

## The Photochemistry of Acetylsalicylic Acid

By S. T. REID and G. SUBRAMANIAN

(Chemical Pharmacology, Experimental Pharmacology Division, Institute of Physiology, The University, Glasgow)

IRRADIATION of phenyl acetate in ethanol has been reported<sup>1</sup> to give *o*- and *p*-hydroxyacetophenone by a photochemical process analogous to a Fries rearrangement. Phenol was also isolated. We report the results of an examination of the photochemistry of acetylsalicylic acid (aspirin) and certain related substances.

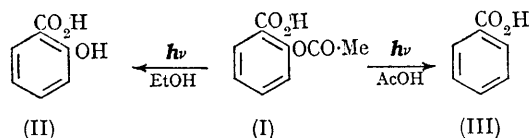
An ethanolic solution (1 mg. per ml.) of acetylsalicylic acid (I) was irradiated in a Hanovia quartz photochemical reactor with a medium-pressure mercury arc until the original ester-carbonyl band ( $\nu_{\max}$  1760  $\text{cm}^{-1}$ ) in the infrared spectrum had disappeared. Salicylic acid<sup>2</sup> (II) (80%) was isolated after chromatography on silica gel, together with a small amount of recovered acetylsalicylic acid (5%). There was no evidence for the formation of any product arising *via* a photochemically-induced Fries rearrangement, although acetylsalicylic acid is known to undergo a normal Fries rearrangement with aluminium chloride.<sup>3</sup> Partial hydrolysis of acetylsalicylic acid by ultraviolet light has been previously reported<sup>4</sup> in aqueous solution at 33°C; hydrolysis of acetylsalicylic acid is also known<sup>5</sup> to take place slowly in the presence of water by an intramolecular process.

Similar photochemical transformations were observed for *m*- and *p*-acetoxybenzoic acid, and, in all three cases, control reactions in the dark gave complete recovery of starting material.

The inability of these substances to undergo a photochemical Fries rearrangement is probably due to the presence of the carboxylic acid grouping. Furthermore, *o*-methoxybenzoic acid gave only salicylic acid (80%) and recovered starting material (10%) on irradiation in either ethanol or acetic acid solution, although other phenolic

ethers are known to undergo photochemical rearrangement to *o*- and *p*-substituted phenols.<sup>6,7</sup>

On irradiation of acetylsalicylic acid in acetic acid solution under identical conditions, a novel photochemical cleavage occurred to give benzoic acid (III) (80%). Benzoic acid (15%) was also isolated in addition to salicylic acid (70%) by the irradiation of acetylsalicylic acid in ethanol solution containing concentrated hydrochloric acid (0.05% HCl).



This photochemical cleavage was not observed with *m*- or *p*-acetoxybenzoic acid; irradiation of either of these acids in acetic acid solution gave the corresponding hydroxybenzoic acid (90%). Esterification of the acid group in acetylsalicylic acid also inhibited this cleavage, and ethyl *o*-acetoxybenzoate was photochemically transformed in acetic acid solution into ethyl salicylate<sup>8</sup> (90%).

In the compounds under study, the photochemical acetoxy cleavage is confined to acetylsalicylic acid in acetic acid or HCl/ethanol solution. It is thus tempting to speculate that the unionised carboxylic acid *ortho* to the acetoxy-group is involved in the cleavage. The precise mechanism of the reaction is under investigation. An attempt to extend this reaction to a

naphthalene derivative has so far proved unsuccessful; the major product from the photolysis of 3-acetoxy-2-naphthoic acid in ethanol or

acetic acid solution is 3-hydroxy-2-naphthoic acid.

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<sup>1</sup> J. C. Anderson and C. B. Reese, *Proc. Chem. Soc.*, 1960, 217.

<sup>2</sup> All products were identified by comparison with authentic samples.

<sup>3</sup> D. N. Shah and N. M. Shah, *J. Indian Chem. Soc.*, 1949, **26**, 235.

<sup>4</sup> A. Guillaume and G. Tanret, *Bull. Soc. Chim. biol.*, 1936, **18**, 556.

<sup>5</sup> L. J. Edwards, *Trans. Faraday Soc.*, 1950, **46**, 723.

<sup>6</sup> D. P. Kelly and J. T. Pinhey, *Tetrahedron Letters*, 1964, 3427.

<sup>7</sup> M. S. Kharasch, G. Stampa, and W. Nudenberg, *Science*, 1952, **116**, 309.

<sup>8</sup> Identified by g.l.c. using a 10% poly(ethylene glycol adipate) column.