Base-induced Hydrolytic Rearrangement of *trans*-γ-Bromodypnone to 1,2-Dibenzoylethane[1,2]

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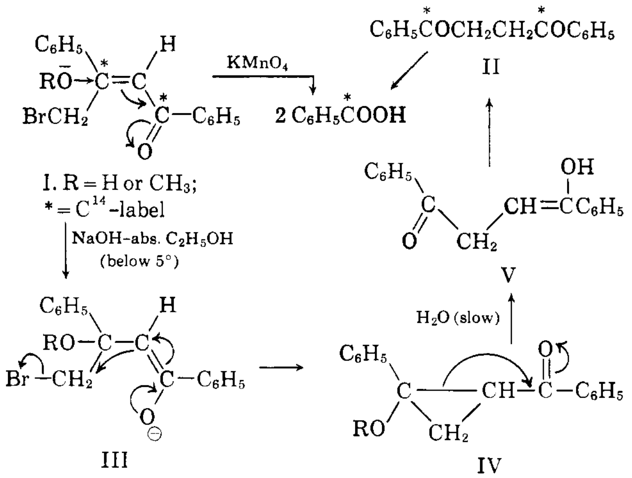
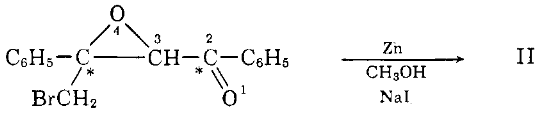
Sodium hydroxide in ethanol induces hydrolytic rearrangement of *trans*-γ-bromodypnone to 1,2-dibenzoylethane. Phenyl group migration from the 3- to the 4-position of the dypnone skeleton during this rearrangement and during the similar reductive rearrangements of *cis*- and *trans*-γ-bromodypnone oxides[5] was excluded by repeating the three reactions upon materials C^{14}-labeled at the 1- and 3-carbons, followed by permanganate oxidation of the respective products to benzoic acid, in each case with retention of the full C^{14}-activity. A rearrangement mechanism is suggested in terms of cyclopropane intermediates.

trans-γ-Bromodypnone (I), the vinylog of an α-bromo ketone, is at the right oxidation level for furanization, and at times[2,3] under weakly acidic or basic conditions it undergoes this reaction rather than displacement of the γ-bromine atom. We were then led to investigate the action of strong base, sodium hydroxide or methoxide, conditions under which furanization was not expected. At reaction temperatures below 5° in absolute ethanol containing a small excess of sodium hydroxide, the only crystalline product isolated proved unexpectedly to be 1,2-dibenzoylethane (II) in which the originally beta phenyl group appeared in the terminal position gamma to the original carbonyl group; it was obtained in varying yields, in one case 49%. After the bulk of the γ-bromodypnone had been used up, dibenzoylethane did not crystallize immediately from the cold ethanol solution as it would have done if it had directly been formed and if it had then been present in an amount approaching that ultimately obtained upon work-up. Preliminary attempts so far to isolate a crystalline intermediate have not been successful.



Because of interest in this as a rearrangement under alkaline conditions, and because of its relation to Favorskiĭ rearrangements[4] and to the reductive rearrangements of *cis*- and *trans*-γ-bromodypnone oxides[5] (VI) to 1,2-dibenzoylethane, a rigorous test was carried out to exclude the possibility that in these reactions the phenyl group had migrated from the 3- to the 4-carbon atom of the dypnone skeleton, even through such a migration seemed unlikely on mechanistic grounds. For this purpose *trans*-dypnone, phenacyl bromide and the *cis*- and *trans*-γ-bromodypnone oxides C^{14}-labeled at the β and at the carbonyl carbon atoms were made from acetophenone C^{14}-labeled at its carbonyl carbon. Permanganate oxidations of these intermediates and of the samples of dibenzoylethane obtained in the three rearrangements, each gave benzoic acid of the same C^{14}-activity; and proportional C^{14}-activity was directly demonstrated in the C^{14}-labeled γ-bromodypnone. Had phenyl group migration occurred from the β- to the γ-position at any point during the rearrangements to dibenzoylethane, the benzoic acid molecule produced from the original benzoyl group would have contained the original C^{14}-activity of that group, whereas the other molecule of benzoic acid with its phenyl group attached to the carbon atom originally terminal in γ-bromodypnone or its oxides, would have been inactive; and the benzoic acid sample obtained from each oxidation would have had close to half of the total C^{14}-activity of the starting material and of the benzoic acid obtained from it by oxidation. Phenyl group migration during the three rearrangements to dibenzoylethane, and any mechanism involving it, are thereby excluded.



VI. *cis* and *trans*

The base-induced rearrangement of γ-bromodypnone to dibenzoylethane can be explained in conventional terms as reversible hydroxide or methoxide ion attack or addition-enolization of the α,β-unsaturated ketone system with approach toward or actual formation of the enolate ion III, intramolecular carbon-alkylation to a cyclopropanol or its ether IV, fission of the cyclopropane ring by retrograde aldolization to the enol V or its equivalent and ketonization to II.[6]

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[1] Supported by National Science Foundation grant G 9494.

[2] R. E. Lutz and L. T. Slade, a paper presented at the 138th National Meeting of the American Chemical Society, New York, N. Y. September, 1960; Abstracts, p. 99P.

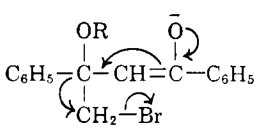
[3] (a) L. T. Slade, Ph.D. dissertation, University of Virginia, 1960; (b) R. E. Lutz and L. T. Slade, *J. Org. Chem.*, **26**, 4888 (1961).

[4] (a) A. S. Kende, *Org. Reactions*, **11**, 261 (1960); (b) C. L. Stevens and E. Farkas, *J. Am. Chem. Soc.*, **74**, 5352 (1962); (c) R. B. Loftfield, *ibid.*, **72**, 632 (1950); (d) E. E. Smissman and G. Hite, *ibid.*, **83**, 3980 (1961).

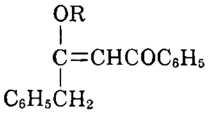
[5] H. H. Wasserman, N. E. Aubrey, and H. E. Zimmerman, *ibid.*, **75**, 96 (1953).

[6] In the reductive rearrangement of *cis*- and *trans*-γ-bromodypnone oxides (VI) to 1,2-dibenzoylethane (II) Wasserman[5] has postulated an intermediate cyclopropoxy anion corresponding to IV. This reaction might be expressed in terms of conjugate reduction, *e.g.*, of the epoxy ketone system with expulsion of bromide ion as in III–IV, which possibly would meet steric and conformational exigencies and explain the difference in yields of II from the stereoisomers of VI (28% *vs.* 8%). For analogies see Boord type reductions of β-halo ethers [(a) C. G. Schmitt and C. E. Boord, *J. Am. Chem. Soc.*, **54**, 751 (1932); (b) L. F. Small and R. E. Lutz, *ibid.*, **56**, 1738 (1934)] and 1,4-reductive-enolization of α-bromo ketone and epoxy ketone systems [(c) R. E. Lutz and W. G. Reveley, *ibid.*, **63**, 3180 (1941); (d) R. E. Lutz and F. N. Wilder, *ibid.*, **56**, 2065 (1934)].

A vinylogous Favorskiĭ hydrolytic rearrangement[4b] of γ-bromodypnone might be envisioned in terms of the intermediate of base attack VII and reaction along the lines indicated, involving migration of the phenyl group from the β to the γ-carbon with expulsion of bromide ion; this would lead to the β-diketone enol VIII or cleavage products from it, but not to dibenzoylethane. Although no such products related to or derivable from VII were observed, losses of material were considerable and this mode of reaction is not excluded as a competing process.



VII. R = H or CH_3



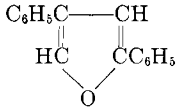
$$C_6H_5CH_2-\overset{OR}{C}=CHCOC_6H_5$$

VIII

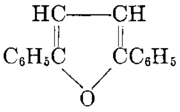
Further studies on hydrolytic rearrangement of γ-bromodypnones and of furanizations and pyrrole formation are in progress.

Experimental

In one base-induced rearrangement of γ-bromodypnone at 0 to −10° in which not all of the starting material had been used up, the total isolated product mixture including the unchanged γ-bromodypnone was subjected in work-up to the prolonged action of ethanol under reflux, and the solution had become sharply acidic through alcoholysis of the unreacted γ-bromodypnone. Upon partial separation and isolation of the crystalline products there was obtained a very small amount of dibenzoylethane and a considerable amount of a mixture of two diphenylfurans consisting of roughly comparable quantities of the 2,4 and 2,5 isomers, XII and XIII. Mixtures of authentic samples of these isomers showed melting point depressions of only a few degrees. The presence and identity of the two isomers in the mixture was demstrated semiquantitatively by the approximately equal intensities of the two infrared absorption peaks of 12.3 and 12.5 μ, which are characteristic respectively of the 2,4 and 2,5 isomers, and by comparison with the spectrum of a known mixture. These two wave lengths of strong absorption constitute the most significant difference in the very similar absorption spectra of these two isomers.



XII



XIII

The unlikely possibility that 2,4-diphenylfuran would be formed as an intermediate in the formation of dibenzoylethane in the above rearrangements was excluded by direct test which showed that both it and 2,5-diphenylfuran are stable under the alkaline conditions used for the rearrangements. The source of the 2,5-diphenylfuran in the above experiments evidently is the dibenzoylethane produced by the rearrangement, which in separate experiment actually was shown to furanize under the work-up conditions. The source of the 2,4-diphenylfuran must be hydrolytic furanization of the starting material, γ-bromodypnone, which had survived the initial alkali reaction; in a separate experiment under the work-up conditions the actuality of this reaction was demonstrated.

Hydrolytic Rearrangement of *trans*-γ-Bromodypnone (I).—A solution of 3 g. (0.01 mole) of I in 100 ml. of absolute ethanol at *ca.* 5–8° was treated dropwise under stirring with a 25-ml. absolute ethanol solution of 0.4 g. (0.01 mole) of sodium hydroxide (30 min. or longer), and the mixture was then allowed to stand at *ca.* 0°. No dibenzoylethane (II) precipitated at this point, but at times small amounts of unchanged material (I) was present and was filtered off and identified. Since II is less soluble than I and crystallizes very easily, it could not have yet been formed as such in significant amounts. Treatment of the reaction mixture with ether and sodium chloride solution, drying the ether extract over sodium sulfate, and concentrating then gave a crystalline residue melting in the range 143–145° (yields widely varying, in one case 49%) which was identified as nearly pure dibenzoylethane (II) by recrystallizations, analysis, ultraviolet and infrared absorption spectra, and mixture melting point with an authentic sample. (Absorption maxima: 243, 278 mμ, ε 26,900, 244; μ, 2.80w, 3.44w, 5.94s, 6.26m, 6.90m, 7.15m, 7.25w, 7.39m, 8.16s, 8.46m, 10,06m, 10.52w).

In a similar experiment in a mixture of 50 ml. each of absolute methanol and ether at −10° with dropwise addition of a solution of 0.01 mole of sodium in 50 ml. of methanol, work-up as above gave a yield of 36% of II.

A sample of 2,4-diphenylfuran (and similarly 2,5-diphenylfuran) after treatment with alcoholic sodium hydroxide under the above conditions, was recovered unchanged (88%).

Preparations of C^{14}-labeled materials, based on the above and on references cited in the discussion, were made in a series of practice experiments to gain experience and test yields. C^{14}-Activities were determined as counts per minute in the usual way and are summarized in the following table.

Table I

C^{14}-Activities

C_6H_5COOH, obtained by $KMnO_4$ oxidations[a] of the following compounds[b]	% C^{14}-activity relative to C_6H_5COOH obtained by $KMnO_4$ oxidation of the C^{14}-labeled reference compound, $C_6H_5COCH_2Br$ [b,c]
trans-Dypnone[1b]	102
Dibenzoylethane (II) from base-induced rearrangement of γ-bromodypnone (I)	98
Dibenzoylethane from reductive rearrangement[d,e] of γ-bromodypnone *cis* epoxide[5] (VIII), m.p. 129–130°	98
Noncrystalline residue from this reaction	100
Dibenzoylethane from reductive rearrangement[e] of γ-bromodypnone *trans* epoxide[5] (VIII), m.p. 166–167°	105
Noncrystalline residue from this reaction	101
γ-Bromodypnone, compared directly with unoxidized γ-bromodypnone with correction for the difference in molecular weight (m.p. 68–70°)	97

[a] In refluxing water–sodium hydroxide mixture. [b] All C^{14}-labeled compounds were synthesized from C^{14}-labeled acetophenone. [c] The C^{14}-labeled phenacyl bromide was oxidized to benzoic acid by dioxane–water–iodine–potassium iodide–sodium hydroxide mixture. [d] In one experiment following the reported procedure for preparing the α-phenacyl bromide (*cis*-VIII[5]), with fractional crystallization of the product from ether, we obtained *ca.* 50% of the high-melting and 15% of the low-melting isomer. [e] The yields of dibenzoylethane in the reductive rearrangements were low, and distressingly so in the case of the low-melting isomer, and they corresponded to those reported[5] (28% from the high-melting isomer and 8% from the low-melting isomer). A reaction path involving simple deoxygenation of VIII seems excluded by separate test which indicates that the necessarily intermediate γ-bromodypnone does not produce dibenzoylethane under similar conditions.