2) Lutz and Gillespie, *THIS JOURNAL*, **72**, 344 (1950).

(3) (a) Nystrom and Brown, *ibid.*, **70**, 1197, 2548, 3738 (1948). (b) Hochstein and Brown, *ibid.*, **70**, 3484 (1948); Hochstein, *ibid.*, **71**, 305 (1949).

(IVa).² Doubtless *cis*-to-*trans* isomerization occurred before reduction, as has been shown to occur in the case of aluminum isopropoxide reduction.²

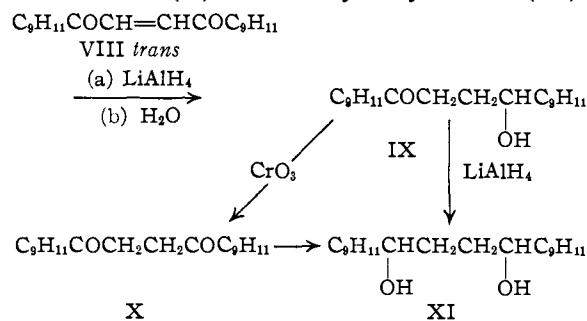
Identification of the second and main product of the reduction as the partially reduced compound, 1,4-diphenyl-4-hydroxy-1-butanone (III), was accomplished by analysis, chromic acid oxida-

tion to the saturated diketone (V), platinum-catalyzed or further lithium aluminum hydride reduction to the same mixture of saturated glycols (IVa and b) as was obtained upon comparable reductions of the saturated diketone (V), aluminum isopropoxide reduction to the lower-melting glycol (IVb) exclusively, conversion into the methyl ether (VI) by the action of methanolic hydrogen chloride and conversion into the chloro ketone (VII) by the action of ethereal hydrogen chloride. The presence of the carbonyl group and exclusion of a cyclic hemiacetal structure was demonstrated by the ultraviolet absorption maximum in the region 240 m μ which is shown also by the methyl ether (VI),



the chloro compound (VII) and the related saturated diketone (V) (see Fig. 1), and which is characteristic for a carbonyl in conjugation with a phenyl.

Reduction of *trans*-dimesitylolethylene (VIII) by an excess of lithium aluminum hydride also proceeded rapidly but in this case only a single product was obtained, namely, the hydroxyketone (IX) which had previously been made by the catalytic reduction of 1,4-dimesityl-4-hydroxy-2,3-epoxy-1-butanone.⁴ This product was readily oxidized by chromic acid to the saturated diketone (X), and it was reduced by lithium aluminum hydride to a mixture from which could be isolated previously in the sodium-alcohol reductions of both the diketone (X) and the hydroxy ketone (IX).



Neither the hydroxyketone (IX) nor the diketone (X) showed ultraviolet absorption maxima in the region 240 m μ (see Fig. 1) which is characteristic for a carbonyl group in conjugation with a phenyl nucleus.⁵ These results are comparable with the non-appearance of maxima in this region in the case of aceto-

(4) Lutz and Wood, *THIS JOURNAL*, **60**, 229 (1938).

(5) Burawoy, *Ber.*, **63**, 3155 (1930); Weissberger, "Physical Methods of Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1946, p. 816.

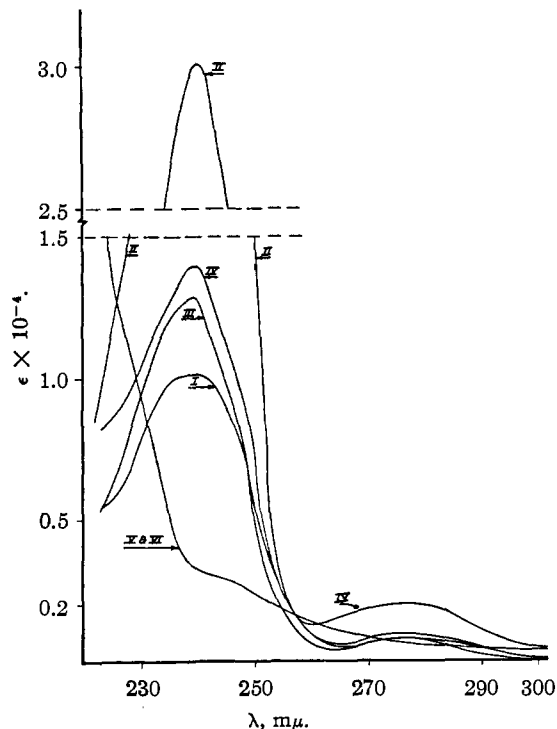
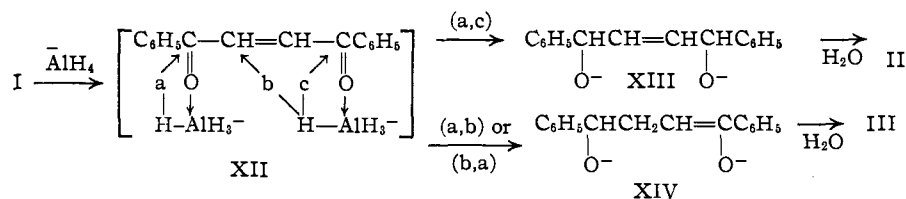


Fig. 1.—Ultraviolet absorption spectra determined in a Beckman DU quartz spectrophotometer using 0.0001 molal solutions in purified isoöctane, except for V which was run at 0.00001 molal concentration: I, C₆H₅COCH₂CH₂CHOHC₆H₅; II, C₆H₅COCH₂CH₂COC₆H₅; III, C₆H₅COCH₂CH₂CHC₆H₅; IV, C₆H₅COCH₂CH₂CHC₆H₅; V, C₉H₁₁COCH₂CH₂CHOHC₉H₁₁; VI, C₉H₁₁COCH₂CH₂CH₂C₉H₁₁.

mesitylene and 2,4,6-triisopropylacetophenone.⁶ The unsaturated 1,4-glycol (II) formed in small amounts in the lithium aluminum hydride reduction of dibenzoylolethylene (I) is the expected result of successive 1,2-reductions of the two carbonyl groups. The hydroxyketone (III), on the other hand, with its reducible carbonyl group, must have been stabilized in the form of an enolate (XIV) and liberated upon hydrolysis of the



reaction mixture. The only mechanism which adequately explains this result is 1,4-addition of the reagent to the α,β -unsaturated ketone system (cf. XIIb) with prior or subsequent 1,2-reduction (XIIa) independently of the other carbonyl

(6) O'Shaughnessy and Rodebush, *THIS JOURNAL*, **62**, 2906 (1940).

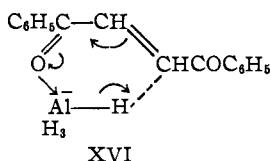
group. These several possibilities are pictured in formulas XII–XIV as three two-step paths, (a, c), (a, b) and (b, a).

The possibility, after initial 1,4-addition (b), of enolization at the second carbonyl to give the diene-diolate, is excluded because there was isolated none of the saturated diketone (V) which would be produced on subsequent hydrolysis.

By way of comparison, the action of phenylmagnesium bromide on dibenzoyl ethylene,⁷ like that of lithium aluminum hydride, involves chiefly 1,4-addition as the first step, but differs in the second step by causing enolization at the remaining carbonyl. This difference may be accounted for by the different influences of the nucleophilic addends, phenyl *vs.* hydrogen, which enter the molecule alpha to the second carbonyl and which would be expected to affect differently the ability of this second carbonyl subsequently to add and to enolize.

In the case of dimesitylolethylene (VIII) it would be expected that steric hindrance would diminish the facility of the 1,2-attack at the carbonyls but would not affect the 1,4-reaction; this would account for the isolation in this case of just the one product, the hydroxy ketone (IX).

The expression of lithium aluminum hydride reductions as nucleophilic displacements⁸ applies in the present case, although here an intermediate cyclic resonating transition state (XVI) somewhat analogous to those proposed in reactions of the Grignard⁹ reagent and in aluminum alkoxide reduction,² may be possible.¹⁰



Experimental

1,4-Diphenyl-4-hydroxy-1-butanone (III).—Reduction of *cis* and *trans* dibenzoyl ethylene (I) was effected with practically identical results by extracting a 10-g. sample of the solid over a period of five hours from a Soxhlet thimble by refluxing a solution of 1.5 g. of lithium aluminum hydride in 500 ml. of dry ether. This procedure was employed because the reaction was vigorous and the compound I, which is difficultly soluble in ether, could thereby be introduced slowly. A white precipitate formed. The mixture was cooled in ice and hydrolyzed by dropwise addition of 100 ml. of water and then 100 ml. of 10% sulfuric acid. The ether extracts upon drying over sodium sulfate and evaporation gave an oil which solidified. Crystallization from chloroform gave 1.0 g. of II; m. p. 150–151° (identified by mixture melting point²). Additions of petroleum ether gave 9.0 g. of III of m. p. 92–93°, which was recrystallized in the same way. It gave a mixture melting point depression with IVb.

(7) Lutz and Tyson, *THIS JOURNAL*, **56**, 1341 (1934).

(8) Trevo and Brown, *ibid.*, **71**, 1675 (1949).

(9) Lutz and Reveley, *ibid.*, **68**, 3184 (1941).

(10) This type of quasi-ring mechanism has been criticized on the basis of possible steric interference by the β -hydrogen of the conjugated system. We had long ago considered this question but had dismissed it as inconsequential.

Anal. (of III). Calcd. for $C_{18}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.14; H, 6.99.

Numerous attempts to isolate a derivative of the enolate of III which was presumed to be formed first in the above reduction, by methylation with methyl iodide or dimethyl sulfate, or by bromination, were unsuccessful.

Oxidation of 2.4 g. in 100 ml. of concd. acetic acid by adding 2 g. of chromic oxide in 30 ml. of 80% acetic acid over forty minutes at 20°, followed by hydrolysis in ice, and recrystallization of the precipitate from ethanol, gave 2 g. (83%) of V (identified by mixture m. p.).

Reduction of III by platinum and hydrogen in ethanol, and by lithium aluminum hydride according to the procedure outlined above, gave similar mixtures from which in each case both saturated glycols were isolated by fractional crystallization from chloroform by the addition of petroleum ether. The lithium aluminum hydride reduction products were separated almost completely into equal amounts of the pure glycols which melted, respectively, at 98–99° and 113–114°. Reduction of III by aluminum isopropoxide in the usual way (refluxing one and one-half hours) gave a product from which only the glycol (IVb) of m. p. 89–90° could be isolated (yield 63%).

TABLE I

ULTRAVIOLET ABSORPTION MAXIMA AND MINIMA OF SOME MONO- AND DIKETONES

Compound	Curve no. Fig. 1	Maxima λ (m μ) $\times 10^{-4}$	Minima λ (m μ) $\times 10^{-4}$
1,4-Diphenyl-4-hydroxy-1-butanone	I	280	265 0.05
		239	1.10
1,4-Diphenylbutane-1,4-dione	II	280	260 0.12
		240	3.01
1,4-Diphenyl-4-methoxy-1-butanone	III	280	265 0.09
		239	1.29
4-Chloro-1,2-diphenyl-1-butanone	IV	280	0.09
		239	1.39 265 0.05
4-Hydroxy-1,4-dimesityl-1-butanone	V	245 ^a	0.29
1,4-Dimesityl-1-butanone	VI	245 ^a	0.29

^a These are inflection points.

Reduction of dibenzoyl ethane (V) by lithium aluminum hydride as above gave an almost quantitative yield of a mixture of the two crystalline glycols (IVa and b) which was separated into approximately equal amounts of each by fractional crystallization from chloroform by the addition of petroleum ether.

1,4-Diphenyl-4-methoxy-1-butanone (VI).—A solution of 4 g. of III in 100 ml. of methanol and 5 ml. of saturated ethereal hydrogen chloride was refluxed for one hour, concentrated and added to 100 ml. of cold 10% sodium carbonate. The resulting precipitate was crystallized from isoctane using an ice-salt-bath; yield 2 g. of m. p. 61–62° (50%).

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13; OCH_3 , 12.20. Found: C, 80.00; H, 7.07; OCH_3 , 12.30.

1,4-Diphenyl-4-chloro-1-butanone (VII). was prepared by allowing a solution of 1 g. of III in 25 ml. of saturated ethereal hydrogen chloride to stand for twenty-four hours at room temperature; the product was recrystallized from ethanol; 0.8 g. (75%); m. p. 89–90°.

Anal. Calcd. for $C_{16}H_{15}ClO$: C, 74.27; H, 5.88. Found: C, 74.38; H, 5.87.

Phosphorus oxychloride was somewhat less successful in the above reaction; pyridine-thionyl chloride, however, did not give a tractable product.

Reduction of dibenzoyl acetylene by lithium aluminum hydride in ether by the above method gave dark red resinous products.

Reduction of *trans*-dimesitylolethylene (VIII), also as above, gave a 94% yield of product of m. p. 129–132°

which on crystallization from ethanol melted at 132–133° and was identified by mixture melting point as IX⁴ (it gave a mixture melting point depression with X).

Reduction of dimesitoylthane (X) as above gave an 80% yield of product which was recrystallized from ethanol; it melted at 128–132°. Fractional precipitation from chloroform by means of petroleum ether gave first fractions of m. p. 184–185°, which were identified as XI⁴ by mixture melting point.

Summary

Lithium aluminum hydride reductions of *cis*- and *trans*-dibenzoylthylenes gave chiefly 1,4-diphenyl-4-hydroxybutanone and a small amount

of the *trans* unsaturated 1,4-glycol. The structure of the hydroxyketone was shown by reactions and by ultraviolet absorption spectra. In reduction of dimesitoylthylene only the hydroxyketone was isolated.

These reductions are explained in terms of competing 1,2- and 1,4-reductions; 1,4-reduction is predominant and involves protection of the carbonyl involved, in the form of the monoenolate. These reductions are compared with additions of the Grignard reagent.

CHARLOTTESVILLE, VIRGINIA RECEIVED JULY 20, 1949

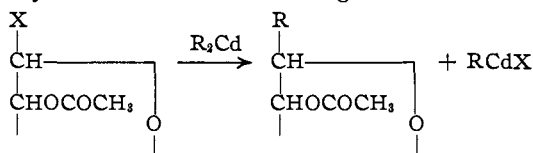
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Reactions of Polyacylglycosyl Halides with Organocadmium Reagents

BY CHARLES D. HURD AND ROMAN P. HOLYSZ¹

In recent years the use of organocadmium reagents has been recognized as a convenient means of preparing ketones from acyl halides.² As a result of the generally lower reactivity of organocadmium reagents as compared to that of Grignard reagents, the coupling reaction with acyl halides usually stops at the ketone stage. In contrast, Grignard reagents are capable of further reaction with the ketones to yield tertiary alcohols, except at very low temperatures. Furthermore, organocadmium reagents usually do not react readily with esters under ordinary conditions. For instance, cadmium alkyls react with carbethoxyacyl halides of the type EtOOC-(CH₂)_n-COX to give good yields of keto esters, EtOOC-(CH₂)_n-CO-R, with no appreciable attack on the ester function.³ Reactions of organocadmium reagents with active halogen in compounds other than acyl halides have not been investigated extensively. Gilman and Nelson⁴ reported that dialkylcadmium did not couple with *t*-butyl chloride, and that diphenylcadmium reacted with benzenesulfonyl chloride to yield diphenyl sulfone, benzenesulfinic acid and chlorobenzene. Summerbell and Bauer⁵ obtained a 44% yield of 2,3-dibutyl-1,4-dioxane by the action of dibutylcadmium on 2,3-dichloro-1,4-dioxane, which is an *alpha* halogen ether.

With these facts in mind one might then expect a polyacylglycosyl halide, which may be visualized as an *alpha* halogen ether, to react with dialkyl- or diarylcadmium in the following manner,



(1) Corn Products Refining Company Fellow, 1945–1947; du Pont Fellow, 1947–1948.

(2) Cason, *Chem. Rev.*, **40**, 15 (1947).

(3) Cason and Prout, *THIS JOURNAL*, **66**, 46 (1944).

(4) Gilman and Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

(5) Summerbell and Bauer, *THIS JOURNAL*, **58**, 759 (1936).

The ester functions would remain intact, thereby making possible the use of only one mole (or a slight excess) of the organocadmium reagent per mole of polyacylglycosyl halide instead of the nine moles of Grignard reagent theoretically necessary in the Grignard glycosylation.⁶ The attack of the ester functions by the Grignard reagent results in the major product being an unwanted carbinol, while the carbohydrate derivative is water soluble, necessitating lengthy isolation and acylation procedures.

The anticipated reactions were realized both in the glucose and mannose series with diphenylcadmium, although the yields were low. Tetraacetyl- α -D-glucopyranosyl bromide coupled with diphenylcadmium in refluxing benzene solution to give tetraacetyl- β -D-glucopyranosylbenzene in approximately 20% yield. The remaining sirupy product darkened considerably on standing and eventually became a black tar. The presence of bromine in the tarry product suggested that the reaction probably was not completed. There was no significant improvement of the yield of tetraacetyl- β -D-glucopyranosylbenzene when the reaction mixture was refluxed for a much longer period or the reaction carried out in refluxing toluene. Similarly, in the mannose series coupling to a limited extent without apparent attack of the ester functions was observed between diphenylcadmium and tetraacetyl- α -D-mannopyranosyl bromide in refluxing toluene solution. In this instance tetraacetyl- α -D-mannopyranosylbenzene was isolated in 29% yield in addition to sirupy products.

However, with dibutyl- and dibenzylcadmium entirely different and unexpected types of products were obtained. Dibenzylcadmium reacted with tetraacetyl- α -D-glucopyranosyl bromide in refluxing toluene solution to form in approximately 30% yield a crystalline substance which was not the anticipated α -(tetraacetylglucosyl)-toluene but an acetal-like compound (I).

(6) Hurd and Bonner, *ibid.*, **67**, 1972 (1945).