

**444.** *Acetylenic Compounds Related to Stilbæstrol. Part IV.<sup>1</sup> The Preparation of  $\alpha$ -Alkyl- $\beta$ -ethynyl-4,4'-dihydroxystilbenes.*

By C. W. SHOPPEE, J. CYMERMAN CRAIG, and RUTH E. LACK.

Although attempted demethylation of 1,2-di-(*p*-methoxyphenyl)but-1-en-3-yne (IIa) led to decomposition, use of the 1,2-di-(*p*-tetrahydropyranyloxyphenyl)-derivative, obtained from 4,4'-bis(tetrahydropyranyloxy)deoxybenzoin and ethynylmagnesium bromide, gave 1,2-di-(*p*-hydroxyphenyl)but-1-en-3-yne.

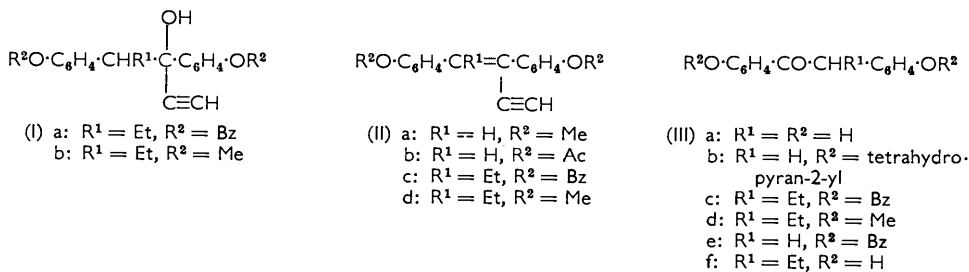
Conversion of 4,4'-dibenzoyloxy- $\alpha$ -ethyldeoxybenzoin into the acetylenic alcohol (Ia) was accomplished with preservation of the benzoate groups. Attempted dehydration of the alcohol (Ia) with phosphorus trichloride in pyridine or triethylamine gave only insoluble phosphate esters, but use of thionyl chloride in triethylamine afforded the chloroallene (Va), the chloroacetylene (IX), and the *trans*-isomer of 1,2-di-(*p*-benzoyloxyphenyl)hex-1-en-3-yne (IIc), whose structure was proved by hydrogenation to stilbæstrol dibenzoate.

PRECEDING papers of this series<sup>1</sup> have described methods for obtaining 1-alkyl-1,2-di-(*p*-methoxyphenyl)but-3-yn-2-ols (as Ib) and 1-alkyl-1,2-di-(*p*-methoxyphenyl)but-1-en-3-yne (as IID). The preparation of the corresponding phenolic compounds has now been investigated.

Preliminary experiments showed that demethylation of compounds of type (Ib) and

<sup>1</sup> Shoppee, Craig, and Lack, Part III, *J.*, 1961, 1311.

(II<sub>d</sub>) with alcoholic alkali<sup>2</sup> or with hydriodic acid<sup>3,4</sup> at high temperatures caused extensive decomposition of the acetylenic compounds; whilst the use of aluminium bromide in benzene<sup>5</sup> or in collidine<sup>6</sup> (172°) also failed.



Attempted demethylation of 1,2-di-(*p*-methoxyphenyl)but-1-en-3-yne (II<sub>a</sub>) by aluminium bromide in xylene (140°) gave no phenolic material after 2 hr., but extensive polymerisation of the starting material occurred to give the known dimeric product.<sup>1</sup> The instability of acetylenic stilbenes of type (II) to both acidic reagents and temperatures above 140° thus required use of protecting groups, other than methoxyl, removable under milder conditions; tetrahydropyranyl ethers proved satisfactory.

The preparation of 4,4'-dihydroxydeoxybenzoin has been described,<sup>7</sup> by the action of boiling water on the diazonium salt from 4,4'-diaminotolan or 4,4'-diaminodeoxybenzoin. Treatment of the readily accessible deoxyanisoin<sup>8</sup> with hydriodic acid in the presence of either phenol or acetic acid gave excellent yields of 4,4'-dihydroxydeoxybenzoin (III<sub>a</sub>). Anisoin with hydriodic acid in phenol gave also 4,4'-dihydroxydeoxybenzoin.

4,4'-Dihydroxydeoxybenzoin was converted into its bistetrahydropyranyl ether (III<sub>b</sub>) in 93% yield by a modification of Parham's method<sup>9</sup> in the absence of solvents. Addition of sodium hydroxide at the end of the reaction was essential to prevent hydrolysis to the starting phenol, whilst the use of dioxan resulted in considerably reduced yields (cf. ref. 10) and isolation of appreciable quantities of the hydrolysis product  $\delta$ -hydroxyvaleraldehyde. Treatment of the bistetrahydropyranyl ether (III<sub>b</sub>) with ethynylmagnesium bromide<sup>11</sup> gave solely phenolic material, consisting of a mixture of ketone and alcohol which decomposed on chromatography. Alternatively, the product was converted, after removal of unchanged ketonic material by Girard's reagent D,<sup>12</sup> directly into the stilbene diacetate (II<sub>b</sub>). Its ultraviolet spectrum showed absorption characteristic of the *trans*-stilbene chromophore and was transformed, on irradiation of the compound, into that of the *cis*-isomer with the previously observed<sup>1</sup> changes in intensities (cf. Table).

Demethylation of  $\alpha$ -ethyldeoxyanisoin<sup>1</sup> by hydriodic and acetic acids, as described by Dodds *et al.*,<sup>4</sup> gave a product consisting mainly of 1-*p*-hydroxyphenyl-2-*p*-methoxyphenylbutan-1-one which on further treatment with the same reagent afforded the known amorphous 4,4'-dihydroxy- $\alpha$ -ethyldeoxybenzoin.<sup>4</sup>

Reaction of the dibenzoate (III<sub>c</sub>) with a large excess of ethynylmagnesium bromide in

<sup>2</sup> Salzer, *Z. physiol. Chem.*, 1942, **5**, 39; Biggerstaff and Wilds, *J. Amer. Chem. Soc.*, 1949, **71**, 2132; Spath, *Monatsh.*, 1914, **35**, 319.

<sup>3</sup> Dodds, Golberg, Lawson, and Robinson, *Nature*, 1938, **142**, 1121; La Forge, *J. Amer. Chem. Soc.*, 1933, **55**, 3040.

<sup>4</sup> Dodds, Golberg, Lawson, and Robinson, *Proc. Roy. Soc.*, 1939, **B**, **127**, 140.

<sup>5</sup> Burckhalter and Sam, *J. Amer. Chem. Soc.*, 1952, **74**, 187.

<sup>6</sup> Marshall and Whiting, *J.*, 1957, 537.

<sup>7</sup> Zincke and Fries, *Annalen*, 1902, **325**, 75.

<sup>8</sup> Carter, Craig, Lack, and Moyle, *J.*, 1959, 476.

<sup>9</sup> Parham and Anderson, *J. Amer. Chem. Soc.*, 1948, **70**, 4187; Parham and De Laitsch, *ibid.*, 1954, **76**, 4962.

<sup>10</sup> Gaspert, Halsall, and Willis, *J.*, 1958, 624; Cocker and Halsall, *J.*, 1957, 3441.

<sup>11</sup> Jones, Skattebol, and Whiting, *J.*, 1956, 4765.

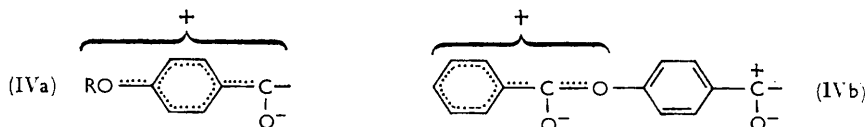
<sup>12</sup> Viscontini and Meier, *Helv. Chim. Acta*, 1950, **33**, 1773.

*Ultraviolet absorption spectra.*

Compound	$\lambda_{\max.}$ (m $\mu$ )	$\epsilon$	Compound	$\lambda_{\max.}$ (m $\mu$ )	$\epsilon$
(IIb): <i>trans</i> .....	230, 315	15,550, 28,000	(IIId): <i>trans</i> ...	223, 284	14,600, 12,200
(IIb): <i>cis</i> .....	234, 302	17,900, 17,800	Stilbaestrol di-		
(IIc): <i>trans</i> .....	232, 272	50,800, 25,350	benzoate .....	232, 270 infl.	34,600, 12,000
(IIc): <i>cis</i> .....	232, 270 infl.	58,000, 24,800	(Va) .....	233, 260	47,600, 29,000
			(Vb) .....	224, 278	18,100, 14,900

tetrahydrofuran under reflux (66°) gave a phenolic product which on re-benzoylation yielded the acetylenic alcohol (Ia): there was extensive decomposition and the neutral fraction contained only polymeric material. At 0° the Grignard reaction gave no phenolic product, and the neutral portion consisted of a mixture of the acetylenic alcohol (Ia) with unchanged starting material. When the reaction period (2 hr. at 0°) was extended (72 hr. at 20°) considerable decomposition ensued, but an excellent yield of the alcohol (Ia), free from starting ketone and decomposition products, was obtained by interaction for 2 hr. at 0° with a further 2 hr. at 20° only.

It is noteworthy that the 4,4'-dibenzoyloxy-grouping is retained even in the presence of a large excess of the Grignard reagent at 0° and 20°, while refluxing resulted in the removal of the ester groups. The same dibenzoate was found<sup>4</sup> to be converted entirely into the phenolic tertiary alcohol by refluxing with ethereal ethylmagnesium bromide. While the related  $\alpha$ -ethyldeoxyanisoin (IIIId) required 18 hours' refluxing (66°) to react with ethynylmagnesium bromide,<sup>1</sup> the 4,4'-dibenzoyloxy-compound (IIIc) was completely converted into the tertiary alcohol (Ia) under the mild conditions (0° to 20°) described above. This difference in the reactivity of the carbonyl function in these two ketones is due to the greater electron-withdrawing effect of the *p*-benzoyloxy- than of the *p*-methoxy-group. Contributions from resonance structures such as (IVa), which will reduce the reactivity of the carbonyl carbon atom in (III), will be large in the case of the *p*-methoxy- but small in that of the *p*-benzoyloxy-ketone, because of the alternative resonance possibilities in the benzoyloxy-system (IVb).

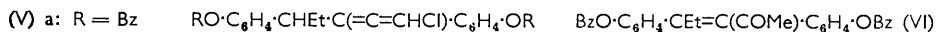


Attempted dehydration of the acetylenic alcohol (Ia) by means of phosphorus trichloride in pyridine<sup>1</sup> at  $-20^\circ$ , which gave the chloroallene (Vb) from the corresponding di-*p*-methoxyphenyl compound, gave only a low yield of an ether-soluble product, shown to contain the chloro-allene (Va),  $\nu_{\max.}$  1930  $\text{cm}^{-1}$ , and the  $\alpha\beta$ -unsaturated ketone (VI),  $\nu_{\max.}$  1670  $\text{cm}^{-1}$ . The major portion of the product was ether-insoluble and appeared to consist of phosphate esters. Use of phosphorus trichloride in triethylamine at  $-40^\circ$  again gave a phosphate ester which resisted alkaline or acid hydrolysis and was not further investigated.

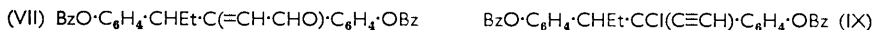
The different behaviour of the *p*-benzoyloxyphenyl compound (Ia) and its *p*-methoxyphenyl analogue may again be due to the electron-withdrawal inequality  $p\text{-BzO} > p\text{-MeO}$ , leaving an electron-deficiency on the  $\alpha$ -carbon atom in the former case and thus preventing the fission of the C-O bond shown<sup>1</sup> to occur in the latter case.

The acetylenic alcohol (Ia), when treated with thionyl chloride in triethylamine at  $-40^\circ$  for 0.5 hr., afforded the chloro-allene (Va),  $\nu_{\max.}$  1925 and 1890  $\text{cm}^{-1}$  (conjugated C=C=C) and 753 and 740  $\text{cm}^{-1}$  (C-Cl), the desired *trans*-3,4-di-*p*-benzoyloxyphenylhex-3-en-1-yne (IIc) (changed by irradiation to the *cis*-isomer; see Table), and the  $\alpha\beta$ -unsaturated ketone (VI), m. p.  $156^\circ$ , formed by the Meyer-Schuster rearrangement previously discussed.<sup>1</sup> When an improved chromatographic technique was employed in a similar experiment, in which treatment with thionyl chloride was for only 5 min. at

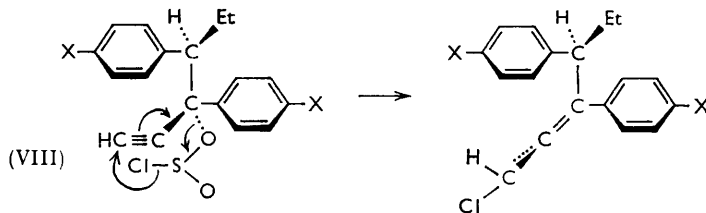
—40°, the products were the chloro-allene (Va), the chloro-acetylene (IX), and the



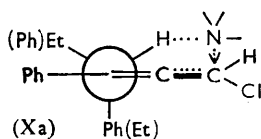
b: R = Me



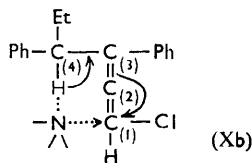
*trans*-stilbene (IIc): absence of the ketone (VI) may be ascribed to the fact that alkaline conditions were preserved during the working-up. The reaction with thionyl chloride presumably proceeds through the chlorosulphite (VIII).<sup>13</sup> It is known that the halogen atom in ester halides formed from phosphorus or thionyl halides is easily ionised and can,



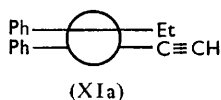
by a unimolecular or bimolecular process, give the chloro-compound (IX) by attack on the oxygen-bearing carbon atom.<sup>13</sup> In the chlorosulphite ester (VIII), however, this carbon atom is in a highly hindered environment of a *t*-butyl nature. Molecular models show that the halogen atom is close to the terminal carbon atom of the ethynyl group, and attack of the halogen on this carbon atom also occurs, with the concerted electron-shifts shown in (VIII), resulting in the simultaneous formation of the chloro-allene (Va) and elimination of sulphur dioxide. That only a trace of the chloroallene was obtained when phosphorus trichloride was employed as the reagent agrees with the known lower tendency of chlorophosphates than of chlorosulphites to rearrange.<sup>13</sup>



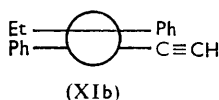
(Xa)



(Xb)



(XIa)



(XIb)

The process, whereby dehydrohalogenation of the chloro-allene (Vb) gave both the *cis*- and the *trans*-form of the ethynyl-stilbene (IIc) may be envisaged as the concerted elimination (Xb), in which attack by the tertiary nitrogen atom, from the direction indicated, on the terminal carbon atom of the chloroallene group results in ionisation of the chlorine atom and loss of a proton from C<sub>(4)</sub> to give either of the two possible stilbenes (XIa) and (XIb). The same products would result if the intermediate chloroallene existed in the diastereoisomeric form shown in parentheses in (Xa). Only the *trans*-form of the stilbene (IIc) could be isolated, however, on treatment of the alcohol (Ia) with thionyl chloride in triethylamine.

Treatment of the chloroallene (Va) with sodamide in liquid ammonia gave a completely phenolic product, which after rebenzoylation was shown to contain a small proportion of an acetylenic substance but was mainly an  $\alpha\beta$ -unsaturated carbonyl compound, m. p. 193°, isomeric with the ketone (VI) of m. p. 156° previously obtained, and believed to be the aldehyde (VII), formed by the Rupe rearrangement.<sup>1</sup>

<sup>13</sup> Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252.

The considerable steric hindrance at the central double bond of  $\alpha\beta$ -disubstituted stilbenes is shown by their ultraviolet absorption spectra, in which interference between both pairs of alkyl and aryl groups has largely destroyed the coplanarity of the chromophoric system,<sup>14</sup> resulting in a lower intensity, and a shift to shorter wavelengths, of the absorption maximum in the 230—240  $m\mu$  region with increasing size of the  $\alpha\beta$ -substituents.<sup>15</sup> The dibenzoyloxy-compound (IIc) showed a main absorption band at 232  $m\mu$ , much more intense than that of the dimethoxy-compound (IIId) and the second (weaker) band was shifted from 284 to 272  $m\mu$ .<sup>1</sup> The same shifts are shown by the chloroallenes (V), where the 4,4'-dibenzoyloxy-compound had high-intensity absorption at 233 and 260, and the 4,4'-dimethoxy-analogue<sup>1</sup> at 224 and 278  $m\mu$ .

It is known that the hindered olefinic linkage in stilboestrol required greatly prolonged reaction periods<sup>4</sup> for catalytic hydrogenation, and we found that stilboestrol dibenzoate was recovered unchanged after attempted hydrogenation with platinum oxide in ethyl acetate. Under the same conditions, the 4,4'-dibenzoyloxystilbene (IIc) was reduced smoothly to stilboestrol dibenzoate, the central double bond proving resistant to further hydrogenation; the structure of the acetylenic stilbene (IIc) is thus confirmed.

#### EXPERIMENTAL

M. p.s were determined on a Kofler block (error  $\pm 2^\circ$ ). Ultraviolet absorption spectra were determined for 95% EtOH solutions on a Hilger "Uvispek" instrument, and infrared spectra on a Perkin-Elmer "Infracord" spectrophotometer. Aluminium oxide used was Woelm (neutral) or Spence type H, activity II (alkaline).

*Attempted Demethylation of 1,2-Di-(p-methoxyphenyl)but-1-en-3-yne (IIa).*—1,2-Di-(*p*-methoxyphenyl)but-1-en-3-yne (100 mg.) was treated with aluminium bromide (500 mg.) in xylene (10 ml.) at 140° for 2 hr. or in benzene (10 ml.) at 80° for 5 hr. Extraction with sodium hydroxide solution gave no phenolic material whilst evaporation of the washed and dried solvent layer at 80° under reduced pressure gave dark polymers, m. p. 140—150°.

*4,4'-Dihydroxydeoxybenzoin (IIIa).*—(a) Deoxyanisoin (60 g.) was treated with 50% aqueous hydrogen iodide (200 ml.) and phenol (40 g.) for 0.5 hr. at the b. p. (cf. La Forge<sup>3</sup>). After removal of phenol in steam the product was extracted into ether, washed with sodium hydrogen sulphite and sodium hydrogen carbonate solution, dried, and evaporated. The pink solid recrystallised from aqueous ethanol, to give 4,4'-dihydroxydeoxybenzoin as colourless prisms (49.6 g., 93.5%), m. p. 217°,  $\lambda_{\max}$ . 222, 280  $m\mu$  ( $\epsilon$  24,130 and 24,130),  $\nu_{\max}$ . 3490, 3390 (OH), 1670 (C=O)  $\text{cm}^{-1}$  [Found (after drying at 20°/1 mm. for 16 hr.): C, 73.4; H, 5.4; O, 21.0. Calc. for  $\text{C}_{14}\text{H}_{12}\text{O}_3$ : C, 73.65; H, 5.3; O, 21.0%]. Zincke and Fries<sup>7</sup> give m. p. 214°.

(b) Treating deoxyanisoin (20 g.) with 50% hydrogen iodide (65 ml.) and phenol (27 g.) gave 4-hydroxy-4'-methoxydeoxybenzoin (12.5 g.), m. p. 157°,  $\lambda_{\max}$ . 222, 279  $m\mu$  ( $\epsilon$  21,200 and 18,800),  $\nu_{\max}$ . 3440 (OH), 1668 (C=O)  $\text{cm}^{-1}$  [Found (after drying at 50°/1 mm. for 6 hr.): C, 74.2; H, 5.8; OMe, 12.6.  $\text{C}_{15}\text{H}_{14}\text{O}_3$  requires C, 74.35; H, 5.85; OMe, 12.8%].

(c) Hydriodic acid (50 ml.; *d* 1.7) and deoxyanisoin (10 g.) in acetic acid (10 ml.) were heated at 135—140° for 10 min. The cooled solution was poured into water and clarified with sodium hydrogen sulphite, and the precipitate was filtered off, to give 4,4'-dihydroxydeoxybenzoin (9.0 g.), m. p. 217°.

(d) Anisoin (5 g.) was treated with hydriodic acid (*d* 1.7, 25 ml.) and phenol (3.5 g.) for 0.5 hr. under reflux. After removal of phenol by steam distillation, the product was ether extracted to give 4,4'-dihydroxydeoxybenzoin, m. p. and mixed m. p. 217°.

(e) 4,4'-Dihydroxydeoxybenzoin (IIIa) (500 mg.) in 5% aqueous sodium hydroxide (5 c.c.) was treated with benzoyl chloride (500 mg.) at 0°. Recrystallisation of the white solid from ethyl acetate gave 4,4'-*di*-(*p*-benzoyloxy)deoxybenzoin (IIIe), m. p. 183°,  $\lambda_{\max}$ . 238  $m\mu$  ( $\epsilon$  27,000),  $\nu_{\max}$ . 1740 (benzoate), 1690 (C=O)  $\text{cm}^{-1}$  [Found (after drying at 40°/1 mm. for 6 hr.): C, 76.8; H, 4.7.  $\text{C}_{28}\text{H}_{20}\text{O}_5$  requires C, 77.05; H, 4.6%].

*Treatment of 4,4'-Dihydroxydeoxybenzoin with Dihydropyran.*—(a) 4,4'-Dihydroxydeoxybenzoin (10 g.), dried at 100° for 24 hr., in redistilled dihydropyran (20 c.c.) was heated with

<sup>14</sup> Braude, *J.*, 1949, 1902.

<sup>15</sup> Suzuki, *Bull. Chem. Soc. Japan*, 1952, **25**, 145; Oki, *ibid.*, 1953, **26**, 37, 161, 331.

16N-hydrochloric acid (3 drops) at 50° until a clear solution resulted; N-sodium hydroxide (10 ml.) was added to the mixture, which solidified after 1 hr. at 20°. Filtration gave 4,4'-bistetrahydroxyran-2-yloxydeoxybenzoin (IIIb) (16.2 g.) (93%), m. p. 125°,  $\lambda_{\max}$  222, 273 m $\mu$  ( $\epsilon$  17,000 and 17,000),  $\nu_{\max}$  1685 (C=O) cm.<sup>-1</sup> [Found (after drying at 20°/1 mm. for 4 hr.): C, 72.55; H, 7.0. C<sub>24</sub>H<sub>28</sub>O<sub>5</sub> requires C, 72.7; H, 7.1%].

(b) 4,4'-Dihydroxydeoxybenzoin (2.5 g.) in dry dioxan (20 ml.) was treated with 16N-hydrogen chloride (3 drops). Dihydropyran (1.85 g.) was added and the mixture left at 25° for 18 hr. Ether was added and the phenolic material extracted with sodium hydroxide. Evaporation of the ether layer left an oil, b. p. 55—57°/5 × 10<sup>-3</sup> mm., which by treatment with 2,4-dinitrophenylhydrazine gave  $\delta$ -hydroxyvaleraldehyde 2,4-dinitrophenylhydrazone, m. p. 115°, identical with a sample prepared from dihydropyran [Found (after drying at 20°/1 mm. for 4 hr.): C, 47.1; H, 5.3. C<sub>11</sub>H<sub>14</sub>O<sub>5</sub>N<sub>4</sub> requires C, 46.8; H, 5.0%]. The residue crystallised from ethanol to give 4,4'-bistetrahydroxyran-2-yloxydeoxybenzoin (IIIb) (500 mg.), m. p. and mixed m. p. 125°. Acidification of the alkaline layer followed by ether extraction gave unchanged 4,4'-dihydroxydeoxybenzoin (1.7 g.), m. p. 215°.

*Treatment of 4,4'-Bistetrahydroxyran-2-yloxydeoxybenzoin with Ethynylmagnesium Bromide.*—The bistetrahydroxyranyl ether (IIIb) (4 g.) was treated with an excess of ethynylmagnesium bromide<sup>1</sup> at 0°, and the mixture refluxed for 3 hr. and kept at 20° for 1.5 hr. After the usual isolation the brown oil (3.5 g.) was treated with Girard reagent D (2 g.) in ethanol (20 ml.) and acetic acid (2.0 g.) at 100° for 0.5 hr. The solution was poured into ice-water (200 ml.) containing enough potassium carbonate (2.07 g.) to neutralize 90% of the acid present. Benzene extracted an oil that was immediately treated with acetic anhydride (5 ml.) at 100° for 10 min. The dark brown mixture was extracted with ether, and the extract washed with sodium hydrogen carbonate solution, and evaporated to give a brown oil (3 g.), which was adsorbed on a column of aluminium oxide (90 g.) in hexane. Elution with hexane (3 × 20 ml.) and benzene-hexane (5 : 1; 7 × 20 ml.) gave 1,2-di-(p-acetoxyphenyl)but-1-en-3-yne (IIb) (1.3 g.), m. p. 142°,  $\nu_{\max}$  3220 (C≡CH), 2150 (C≡C), 1740 cm.<sup>-1</sup> (C=O in Ac),  $\lambda_{\max}$  230, 315 m $\mu$  ( $\epsilon$  15,550 and 28,000) [Found (after drying at 20°/1 mm. for 3 hr.): C, 74.8; H, 5.15; O, 20.6; active H, 0.3. C<sub>20</sub>H<sub>18</sub>O<sub>4</sub> requires C, 75.0; H, 5.0; O, 20.0; active H, 0.3%]. After being kept in sunlight for 12 hr., it had  $\lambda_{\max}$  234, 302 m $\mu$  ( $\epsilon$  17,900 and 17,800). The ketone layer from the Girard separation was acidified with hydrochloric acid to give 4,4'-dihydroxydeoxybenzoin (IIIa), m. p. and mixed m. p. 216°.

$\alpha$ -Ethyl-4,4'-dihydroxydeoxybenzoin (IIIc).—Hydriodic acid (300 ml.; *d* 1.7) and  $\alpha$ -ethyldeoxyanisoin (60 g.) in acetic acid (60 ml.) were gradually heated to 135—140° and kept at this temperature for 15 min., then poured into water and extracted with ether. The ether layer was decolorised with sodium hydrogen sulphite solution, extracted with N-sodium hydroxide, and evaporated, giving unchanged  $\alpha$ -ethyldeoxyanisoin (7.5 g.). Acidification of the alkaline layer followed by ether-extraction gave mainly 1-p-hydroxyphenyl-2-p-methoxyphenylbutan-1-one (50 g.), m. p. 105—109° [Found (after drying at 20°/1 mm. for 3 hr.): C, 74.9; H, 6.8; OMe, 10.4. C<sub>17</sub>H<sub>18</sub>O<sub>3</sub> requires C, 75.5; H, 6.7; OMe, 11.7%].

This product (50 g.) was treated with hydriodic acid (200 ml.; *d* 1.7) in acetic acid (60 ml.) at 140° for 10 min. Isolation in the usual way gave amorphous  $\alpha$ -ethyl 4,4'-dihydroxydeoxybenzoin (42 g.) [dibenzoate,<sup>4</sup> m. p. 137—138°,  $\lambda_{\max}$  236 m $\mu$  ( $\epsilon$  23,500)].

3,4-Di-(p-benzoyloxyphenyl)hex-1-yn-3-ol (Ia).—(a) Ethylmagnesium bromide (from ethyl bromide, 22 ml., 0.3 mol., and magnesium, 6 g., 0.25 mol.) in tetrahydrofuran (100 ml.) was slowly added to a large excess of acetylene in tetrahydrofuran (100 ml.) at 0°. 1,2-Di-(p-benzoyloxyphenyl)butan-1-one (IIIe) (23.2 g., 0.05 mol.) was added at 0° and the mixture refluxed for 2 hr. The dark brown solid product obtained by decomposition with ammonium chloride and acidification with 2N-sulphuric acid, was extracted with ether. The extract was washed with sodium hydrogen carbonate, and the phenolic product was removed in 2N-sodium hydroxide, and recovered by acidification and ether-extraction. It formed a dark brown oil (15 g.), which, after treatment with benzoyl chloride (15 g.) in 2N-sodium hydroxide, was adsorbed on aluminium oxide (500 g.) in hexane. Elution with benzene gave dark amorphous material (4.63 g.); elution with ether-benzene (1 : 1; 3 × 100 ml.) and ether (6 × 100 ml.) afforded 3,4-di-(p-benzoyloxyphenyl)hex-1-yn-3-ol (Ia) (9.4 g.), m. p. 170—171°,  $\lambda_{\max}$  230 m $\mu$  ( $\epsilon$  43,000), inflexion 270 m $\mu$  ( $\epsilon$  8000),  $\nu_{\max}$  3480 (OH), 3300 (C≡CH), 1750, 1270, and 1160 cm.<sup>-1</sup> (benzoate) [Found (after drying at 20°/1 mm. for 2 hr.): C, 78.2; H, 5.55. C<sub>32</sub>H<sub>26</sub>O<sub>8</sub> requires C, 78.35; H, 5.55%].

(b) 1,2-Di-(*p*-benzoyloxyphenyl)butan-1-one (IIIc) (4.64 g.) was treated with ethynylmagnesium bromide (from ethyl bromide, 4.5 ml., and magnesium, 1.2 g.) in tetrahydrofuran (75 ml.) at 0° for 1.5 hr. The usual working-up gave a pale yellow oil (5.2 g.) from which unchanged ketone (2.5 g.), m. p. 136°, separated on the addition of ethanol; removal of the solvent gave a yellow oil which was chromatographed on aluminium oxide (60 g.) in hexane. Elution with benzene (5 × 50 ml.) gave 3,4-di-(*p*-benzoyloxyphenyl)hex-1-yn-3-ol (2.15 g.), m. p. and mixed m. p. 171°.

(c) When the ketone (IIIc) was treated with ethynylmagnesium bromide at 0° for 2 hr. and 20° for 72 hr., it gave a dark phenolic product from which no pure compound was isolated.

(d) Di-(*p*-benzoyloxyphenyl)butan-1-one (IIIc) (23.2 g.) was treated with ethynylmagnesium bromide (from ethyl bromide, 22 ml., and magnesium, 6 g.) in tetrahydrofuran (150 ml.) at 0°, and the mixture was stirred for 2 hr. at 0° and for 2 hr. at 20°. Decomposition of the complex followed by ether-extraction gave 3,4-di-(*p*-benzoyloxyphenyl)hex-1-yn-3-ol (Ia) (19.8 g.), m. p. and mixed m. p. 170—171°.

*Dehydration of 3,4-Di-(p-benzoyloxyphenyl)hex-1-yn-3-ol (Ia).*—(a) The alcohol (Ia) (2 g.) in pyridine (20 ml.) was treated with phosphorus trichloride (2 ml.) at -20° for 5 hr. The mixture was poured into ice-water and extracted with ether. The extract was filtered from phosphorus esters and evaporated, yielding a yellow oil (200 mg.),  $\nu_{\max}$ . 1930 (C=C=C), 1740 (OBz) and 1670 (C-C-C=O)  $\text{cm}^{-1}$ .

(b) The alcohol (Ia) (1 g.) in triethylamine (5 ml.) and tetrahydrofuran (5 ml.) was treated with phosphorus trichloride (2 ml.) at -40° for 5 min. The mixture was poured on ice and extracted with methylene dichloride. The extract was washed with ice-cold *N*-sodium hydroxide, *N*-sulphuric acid, and then immediately with sodium hydrogen carbonate solution. Evaporation of the solvent gave a product which did not crystallise, but reprecipitation from benzene with pentane gave a pale yellow amorphous solid, m. p. 140—142°, containing phosphorus (ammonium molybdate test) [Found (after drying at 50°/1 mm. for 6 hr.): C, 60.6; H, 5.4; O, 16; residue, *ca.* 16%]. This material is considered to be a stable phosphorus ester and was not further investigated.

(c) The alcohol (Ia) (2 g.) in tetrahydrofuran (20 ml.) and triethylamine (30 ml.) was treated with thionyl chloride (2 ml.) at -40°. After 0.5 hr. at 0° the product was poured on ice and extracted with ether, and the extracts were washed as in (b). Evaporation gave a product, m. p. 95—110°, which was adsorbed from hexane-benzene on aluminium oxide (40 g.) prepared in hexane. Elution with benzene-hexane (1 : 20; 3 × 50 ml.) gave 1-chloro-3,4-di-(*p*-benzoyloxyphenyl)hexa-1,2-diene (Va) (450 mg.), m. p. 96—97°,  $\lambda_{\max}$ . 233, 260  $\text{m}\mu$  ( $\epsilon$  47,600 and 29,000),  $\nu_{\max}$ . (in  $\text{CS}_2$ ) 1925, 1890 (C=C=C), 1740 (OBz), 740, 753 ( $\text{CCl}$ )  $\text{cm}^{-1}$  [Found (after drying at 20°/1 mm. for 4 hr.): C, 75.5; H, 4.95.  $\text{C}_{32}\text{H}_{25}\text{O}_4\text{Cl}$  requires C, 75.5; H, 4.95%]. Further elution with benzene-hexane gave crystals shown by infrared analysis to be a mixture of allenic and acetylenic material. Elution with benzene gave *trans*-3,4-di-(*p*-benzoyloxyphenyl)hex-3-en-1-yne (IIc) (102 mg.), m. p. 185—187°,  $\lambda_{\max}$ . 232, 272  $\text{m}\mu$  ( $\epsilon$  50,800, 25,350) changing in 24 hr. in sunlight to 232  $\text{m}\mu$  ( $\epsilon$  58,600), inflexion *ca.* 270  $\text{m}\mu$  ( $\epsilon$  24,800),  $\nu_{\max}$ . (in  $\text{CS}_2$ ) 3300 (C≡CH) and 1740  $\text{cm}^{-1}$  (OBz) [Found (after drying at 20°/1 mm. for 48 hr.): C, 79.8; H, 5.35; O, 14.5.  $\text{C}_{32}\text{H}_{24}\text{O}_4, \frac{1}{2}\text{H}_2\text{O}$  requires C, 79.8; H, 5.25; O, 14.95%]. Elution with ether-benzene (1 : 10; 2 × 50 ml.) and ether (5 × 50 ml.) gave 3,4-di-(*p*-benzoyloxyphenyl)hex-3-en-2-one (VI) (460 mg.), colourless needles (from ethanol), m. p. 156° (positive iodoform reaction),  $\lambda_{\max}$ . 232  $\text{m}\mu$  ( $\epsilon$  58,000), inflexion *ca.* 270  $\text{m}\mu$  ( $\epsilon$  23,000),  $\nu_{\max}$ . 1740 (OBz), 1650 (C-C-C=O)  $\text{cm}^{-1}$  [Found (after drying at 20°/1 mm. for 4 hr.): C, 78.6; H, 5.9.  $\text{C}_{32}\text{H}_{26}\text{O}_5$  requires C, 78.35; H, 5.35%].

(d) The alcohol (Ia) (2 g.) was treated with thionyl chloride as in (c) but for only 5 min. at -40°; the mixture was poured into ice-cold *N*-sodium hydroxide, and the product isolated in the usual manner to give an oil. This was adsorbed on aluminium oxide (60 g.) prepared in hexane. Elution with benzene-hexane (1 : 20; 3 × 50 ml.) gave the chloroallene (Va) (620 mg.), m. p. and mixed m. p. 95—97°; further elution with benzene-hexane (1 : 5; 5 × 50 ml.) gave 3-chloro-3,4-di-(*p*-benzoyloxyphenyl)hex-1-yne (IX) (150 mg.), m. p. 130°,  $\lambda_{\max}$ . 232  $\text{m}\mu$  ( $\epsilon$  58,500),  $\nu_{\max}$ . (in  $\text{CS}_2$ ) 3300 (C≡CH) and 1740  $\text{cm}^{-1}$  (OBz) [Found (after drying at 20°/1 mm. for 8 hr.): C, 75.65; H, 4.9; active H, 0.17.  $\text{C}_{32}\text{H}_{25}\text{ClO}_4$  requires C, 75.5; H, 4.95; active H, 0.19%]. Further elution with benzene gave *trans*-3,4-di-(*p*-benzoyloxyphenyl)hex-3-en-1-yne (IIc) (105 mg.), m. p. 184—186°, undepressed on admixture with the material obtained as above and exhibiting identical infrared absorption. No trace of the ketone (VI) was found.

*Reaction of the Chloro-allene (Va) with Sodamide in Liquid Ammonia.*—Ferric nitrate (20 mg.)

and sodium (500 mg.) were added to liquid ammonia (200 ml.) at  $-35^{\circ}$ ; no blue colour remained after 0.5 hr. 1-Chloro-3,4-di-(*p*-benzoyloxyphenyl)hexa-1,2-diene (Va) (200 mg.) in dry ether (10 ml.) was added dropwise at  $-40^{\circ}$ . After 0.5 hr., the usual working-up gave a dark brown oil which was phenolic, dissolving in 2*N*-sodium hydroxide, and was treated therein with benzoyl chloride (0.5 ml.) at  $0^{\circ}$ . Extraction with ether gave a yellow oil that was adsorbed on aluminium oxide (5 g.) from benzene. Elution with benzene-pentane (1:1;  $2 \times 10$  ml.) gave a yellow oil (50 mg.),  $\nu_{\max}$  3250 (C $\equiv$ CH), 1740 (OBz), 1650  $\text{cm}^{-1}$  (C=C=O): insufficiency of material prevented further investigation. Elution with benzene and with ether gave a crystalline product thought to be 3,4-di-(*p*-benzoyloxyphenyl)hex-2-enal (VII), m. p.  $192^{\circ}$ ,  $\lambda_{\max}$  232  $\mu$  ( $\epsilon$  48,000), inflexion *ca.* 270  $\mu$  ( $\epsilon$  17,100),  $\nu_{\max}$  1740 (OBz), 1650 (C=C=O)  $\text{cm}^{-1}$  [Found (after drying at  $20^{\circ}/1$  mm. for 4 hr.): C, 78.1; H, 5.5.  $\text{C}_{32}\text{H}_{26}\text{O}_5$  requires C, 78.35; H, 5.35%].

*Hydrogenation of 3,4-Di-(p-benzoyloxyphenyl)hex-3-en-1-yne (IIc).*—(a) Stilbœstrol dibenzoate (50 mg.), m. p.  $216^{\circ}$ , in ethyl acetate (100 ml.) was shaken in hydrogen with pre-reduced Adams catalyst (20 mg.) for 4 hr. Filtration from the catalyst and evaporation of the solvent gave a quantitative recovery of unchanged starting material.

(b) 3,4-Di-(*p*-benzoyloxyphenyl)hex-3-en-1-yne (IIc) (30 mg.) in ethyl acetate (50 ml.) was hydrogenated as above. The solid product was chromatographically purified on aluminium oxide (1 g.) prepared in benzene. Elution with benzene gave stilbœstrol dibenzoate, m. p. and mixed m. p.  $216^{\circ}$ , having the correct infrared spectrum.

DEPARTMENT OF ORGANIC CHEMISTRY, THE UNIVERSITY OF SYDNEY,  
NEW SOUTH WALES, AUSTRALIA.

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