TABLE I

PERCENTAGES OF ALANINE AND GLYCINE IN SILK FIBROIN[a]

Amino acid			Alanine	Glycine
Analysis of filter paper chromatograms	Indirect photometric, Polson *et al.*[2]		37.6	39.9
	Direct	Visual Polson, *et al.*[2]	34.0	42.4
		Photometric, authors	34.9	43.4
Selective pptn., Bergmann and Niemann,[21]			26.4	43.8
Microbiological, Shankman, *et al.*[20]			..	43.6

[a] Corrected for moisture and ash.

The data obtained for glycine and alanine in silk fibroin are given in Table I. It may be noted that the value (43.4%) found for glycine in silk fibroin is in good agreement with the values (39.9 to 43.8%) reported by earlier workers who used microbiological,[20] selective precipitation[21] and analogous photometric-chromatographic[2] procedures. Although the value 34.9% found for alanine is in good agreement with the values, 34.0 and 37.6%, reported by Polson, *et al.*,[2] it is much higher than the value of 26.4%, obtained by Bergmann and Niemann.[21]

Summary

A method has been described for the quantitative determination of amino acids on filter paper chromatograms by direct photometry. It has been found by this method that silk fibroin contained 43.4 per cent. of glycine and 34.9 per cent. of alanine. These values are in good agreement with others given in the literature.

[20] Shankman, Camien and Dunn, *J. Biol. Chem.*, **168**, 51 (1947).

[21] Bergmann and Niemann, *ibid.*, **122**, 577 (1937-1938).

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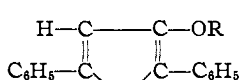
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

The Transetherification of 3-Alkoxy-2,5-diphenylfurans[1]

BY PHILIP S. BAILEY AND JOHN D. CHRISTIAN

The conversions of 3-methoxy- and 3-ethoxy-2,5-diphenylfurans (I), one into the other, in solutions of the opposite alcohol, triethylamine hydrochloride and a trace of hydrogen chloride was reported in an earlier paper.[2] In the present paper is described a further study of this reaction which might be termed a transetherification[1b] by comparison to the corresponding transesterification reaction which esters undergo. Both employ an acid catalyst and both involve the displacement of an alkoxy group directly attached to an unsaturated grouping.



I (a) $R = CH_3$
(b) $R = C_2H_5$
(c) $R = C_3H_7\text{-}n$
(d) $R = C_4H_9\text{-}n$
(e) $R = C_4H_9\text{-}i$
(f) $R = -\underset{\underset{O}{\|}}{C}-CH_3$

Concerning the minimal conditions necessary for the reaction, it was found in the study that the hydrogen chloride was essential, whereas the amine hydrochloride was not. No conversion was observed in the absence of the hydrogen chloride even though the amine hydrochloride was present. Under the opposite conditions, conversion did occur, but in poorer yield than when both reagents were present. In all subsequent runs, therefore, both reagents were used.

The reaction using 3-methoxy-2,5-diphenylfuran was found to occur with ethanol, *n*-propyl alcohol, *n*-butyl alcohol and isobutyl alcohol. The yields varied from 68 to 55%. Isopropyl alcohol and *t*-butyl alcohol gave no reaction, and *s*-butyl alcohol, *n*-amyl alcohol and isoamyl alcohol gave principally non-crystalline products which are assumed to be of a different nature, since the corresponding alkoxyfurans should be crystalline by comparison to the others known.[3] Transetherifications of alkoxyfurans of higher molecular weight to alkoxyfurans of lower molecular weight were also carried out.

The alcoholysis reaction was extended also to 3-acetoxy-2,5-diphenylfuran, using methanol and *n*-propanol. Isopropyl alcohol, *n*-butyl alcohol and isobutyl alcohol reacted differently to yield oils plus a dimolecular oxidation product, 2,2'-bis-(2,5-diphenylfuranone-3).[4] The reaction failed with 3-(4-morpholinyl)-2,5-diphenylfuran (II) and, as reported earlier,[2] with 3-chloro-2,5-diphenylfuran. All of the above described transformations are listed in Table I.

From the viewpoint of synthesis of alkoxyfurans, the alcoholysis of 3-methoxy-(or 3-ethoxy-) and 3-acetoxy-2,5-diphenylfurans is of limited value. However, since only 3-methoxy- and 3-ethoxy-2,5-diphenylfurans can be made from 1,2-dibenzoyl-1,2-dibromoethane,[2,5,6] these transfor-

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[1] (a) From the M. A. Thesis of J. D. Christian, January, 1949. (b) Since the paper was accepted for publication, similar transetherification reactions have been reported with different systems: see Croxall, Van Hook and Luckenbaugh, THIS JOURNAL, **71**, 2736 (1949), and Ogata and Okano, *ibid.*, **71**, 3211 (1949).

[2] Bailey and Kelly, THIS JOURNAL, **70**, 3442 (1948).

[3] Melting points: Me, 114-115°, Et, 94-95°, Pr, 86-87°, iso-Pr, 87-88°, Bu, 60-61°, iso-Bu, 71-72°.

[4] Previously reported by Lutz, McGinn and Bailey, THIS JOURNAL, **65**,843 (1943); and Kohler and Woodward, *ibid.*, **58**, 1933 (1933).

[5] Bailey and Lutz, *ibid.*, **69**, 498 (1947).

[6] Conant and Lutz, *ibid.*, **47**, 881 (1925).

mations constitute the best known method for the cases applicable. Very poor yields are obtained from the addition of alcohols to 1,2-dibenzoylethylene.[2,5]

It is interesting to note that under the conditions of the transetherification reaction the purely aliphatic, unsaturated alkyl vinyl ethers undergo addition[7] and the purely aromatic anisole (III) gives no reaction. Other alkoxyunsaturates, in between these two extremes as far as stability of the unsaturated nucleus is concerned, should, like the alkoxydiphenylfurans (I), react by displacement. This displacement perhaps occurs by an addition mechanism similar to that of the transesterification reaction. Such a mechanism has previously been suggested for the etherification of β-naphthol by alcoholic hydrogen chloride.[8]

The similarity between the alkoxyfurans (I) and esters does not extend too well to other reactions. No reaction was observed between 3-methoxy-2,5-diphenylfuran and ammonia (in methanolic solution) or hot morpholine. Hydrolysis occurred, however, when the methoxyfuran was refluxed with 6 *N* hydrochloric acid. The product was 2,2′-bis-(2,5-diphenylfuranone-3)[4] (IV), presumably formed by the oxidation of 3-hydroxy-2,5-diphenylfuran.

The characteristic nitric acid oxidation of Lutz and Wilder[9] has been carried over to several 3-alkoxy-2,5-diphenylfurans in order to facilitate identification.

Experimental[10]

Typical Experiment. Reaction of 3-Methoxy-2,5-diphenylfuran with Ethanol.—A solution of 1 g. of 3-methoxy-2,5-diphenylfuran, 1 g. of triethylamine hydrochloride, 30 ml. of ethanol (distilled from sodium ethoxide) and enough ethanolic hydrogen chloride to give an indicated *p*H of 2 (*p*-Hydrion paper) was refluxed for thirty hours, during which time the *p*H was maintained at 2–3. The solution was evaporated to dryness, the residue was extracted with ether and the ether extract was washed and evaporated. Crystallization of the residue from ethanol gave 0.7 g. (66% yield) of 3-ethoxy-2,5-diphenylfuran (m. p. 90.5–92.5°; identified by a mixture melting point with an authentic sample).[5] A red viscous oil remained.

When the triethylamine hydrochloride was omitted, everything else remaining the same, only a 33% yield of the ethoxyfuran was obtained. No reaction was obtained when the hydrogen chloride was omitted and the triethylamine hydrochloride was present (80% recovery of methoxyfuran plus an intractable oil) nor when both the hydrogen chloride and triethylamine hydrochloride were omitted (96% recovery of methoxyfuran).

Attempted reaction of 3-methoxy-2,5-diphenylfuran with morpholine (1 g. of furan and 40 ml. of morpholine for thirty hours at 70°) gave a 87% recovery of the methoxyfuran (m. p. 112–114°, identified by a mixture melting point) and a red oil. A similar reaction with a saturated methanolic solution of ammonia (1 g. furan, 80 ml. solution) was attempted for eight days at room temperature. The recovery of methoxyfuran was 99%.

Acid Hydrolysis of 3-Methoxy-2,5-diphenylfuran.—A mixture of 1 g. of the 3-methoxyfuran and 50 ml. of 6 *N* hydrochloric acid was refluxed with stirring for thirty hours. The mixture was evaporated to dryness by a stream of air, the residue was treated with ether, and the resulting mixture was filtered. On the filter paper was obtained 0.33 g. (34% yield) of 2,2′-bis-(2,5-diphenylfuranone-3) which melted at 243–246° and was identified by a mixture melting point with an authentic sample.[4] Evaporation of the ether extract gave an oil which resisted crystallization.

TABLE I

Reactants[a]	Products	Yield, %
Ia + ethanol	Ib	66
Ia + *n*-propyl alcohol	Ic	55[b]
Ia + *n*-butyl alcohol	Id	67[c]
Ia + isobutyl alcohol	Ie	68[d]
Ia + isopropyl alcohol	Ia	95
Ia + *s*-butyl alcohol	Ia	33[e]
Ia + *t*-butyl alcohol	Ia	96
Ia + *n*-amyl alcohol[f]	Oil[e]	...
Ia + 3-methyl-1-butanol[f]	Ia	10[e]
Id + ethanol	Ib	84[g]
Ie + methanol	Ia	76[h]
If[i] + methanol	Ia	96
If + *n*-propyl alcohol[f]	Ic	55[e,j]
If + isopropyl alcohol	IV[k]	20[e]
If + *n*-butyl alcohol[f]	IV[k]	20[e]
If + isobutyl alcohol[f]	IV[k]	10[e]
III[l] + ethanol	III[l]	56[m]
II[n] + ethanol	II[n]	85[e]

[a] Conditions were as described in the typical experiment. The reaction time was always thirty hours, the corresponding alcoholic hydrogen chloride solution was used and triethylamine hydrochloride was present. The alcohols were made anhydrous by distillation from the corresponding sodium alkoxide. Temperatures were the reflux temperature except where otherwise indicated. The reactions were worked up as described in the typical experiment. All products were identified by mixture melting points with authentic samples. [b] M. p. 83–84°, see ref. 2. [c] Recryst. from isopropyl alcohol and from ethanol, m. p. 60–61°. *Anal.* Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.90. Found: C, 82.07, H, 7.09. [d] M. p. 70–72°, see ref. 2. [e] A red viscous residue remained which resisted all crystallization efforts. [f] The temperature was 85–95°. [g] A 14% recovery of the *n*-butoxyfuran also was obtained. [h] A 20% recovery of the isobutoxyfuran also was obtained. [i] Prepared by the method of Lutz.[11] [j] A 6% yield of 2,2′-bis-(2,5-diphenylfuranone-3) (IV) also was obtained. See reference 4. [k] 2,2′-Bis-(2,5-diphenylfuranone-3), m. p. 245–250°; see reference 4. [l] Anisole. [m] Identified through the sulfonamide (m. p. 108–109°; no sulfonamide of phenetole (m. p. 149–150°) was isolated).[12] [n] 3-(4-Morpholinyl)-2,5-diphenyl-furan.

The nitric acid oxidation of **3-methoxy-2,5-diphenylfuran** was carried out by the general method of Lutz and Wilder[9] in acetic acid medium at room temperature. The yield of known 1,2-dibenzoyl-1-methoxyethylene, which, incidentally, must be the *cis* isomer,[9] was 14% (m. p. 103–106°, identified by a mixture melting point with a known sample[6]). A red oil also was obtained.

The nitric acid oxidation[9] of **3-ethoxy-2,5-diphenylfuran** was carried out in propionic acid at 0° for ten minutes. The yield of *cis*-1,2-dibenzoyl-1-ethoxyethylene (m. p. 97–100°, identified by a mixture melting point with an authentic sample[6]) was 78%. The lower temperature apparently accounts for the improved yield over that of the preceding experiment.

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[7] For a review of the chemistry of alkyl vinyl ethers see Schildknecht, Zoss and McKinley, *Ind. Eng. Chem.*, **39**, 180 (1947).

[8] (a) Davis, *J. Chem. Soc.*, **77**, 33 (1900); (b) Fieser and Lothrop, THIS JOURNAL, **57**, 1459 (1935).

[9] Lutz and Wilder, *ibid.*, **56**, 978 (1934).

[10] All melting points are corrected.

[11] Lutz, THIS JOURNAL, **48**, 2916 (1926).

[12] See Procedures I and A of Huntress and Carten, *ibid.*, **62**, 511, 603 (1940), for directions for preparation of the sulfonamides.

cis-**1,2-Dibenzoyl-1-*n*-propoxyethylene** was prepared from 2,5-diphenyl-3-*n*-propoxyfuran by the general method[9] described in the experiment just preceding. After several recrystallizations from ethanol and isopropyl alcohol the material melted at 72–73°; the yield was 77%.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.17. Found: C, 77.18; H, 6.16.

The propoxyethylene was converted back to the furan by reduction with zinc and acetic acid.[6]

cis-**1,2-Dibenzoyl-1-isopropoxyethylene** was prepared from 2,5-diphenyl-3-isopropoxyfuran[5] in propionic acid at 0° by the general method[9] described above. The yield of material melting at 108–109° after recrystallization from isopropyl alcohol was 78%.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.17. Found: C, 77.74; H, 6.44.

Zinc and acetic acid reduction[6] converted the material back to the furan from which it was made.

The difference in melting points between 1,2-dibenzoyl-1-*n*-propoxyethylene and 1,2-dibenzoyl-1-isopropoxyethylene makes them easily distinguished. Thus the corresponding furans can easily be distinguished through these derivatives. They are otherwise difficult to differentiate between, since the isopropoxyfuran melts at 87–88°, the *n*-propoxyfuran at 86–87° and the mixture melting point between the two is 82–85°.

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Summary

1. 3-Alkoxy-2,5-diphenylfurans have been found to undergo alcoholysis, termed transetherification, under acidic conditions.

2. A comparison is made of transetherification, transesterification and the addition of alcohols to alkyl vinyl ethers.

3. The nitric acid oxidation of 2,5-diarylfurans to *cis*-1,2-diaroylethylenes has been extended to 3-alkoxy-2,5-diphenylfurans.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF WISCONSIN]

A Glyco-lipide Produced by *Pseudomonas Aeruginosa*[1]

BY F. G. JARVIS[2] AND M. J. JOHNSON

Several crystalline compounds[3,4,5,6,7] and at least two partially purified oils[8,9] have been isolated from *Pseudomonas aeruginosa* cultures. These materials have been primarily investigated with respect to their antibacterial activity. With the exception of pyocyanin,[3,4] none of these metabolic products have been fully characterized. The isolation and investigation of the structure of an acidic, crystalline glyco-lipide produced by *P. aeruginosa* is described in this paper. The compound contains the same structural units (L-rhamnose and *l*-β-hydroxydecanoic acid) as the oil isolated by Bergström, *et al.*,[9] but has a higher molecular weight and a higher rhamnose–hydroxyacid ratio. It is quite possible that the compound is identical to the crystalline material isolated by Birch-Hirschfeld[6] but insufficient data are available for suitable comparison. Our compound was found to be bacteriostatic to *Mycobacterium tuberculosis* H37 Rv in a concentration of about 0.5 mg. per ml. of culture medium. Five mg. given introperitoneally to mice killed in about sixteen hours.[10]

Isolation.—The organism was grown on a 4% Difco peptone–3% glycerol broth at 30° on a reciprocating shaker. Cultures were harvested after from four to five days growth. The acid was produced by each of three strains of *P. aeruginosa* tested (University of Washington strains no. 141, 142, 261). The one strain of *P. florescens* tested failed to produce the compound. Yields as high as 2.5 g. per liter were obtained. The crystalline acid was not produced (or could not be isolated by our procedure) when the peptone was replaced by tryptone or the glycerol replaced by glucose in the growth medium.

The compound was obtained in crystalline form by acidifying the whole culture to *p*H 2 with sulfuric acid and refrigerating for two or three days. The crystals were collected on very coarse filter paper, taken up in a small volume of ethyl ether (insoluble residues discarded) and precipitated by addition of petroleum ether. After the removal of solvent by decantation and evaporation, the precipitate was dissolved in dioxane and crystallized by adding water and chilling. The material could be recrystallized in the cold by acidifying water solutions of its sodium salt or by adding water to dioxane or acetone solutions of the free acid.

Properties.—The compound crystallizes in the form of thin, colorless rectangular platelets. It is very soluble in ether, ethyl alcohol, acetone, dioxane and dilute sodium bicarbonate solution. It is nearly insoluble in water and petroleum ether. The compound (m. p. 86°, $\alpha_D = -84°$, 3% in chloroform) has a neutral equivalent of about 665. Molecular weight determinations by the Rast method gave a value of about 650.

Anal.[11] Calcd. for $C_{32}H_{58}O_{14}$: C, 57.64; H, 8.77. Found: C, 57.62; H, 8.74.

Other data (see below) indicate that the true formula is $C_{32}H_{60}O_{14}$. Quantitative acetylation of the material showed 4.3 hydroxyl groups per mole; however, chromatographic analysis of the acetylated material gave three acidic bands indicating either incomplete acetylation or decomposition during the reaction. The chromatographic

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(1) Published with the approval of the Director of the Wisconsin Experiment Station.

(2) National Institute of Health Predoctorate Research Fellow.

(3) F. Wrede and E. Strack, *Ber.*, **62B**, 2051 (1929).

(4) H. Hillemann, *ibid.*, **71B**, 46 (1938).

(5) S. Hosoya, *Compt. rend. soc. biol.*, **99**, 771 (1928).

(6) L. Birch-Hirschfeld, *Z. Hyg. Infektionsrank.*, **116**, 304 (1935).

(7) E. E. Hays, *et al.*, *J. Biol. Chem.*, **159**, 725 (1945).

(8) R. Schoental, *Brit. J. Exp. Path.*, **22**, 137 (1941).

(9) S. Bergström, H. Theorell and H. Davide, *Arkiv Kemi Mineral. Geol.*, **23A**, No. 13 (1947).

(10) The authors are indebted to Dr. Russell S. Weiser, University of Washington, for the antibiotic and mouse toxicity tests.

(11) The carbon-hydrogen analyses were performed by the Clarke Microanalytical Laboratory, Urbana, Illinois.