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FORMATION OF SPIRO COMPOUNDS BY AN UNUSUAL INTRA-MOLECULAR NUCLEOPHILIC SUBSTITUTION IN *o*-BROMOMETHYL-SUBSTITUTED BENZILS AND BENZOPHENONES

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During attempted preparation of aromatic diketones - as starting materials for dioximes - bearing bulky substituents at the ortho position, an unexpected reaction was observed It was our intention to prepare 2,2'-bis(t-butoxymethyl)benzil 3, by bromination of 2,2'-dimethylbenzil[1] 1 with N-bromosuccinimide, followed by substitution with potassium t-butoxide (Fig 1)

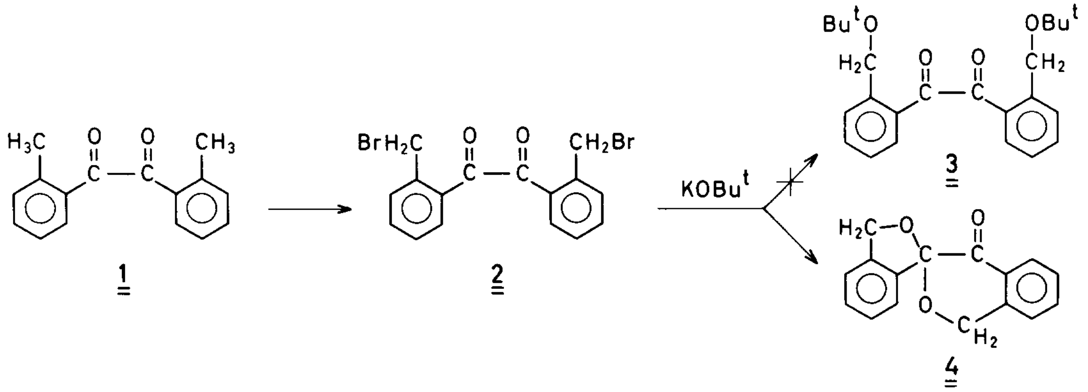

FIGURE 1 The planned and observed reaction scheme for the preparation and substitution of 2,2'-bis(bromomethyl)benzil

The main product of the reaction of 2,2'-bis(bromomethyl)benzil 2 with potassium t-butoxide showed, however, the presence of two overlapping AB systems in its ^{1}H NMR spectrum, indicating a cyclic structure with two different non-aromatic rings The same compound was obtained when 2 was refluxed during 3 minutes in the presence of 4 equivalents of sodium hydroxide in aqueous ethanol (50% v/v) When the latter reaction mixture was cooled slowly, small colorless needly crystals were obtained Recrystallization from aqueous ethanol (50% v/v) yielded a pure compound (mp 123 7-123 8^o), having the following spectroscopic properties

IR (KBr), 1700 (C = O), 1285, 1238, 1073, 1007, 972, 777, 738 cm^{-1}

^{1}H NMR (60 MHz, $CDCl_3/CD_3COCD_3$) δ = 4 92, 5 45 (AB system, J = 16 Hz, CH_2), 5 15, 5 30 (AB system, J = 13 Hz, CH_2), 7 15-8 13 (m, C_6H_4)

^{13}C NMR (20 MHz, CD_3COCD_3) δ = 63 29 (t, CH_2), 73 85 (t, CH_2), 109 06 (s, spiro-C), 121 60 (d), 124 44 (d), 125 29 (d), 127 62 (d), 128 24 (d), 128 34 (d), 129 75 (s), 130 23 (d), 134 76 (d),

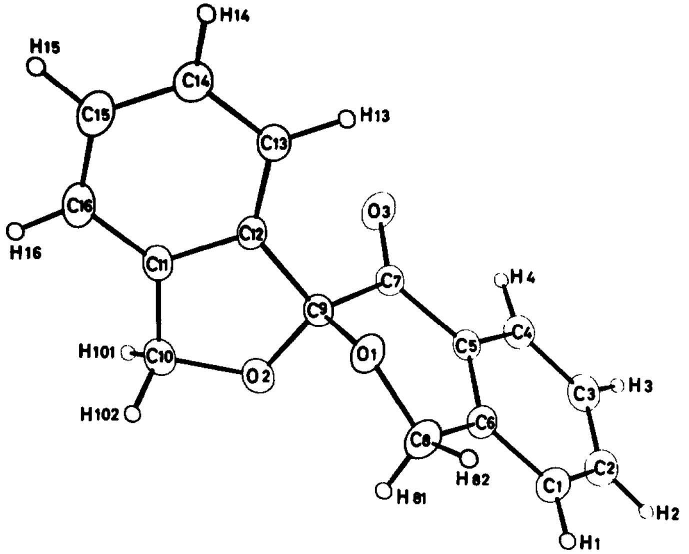

FIGURE 2. The molecular structure of 4. Some relevant bond distances (Å) and bond angles (°) are

C_5–C_7 = 1 476 C_{12}–C_9 = 1 499 $C_6C_8O_1$ = 113 4 $C_{10}O_2C_9$ = 110.7
C_7–C_9 = 1.531 C_9–O_2 = 1.421 $C_8O_1C_9$ = 114 3 $O_2C_9C_{12}$ = 105.2
C_9–C_1 = 1.413 O_2–C_{10} = 1 442 $O_1C_9C_7$ = 109 4 $C_7C_9C_{12}$ = 117.1
O_1–C_8 = 1 431 C_{10}–C_{11} = 1 489 $C_9C_7C_5$ = 115.7 $O_1C_9O_2$ = 111 9
C_8–C_6 = 1.491 C_7–O_3 = 1.210 $C_{11}C_{10}O_2$ = 104 7

138 18 (s), 141 47 (s), 142 91 (s), 188 53 (s, C = 0)
MS, m/e = 252 (0 14%, M^+), 251 (0 48%), 236 (0 16%), 165 (3%), 133 (3%), 119 (18%), 118 (100%) 91 (10%), 90 (81%), 89 (40%), 77 (15%), 63 (13%), 51 (11%)

Judging from the physical properties and the elemental analysis (Calcd for $C_{16}H_{12}O_3$ (252 27) C, 76 18, H, 4 79. Found C, 76 15, H, 4 71) we came to believe that we were dealing with 4'-oxo-spiro[isobenzofuran-1(3H),3'-isochroman] 4 This structure was confirmed by an X-ray structure analysis^3 (Fig 2) The formation of 4 is proposed to proceed according to the mechanism depicted in Figure 3

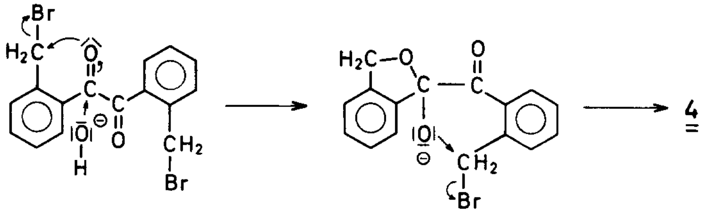

FIGURE 3. Mechanism proposed for the formation of 4

The present observation bears some relation to the anchimeric assistance of an ortho carbonyl group in the hydrolysis of aromatic esters[4] and imides[5] In these reactions the increase in rate of the hydrolysis is ascribed to catalysis involving a nucleophilic attack by OH$^-$ or CH$_3$O$^-$ on the ketonic or aldehydic carbonyl group, followed by an attack of the activated carbonyl oxygen on the ester carbonyl. A similar accelerating influence of an ortho carboxylic ester group was found in the hydrolysis of benzyl and benzhydryl bromides, resulting in ring-closure to phthalides[6]

Three additional experiments were performed to explore the scope and limitations of the present reaction. First, compound 2 was brought into reaction with SH$^-$ in an aqueous-alcoholic medium (50% v/v) The spiro compound 5 with a sulphur atom built in at the 2'-position was obtained as the main product. This indicates a similar reaction mechanism as depicted above, however, now initiated by SH$^-$ as the nucleophilic agent A small amount of the spiro compound 6, having sulphur atoms at the 2- and 2'-position, was obtained as a side product

In a second experiment compound 3 was brought into reaction with CH$_3$O$^-$ in methanol. A product, identified as 1,1'-bi(1-methoxy-3*H*-isobenzofuran) 7, was obtained by direct crystallization from the reaction mixture Another product of this reaction was found to be 2,2'-bis(methoxymethyl)-benzil This indicates a competition between the mechanism depicted above and a direct nucleophilic substitution of the bromine atom by the methoxide group The fact that different reaction products are obtained when using t-butoxide or methoxide as the nucleophile may possibly be explained on the basis of the following causes Firstly steric hindrance may oppose the addition of a second t-butoxide. Secondly the branched alkyl group is more easily eliminated from the molecule leading to closure of the second ring

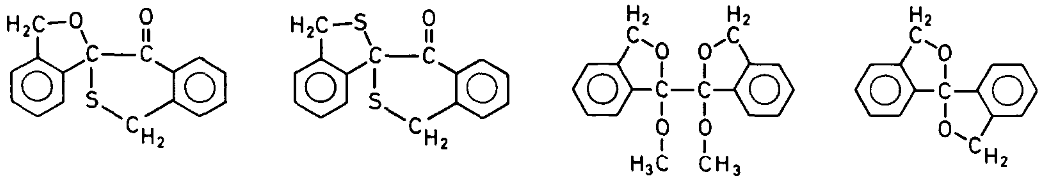
5 6 7 8

FIGURE 4 The molecular structure of some cited compounds.

In a third experiment 2,2'-dimethylbenzophenone, prepared according to Cook[7], was brominated with N-bromosuccinimide. Reaction of the 2,2'-bis(bromomethyl)benzophenone with sodium hydroxide in aqueous ethanol (50% v/v) yielded 1,1'-spirobi(3*H*-isobenzofuran) 8, in high yield, giving additional support to the mechanism proposed in Figure 3.

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REFERENCES

1 The 2,2'-dimethylbenzil was prepared from 2-methylbenzaldehyde by a benzoin condensation, followed by oxidation according to the method of Moureu et al [2]

2 H. Moureu, P. Chovin, and R Sabourin, Bull Soc Chim Fr 22, 1155-57 (1955)

3 H van Koningsveld, submitted for publication in Cryst Struct Commun

4 M.L Bender, F Chloupek, and M C Neveu, J Am Chem Soc 80, 5384-87 (1958), M L Bender and M C Neveu, J Am Chem Soc. 80, 5388-91 (1958), M L Bender and M.S Silver, J Am Chem Soc 84, 4589-90 (1962), Y. Shalitin and S A Bernhard, J Am Chem Soc 86, 2292 (1964); M S. Newman and A L Leegwater, J Am Chem Soc 90, 4410-13 (1968), K Sano, J Org Chem 34, 2076-80 (1969), H D Burrows and R Macolm Topping, J. Chem Soc B, 1970, 1323-29, K Bowden and G R Taylor, J Chem Soc B, 1971, 145-48, 149-56, G H Hurst and M L Bender, J Am Chem Soc. 93, 704-11 (1971)

5 B Zerner and M L Bender, J Am Chem Soc 83, 2267-74 (1961)

6 A Singh, L J Andrews, and R M Keefer, J Am Chem Soc 84, 1179-85 (1962)

7 J.W Cook, J. Chem Soc 1930, 1087-91.

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