kept at 55°. Dry hydrogen was bubbled through the hot mixture during the period of reduction (5 hours). Ether (100 ml.) was added to the final reaction mixture, the precipitate filtered and repeatedly washed with ether (30 ml.). Further purification was effected by boiling the reduced polymer with 0.1 *N* hydrochloric acid for 10 minutes.

Anal. Calcd. for VI (*n* average = 80): C, 41.7; H, 4.3; N, 12.2; amino-N, 0.15. Found: C, 41.0; H, 4.3; N, 12.0; amino-N, 0.15[11]; carboxyl-N, 0.13.[10]

The equivalent weight of the polymer determined by dissolving in excess of 0.1 *N* sodium hydroxide and potentiometric back-titration with 0.1 *N* hydrochloric acid was 125; the value calculated for complete reduction is 115; $[\alpha]^{25}\text{D}$ −11.2° (*c* 5 in water in the presence of one equivalent of sodium hydroxide); $[\alpha]^{25}\text{D}$ −10.8° (*c* 5 in water in the presence of 0.67 equivalent of sodium hydroxide); $[\alpha]^{25}\text{D}$ −10.4° (*c* 5 in water in the presence of 0.33 equivalent of sodium hydroxide).

Two other poly-L-aspartic acid preparations gave the following analysis: Preparation (a) prepared under conditions similar to those described above): N, 12.0; amino-N, 0.20; carboxyl-N, 0.18 (*n* average calcd. = 61).

Preparation (b) (prepared from IV kept in a desiccator over sulfuric acid for 5 months): N, 12.2; amino-N, 0.61; carboxyl-N, 0.52 (*n* average calcd. = 20).

Total Hydrolysis of VI (*n* average = 80).—Poly-L-aspartic acid (50 mg.) was hydrolyzed by refluxing in 6 *N* hydrochloric acid (4 ml.) for 24 hours. The resulting clear hydrolysate was diluted to a volume of 25 ml. and the amino-N[11] and carboxyl-N[10] determined in 1-ml. aliquots after neutralization.

Anal. Calcd. for a hydrolysate of 100 mg. VI (*n* average = 80); amino-N, 12.2 mg.; carboxyl-N, 12.2 mg. Found: amino-N, 11.8 mg. carboxyl-N, 11.5 mg.

In order to determine the specific rotation of the aspartic acid derived from the polymer on acid hydrolysis, the following experiment was carried out: Poly-L-aspartic acid (50 mg.) was hydrolyzed, as above. The hydrolysate was brought to dryness, the residue dissolved in 6 *N* hydrochloric acid (0.5 ml.) and brought to a volume of 1 ml. with the same solvent. From the optical rotation of this solution the specific rotation of the monomeric aspartic acid (56.9 mg., *cf.* amino-N of previous experiment) was calculated: $[\alpha]^{25}\text{D}$ 24.9.[19] On isolation of the aspartic acid from the hydrolysate, it was found that the acid showed the normal specific rotation of L-aspartic acid.

The ammonium salt of poly-L-aspartic acid (*n* = 80) was obtained by dissolution of VI in an excess of 3 *N* ammonium hydroxide and evaporation to dryness on a water-bath. The salt was dried over sulfuric acid for two days before analysis.

Anal. Calcd. for $(C_4H_8O_3N_2)_n$: N, 21.2. Found: N, 20.7.

Sodium Salt of VI (*n* = 80).—VI was dissolved in a slight excess of 1 *N* sodium hydroxide and absolute ethanol (10 volumes) added. The flocculent precipitate was washed with ethanol, redissolved in a small amount of water and reprecipitated with absolute ethanol (10 volumes). The purified salt was collected, washed with absolute ethanol and anhydrous ether and dried *in vacuo* over sulfuric acid.

Anal. Calcd. for $(C_4H_4O_3NNa)_n$: Na, 16.8. Found: Na: 14.8.

The copper salt of VI (*n* = 80) was obtained as a green voluminous precipitate on adding an excess of aqueous copper sulfate to an aqueous solution of sodium poly-aspartate.

Anal. Calcd. for $(C_4H_4O_3N^1/_2Cu)_n$: Cu, 21.8; N, 9.6. Found: Cu, 22.0; N, 10.0.

The silver salt of VI (*n* = 80) was precipitated from an aqueous solution of sodium poly-aspartate on adding an excess of aqueous silver nitrate.

Anal. Calcd. for $(C_4H_4O_3NAg)_n$: Ag, 48.7. Found: Ag, 40.0.[21]

Carboxyl-N of **L-Isoasparagine.**—L-Isoasparagine hydrate was prepared according to Bergmann and Zervas[4] and analyzed for carboxyl-N.[10]

Anal. Calcd. for L-isoasparagine hydrate: carboxyl-N, 9.3. Found: carboxyl-N, 9.5.

Potentiometric Titration of VI (*n* average = 61).—The titration curve given in Fig. 1 was obtained by the back-titration of an aqueous solution of sodium poly-L-aspartate (*n* = 61; 30.0 mg. in 20 ml.) with 0.05 *N* hydrochloric acid. The titration was carried out at 25° in a nitrogen atmosphere, using the Beckman *p*H-meter with a glass electrode.

The influence of potassium chloride at various concentrations on the *p*H of an aqueous solution of a 50% neutralized poly-L-aspartic acid is given in Fig. 3.

Viscosity of Poly-L-aspartic Acid (*n* = 61) Solutions.—The viscosity of poly-L-aspartic acid (*n* = 61) in aqueous solution at various degrees of neutralization was measured at 30 ± 0.02° in a modified Ostwald–Fenske viscosimeter (A.S.T.M. D445) of efflux time 180.6 seconds for water. The results are summarized in Fig. 4. Concentrations are given in basic moles per liter (1 basic mole 115 g.).

Acknowledgment.—The authors are indebted to Mr. J. H. Jaffe and Dr. S. Pinchas for carrying out the infrared measurements, and to Dr. A. Katchalsky for the benefit of helpful discussion.

[21] The silver salt of poly-glutamic acid obtained by Hanby, Waley and Watson[8] contained silver in a percentage (40.7%) considerably less than the theoretical (45.8%).

REHOVOTH, ISRAEL RECEIVED FEBRUARY 15, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Synthesis and Reaction with Morpholine of *cis*-1,2-Dibenzoyl-1-*p*-tolylethylene[1]

BY PHILIP S. BAILEY, ELIAS E. KAWAS AND LELAND L. SMITH[2]

cis-1,2-Dibenzoyl-1-*p*-tolylethylene, a vinylog of 1,2-dibenzoylpropene, has been synthesized and shown to react with morpholine by simple addition, in contrast to 1,2-dibenzoylpropene which undergoes a novel reaction with morpholine to give 1,2-dibenzoyl-3-(4-morpholinyl)-propane.

Earlier work has shown that 1,2-dibenzoylpropene and similar compounds will react with secondary amines to give 3-amino-1,2-dibenzoylalkanes.[3,4,5] In view of certain addition reactions of conjugated systems involving aromatic rings found in the literature[6] it seemed desirable to make 1,2-dibenzoyl-1-*p*-tolyl- and *o*-tolylethylenes in order to see if the amine reaction could be extended to vinylogs (through the benzene ring) of 1,2-dibenzoylpropene. Of these only the first one could be prepared.

1,2-Dibenzoyl-1-*p*-tolylethylene (I) was made by well known and general reactions[7] involving the

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[1] This is the fifth in a series of papers concerning 1,3-shifts of hydrogen in the reactions of dibenzoylalkenes and related compounds. For the first four see (a) R. E. Lutz and P. S. Bailey, THIS JOURNAL, **67**, 2229 (1945); (b) P. S. Bailey and R. E. Lutz, *ibid.*, **67**, 2232 (1945); (c) P. S. Bailey and G. Nowlin, *ibid.*, **71**, 732 (1949); (d) P. S. Bailey and W. W. Hakki, *ibid.*, **71**, 2886 (1949).

[2] Taken in part from the M.A. Thesis of Leland L. Smith, May, 1948.

[3] R. E. Lutz and P. S. Bailey, THIS JOURNAL, **67**, 2229 (1945).

[4] P. S. Bailey and G. Nowlin, *ibid.*, **71**, 732 (1949).

[5] P. S. Bailey and W. W. Hakki, *ibid.*, **71**, 2886 (1949).

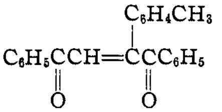
[6] (a) E. P. Kohler and E. M. Nygaard, *ibid.*, **52**, 4128 (1930); (b) M. Couper and R. E. Lutz, *J. Org. Chem.*, **7**, 79 (1942); (c) H. Gilman, J. E. Kirby and C. R. Kinney, THIS JOURNAL, **51**, 2252 (1929).

[7] (a) R. E. Lutz and W. R. Tyson, *ibid.*, **56**, 1341 (1934); (b) R. E. Lutz and C. J. Kibler, *ibid.*, **61**, 3007 (1939); (c) R. E. Lutz and F. N. Wilder, *ibid.*, **56**, 978 (1934).

addition of *p*-tolylmagnesium bromide to 1,2-dibenzoylethylene and cyclization to form 2,5-diphenyl-3-*p*-tolylfuran, followed by the nitric acid oxidation of the furan to form the ethylene, which should be *cis* by analogy to other such oxidations.[7c] Evidence for the dibenzoyltolylethylene (I) structure, besides the generality of the preparative method, was its reductive cyclization back to the diphenyltolylfuran from which it was made and its reaction which acetic anhydride and sulfuric acid to give an acetoxyfuran, 3-acetoxy-2,5-diphenyl-4-*p*-tolylfuran. Both reactions are characteristic of 1,2-dibenzoylethylene derivatives.[8] It is interesting to note that I completely resisted reduction by means of zinc and acetic acid. In comparison, 1,2-dibenzoyl-1-phenylethylene is easily reduced.

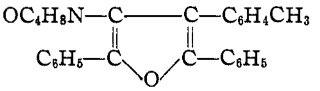
1,2-Dibenzoyl-1-*o*-tolylethane and 2,5-diphenyl-3-*o*-tolylfuran were made by analogous reactions. The nitric acid oxidation[7c] of the latter, however, gave only an oily substance which could not be characterized.

1,2-Dibenzoyl-1-*p*-tolylethylene (I) did not react with morpholine under mild conditions. However, when a solution of the two was refluxed for 60 hours there was obtained a morpholinylfuran as the major product and the corresponding morpholinyldiketone as a minor product. The morpholinyldiketone was cyclized to the morpholinylfuran by means of acetic anhydride and sulfuric acid and was easily deaminated to I by means of hot acetic acid. Upon nitric acid oxidation[7c] the morpholinylfuran gave an unsaturated morpholinyldiketone which, upon ozonolysis followed by hydrogen peroxide oxidation of the product, gave a mixture of benzoic and *p*-toluic acids. These reactions show that the morpholinylfuran is II, the saturated diketone is III and the unsaturated diketone is IV. Therefore the addition of morpholine to I occurred through its α,β-unsaturated ketone system and I did not behave in this reaction as a vinylog of 1,2-dibenzoylpropene.

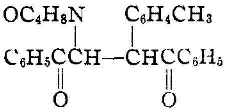


$$C_6H_5\underset{\displaystyle\overset{\|}{O}}{C}CH{=}\overset{\displaystyle C_6H_4CH_3}{\overset{|}{C}}\underset{\displaystyle\overset{\|}{O}}{C}C_6H_5$$

I

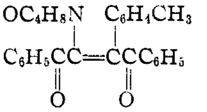


II



$$C_6H_5\underset{\displaystyle\overset{\|}{O}}{C}\overset{\displaystyle OC_4H_8N}{\overset{|}{C}}H{-}\overset{\displaystyle C_6H_4CH_3}{\overset{|}{C}}H\underset{\displaystyle\overset{\|}{O}}{C}C_6H_5$$

III



$$C_6H_5\underset{\displaystyle\overset{\|}{O}}{C}\overset{\displaystyle OC_4H_8N}{\overset{|}{C}}{=}\overset{\displaystyle C_6H_4CH_3}{\overset{|}{C}}\underset{\displaystyle\overset{\|}{O}}{C}C_6H_5$$

IV

Experimental[9]

2,5-Diphenyl-3-*p*-tolylfuran.—To 160 ml. of a well-stirred 1.9 *N* ethereal solution of *p*-tolylmagnesium bromide was added, over a period of 30 minutes, 20 g. of finely divided *trans*-1,2-dibenzoylethylene. After 15 minutes warming, the mixture was poured onto ice and hydrochloric acid. The resulting mixture was extracted with ether and the ether extract was washed, dried and evaporated. The clear yellow residue (34 g.) resisted all crystallization efforts. It was dissolved in 80 ml. of acetic anhydride and 25 drops of concentrated sulfuric acid was added. After five minutes the mixture was poured onto ice and neutralized with sodium carbonate. A gummy solid separated and was crystallized from acetone yielding 15.5 g. (59%) of crystals melting at 125–133°. In another experiment, 6.5 g. of the yellow oil was obtained from 5 g. of dibenzoylethylene. This was molecularly distilled and the distillate (4.2 g.) was partially crystallized from a warm acetone–ethanol mixture, yielding 1.5 g. (23%) of crystals which melted at 127–130° and showed no depression in a mixture melting point with the crystals described above.[10] An analytical sample (from ethanol) melted at 135–136°.

Anal. Calcd. for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 88.97, 89.10; H, 5.91, 5.89.

1,2-Dibenzoyl-1-*o*-tolylethane.—This substance was made by the addition of *o*-tolylmagnesium bromide to 1,2-dibenzoylethylene using the procedure described in the first part of the preceding experiment. The yield was 86% and the melting point was 119–120° after several recrystallizations from ethanol.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 83.82, 83.88; H, 6.02, 6.10.

2,5-Diphenyl-3-*o*-tolylfuran.—A suspension of 2 g. of the *o*-tolylethane in 20 ml. of hydriodic acid (sp. gr. 1.7) was heated with stirring for 17 hours. The hydriodic acid was decanted off and the residual material was crystallized from ethanol solution by the addition of water; 1.8 g. (95%), recrystallized from ethanol–water, m.p. 90–91°. The material was also made in 26% yield by the acetic anhydride–sulfuric acid method and in 40% yield by the acetyl chloride–sulfuric acid method.[8a] The analyses were somewhat low due to an impurity which could not be removed.

Anal. Calcd. for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 88.47, 88.36; H, 5.93, 5.66.

1,2-Dibenzoyl-1-*p*-tolylethylene (I) was made from 2,5-diphenyl-3-*p*-tolylfuran by the general procedure of Lutz and Wilder[7c] using propionic acid solvent at 0° in place of acetic acid at room temperature. The yield of material, melting at 148–149° after several recrystallizations from ethanol, was 79%. The compound decolorized an acetone solution of potassium permanganate.

Anal. Calcd. for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56. Found: C, 84.67, 84.85; H, 5.51, 5.57.

Attempted synthesis of 1,2-dibenzoyl-1-*o*-tolylethylene from 2,5-diphenyl-3-*o*-tolylfuran using the same general[7c] procedure described above at 0° and at −23° gave a resiny material which resisted all crystallization efforts. Similar results were also obtained when 1,2-dibenzoylethylene was treated with *o*-tolylmagnesium bromide and the resulting solution was poured into an ethanol solution of iodine at 0°.

3-Acetoxy-2,5-diphenyl-4-*p*-tolylfuran.—This compound was made from 1,2-dibenzoyl-*p*-tolylethylene (I) by the general method of Lutz.[8a] It was necessary, however, to warm the reaction mixture over a steam-bath for eight minutes. The yield of material, which melted at 139–141° after recrystallizations from ethanol and acetone and molecular distillation, was 88%.

Anal. Calcd. for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.45; H, 5.49.

Reduction of 1,2-Dibenzoyl-1-*p*-tolylethylene (I).—To a warm solution of 4 g. of stannous chloride in 8 ml. of concentrated hydrochloric acid and 6 ml. of glacial acetic acid was added a solution of 1 g. of 1,2-dibenzoyl-1-*p*-tolylethylene in 5 ml. of hot glacial acetic acid. After 15 minutes of reflux the mixture was cooled and filtered, yielding 0.84 g. (88%) of 2,5-diphenyl-3-*p*-tolylfuran (m.p. 132–133°). Catalytic reduction in acetic acid solution using platinum catalyst at atmospheric pressure gave a 30% yield of the furan (m.p. 129–132°). Identifications were by the mixture melting point method.

Attempted reduction with zinc and acetic acid using 1 g. of the ethylene (I) and 10 ml. of acetic acid and refluxing in the presence of zinc dust for 30 minutes gave a 70% recovery of starting material. A similar reduction of 1,2-dibenzoyl-1-phenylethylene using zinc from the same source gave 1,2-

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[8] (a) R. E. Lutz, THIS JOURNAL, **48**, 2916 (1926); (b) R. E. Lutz, L. Love, Jr., and F. S. Palmer, *ibid.*, **57**, 1953 (1935); (c) R. E. Lutz and F. S. Palmer, *ibid.*, **57**, 1957 (1935).

[9] Some of the microanalyses were done by the Microchemical Laboratories of Skokie, Illinois, and by Clark Microanalytical Laboratory of Urbana, Illinois.

[10] It is not unusual to obtain a furan rather than a saturated 1,4-diketone from Grignard additions to dibenzoylethylene derivatives. See reference 7b.

dibenzoyl-1-phenylethane (m.p. 124–126°)[11] after five minutes reflux; no starting material was recovered.

3-(4-Morpholinyl)-2,5-diphenyl-4-*p*-tolylfuran (II).—A mixture of 45 g. of 1,2-dibenzoyl-1-*p*-tolylethylene and 250 ml. of morpholine was refluxed for 60 hours. The morpholine was evaporated by a stream of air and the residue was crystallized from ethanol. The first batch of crystals weighed 24 g. (42%) and melted at 195–197°. An analytical sample (from ethanol) melted at 199–200°.

Anal. Calcd. for $C_{27}H_{25}NO_2$: C, 81.99; H, 6.37; N, 3.54. Found: C, 82.18; H, 6.71; N, 3.71.

From the preceding experiment there was also obtained a second batch of crystals which melted at 150–180° and weighed 22 g. Tedious fractional recrystallizations from ethanol gave small amounts of I and II. When II in the mixture was destroyed by nitric acid oxidation[7c] it was possible to isolate, by fractional recrystallization (ethanol) of the resulting mixture, a small amount of material melting at 180–181° which was subsequently shown to be 1,2-dibenzoyl-1-(4-morpholinyl)-2-*p*-tolylethane (III).

Anal. Calcd. for $C_{27}H_{27}NO_3$: C, 78.42; H, 6.58. Found: C, 78.26; H, 6.45.

The relationship of this material (III) to 3-(4-morpholinyl)-2,5-diphenyl-4-*p*-tolylfuran (II) was shown by conversion of the diketone to the furan upon treatment with acetic anhydride and sulfuric acid[8a] and the relationship of the morpholinyldiketone (III) to 1,2-dibenzoyl-1-*p*-tolylethylene (I) was shown by the conversion of the former to the latter by treatment with hot acetic acid.

1,2-Dibenzoyl-1-(4-morpholinyl)-2-*p*-tolylethylene (IV).—To a suspension of 22 g. of 3-(4-morpholinyl)-2,5-diphenyl-4-*p*-tolylfuran in 125 ml. of glacial acetic acid was added a solution of 25 ml. of nitric acid and 75 ml. of acetic acid. After the mixture had stood for five minutes, it was poured onto cracked ice. Twenty-four grams (91%) of yellow crystals melting at 140–145° was obtained. An analytical sample (from ethanol) melted at 157–158°. The material was subsequently shown to be the nitrate of 1,2-dibenzoyl-1-(4-morpholinyl)-2-*p*-tolylethylene.

Anal. Calcd. for $C_{27}H_{26}N_2O_6$: C, 68.34; H, 5.52. Found: C, 68.56; H, 5.59.

Treatment of 10 g. of the crude nitrate with ether and ammonium hydroxide converted it to 9 g. of the free base which was obtained upon evaporation of the ether. The material melted at 123–124° after several recrystallizations from isopropyl alcohol.

Anal. Calcd. for $C_{27}H_{25}NO_3$: C, 78.80; H, 6.12. Found: C, 79.03, 78.64; H, 6.26, 6.08.

The morpholinyldiketone was converted to its nitrate by treatment with dilute nitric acid. Identification was by the mixture melting point method. The free amine was also converted to a hydrochloride by treatment with ethereal hydrogen chloride. The melting point after several recrystallizations from ethanol was 196–197°.

Anal. Calcd. for $C_{27}H_{26}ClNO_3$: C, 72.39; H, 5.85. Found: C, 72.69; H, 5.73.

In order to show the relationship between the morpholinylfuran (II) and the morpholinylethylene (IV) the latter was reduced by means of zinc and acetic acid and the product was treated with acetic anhydride and sulfuric acid which constitutes cyclizing conditions.[8a] The products were the morpholinylfuran (II) (m.p. 193–195°) and 2,5-diphenyl-3-tolylfuran (m.p. 125–130°). The former was separated from the latter by means of its solubility in dilute hydrochloric acid. Identifications were by the mixture melting point method.

Proof of Structure of 1,2-Dibenzoyl-1-(4-morpholinyl)-2-*p*-tolylethylene.—Ozonolysis of 4 g. of morpholinylethylene was carried out in carbon tetrachloride solution. The ozonide was decomposed with water and the carbon tetrachloride solution was extracted first with sodium carbonate solution and then with dilute hydrochloric acid. From the sodium carbonate extract 0.1 g. of benzoic acid was obtained and from the hydrochloric acid extract only a slight residue was obtained upon neutralization, extraction with ether and evaporation of the ether extract. Evaporation of the carbon tetrachloride solution gave a yellow oily material which completely resisted crystallization, except for 0.1 g. of material melting at 235–240° which was obtained from acetone and which was not given study. On the basis that the yellow oil was an impure benzil type compound it (3 g.) was treated with 10 ml. of 40% sodium hydroxide solution and 10 ml. of 30% hydrogen peroxide solution. Heat was evolved. After three hours the solution was neutralized with hydrochloric acid and filtered. The colorless crystals thus obtained weighed 2 g. and melted at 97–135°. Tedious fractional recrystallizations from water gave 0.3 g. of *p*-toluic acid (m.p. 178–181°) and 0.6 g. of benzoic acid (m.p. 115–120°). Identifications were by mixture melting points with authentic samples.

Acknowledgment.—The authors gratefully acknowledge a grant-in-aid from the Research Corporation, New York, N. Y., which helped make this work possible.

AUSTIN, TEXAS RECEIVED DECEMBER 26, 1950

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[11] Lutz, THIS JOURNAL, **51**, 3020 (1929).