Tetrahedron Letters No. 21, pp 2145 - 2148, 1972. Pergamon Press. Printed in Great Britain.

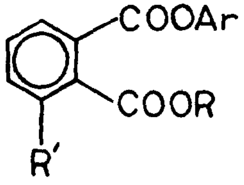
AN ABNORMAL PHOTO-FRIES REARRANGEMENT OF ARYL PHTHALATES

A. S. Kende and J. L. Belletire

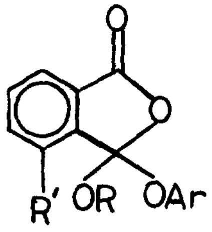
Department of Chemistry, University of Rochester, Rochester, New York 14627

(Received in USA 9 March 1972; received in UK for publication 18 April 1972)

In exploring photochemical steps towards the total synthesis of the anthracycline antibiotics[1] we have discovered an unusual reaction during attempted photo-Fries rearrangement[2] of aromatic phthalate esters. This abnormal variant of the Fries reaction is exemplified by the photolysis of methyl p-tolyl phthalate 1a[3] under Kobsa's[4] conditions. After one hour, 1a leads to a mixture of unchanged starting material (ca 30%), some polymer, and the isomerization product 2a (ca 20%[5]) which was isolated as a viscous oil (λ_{film} 5.60,6.62,7.41,7.80,8.25, 8.75,8.95,9.48,10.52,11.12,12.90; $\frac{m}{e}$ 270 (1.1), 239 (7.6), 226(7.6), 163(100); δ_{CDCl_3} 7.9-7.3(broad s,ArH,3H), 6.84(s,p-tolyl ArH,4H), 3.58(s,OCH_3,3H), 2.17(s,$ArCH_3$,3H)). Under comparable photolysis conditions phenyl benzoate gives the expected mixture of o-hydroxybenzophenone (ca 30%), starting material (ca 30%), and some polymer, whereas dimethyl phthalate remains essentially unchanged.



1



2

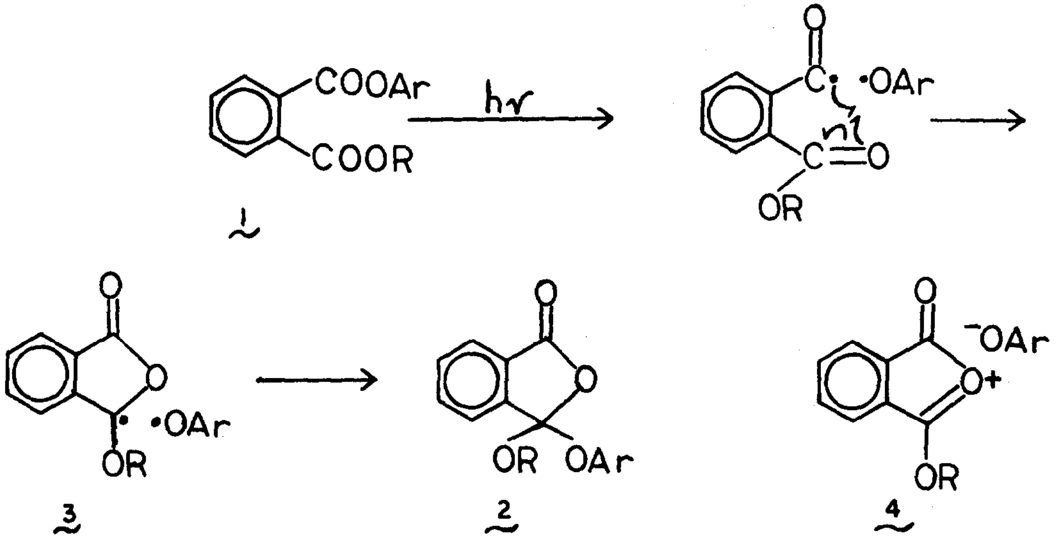
a R' = H; R = CH_3; Ar = p-C_6H_4-CH_3

b R' = H; R, Ar = p-C_6H_4-CH_3

c R' = OCH_3; R = CH_3; Ar = p-C_6H_4-CH_3

The rare orthoanhydride structure 2a rests upon its conversion by aqueous acid into phthalic acid (85% yield), the cited spectroscopic data, and the mechanistic considerations outlined in Scheme I. Homolysis of the carbonyl-aryloxy bond in excited singlet 1[6], followed by bonding of the acyl radical to the adjacent carbonyl oxygen, leads to the delocalized benzyl radical 3 which upon rebonding to the nearby phenoxy radical yields the observed product[7]. Formulation of the delocalized intermediate as a radical pair rather than an ion pair (cf 4) is consistent with the failure to incorporate a t-butoxy group when the photochemical formation of 2a is carried out in t-butanol/benzene mixtures. The abnormal rearrangement by way of 3 effectively swamps the conventional photo-Fries pathway since none of the normal product could be detected by spectroscopic methods.

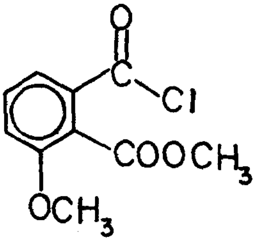
Scheme I



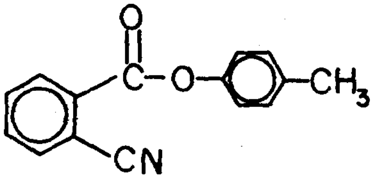
The symmetrical substrate di-p-tolyl phthalate 1b[8] upon photolysis gave the corresponding rearrangement product 2b as colorless needles (mp 105-106°; λ_{KBr} 5.61,6.70,7.45,7.83,8.35,8.60,9.10,9.48,9.80,11.09,11.22,12.08,12.72,13.31, 13.95,14.40μ; $\frac{m}{e}$ 346(0.7),239(100); δ_{CDCl_3} 7.9-7.6(broad s,ArH,4H), 7.00(s,p-tolyl ArH,8H), 2.27(s,$ArCH_3$,6H)).

The presence of an additional ortho substituent did not hinder the reaction sequence. Thus, diesterification of 3-methoxyphthalic acid, selective saponification of the less hindered ester, careful conversion to the acid chloride 5[9], and reaction with p-cresol afforded the crystalline diester 1c (mp 114-115°; λ_{KBr} 5.79,7.80,8.39,8.94,9.60,13.15μ; δ_{CDCl_3} 8.0-6.95(multiplet, ArH,7H), 3.90(s,OCH_3,6H),2.38(s,$ArCH_3$,3H)). Photolysis of this diester gave isomerization product 2c as a viscous oil (λ_{film} 5.59,6.11,6.60,6.70,7.33,7.75, 8.30,8.65,8.80,9.41μ; $\frac{m}{e}$ 300(0.2),269(15),193(100); δ_{CDCl_3} 7.8-6.8 (multiplet, ArH,3H),6.92(s,p-tolyl ArH,4H),4.00,3.68(s,OCH_3,6H),2.20(s,$ArCH_3$,3H)).

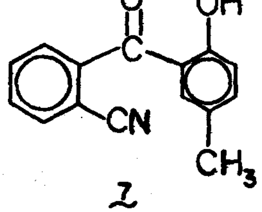
In accord with the mechanism proposed above, this abnormal variant of the photo-Fries rearrangement can be entirely circumvented by employing o-cyanobenzoates rather than phthalates as starting materials. Carpino's method[10] was used to prepare nitrile 6 (mp 99-100.5°; λ_{KBr} 4.50,5.80,11.29,12.28,13.12,14.50μ; δ_{CDCl_3} aromatic multiplets centered 8.38(1H), 7.85(3H), 7.23(s,p-tolyl ArH,4H), 2.39(s,$ArCH_3$,3H)). Photolysis gave the benzophenone 7 as yellow prisms (24%; mp 106-108°; λ_{KBr} 2.95,4.50,6.11,7.50,7.70,8.00,8.15,8.70,10.38,11.48,11.81, 12.35,12.91,13.71μ; δ_{CDCl_3} 11.63(s,OH,1H),8.15-6.90(multiplet,ArH,7H),2.25 (s,$ArCH_3$,3H); $\frac{m}{e}$ 237; λ_{CH_3OH} 355nm). No byproducts corresponding to cyano participation were detected.[11]



5



6



7

Work is currently in progress to extend our results to aryl esters of aliphatic 1,2-dicarboxylic acids[12].

FOOTNOTES AND REFERENCES

1. H. Brockmann, Fortschr. Chem. Org. Naturstoffe., 21, 121 (1963).
2. V. Stenberg, Organic Photochemistry, Vol. 1, O. L. Chapman, ed., M. Dekker, New York, 1967, p. 127.
3. P. J. Bunyan and D. H. Hey, J. Chem. Soc., 324 (1962).
4. H. Kobsa, J. Org. Chem., 27, 2293 (1962). This procedure involves direct irradiation through quartz of deaerated benzene solutions at moderate substrate concentrations (.01-.05M).
5. In all cases an nmr of the crude photolysis mixture was taken to ensure no artifacts were introduced during purification. Chromatography over 50 weight equivalents of silica gel using benzene as eluent gave a clean separation of non-polymeric distillable products from polymeric residue. Repeated (3-5 times) column chromatography was necessary to completely separate product 2 from starting material.
6. Attempts to sensitize the photolysis with benzophenone led only to unchanged starting material.
7. Cf A. Shah, S. N. Singh, and M. V. George, Tetrahedron Letters, 3983 (1968).
8. R. Meyer, Ber., 26, 204 (1893).
9. Oxalyl chloride in benzene at 40° was used to avoid scrambling the position of the methyl ester [cf S. Stallberg-Stenhagen, J. Amer. Chem. Soc., 69, 2568 (1947)].
10. L. A. Carpino, ibid, 84, 2196 (1962).
11. All new compounds reported in this work gave satisfactory elemental or mass spectral analyses.
12. We are indebted to the National Institutes of Health for generous support of this research through grants IF02GM51050 and CA-11326.