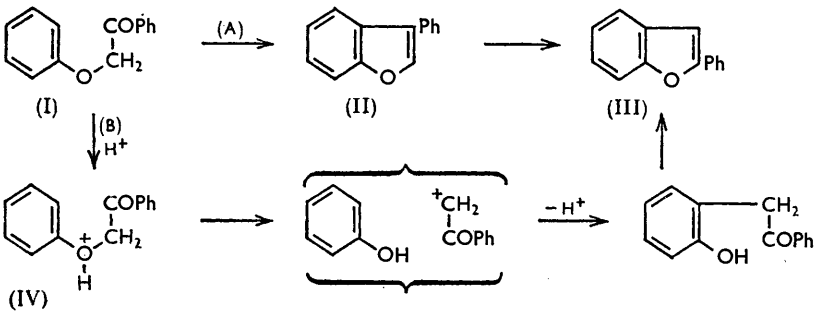
711. *Cyclodehydration Processes. Part II.* Migration of a Phenyl Group during Cyclisation of ω-Phenoxyacetophenone.*

By W. Davies and S. Middleton.

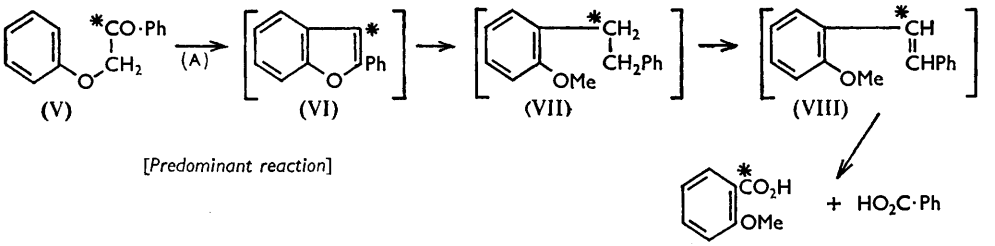
The use of a ^{14}C has shown that formation of 2-phenylbenzofuran during cyclisation of ω-phenoxyacetophenone with polyphosphoric acid at 132° is due to rearrangement of the normal cyclisation product, 3-phenylbenzofuran. The mechanism of this rearrangement is discussed.

In Part I * it was shown that cyclising ω-phenoxyacetophenone (I) by polyphosphoric acid at 80° for 3½ hr. gave an 82% yield of 3-phenylbenzofuran (II), but 132° for 2 hr. gave a 71% yield of 2-phenylbenzofuran (III); a mixture of the two was obtained at 110° in 2 hr. Further, since the 3- was rearranged to the 2-phenyl compound in 80% yield when heated with polyphosphoric acid at 132° for 2 hr., it was suggested that in condensations



the higher temperatures the latter was formed by rearrangement of the former (mechanism A). However, an alternative mechanism (B) involves fission between the oxygen atom and the CH_2 group [which could well occur if the oxonium salt (IV) was initially formed]. It was decided to distinguish between these mechanisms by use of [^{14}C].

ω-Phenoxy[*carbonyl*-^{14}C]acetophenone (V) was prepared from [1-^{14}C]acetyl bromide by standard procedures and treated with polyphosphoric acid at 132° for 3 hours, to give



predominantly compound (VI). This was reduced with sodium and ethanol to *o*-hydroxybibenzyl, which with methyl iodide gave the *o*-methoxy-compound (VII). Bromination with *N*-bromosuccinimide, followed by dehydrobromination with triethylamine, then gave *o*-methoxystilbene (VIII) which was oxidised with potassium permanganate to a mixture of benzoic and *o*-methoxybenzoic acid.

In this sequence mechanism A would give inactive benzoic and active *o*-methoxybenzoic acid, and mechanism B would give active benzoic and inactive *o*-methoxybenzoic acid.

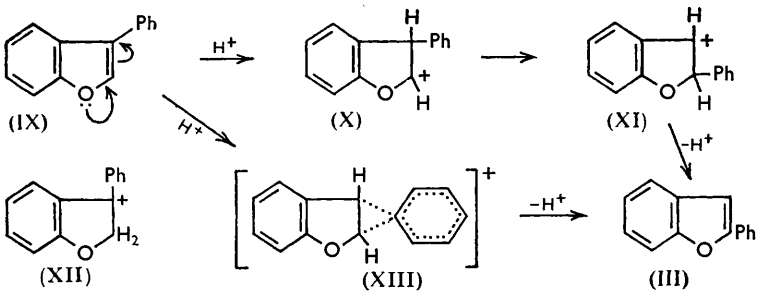
The mixed acids were treated with *p*-phenylazophenacyl bromide, and the azo-esters separated by chromatography. The benzoic ester contained only 0·3% of the combined

* Part I, *J.*, 1958, 822.

activities of both esters. Thus, under the conditions used, $\gtrsim$0·3% of the 2-phenylbenzofuran can be formed by mechanism B or other mechanism not involving migration of the phenyl group.

The rearrangement of 3- to 2-phenylbenzofuran is apparently acid-catalysed since the 3-phenyl compound is not rearranged when heated alone; the reaction may be initiated by proton attack on the benzofuran nucleus. Since benzofuran undergoes electrophilic attack predominantly at the 2-position,[1] it would be expected that proton attack on 3-phenylbenzofuran would afford the carbonium ion (XII). This, however, would not be expected to rearrange, so reaction should not proceed further.

It is probable, however, that some proton-attack would take place at the 3-position (cf. IX). If the resulting carbonium ion had the classical structure (X), it could rearrange to the ion (XI) which could yield 2-phenylbenzofuran by loss of a proton. Alternatively,



Although the steps are represented as irreversible, this need not necessarily be so.

if the intermediate were the synartetic ion (XIII), it could rearrange to the 2-phenylbenzofuran by elimination of a proton. Rearrangements involving these types of intermediate are common; for example, carbonium ions similar to (X) and (XI) are involved in the formation of rearranged products during the deamination of 2-amino-1,1-diphenylpropan-1-ol,[2] and a bridged phenonium ion similar to (XIII) precedes formation of 1-phenylcyclohexene from *trans*-2-phenylcylohexanol.[3] The driving force for the rearrangement doubtless arises from the fact that isomer (III) is more conjugated than (II); that rearranged products have so far not been isolated during the cyclisation of compounds with an aliphatic side chain may be due to the absence of any marked difference between the degrees of conjugation of isomeric 2- and 3-alkylbenzofurans.

Experimental

ω-Phenoxy[carbonyl-^{14}C]*acetophenone* (V).—[1-^{14}C]Acetyl bromide (0·05 mc.), diluted with freshly distilled inactive material (5·0 ml.) was added dropwise during 10 min. to a stirred suspension of powdered aluminium bromide (23 g.) in dry benzene (20 ml.). The mixture was refluxed for 1 hr., cooled, decomposed with ice, and extracted with ether. The dried ($MgSO_4$) ether layer was evaporated on the steam-bath, the residue diluted with a " chaser " (15 ml. of α-bromonaphthalene), and the labelled acetophenone distilled at 90—91°/19 mm. (5·35 g., 67%). Bromination of an ether solution of this acetophenone by the method of Cowper and Davidson [4] gave [α-^{14}C]phenacyl bromide (82%) which with phenol (as described in Part I) gave ω-phenoxyacetophenone (V), m. p. 72·5—73° (73%).

Cyclisation.—The labelled compound was stirred with 10 parts of polyphosphoric acid (prepared as described in Part I) at 132° for 3 hr., after which the mixture was treated as described in Part I to give the labelled 2-phenylbenzofuran (VI), m. p. 120—121° (75%).

Labelled 2-Methoxystilbene (cf. VII).—2-Phenylbenzofuran (VI) was reduced with sodium

[1] Hartough and Meisel, " Compounds with Condensed Thiophene Rings," Interscience, New York, 1954.
[2] Benjamin, Schaeffer, and Collins, *J. Amer. Chem. Soc.*, 1957, **79**, 6160.
[3] Schaeffer and Collins, *ibid.*, 1956, **78**, 125.
[4] Cowper and Davidson, *Org. Synth.*, 1939, **19**, 24.

and ethanol by the method of Stoermer and Reuter [5] to *o*-hydroxybibenzyl, m. p. 83—84° (43%), which with methyl iodide (10 mol.) and potassium carbonate in boiling acetone gave the methoxy-compound (VII), b. p. 180—184°/18 mm. (93%).

o-Hydroxybibenzyl, like the *m*-hydroxy-compound,[6] could not be methylated by diazomethane.

Labelled 2-Methoxystilbene (VIII).—The bibenzyl derivative (0·81 g.) was refluxed with *N*-bromosuccinimide (0·68 g.) and benzoyl peroxide (10 mg.) in dry carbon tetrachloride (50 ml.) for 3 hr., cooled, and filtered to remove succinimide. Excess of triethylamine (2 ml.) was then added, and the mixture refluxed for 10 min., cooled, filtered to remove triethylamine hydrobromide, and evaporated. The residue was extracted with 1 : 1 benzene–light petroleum (b. p. 40—60°), and the extract chromatographed on silica with the same solvent mixture as developer. The fraction with blue fluorescence in ultraviolet light was collected and evaporated, to give the pale yellow stilbene derivative, m. p. 60—62° (0·68 g., 85%).

Oxidation. The stilbene (0·68 g.) was refluxed with potassium permanganate (4·5 g.) for 15 min. in acetone (50 ml., previously treated with permanganate) and water (30 ml.). The mixture was then diluted with water and acidified with concentrated hydrochloric acid, and solid sodium sulphite added to remove manganese dioxide. An ether extract of the resultant solution was extracted with sodium carbonate solution, which, after acidification with hydrochloric acid, yielded to methylene chloride the mixed acids as a pale brown solid.

During preliminary experiments with inactive material, it was found that neither *o*-hydroxy- nor *o*-methoxy-bibenzyl could be satisfactorily oxidised by chromic oxide–acetic acid, or acid, neutral or alkaline potassium permanganate.

p-*Phenylazophenacyl Bromide.*—*p*-Aminoacetophenone [7] (1 mol.) and nitrosobenzene (1 mol.) in glacial acetic acid overnight gave *p*-phenylazoacetophenone as orange-red plates (from ethanol), m. p. 114—115° (lit.,[8] m. p. 114·5—116°). Bromination in acetic acid [9] then gave the bromo-compound (54%) as red-orange prisms, m. p. 103—104° (lit., m. p. 104—105° [10], 92° [11], 103° [12], 104—105° [9]).

Separation of the Mixed Acids.—The mixed acids obtained by oxidation as above were dissolved in 10% sodium hydroxide solution (50 ml.), and the mixture made just acid to Cresol Red by addition of dilute sulphuric acid. A hot solution of *p*-phenylazophenacyl bromide (2·0 g.) in ethanol (150 ml.) was then added, the mixture refluxed for 1 hr. and cooled, and the resultant orange crystals were filtered off. After drying, these were chromatographed in benzene on silica, with benzene as developer.

Three distinct bands separated. The first, a narrow orange-red band, was readily eluted from the column; evaporation of the eluant gave an orange solid of indefinite m. p. which was rejected since it gave a positive Beilstein–Welch test for halogen and so presumably contained some unchanged *p*-phenylazophenacyl bromide. The second, orange band was broad and was also readily eluted by benzene. Evaporation of the eluant gave *p*-phenylazophenacyl benzoate, orange needles (from ethanol), m. p. and mixed m. p. 171—172° (Sugiyama *et al.*[12] report m. p. 169—169·5°).

The third, red-orange band was also broad but moved much more slowly. It was readily eluted, however, by benzene–ethyl acetate (10 : 1). Evaporation gave p-*phenylazophenacyl* o-*methoxybenzoate*, orange plates (from ethanol), m. p. and mixed m. p. 117—118° (Found: C, 70·5; H, 5·0; N, 7·7. $C_{22}H_{18}O_4N_2$ requires C, 70·6; H, 4·8; N, 7·5%).

Determination of Activities.—Infinitely thick samples of the separated azo-esters were counted under the same geometrical conditions with an end-window Geiger–Müller counter. Counting rates (per minute) and σ values were: background 10·2, 0·18; background + benzoic ester 12·4, 0·19; background + *o*-methoxybenzoic ester, 1056, 4·2. Thus, R = (activity of benzoic ester)/(total activity of both esters) = $(12{\cdot}4 - 10{\cdot}2)/[(12{\cdot}4 - 10{\cdot}2) + (1056 - 10{\cdot}2)] = 0{\cdot}0021$, and $\sigma_R = 0{\cdot}0025$. Thus, with a certainty of 0·99, $R = 0{\cdot}0021 \pm 0{\cdot}00075$, *i.e.*, the benzoic ester contains $> 0{\cdot}3\%$ of the total activity of both esters.

[5] Stoermer and Reuter, *Ber.*, 1903, **36**, 3982.
[6] Brunn, *Kgl. norske Videnskab. Selskab. Forhandl.* 1950, No. 4; *Chem. Abs.*, 1953, 11163.
[7] Kunckell, *Ber.*, 1900, **33**, 2641.
[8] Angeli, *Atti R. Accad. Lincei*, 1915, **24**, 1187.
[9] Ikeda, Webb, and Kepner, *Analyt. Chem.*, 1954, **26**, 1228.
[10] Schmid and Leyman, *Helv. Chim. Acta*, 1950, **33**, 1494.
[11] Masuyama, *J. Chem. Soc. Japan, Pure Chem. Sect.*, 1950, **71**, 402.
[12] Sugiyama, Harada, Mita, and Ueno, *ibid.*, 1951, **72**, 152.

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CHEMISTRY DEPARTMENT, UNIVERSITY OF MELBOURNE,
CARLTON, N.3, AUSTRALIA. [*Received, April 27th,* 1959.]