930. *Some Derivatives of Cyclopenta*[c]*pyran, a New Heteroaromatic System.*

By JOHN HARLEY-MASON and CHARLES R. HARRISON.

The red by-product obtained on thermal decomposition of phenacyltrimethylammonium hydroxide has been shown to be 6,7-dibenzoyl-1,3,5-triphenylcyclopenta[*c*]pyran (IVa), the first example of this heteroaromatic system. Its reactions, degradation, and an alternative synthesis are described. Some bromo-derivatives have been prepared, together with some related pyrindines.

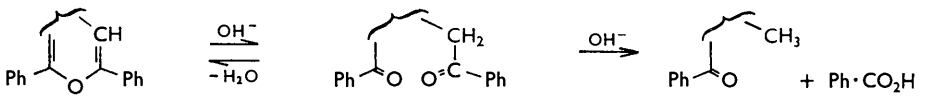
EARLIER work by one of us [1] on the thermal decomposition of phenacyltrimethylammonium hydroxide had shown that the main product was 1,2,3-tribenzoylcyclopropane.* The presence of a small amount of an intensely red by-product was noted, but this was not investigated at the time. By repetition of this work on a larger scale, with chromatography on alumina, the red substance has been isolated and characterised, and its structure elucidated by degradation and an alternative synthesis.

The compound was obtained in very low yield (*ca.* 1·5%) as deep red needles. Microanalysis and molecular-weight determination indicated the formula $C_{40}H_{26}O_3$, corresponding to five Ph·CO·CH: units less two molecules of water. Infrared and nuclear magnetic resonance spectroscopy showed only aromatic protons, and there was no peak above 1666 cm.$^{-1}$ in the carbonyl region. Oxidation with potassium permanganate gave benzoic acid in high yield as the only isolable product. The compound was stable to acids, but

* This was then described as the *cis*-compound on the basis of the early work of Paal and Schulze,[2] but it has recently [3] been shown to be the *trans*-isomer (XV).

[1] Harley-Mason, *J.*, 1949, 518.
[2] Paal and Schulze, *Ber.*, 1903, **36**, 2425.
[3] Maier, *Chem. Ber.*, 1962, **95**, 611.

with hot dilute alcoholic potassium hydroxide gave an orange-yellow substance, $C_{40}H_{28}O_4$, corresponding to the addition of a molecule of water. The infrared spectrum of this showed carbonyl peaks at 1692 and 1642 cm.$^{-1}$, but no peak corresponding to a hydroxyl group. In the nuclear magnetic resonance (n.m.r.) spectrum there was a single peak at τ 6·1, interpreted as due to the methylene group in Ph·CO·CH_2– attached to a conjugated system. This substance was smoothly reconverted into the original red substance by long boiling in ethanol or treatment with acid. On prolonged boiling with 30% methanolic potassium hydroxide the red compound gave benzoic acid and a second degradation product, a yellow solid, $C_{33}H_{24}O_3$, having peaks at 1657 cm.$^{-1}$ and below in the carbonyl region of the infrared spectrum and having a single resonance at τ 8·15 in the n.m.r. spectrum interpreted as due to CH_3 attached to a conjugated system. These reactions suggest a system of the type below:

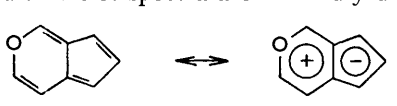


In accord with this was the reaction of the red compound with ethanolic ammonia to give an orange material, $C_{40}H_{27}NO_2$, and with methylamine to give a similar substance, $C_{41}H_{29}NO_2$, corresponding to the replacement of the pyran oxygen by >NH and >NMe, respectively.

It was noted that the ultraviolet and infrared spectra of the second alkaline degradation product were similar to those of the known [4] 1,2,3-tribenzoyl-4-phenylcyclopentadiene * (I), and it was therefore formulated as 1-methyl-2,3,4-tribenzoyl-5-phenylcyclopentadiene (II). The first alkaline degradation product is therefore 1-phenacyl-2,3,4-tribenzoyl-5-phenylcyclopentadiene (III) and the red compound is 6,7-dibenzoyl-1,3,5-triphenylcyclopenta[*c*]pyran (IVa). This is the first example of the cyclopenta[*c*]pyran system to be prepared, and like other pseudoazulenes (*e.g.*, the known sulphur and nitrogen analogues [5]) classical (V) and zwitterion (VI) structures may be written for it.

Structure (IVa) was confirmed by an alternative synthesis. On fusing the potassium salt of tribenzoylphenylcyclopentadiene with an excess of phenacyl chloride the cyclopentapyran (IVa) was obtained in fair yield, presumably *via* (III) formed by *C*-alkylation of the cyclopentadiene. Vigorous conditions are necessary owing to the steric hindrance involved.

The compounds obtained by the action of ammonia and methylamine on the cyclopentapyran are plainly the 2-pyrindines (VII; R = H and Me). It is of interest that their ultraviolet spectra are markedly different, suggesting that in the case of the parent (VII; R = H) the prototropic isomer (VIII) must be considered. As would be expected, their spectra in concentrated sulphuric acid solution are almost identical. The cyclopentapyran also reacts readily with hydrazine to give a yellow compound, $C_{40}H_{28}N_2O_2$. This has a peak at 1689 cm.$^{-1}$ in the infrared spectrum and therefore very probably contains a phenacyl group (cf. III), indicating the cyclopentapyridazine structure (IX or X); we are at present unable to distinguish between these. A similar system was earlier prepared by Hale.[6]



(V) (VI)

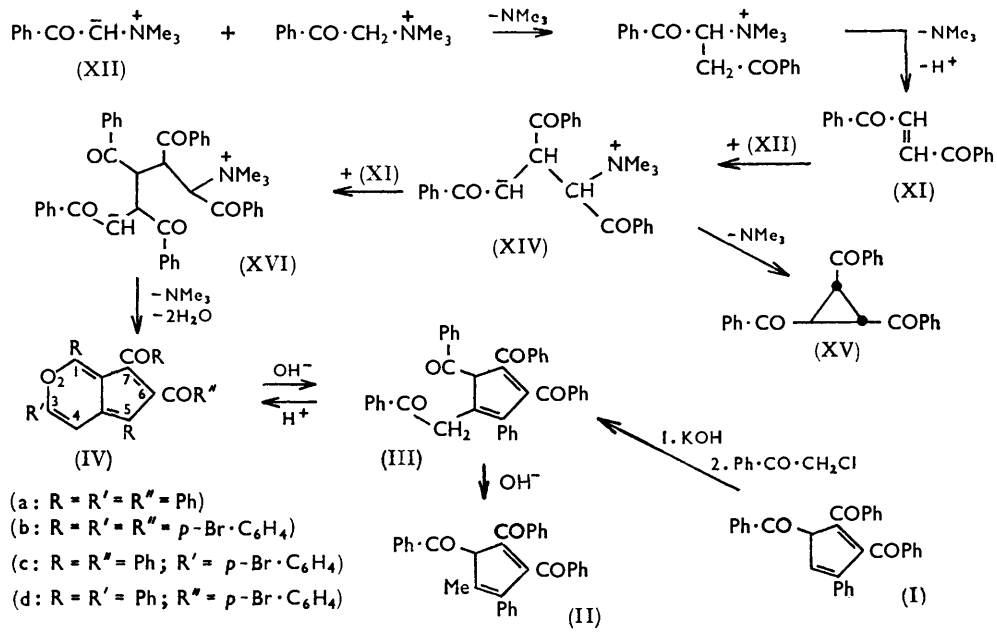
* The original authors [4a] proposed this structure. Fuson *et al.*,[4b] although agreeing with the basic skeleton, favoured a tautomeric hydroxyfulvene structure. We prefer the latter since we observed a peak at τ −8·52 in the n.m.r. spectrum, attributed to a strongly chelated hydroxyl group, but we use the older structure for simplicity.

[4] (*a*) Gardner and Rydon, *J.*, 1938, 45; (*b*) Fuson, Fleming, Warfield, and Wolf, *J. Org. Chem.*, 1945, **10**, 121.

[5] A. G. Anderson, jun., Harrison, R. G. Anderson, and Osbourne, *J. Amer. Chem. Soc.*, 1959, **81**, 1255.

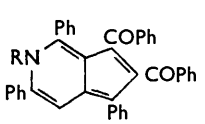
[6] Hale, *J. Amer. Chem. Soc.*, 1916, **38**, 2535.

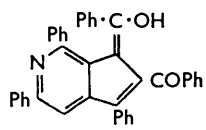
Thermal decomposition of 4-bromophenacyltrimethylammonium hydroxide gave the purple-red penta-*p*-bromo-derivative (IVb) of the cyclopentapyran together with *trans*-tri-*p*-bromobenzoylcyclopropane, while reaction of 4-bromophenacyl chloride with the



potassium salt of tribenzoylphenylcyclopentadiene gave the mono-*p*-bromo-derivative (IVc), which on vigorous treatment with alkali gave *p*-bromobenzoic acid and the cyclopentadiene (II).

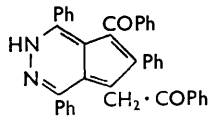
The mechanism of formation of the cyclopentapyran system and of tribenzylcyclopropane is of considerable interest. We suspected that 1,2-dibenzoylethylene (XI), formed *via* the ylid (XII) as indicated in the sequence (XII) ⟶ (XI), was a common intermediate since the analogous compound [7] (XIII) is known [8] to give dibenzoylethylene when heated at 150° under a vacuum. This was confirmed when we found that addition of *trans*-dibenzoylethylene to the reaction mixture before pyrolysis lowered the reaction temperature and increased the yield of the cyclopentapyran twenty-fold (thus greatly facilitating the preparation of this material in sufficient amount). Michael addition of the ylid (XII) to dibenzoylethylene would lead to the intermediate (XIV) which by a

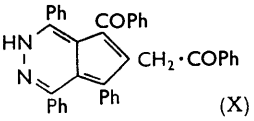

(VII)


(VIII)

1,3-elimination of trimethylamine can give the tribenzoylcyclopropane (XV). On the other hand a further Michael addition of (XIV) to dibenzoylethylene leads to the intermediate (XVI), which by loss of trimethylamine and water gives the cyclopentapyran (IVa). Some support for this mechanism is provided by the fact that thermal decomposition of 4-bromophenacyltrimethylammonium hydroxide in the presence of *trans*-dibenzoylethylene gives a *p*-bromophenylcyclopentapyran [very probably (IVd)], different from the isomer (IVc) mentioned above and giving benzoic acid on vigorous alkaline treatment.

[7] Kröhnke, *Ber.*, 1935, **68**, 1184.
[8] Cook, Downer, and Hornung, *J.*, 1941, 503.


(IX)


(X)

This rules out tribenzoylphenylcyclopentadiene (I) as an intermediate—and, indeed, addition of the latter in place of dibenzoylethylene to the pyrolysis mixture gave no increase in the yield of the cyclopentapyran. The second product was 1,2-dibenzoyl-3-*p*-bromobenzoylcyclopropane. The n.m.r. spectrum of this cyclopropane was identical in pattern


(XIIIa) (XIIIb)

with that of *trans*-tribenzoylcyclopropane [9] and *trans*-tri-*p*-bromobenzoylcyclopropane. This is characteristic of an AX_2 system,[10] showing that the compound has the two benzoyl groups *cis* to one another with the *p*-bromobenzoyl group *trans* to them. Thus, rotation of one of the benzyl groups in the *trans*-dibenzoylethylene must have occurred. This is certainly easily possible in the mechanism outlined above. However, if the cyclopropane were formed by addition of *p*-bromobenzoylcarbene to *trans*-dibenzoylethylene, the benzoyl groups should remain *trans* to one another.

Experimental

Infrared spectra were recorded on a Perkin-Elmer model 21 instrument with a sodium chloride prism, for Nujol mulls. Ultraviolet spectra were measured for 95% ethanol solutions with a Cary model 14 recording spectrometer. N.m.r. spectra were obtained at 40 Mc./sec. by using a Varian associates V4300B spectrometer. Frequencies are measured on the τ scale relative to tetramethylsilane ($\tau = 10{\cdot}00$). Chromatography was carried out with chloroform solutions on alumina activated at 360°.

6,7-*Dibenzoyl*-1,3,5-*triphenylcyclopenta*[c]*pyran* (IVa).—To a solution of phenacyltrimethylammonium bromide (20 g.) in water (40 ml.), silver oxide (15 g.) was added. After 15 minutes' shaking, the solution was filtered and evaporated to dryness under reduced pressure. The waxy residue was slowly heated in an oil-bath. At about 150° (internal temperature) a vigorous reaction commenced with the evolution of trimethylamine. As it subsided the temperature was raised to 180° and kept there for 10 min. The dark red-brown melt was allowed to cool to 120—130° and glacial acetic acid was added. After refluxing for 5 minutes the hot solution was filtered and the acetic acid removed under reduced pressure. The residue was chromatographed and the prominent red band collected. This fraction, which contained a considerable amount of tribenzoylcyclopropane, was dissolved in an excess of ethanol, and the ethanol was slowly distilled off. After a time the red solid began to separate. When sufficient had separated, it was filtered off from the boiling solution and recrystallised from ethanol (if the distillation was continued too long the product was heavily contaminated by the cyclopropane). The *cyclopenta*[c]*pyran* (0·13 g.) formed deep red needles, m. p. 212·5—213·5° (Found: C, 86·5; H, 4·75%; *M*, 530 and 560 by thermistor vapour-pressure method. $C_{40}H_{26}O_3$ requires C, 86·6; H, 4·75%; *M*, 555), $\nu_{max.}$ 1667, 1640, 1620, 1600, and 1581 cm.$^{-1}$, $\lambda_{max.}$ 264 (ε 41,700), 319 (ε 24,800), and 493 mμ (ε 5460); $\lambda_{min.}$ 226 (ε 24,200), 309 (ε 24,000), and 433 mμ (ε 2070).

When dibenzoylethylene (20 g.) was added before decomposition, the reaction temperature was lowered to *ca.* 90°, and the yield increased approximately twenty-fold.

6,7-*Di*-p-*bromobenzoyl*-1,3,5-*tri*-p-*bromophenylcyclopenta*[c]*pyran* (IVb) *and* trans-*tri*-p-*bromobenzoylcyclopropane*.—4-Bromophenacyltrimethylammonium bromide (from 4-bromophenacyl bromide and trimethylamine) was treated as above for the unsubstituted compound. After chromatography the red fraction was treated with diethyl ether. The white residue gave needles of trans-*tri*-p-*bromobenzoylcyclopropane*, m. p. 197° (from ethanol) (Found: C, 48·4; H, 2·75. $C_{24}H_{15}Br_3O_3$ requires C, 48·75; H, 2·55%), $\nu_{max.}$ 1695, 1663, and 1589 cm.$^{-1}$, $\lambda_{max.}$ (in

[9] Shoolery, *Svensk Kem. Tidskr.*, 1957, **69**, 185.

[10] Pople, Schneider, and Bernstein, " High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959.

dioxan) 265 (ε 56,700), $\lambda_{min.}$ 231 mμ (ε 13,440). The ethereal solution was diluted with ethanol and the ether distilled off. The precipitated solid was dissolved in chloroform, ethanol added, and the chloroform slowly distilled off until the solution began to become cloudy. Cooling yielded the *cyclopenta*[c]*pyran* as a microcrystalline purple solid, m. p. 244°, $\nu_{max.}$ 1666, 1630, 1591, and 1581 cm.$^{-1}$, $\lambda_{max.}$ 276 (ε 57,100), 325 (ε 31,200), and 492 mμ (ε 6625), $\lambda_{min.}$ 232 (ε 30,200), 318 (ε 31,080), and 439 mμ (ε 4275) (Found: C, 50·7; H, 2·6. $C_{40}H_{21}Br_5O_3$ requires C, 50·6; H, 2·25%).

7-*Benzoyl*-6-p-*bromobenzoyl*-1,3,5-*triphenylcyclopenta*[c]*pyran* (IVd) *and* 1,cis-2-*Dibenzoyl*-trans-3-p-*bromobenzoylcyclopropane*.—4-Bromophenacyltrimethylammonium bromide (10 g.) was decomposed as above, except that *trans*-dibenzoylethylene (20 g.) was added to the quaternary ammonium hydroxide before decomposition and the reaction was completed by heating at 190° for 20 min. After chromatography the red fraction was treated with ether to yield a dark solution and a pink solid. The solid was recrystallised twice from glacial acetic acid and once from ethanol to give the *cyclopropane* as needles, m. p. 167° (Found: C, 66·8; H, 4·15. $C_{24}H_{17}BrO_3$ requires C, 66·5; H, 3·95%), $\nu_{max.}$ 1675, 1598, and 1580 cm.$^{-1}$, $\lambda_{max.}$ 256 (ε 43,020), $\lambda_{min.}$ 226 mμ (ε 11,400). The ethereal solution obtained above was refluxed for 8 hr. and the solid which separated filtered off. The solid was recrystallised twice from ethanol to yield the *cyclopenta*[c]*pyran* (0·6 g.) as dark red needles, m. p. 233° (Found: C, 75·75; H, 3·95. $C_{40}H_{25}BrO_3$ requires C, 75·8; H, 3·95%), $\nu_{max.}$ 1671, 1628, 1602, and 1580 cm.$^{-1}$, $\lambda_{max.}$ 266 (ε 44,200), 322 (ε 28,220), and 492 mμ (ε 5484), $\lambda_{min.}$ 224 (ε 30,000), 308 (ε 27,000), and 434 mμ (ε 3125).

6,7-*Dibenzoyl*-1,3,5-*triphenylcyclopenta*[c]*pyran by Phenacylation of Tribenzoylphenylcyclopentadiene*.—Tribenzoylphenylcyclopentadiene was prepared by the method of Fuson *et al.*[4b] and formed yellow needles, m. p. 164°, $\nu_{max.}$ 1654, 1611, 1590, and 1527s cm.$^{-1}$, $\lambda_{max.}$ 247 (ε 28,900), 292 (ε 20,260), and 431 mμ (ε 10,220), $\lambda_{min.}$ 221 (ε 24,200), 276 (ε 19,700), and 406 mμ (ε 9700), $\lambda_{infl.}$ 370 mμ (ε 11,900). The cyclopentadiene (0·5 g.) was dissolved in warm ethanol (20 ml.) containing potassium hydroxide (0·07 g.). The solution was evaporated to dryness and phenacyl chloride (5 g.) added to the residue. The mixture was heated at 180° for 20 min. After cooling to 120° it was refluxed with glacial acetic acid for 5 min. The excess of phenacyl chloride was removed by steam-distillation and the residue chromatographed. The prominent orange-red band was collected and recrystallised twice from methanol, giving red needles (0·11 g.), m. p. 210°, identical (i.r. spectrum) with the product obtained from thermal decomposition of phenacyltrimethylammonium hydroxide.

6,7-*Dibenzoyl*-3-p-*bromophenyl*-1,5-*diphenylcyclopenta*[c]*pyran* (IVc).—Tribenzoylphenylcyclopentadiene (1 g.) was converted into its potassium salt as above. 4-Bromophenacyl chloride (10 g.) was added, and the mixture heated at 180° for 30 min. After treatment with glacial acetic acid, steam-distillation, and chromatography as for the previous compound, it gave an orange-red fraction which was refluxed with light petroleum (b. p. 60—80°) for 30 min. The residue was filtered off and treated twice more in this way. The *cyclopenta*[c]*pyran* formed bright red needles, m. p. 242° (from methanol) (Found: C, 75·7; H, 4·2. $C_{40}H_{25}BrO_3$ requires C, 75·8; H, 3·95%), $\nu_{max.}$ 1676, 1616, 1601, and 1564 cm.$^{-1}$, $\lambda_{max.}$ 267 (ε 48,400), 320 (ε 27,300), and 488 mμ (ε 6950), $\lambda_{min.}$ 228 (ε 27,050), 314 (ε 27,200), and 436 mμ (ε 4820).

6,7-*Dibenzoyl*-1,3,5-*triphenyl*-2H-2-*pyrindine* (VII; R = H).—6,7-Dibenzoyl-1,3,5-triphenylcyclopenta[*c*]pyran (0·1 g.) was dissolved in hot ethanol (50 ml.), and ammonia (*d* 0·88) (1 ml.) was added. After 5 min. the solution (now orange) was diluted with water, and the precipitated solid recrystallised from ethanol–water. The *pyrindine* was obtained as orange-red needles m. p. 203° (decomp.) (Found: C, 86·6; H, 5·4; N, 2·1. $C_{40}H_{27}NO_2$ requires C, 86·75; H, 4·9; N, 2·55%), $\nu_{max.}$ 3500, 3380, 1634, 1615, 1591, 1583, and 1558 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 257 (ε 40,310) and 460 (ε 8030), $\lambda_{min.}$ 226 (ε 29,900) and 432 (ε 7346), $\lambda_{infl.}$ 375—390 (ε 9824). $\lambda_{max.}$ (in conc. H_2SO_4) 279 (ε 29,900), 355 (ε 22,000), 423 (ε 19,220), and 730 (ε 9840), $\lambda_{min.}$ 249 (ε 21,090), 343 (ε 21,100), 385 (ε 16,180), and 580 (ε 6330), $\lambda_{infl.}$ 224 (ε 26,500) and 292 mμ (ε 29,000).

6,7-*Dibenzoyl*-2-*methyl*-1,3,5-*triphenyl*-2H-2-*pyrindine* (VII; R = Me).—This was prepared in the same way as the previous compound, but with ethanolic methylamine in place of ammonia. The *pyrindine* was obtained as orange crystals, m. p. 280° (Found: C, 86·8; H, 5·6; N, 2·4. $C_{41}H_{29}NO_2$ requires C, 86·75; H, 5·2; N, 2·45%), $\nu_{max.}$ 1665, 1593, 1541, and 1515 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 252 (ε 39,100), 293 (ε 35,200), and 469 (ε 7240), $\lambda_{min.}$ 225 (ε 30,300), 276 (ε 32,800), and 420 (ε 4880), $\lambda_{max.}$ (in conc. H_2SO_4) 272 (ε 30,850), 424 (ε 20,110), and 706 (ε 11,180), $\lambda_{min.}$ 249 (ε 25,700), 375 (ε 13,260), and 580 (ε 6560), $\lambda_{infl.}$ 230 (ε 29,350) and 325 mμ (ε 20,400).

7-*Benzoyl*-5(*or* 6)-*phenacyl*-1,4,6(*or* 5)-*triphenylcyclopenta*[d]*pyridazine* (IX or X).—This was prepared in the same way as the previous two compounds, by using hydrazine hydrate. The *pyridazine* was obtained as yellow needles, m. p. 246° (Found: C, 84·7; H, 5·6; N, 5·05. $C_{40}H_{28}N_2O_2$ requires C, 84·5; H, 4·95; N, 4·95%), $\nu_{max.}$ 3310, 3220, 1689, 1624, 1598, 1581, and 1550 cm.$^{-1}$, $\lambda_{max.}$ 248 (ε 42,500), 277 (ε 38,600), and 392 (ε 4970), $\lambda_{min.}$ 223 (ε 31,400), 267 (ε 37,250), and 356 mμ (ε 4070).

1,2,3-*Tribenzoyl*-4-*phenacyl*-5-*phenylcyclopentadiene* (III).—6,7-Dibenzoyl-1,3,5-triphenylcyclopenta[*c*]pyran (0·1 g.) was dissolved in boiling ethanol (50 ml.), and potassium hydroxide (0·1 g.) added. After 10 minutes' refluxing, the solution was cooled and acidified with an excess of dilute hydrochloric acid. The precipitated yellow solid was washed with water, dried at room temperature/0·1 mm., and dissolved in boiling ethanol; this solution was rapidly filtered and cooled (prolonged maintenance at the b. p. caused extensive recyclisation). The *cyclopentadiene* was obtained as yellow prisms, decomposing at 184° (to give the cyclopenta[*c*]pyran) (Found: C, 84·05; H, 5·05. $C_{40}H_{28}O_4$ requires C, 83·9; H, 5·05%), $\nu_{max.}$ 1692, 1643, 1601, and 1525s cm.$^{-1}$, $\lambda_{max.}$ 244 (ε 38,800), 320 (ε 12,600), and 402 (ε 12,850), $\lambda_{min.}$ 220 (ε 27,800), 300 (ε 11,380), and 347 mμ (ε 10,750).

1,2,3-*Tribenzoyl*-4-*methyl*-5-*phenylcyclopentadiene* (II).—A solution of 6,7-dibenzoyl-1,3,5-triphenylcyclopenta[*c*]pyran (0·1 g.) and potassium hydroxide (6 g.) in methanol (20 ml.) and water (0·25 ml.) was refluxed for 4 hr. The solution was then cooled and acidified with dilute hydrochloric acid, and the precipitated solid was filtered off and washed with water. The filtrate, on removal of the methanol and extraction with ether, gave benzoic acid. The solid which had been filtered off was dried thoroughly at 40°/0·1 mm. and recrystallised from light petroleum (b. p. 60—80°) (acetone–carbon dioxide bath). The *tribenzoylmethylphenylcyclopentadiene* was obtained as a yellow microcrystalline solid, m. p. 93—96° (Found: C, 84·65; H, 5·5. $C_{33}H_{24}O_3$ requires C, 84·6; H, 5·15%), $\nu_{max.}$ 1657, 1598, and 1530s cm.$^{-1}$, $\lambda_{max.}$ 247 (ε 25,800) and 400 (ε 11,620), $\lambda_{min.}$ 225 (ε 22,500) and 345 mμ (ε 10,580), λ_{infl} 310 mμ (ε 11,720).

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