

Action of Phenyl Grignard Reagent and Phenyllithium on *cis*- and *trans*-1,2-Dibenzoyl ethylene^{1,2}

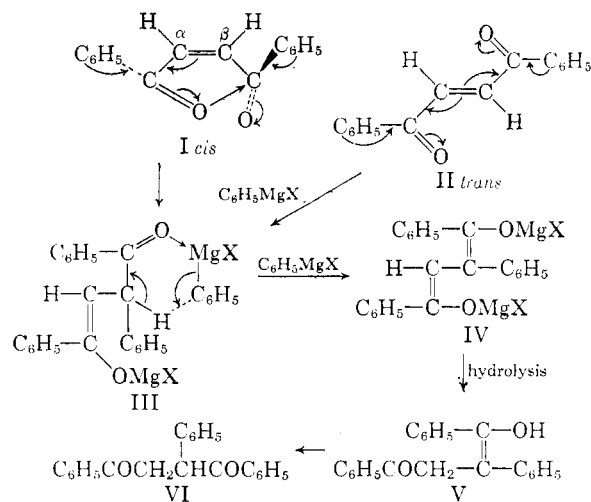
ROBERT E. LUTZ AND CHARLESWORTH L. DICKERSON³

Cobb Chemical Laboratory, University of Virginia, Charlottesville, Va.

Received September 11, 1961

cis-1,2-Dibenzoyl ethylene (1,4-diphenyl-2-butene-1,4-dione), like the *trans* isomer, undergoes 1,4-addition-enolization by phenyl Grignard reagent⁴ with subsequent enolization of the remaining carbonyl group, and hydrolysis gives desylacetophenone (1,2,4-triphenylbutane-1,4-dione). The nonfuranizable configuration is postulated for the more persistent of the two intermediate enolate groups. Phenyllithium adds twice to each stereoisomer, in each case by two competing reaction sequences. One involves successive 1,2-additions to the two carbonyl groups and gives the respective *cis* and *trans* unsaturated glycols. The other involves 1,4-addition-enolization of the α,β -unsaturated ketone system followed by 1,2-addition to the remaining carbonyl group, whereupon hydrolysis gives 1,3,4,4-tetraphenyl-4-hydroxybutanone-1, in 40% yield from the *trans* isomer and 14% from the *cis*. Addition of phenyllithium to desylacetophenone and to the hydroxy ketone, and dehydration of the resulting 1,4-glycol, gave pentaphenyltetrahydrofuran. The evidence for structures and reasons for differences in modes of reactions are discussed.

This investigation extends the earlier study of the action of phenyl Grignard reagent⁴ on *trans*-1,2-dibenzoyl ethylene (II),⁵ to the *cis* isomer I, and to the reactions with phenyllithium. The latter are of particular interest for comparison with the lithium aluminum hydride 1,2:1,4 di-reductions of the dibenzoyl ethylenes to the saturated hydroxy



ketone enolate from which the hydroxy ketone is produced upon hydrolysis.⁶

Phenyl Grignard reagent adds 1,4 to *cis*-dibenzoyl ethylene (I) as it did to the *trans* isomer II⁵ with subsequent enolization of the resulting mono-enolate III to the di-enolate IV which upon hydroly-

ysis yields desylacetophenone (VI). The configuration of the mono-enolate III is assigned on assumed correspondence with the conformations⁷ of the dibenzoyl ethylene molecules depicted in I and II. The *trans*-diphenyl mono-enolate configuration V in the di-enolate IV presumably is produced under stereocontrol at the moment of enolization as indicated in III. These postulates are consistent with the disinclination of the compound toward furanization at the mono-enol stage V, and with the ready furanization during conjugate reduction of *trans*- (but not *cis*)-1,2-dibenzoyl ethylene where the original conformation analogous to II is believed to dictate production of the opposite and furanizable *cis*-diphenyl mono-enolate configuration.⁸

cis-trans inversion by the Grignard reagent did not seem to be taking place prior to addition, but this is not excluded. Such rearrangement has been shown to occur, however, during aluminum isopropoxide reduction.⁹

trans-Dibenzoyl ethylene reacted with two molecules of phenyllithium to give a mixture of the *trans*-glycol¹⁰ VII (15%) and the hydroxy ketone IX¹⁰ (40%). The latter, the 1,2:1,4 di-addition product, must have been formed as its enolate VIII which is incapable of further reaction with the reagent and from which the keto group is released upon hydrolysis of the reaction mixture and ketonization.

The hydroxy ketone IX was first obtained by Scholtis¹⁰ as one of the products of phenyllithium additions to fumaric diester but it was formulated as the cyclic hemiketal. It would not be expected

(1) Work supported by contract with Office of Ordnance Research, U. S. Army, and a research grant from the National Science Foundation.

(2) C. L. Dickerson, Doctorate dissertation, University of Virginia, March, 1954; reported in part at the International Congress of Pure and Applied Chemistry, Paris, July, 1957.

(3) Present location, S. C. Johnson and Son, Inc., Racine, Wis.

(4) The Grignard reagent is assumed to be dimolecular; in the formulations C_6H_5MgX and $-OMgX$, X is noncommittal with respect to the atoms or groups actually attached to magnesium.

(5) R. E. Lutz and W. R. Tyson, *J. Am. Chem. Soc.*, **56**, 1341 (1934).

(6) R. E. Lutz and J. S. Gillespie, *J. Am. Chem. Soc.*, **72**, 2002 (1950).

(7) L. Kuhn, R. E. Lutz, and C. A. Bauer, *J. Am. Chem. Soc.*, **72**, 5058 (1950).

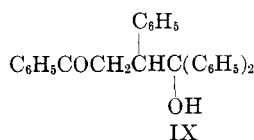
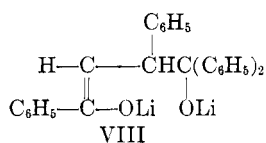
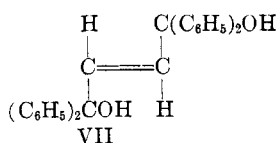
(8) (a) R. E. Lutz and C. R. Bauer, *J. Am. Chem. Soc.*, **73**, 3456 (1951). (b) This reaction, because of its importance, has been repeated, successfully, by John I. Dale.

(9) R. E. Lutz and J. S. Gillespie, *J. Am. Chem. Soc.*, **72**, 344 (1950).

(10) K. Scholtis, *Ann.*, **557**, 82 (1945); cf. also ref. 11 and 12.

(11) T. Purdie and P. S. Arup, *J. Chem. Soc.*, **97**, 1537 (1910).

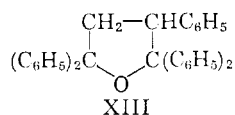
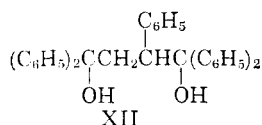
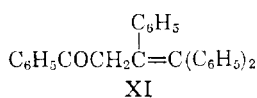
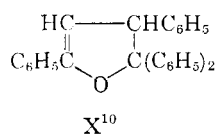
(12) D. S. Tarbell, *J. Am. Chem. Soc.*, **60**, 215 (1938).



to exist in this form, however, without steric support of a *cis* double bond. The acyclic structure is demonstrated by the ultraviolet absorption maximum at 240 $m\mu$, ϵ 14,500, and by the strong infrared hydroxyl and keto absorption bands at 2.81 and 5.95 μ .

The acetic-hydrochloric acid dehydration product of IX, which Scholtis¹⁰ formulated as the cyclic enol ether X, is now shown to be the β,γ -unsaturated ketone XI as follows: It has a high ultraviolet absorptivity of ϵ 14,000 at 275 $m\mu$ in the form of a shoulder on the curve of λ_{max} 237 $m\mu$, ϵ 32,800. This corresponds approximately to expectation as either the sum of the absorptivities of the independent benzoyl and stilbene groups of XI or the absorption of the α -substituted chalcone system of the α,β -unsaturated isomer of XI, whereas the cyclic enol ether X would absorb strongly but only at *ca.* 240 $m\mu$. Structure XI would account for the ready cyclodehydrative condensation to 1,2,4-triphenyl-naphthalene.¹⁰ The NMR spectrum¹³ shows a line at 4.8 p.p.m. at lower field from the tetramethylsilane reference, which can be assigned only to the CH_2 group of XI and not to two CH groups such as would be present in the α,β -unsaturated isomer; and the chemical shift of this line is in agreement with the value 4.3 p.p.m. for the CH_2

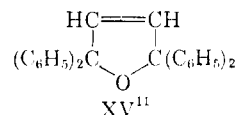
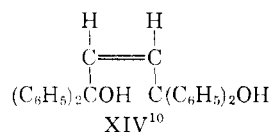
proton resonance of the structure $-\text{COCH}_2\text{C}=\text{C}-$ as determined by Chamberlain.¹⁴



In reactions to test further the above relationships both the hydroxy ketone IX and desylacetophenone VI were treated with phenyllithium and each gave small yields of the same pentaphenyl 1,4-glycol XII, which showed strong hydroxyl group absorptivity at 2.80 μ but no benzoyl absorptivity

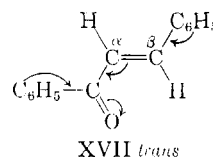
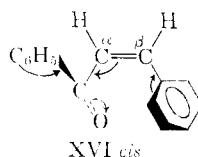
in either the 6.0- μ or the 240- $m\mu$ regions. The glycol structure was confirmed by dehydration with hot concentrated acetic acid to a dehydro compound which corresponds to pentaphenyltetrahydrofuran (XIII).

cis-Dibenzoyl ethylene with phenyllithium gave only a 14% yield of the hydroxy ketone IX through successive 1,2- and 1,4-additions. The main product was in oil which was shown¹⁵ to contain considerable amounts of the *cis*-glycol XIV by dehydration in glacial acetic acid and isolation of the corresponding dihydrofuran XV.¹¹



Although yields of crystalline products in the above metallophenyl additions to *cis*- and *trans*-dibenzoyl ethylenes (I and II) were mediocre, some further mechanistic conclusions may be drawn. To the extent that 1,2;1,4 di-additions of phenyllithium occur to both stereoisomers, giving the hydroxy ketone IX, it may be presumed that the *cis* configuration has been retained up to the point of the first addition step, and that 1,4-addition occurs first with disappearance of the original configuration. Were 1,2-addition of phenyllithium to occur first, steric hindrance at the carbon atom adjacent to the newly formed benzhydryl group must drastically impede subsequent 1,4-addition involving the β -carbon of the remaining α,β -unsaturated ketone system, but it would not prevent enolization of or 1,2-addition to the remaining carbonyl group. The intermediate lithium 1,4-addition enolate, the analog of III, must next undergo 1,2-addition to the remaining keto group in spite of steric resistance, rather than undergo the enolization which is actually induced under similar circumstances by phenyl Grignard reagent. The phenyllithium di-additions by the two competing sequences, 1,2:1,2 *vs.* 1,2:1,4, except for the marked configurational effect on yields, are analogous to the di-reductions by lithium aluminum hydride.⁶

The 14:40% ratio of yields of phenyllithium 1,4-addition product from the *cis*- and *trans*-dibenzoyl ethylenes (I and II) is in contrast to the much more striking and opposite ratio of 97:7% of 1,4-



(13) NMR spectrum by E. G. Brame, Experimental Sta., Du Pont Co.

(14) N. F. Chamberlain, *Anal. Chem.*, **31**, 56 (1959).

(15) R. G. Bass, Ph.D. dissertation, University of Virginia, June, 1961.

(16) R. E. Lutz and J. O. Weiss, *J. Am. Chem. Soc.*, **77**, 1814 (1955).

addition to the *cis*- and *trans*-chalcones (XVI and XVII).¹⁸

Steric interferences and their effect on electron displacements must be at a minimum in the *trans* isomers II and XVII, where the molecules are relatively planar, and it is here that the contrast in the principal modes of phenyllithium addition is most striking. The relatively sizable extent of 1,4-addition to *trans*-dibenzoyl ethylene (II) can be attributed to the marked strengthening of the electrophilic activity of both ethylenic carbons, each of which is the β -carbon of an α,β -unsaturated ketone system and at the same time is subject to the strong electron-withdrawing effect of a directly-attached benzoyl group. *trans*-Chalcone (XVII) on the other hand has only moderate localized electrophilic activity at its β -carbon because of the sterically unimpeded and effective through-conjugation involving the electron-donative coplanar β -phenyl group, and it is here that 1,4-addition is at a minimum and 1,2-addition at the carbonyl group is predominant.

The apparent disinclination of *cis*-dibenzoyl ethylene (I) toward 1,4-addition can be explained in terms of higher steric hindrance at the β -carbon atom imposed by overlap of the β -benzoyl group and increase in the positivity of the α -benzoyl carbonyl-carbon caused by *cis*-interaction of the two benzoyl groups as depicted in I. In contrast to the suppression of 1,4-addition to the *trans* isomer, the predominance of 1,4-addition to the *cis*-chalcone (XVI) is attributed to suppression of 1,2-addition by the greater steric interferences at the carbonyl carbon,¹⁶ coupled with a higher positivity at the β -carbon because of lesser neutralization by and less effective conjugation with the β -phenyl.

Experimental¹⁷

Action of Phenyl Grignard Reagent on *cis*-1,2-Dibenzoyl ethylene (1,4-Diphenyl-2-butene-1,4-dione) (I).—Addition of 10 g. (0.042 mole) of I in 1-g. portions to 0.125 mole of the reagent prepared in the usual way in 100 ml. of dry ether, and processing,⁵ gave desylacetophenone (1,2,4-triphenylbutane-1,4-dione) (VI); crystallized from ethanol: 4.32 g. (35%), m.p. 126° (identified).

1,3,4,4-Tetraphenyl-4-hydroxy-1-butanone (IX). A.

(17) Microanalyses by Miss Patricia Paynter. Absorptions: ultraviolet; 10^{-5} M 95% ethanol, Beckman DU quartz spectrophotometer; infrared, by John I. Dale; KBr pellet, Perkin-Elmer Infracord.

Addition of Phenyllithium to *cis*-Dibenzoyl ethylene (I).—One gram (0.0042 mole) of *cis*-dibenzoyl ethylene (I) was added over 1 min. to 0.02 mole of phenyllithium in 100 ml. of ether (prepared in the usual way from lithium wire under a nitrogen atmosphere). Hydrolysis and concentrating the ether solution gave crystalline hydroxy ketone IX; recrystallized from ethanol-benzene mixture, 0.26 g. (14%), m.p. 219–221° (it showed no mixture melting point depression with a sample of the compound formulated by Scholtis as the cyclic hemiketal).¹⁰

Anal. Calcd. for $C_{28}H_{24}O_2$: C, 85.68; H, 6.16. Found: C, 85.66; H, 5.91.

λ_{max} (shoulder) 240 $m\mu$, ϵ 14,500. Infrared bands: 2.81, 5.95 μ .

In the above experiment and in one run in a Dry Ice-acetone bath, the bulk of the product was noncrystalline. While we were unable to isolate the known *cis*-glycol in crystalline form, treatment with refluxing acetic acid gave yields of ca. 15% of the tetraphenyldihydrofuran (XV) of m.p. 180–183° which was identified by comparison with a known sample.¹¹

B. Addition of Phenyllithium to *trans*-Dibenzoyl ethylene (II) (similar to the above) gave the hydroxy ketone IX in 40% yield; m.p. 216–217°. The more ether-soluble product, the *trans* 1,4-glycol VII, was extracted from the crude crystalline product by means of ether, and was recrystallized from 1:1 alcohol-benzene mixture; yield 15%, m.p. 200–201° (identified by mixture m.p.).¹¹

1,3,4,4-Tetraphenyl-3-butene-1-one (XI) was made by addition of 1 ml. of concd. hydrochloric acid to a solution of 1 g. of the hydroxy ketone IX in 15 ml. of glacial acetic acid. The immediately precipitated unsaturated ketone XI was recrystallized from ethanol, 0.5 g. (52%), m.p. 193.5–198°. It gave no mixture melting point depression with the compound formulated by Scholtis¹⁰ as the cyclic enol ether X.

Anal. Calcd. for $C_{22}H_{22}O$: C, 89.80; H, 5.92. Found: C, 89.81; H, 6.02. λ_{max} 237 $m\mu$, ϵ 32,800; shoulder, 270 $m\mu$, ϵ 14,600. Infrared band; 5.92 μ (none at ca. 2.8 μ).

1,1,2,4,4-Pentaphenylbutane-1,4-diol (XII).—To 50 ml. of ethereal phenyllithium (0.066 mole) was added portionwise 5 g. (0.0127 mole) of IX. After 5 min. the mixture was hydrolyzed and processed. Partial evaporation of the ether gave solid which was filtered, leached with hexane, and recrystallized from a 1:5 toluene-hexane mixture; 0.59 g. (10%), m.p. 179–181°.

Anal. Calcd. for $C_{34}H_{30}O_2$: C, 86.77; H, 6.43. Found: C, 87.12; H, 6.61. Infrared band, 2.80 μ .

A similar reaction with VI gave XII in 8% yield (pure). **2,2,3,5,5-Pentaphenyltetrahydrofuran (XIII)** was obtained by refluxing a solution of 0.35 g. of the 1,4-glycol XII in 10 ml. of glacial acetic acid and 1 ml. of concd. hydrochloric acid for 5 min., and pouring the resulting mixture into water. The resulting solid was recrystallized repeatedly from hexane; 0.13 g. (38%), m.p. 183.5–184°.

Anal. Calcd. for $C_{34}H_{30}O$: C, 90.23; H, 6.24. Found: C, 90.13; H, 6.19.

Acknowledgment.—We are indebted to Robert G. Bass for an important supporting experiment, and to E. G. Brame for NMR interpretation.