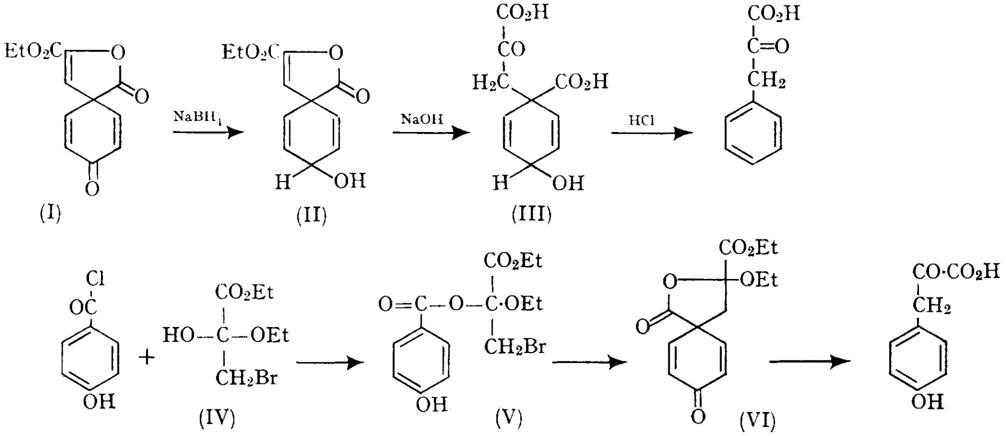
Synthesis of Spirocyclic Cyclohexadienones: New Routes to Prephenate†

By H. PLIENINGER* and K. FRISCHKORN

(*Organisch-Chemisches Institut der Universität, 69, Heidelberg, Tiergartenstrasse*)

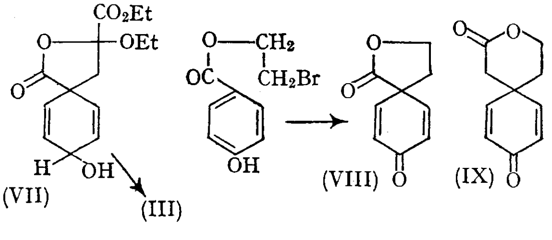
REACTION of ethyl *p*-hydroxyphenylpyruvate with phosgene and potassium t-butoxide in t-butanol gives a mixture from which can be isolated about 4% of a neutral oil which is mainly the dienone (I), λ_{max} 270 mμ. This absorption almost disappears on treatment with $NaBH_4$. In NaOH solution the absorption shifts to λ_{max} 330 mμ (*p*-hydroxyphenylpyruvic acid dianion). The assumed reduction product of (I) with $NaBH_4$, the dienol (II) gives after treatment with NaOH and acidification a mixture of 2,4-dinitrophenylhydrazones which could be separated by t.l.c. The dinitrophenylhydrazone of phenylpyruvate could be identified. Prephenic acid (III) must be assumed as an intermediate of this reaction.



Better yields of the prephenate are obtained as follows: reaction of *p*-hydroxybenzoyl chloride with the product of ethanol and ethyl bromopyruvate (IV) gives the labile ester (V) which can be transformed by refluxing with potassium t-butoxide in t-butanol to the dienone (VI) (yield 6%) which could be isolated nearly pure by chromatography on silica gel. ν_{max} (film) 1805 cm.$^{-1}$ (lactone carbonyl), 1740 cm.$^{-1}$ (ester carbonyl), 1630 cm.$^{-1}$ (C=C) λ_{max} 262 mμ. The absorption in the u.v. spectrum almost disappears with $NaBH_4$. Treatment of (VI) with NaOH gives *p*-hydroxyphenylpyruvate in good yield (u.v. spectrum and isolation of the 2,4-dinitrophenylhydrazone).

The n.m.r. spectrum of (VI) is in agreement with the proposed structure: A_2B_2 spectrum with centres at τ 2·21 and 2·65 (4*H*), *J* 13 c./sec. for the olefinic protons; two very similar ethoxy-groups with multiplet (4H) at τ 6 (OCH_2) and a multiplet (about 7H) at τ 8 (Me) and two protons give a signal at τ 7·6 (CH_2 of the 5-ring).

On reduction of (VI) with $NaBH_4$, the dienol (VII) could be obtained, along with other products; it yielded a crude barium prephenate. The Ba salt contained 25% of the prephenate (determined by rearrangement to phenylpyruvic acid).

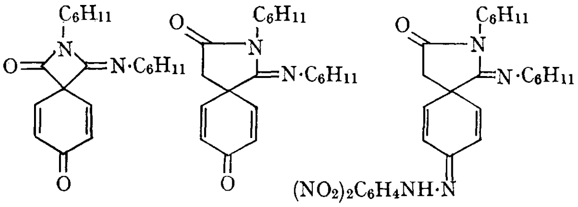


In the same way as (VI), the oily, unstable dienone (VIII) (λ_{max} 272 mμ) and the more stable dienone (IX) (λ_{max} 278 mμ) could be prepared

---

† For former attempts at synthesis see: H. Plieninger, L. Arnold, R. Fischer, and W. Hoffmann, *Chem. Ber.*, 1965, **98**, 1774.

from β-bromoethyl-*p*-hydroxybenzoate and β-bromoethyl-*p*-hydroxyphenylacetate respectively. The u.v. absorption fades with $NaBH_4$. Surprisingly the dienones (VIII) and (IX) give the same dinitrophenylhydrazone.



(X) (XI) (XII)

On treatment of *p*-hydroxybenzoic acid with bromoethanol and dicyclohexylcarbodi-imide, along with the expected ester, an unstable dienone (X) is produced [ν_{max} 1770 cm.$^{-1}$ (C_4-ring lactam) 1630 cm.$^{-1}$ (C=C)]. The structure of the dinitrophenylhydrazone has not yet been clarified. A crystalline stable dienone (XI) could be obtained in good yield, when *p*-hydroxyphenylacetic acid, bromoethanol (possibly as a catalyst), and dicyclo hexylcarbodi-imide are allowed to react (ν_{max} 272 mμ). This dienone gives a dinitrophenylhydrazone of structure (XII).

(*Received, April 8th,* 1968; *Com.* 436.)