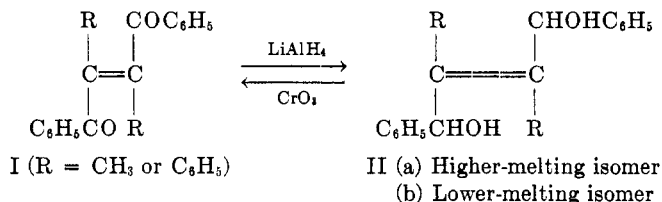


HYDRIDE REDUCTIONS OF THE *CIS* AND  
*TRANS*-DIBENZOYLSTILBENES<sup>1</sup>ROBERT E. LUTZ, C. R. BAUER,<sup>2</sup> R. G. LUTZ,<sup>3</sup> AND J. S. GILLESPIE<sup>4</sup>

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In an earlier paper (3) it was reported that lithium aluminum hydride reduced the  $\alpha,\beta$ -unsaturated ketone system of the 1,2-dibenzoylthylenes (I, III; R = H) largely 1,4 to give the enolate of the saturated 1,4-hydroxyketone as the chief product; there was produced at the same time some of the *trans* unsaturated 1,4-glycol (II, R = H) through 1,2-reduction of the carbonyl groups; but no evidence of reductive-furanization was noted. Aluminum isopropoxide reduction of the dibenzoylthylenes on the other hand gave one *trans* unsaturated glycol (II, R = H) as the only crystalline product isolated (4).

In an extension of this work we have found that *trans*-1,2-dibenzoyldimethyl-ethylene (I, R = CH<sub>3</sub>) reacts with lithium aluminum hydride chiefly by 1,2-reduction at both of the carbonyl groups to give a mixture of two diastereoisomeric unsaturated 1,4-glycols (II, R = CH<sub>3</sub>) which are shown to be *trans* by oxidation with chromic acid back to the *trans* unsaturated diketone. The *cis* isomer (III, R = CH<sub>3</sub>) on the other hand was in several experiments converted into non-crystalline products, but in one isolated experiment it gave a small yield of 3,4-dimethyl-2,5-diphenylfuran (V, R = CH<sub>3</sub>) (2). These results led us to study the action of the hydride reducing agents on the *cis* and *trans*-dibenzoylstilbenes (I, III; R = C<sub>6</sub>H<sub>5</sub>) where similar *cis-trans* differences have appeared and where it has been possible to determine the conditions favorable to reductive furanization (1).



Reduction of *trans*-dibenzoylstilbene (I, R = C<sub>6</sub>H<sub>5</sub>) with an excess of three moles of lithium aluminum hydride, gave two diastereoisomeric *trans* unsaturated glycols (II). The structures of these compounds were shown by the absence of ultraviolet absorptivity in the 240–250 m $\mu$  "benzoyl" range, by the absence of an infrared absorption band in the 6  $\mu$  "carbonyl" region, by the occurrence of

<sup>1</sup> This investigation, initiated under supporting fellowships,<sup>2, 3</sup> was completed under a research grant from the Office of Ordnance Research.

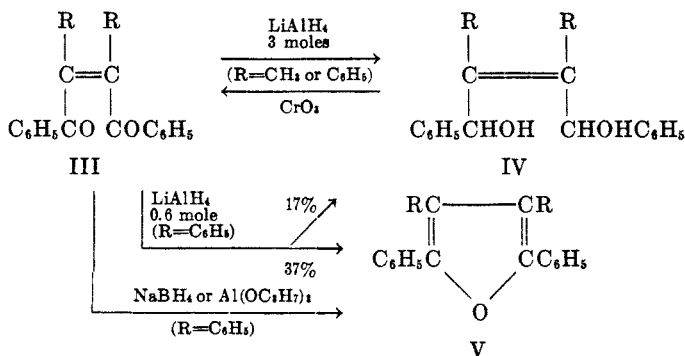
<sup>2</sup> du Pont Company Postgraduate Fellow, 1949–1950 (see ref. 1).

<sup>3</sup> Supported in part by a grant from the Office of Ordnance Research.

<sup>4</sup> Tennessee Eastman Corporation Graduate Scholarship, 1948–1949, under which the preliminary work was done on the reduction of the dimethyldibenzoylthylenes (see ref. 2).

an infrared "hydroxyl" absorption band at  $2.75 \mu$ , and by the chromic acid oxidation back to the *trans* unsaturated diketone.

The *cis* unsaturated diketone (III) similarly underwent 1,2-reduction but gave only one unsaturated glycol (IV) in mediocre yield; no other crystalline product was isolated in careful attempts to find the diastereoisomer. This glycol was characterized by lack of ultraviolet and infrared benzoyl-type absorptivities, by infrared hydroxyl absorptivity ( $2.75 \mu$ ), and by chromic acid oxidation back to the *cis* unsaturated diketone.



It is thus demonstrated that the principal mode of attack with a large excess of the reagent, involving in the main the most active first-hydrogen, is 1,2 directly at the carbonyl groups.

When less than one mole (instead of an excess) of lithium aluminum hydride was used so as to minimize the speed of reaction and to utilize principally the less active hydride hydrogens, a marked difference appeared in facility as well as in mode of reaction of the two dibenzoylstilbenes. The *cis* compound was completely used up and 17% of the *cis* unsaturated glycol (IV) and 37% of tetraphenylfuran (V) were isolated, whereas under comparable conditions the *trans* isomer was recovered largely unchanged and gave only 9% of one of the *trans* unsaturated glycols (IIa).

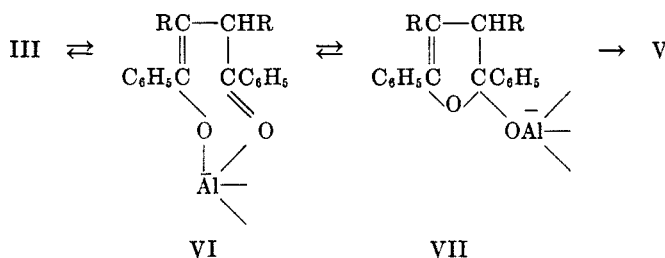
An even more striking configurational effect than the above appears in the reductions of *cis*- and *trans*-dibenzoylstilbenes by sodium borohydride and by aluminum isopropoxide. The *cis* isomer was reduced very slowly but completely by these reagents and the furan was the sole product isolated in crystalline form, whereas the *trans* isomer was not affected under comparable conditions.

#### INTERPRETATION OF RESULTS

The greater difficulty of reduction of the *trans* isomer by the hydride reducing agent and by aluminum isopropoxide may be accounted for in terms of lesser steric interference with the effective planarity of the stilbene conjugated system in that isomer, the consequently greater tendency in that isomer for the two benzoyl groups to function as separate systems, and the suppression of 1,2-reduction by the greater steric shielding of the carbonyl carbons which are each sandwiched between two *trans*-stilbene type phenyls. The greater hindrance at

the carbonyl groups in the *trans* isomer may be seen upon inspection of scalar molecular models. It is analogous to the greater steric hindrance at the carbonyl-carbon in *cis*- $\alpha$ -phenylchalcone which in contrast to the *trans* isomer resists reaction with phenylhydrazine (*cf.* ref. 5) and reduction by aluminum isopropoxide (6).

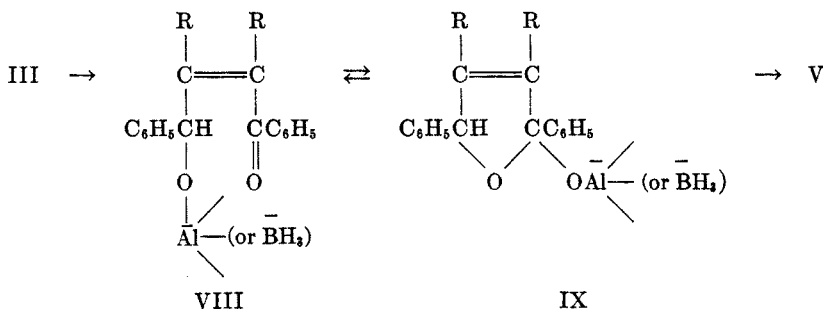
The facilitation of reductive-furanization by the *cis* configuration here is in contrast to the opposite effect of configuration on the zinc-acetic acid reductions of the dibenzoylstyrenes where it is the *trans* isomer which gives the best yield of furan (7). It is believed however that the zinc-acetic acid reductions proceed *via* competing 1,4- and 1,6-reactions and involve electron transfer, that the relative ease of reduction there depends upon the relative degrees of planarity of semiquinone-like intermediates, and that the different ratio of the resulting saturated diketone and furan is determined by the nature of the intermediate enolates involved. The reduction-furanizations of *cis*-dibenzoylstilbene by the hydride reagents and by aluminum isopropoxide evidently involve a quite different mechanism and resemble more the acid-catalyzed nucleophilic addition-furanizations which occur particularly readily with other *cis* unsaturated 1,4-diketones of this type (8).



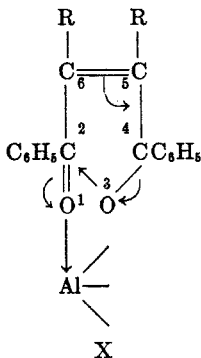
A mechanism involving "1,4"-reduction or nucleophilic attack by hydride hydrogen at the  $\beta$ -carbon of the  $\alpha,\beta$ -unsaturated ketone system of I or III (or of some complex such as X below) to give an enolate (VI) prior to the key cyclization step (*e.g.* VII) would involve at this point (VI) the destruction of the original *cis* or *trans* configurations; and both isomers should then give the same products. Such a mechanism would be possible only if one assumes that steric resistance in the *trans* isomer to 1,4-reduction is significantly greater than toward 1,2-reduction at a carbonyl group, in analogy with steric effects in the *cis* and *trans*- $\alpha$ -phenylchalcones where the *cis* configuration favors 1,4-addition of phenyllithium (6). While this explanation is satisfactory for reductive-furanization by lithium aluminum hydride, it does not account satisfactorily for the aluminum isopropoxide and sodium borohydride reductive-furanizations because the latter two reagents as far as is known at present are carbonyl-specific and have not been able to effect 1,4-reductions.

An adequate explanation for the reductive-furanizations of the *cis* isomer involves stepwise 1,2-reduction of one carbonyl at a time to give an intermediate *cis* unsaturated hydroxy ketone (in its alkoxide form VIII) of sufficient life under

the reducing conditions to cyclize to IX and undergo 1,4-elimination of hydrogen and the oxymetallo group to give the furan V, all of this in successful competition with a second and similar 1,2-reduction at the remaining carbonyl (of VIII). In the case of the *trans* isomer retention of configuration would prevent such cyclization.



An alternative mechanism involves postulation of coordination complexes between the reagent and one carbonyl-oxygen at a time, cyclization through a resonance-stabilized intermediate such as X, and loss of the oxymetallo moiety directly or through IX to give the furan V. The carbonyl carbon (position-2 of X) would be sterically uninhibited toward attack by the other nearby carbonyl oxygen (position-3 of X) which serves as an important part of the steric shield impeding attack by hydride hydrogen at this point; furthermore, such a move toward cyclization (X) would electronically facilitate reduction which could then proceed by direct loss of the oxymetallo group through fission of the remaining 1,2-oxygen-carbon bond of X or through IX by hydrogen transfer (to position-4 of X).



#### EXPERIMENTAL<sup>5</sup>

*Tetrahydrofuran* (V. R. = C<sub>6</sub>H<sub>5</sub>) (9) was made in erratic yields (the best was 25%) by refluxing a solution of 50 g. of benzoin in 100 ml. of water and 100 ml. of conc'd sulfuric acid for 24 hours; crystallized from ethanol, m.p. 171°. It is best prepared by the action of

<sup>5</sup> Microanalyses were by Mrs. J. B. Caliga and Mrs. A. B. Wilgus and Miss Mai Lai.

phenylmagnesium bromide on *cis*-dibenzoylstyrene (10); this procedure was reported as giving first the *cis*-dibenzoylstilbene, but in our hands it gave the tetraphenylfuran directly in 61% yield.

*cis*-1,2-Dibenzoylstilbene (III, R = C<sub>6</sub>H<sub>5</sub>) (9; cf. also 10) was prepared by treating 2 g. of the furan in 30 ml. of conc'd acetic acid with a mixture of 4 ml. of conc'd nitric acid in 10 ml. of conc'd acetic acid, at room temperature for 1 hour, heating to 40° and diluting with water; yield 1.8 g. (86%), m.p. 211–213°; recrystallized from 1:1 ethanol-benzene.

*trans*-1,2-Dibenzoylstilbene (I, R = C<sub>6</sub>H<sub>5</sub>) (11) was obtained in 65% yield by refluxing a suspension of the *cis* isomer in 3% ethanolic potassium hydroxide for 24 hours; recrystallized from conc'd acetic acid; m.p. 232–234°.

*cis*-1,2,3,4-Tetraphenyl-2-butene-1,4-diol (IV, R = C<sub>6</sub>H<sub>5</sub>). Three g. of III (0.008 mole) was added all at once to a vigorously stirred solution of 1 g. (0.026 mole) of lithium aluminum hydride in 300 ml. of dry ether. Refluxing with continued stirring for a half hour, treatment with 40 ml. of water, washing with acid and with water, evaporation, and recrystallization from 50% ethanol, gave 1.9 g. of the *cis* unsaturated glycol IV (63%); m.p. 143°. No crystalline product was obtained from further study of the residues. The furan crystallizes well and would have been detected if formed in significant amounts.

Anal. Calc'd for C<sub>28</sub>H<sub>24</sub>O<sub>2</sub>: C, 85.69; H, 6.16.

Found: C, 85.58; H, 6.55.

Infrared absorption band at 2.75 μ with heavier and broader absorption at 2.90–2.95 μ; no band in the 6 μ region.

The diastereoisomeric *trans*-1,2,3,4-tetraphenyl-2-butene-1,4-diols (IIa and b, R = C<sub>6</sub>H<sub>5</sub>) were obtained according to the above procedure except that a 47% yield of the higher-melting ether-insoluble isomer (IIa) was filtered off. The lower-melting unsaturated glycol (IIb) then was obtained from the ether solution and was recrystallized from dilute ethanol; yield 25%; m.p. 185°.

Anal. Calc'd for C<sub>28</sub>H<sub>24</sub>O<sub>2</sub>: C, 85.69; H, 6.16.

Found: C, 85.70; H, 6.41.

Infrared absorption bands at 2.75 and 2.90 μ; none in the 6 μ region.

The higher-melting isomer (IIa) was recrystallized from xylene-conc'd acetic acid mixtures; m.p. 291–293°.

Anal. Calc'd for C<sub>28</sub>H<sub>24</sub>O<sub>2</sub>: C, 85.69; H, 6.16.

Found: C, 85.80; H, 5.97.

Infrared absorption peaks at 2.75, 2.85 and 6.10 μ (Nujol mull, used because of insolubility in chloroform).

Oxidation of equal weights of the *cis* or either of the two *trans*-glycols (II or IV) by chromic acid in conc'd acetic acid at 50° for a few minutes gave the corresponding unsaturated diketones (I or III) in nearly quantitative yields.

Reduction of *cis*-dibenzoylstilbene (III, R = C<sub>6</sub>H<sub>5</sub>) with lithium aluminum hydride was carried out by adding 0.5 g. (0.0013 mole) of the solid to 0.03 g. (0.0008 mole) of the reagent in 50 ml. of ether and heating the mixture under vigorous reflux for a half hour. Upon crystallizing the product slowly from ethanol and filtering, cooling, addition of a small amount of water at 40°, and cooling, four crops of crystals were obtained and identified as tetraphenylfuran (V); yield 0.176 g. (37%). The last filtrate on further dilution with water and cooling gave 0.07 g. (14%) of the *cis* unsaturated glycol (IV). The rest of the product was non-crystalline. The experiment was repeated with similar results.

Reduction of 1 g. (0.0027 mole) of the *cis* compound (III) with aluminum isopropoxide 4.0 g. (0.020 mole) in 30 ml. of dry isopropyl alcohol under partial reflux for 110 hours, and subsequent hydrolysis with 10% sodium hydroxide and extraction with ether, gave 0.80 g. (80%) of tetraphenylfuran (V) which was crystallized from ethanol. When a similar reaction was stopped after 11 hours of refluxing only impure starting material was recovered (identified), and no other crystalline product was isolated.

Reduction of 1 g. (0.0027 mole) of III with sodium borohydride [0.40 g. (0.011 mole)] in 60 ml. of methanol at room temperature for 2.5 hrs., and subsequent hydrolysis with 10%

hydrochloric acid and extraction with ether, gave 0.68 g. (68%) of tetraphenylfuran (V). Upon addition of water 0.18 g. (18%) of starting material precipitated and was identified.

*Reduction of trans-dibenzoylstilbene* (I, R = C<sub>6</sub>H<sub>5</sub>) with lithium aluminum hydride as in the preceding experiment and concentration of the ether solution, gave 70% of starting material; and after evaporation, the residual material was crystallized from ethanol and gave another 10% of starting material. From the ethanol filtrate upon addition of water was obtained 9% of the *trans* unsaturated glycol (IIa). From the final filtrate no tetraphenylfuran could be isolated. The experiment was repeated with practically identical results.

In separate experiments carried out to determine the magnitude of differences in conditions entailed by the use of solid reactants, it was found that both *cis* and *trans*-dibenzoylstilbenes dissolved rapidly from 0.266-g. samples of the solid into 95 ml. of refluxing ether and reached about 65 and 90% of saturation respectively within five minutes. The solubilities were approximately 1.8 and 0.45 g. per l. respectively. Allowing for these differences, and taking note of the fact that reduction of the *cis* compound was complete during the reaction period in spite of continually diminishing concentrations and reactivity of the reagent, it is clear that the *cis* isomer actually did undergo reduction considerably faster than the *trans* isomer and in a different and unique fashion, under comparable though not precisely identical conditions. More vigorous stirring of the reduction mixtures or/and use of methylal as solvent (12) might diminish or eliminate these differences in conditions, but in view of the obvious validity of the above conclusion it was deemed unnecessary to repeat the work.

*Reduction of trans-dibenzoylstilbene with aluminum isopropoxide or sodium borohydride* under the conditions employed in the corresponding reductions of the *cis* compound, gave only starting material (76 and 96% respectively).

*The diastereoisomeric trans-2,3-dimethyl-1,4-diphenyl-2-butene-1,4-diols* (IIa and b, R = CH<sub>3</sub>). A sample of 7.2 g. of *trans*-dibenzoyldimethylethylene (I, R = CH<sub>3</sub>) in a Soxhlet apparatus was extracted over 5 hrs. by refluxing ether into 1.0 g. of lithium aluminum hydride in a large volume of ether. After hydrolysis 6.0 g. of a solid mixture was recovered upon evaporation. Solution in hot ethanol and cooling caused crystallization of about half of the product, the *higher-melting isomer* (IIa); recrystallized, m.p. 148–149°.

*Anal.* Calc'd for C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>: C, 80.56; H, 7.51.

Found: C, 80.37; H, 7.37.

Concentration or dilution of the filtrate with water gave the second half of the product, the *lower-melting isomer* (IIb); recrystallized, m.p. 109–110°.

*Anal.* Calc'd for C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>: C, 80.56; H, 7.51.

Found: C, 80.56; H, 7.69.

*Chromic acid oxidations of both stereoisomeric trans-glycols* (IIa and b) in conc'd acetic acid under the usual conditions (3) gave the *trans* unsaturated diketone (I) in good yields (identified by mixture m.p.).

*Lithium aluminum hydride reductions of cis-dibenzoyldimethylethylene* (III, R = CH<sub>3</sub>) (of m.p. 96.5–97°)<sup>6</sup> were carried out in ether by adding an ether solution of the compound to the reagent. In several runs only non-crystalline products were isolated; but in one isolated experiment a sizable amount of 3,4-dimethyl-2,5-diphenylfuran (V, R = CH<sub>3</sub>) was isolated and identified by mixture m.p. with an authentic sample (14).

#### SUMMARY

Reduction of *cis*- and *trans*-dibenzoylstilbenes by a large excess of lithium aluminum hydride gave *cis* and *trans* unsaturated glycols. When a small amount of reagent was used the *trans* compound was reduced very slowly to one of the *trans* glycols whereas the *cis* isomer was reduced easily and gave mainly tetra-

<sup>6</sup> This is the true m.p.; the value given in ref. 10 (86.5–87°) is in typographical error.

phenylfuran. The *trans* isomer was not reduced by sodium borohydride or by aluminum isopropoxide, whereas the *cis* isomer was reduced slowly but exclusively to the furan. The reductions are explained in terms of greater steric interferences with the carbonyl groups in the *trans* isomer, and of cyclizability of a *cis* intermediate.

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