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THE ELECTROPHILIC SUBSTITUTION OF BENZOCYCLOBUTENE—II

BENZOYLATION, SULPHONATION, BROMINATION AND CHLORINATION

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Abstract—Benzoylation of benzocyclobutene gives β-phenethyl chloride, 2′-(2-chloroethyl)-benzophenone and 4-benzoylbenzocyclobutene in proportions dependent on solvent and catalyst; β-phenethyl chloride gives no discrete benzoylation product under conditions where benzocyclobutene gives large quantities of the chloroethylbenzophenone. Sulphonation, using dioxan-sulphur trioxide complex, gives β-hydroxyethyl-benzene-*o*-sulphonic acid sultone and benzocyclobutene-4-sulphonic acid in approximately equal amounts. Bromination, in the presence of iodine in 95% acetic acid aq, gives 4-bromobenzocyclobutene (~86% estimated by VPC, 78% isolated) and *o*-bromo-β-phenethyl bromide (~13% estimated, 11% isolated); the yield of 3-bromobenzocyclobutene, if any, is less than 1·2%: similarly chlorination gives 4-chlorobenzocyclobutene (~75% estimated, 69% isolated), *o*-chloro-β-phenethyl chloride (~19% estimated, 13% isolated) and an acetate (~4% estimated); an upper limit of about 1·5% is placed on the extent of chlorination in the 3-position. The interconversions of the substituted benzocyclobutenes obtained with known compounds is examined. On the basis of these and previously reported results a multicentre transition state is proposed for some dealkylation reactions, a reinterpretation of Jensen and Maciel's kinetic data for the benzoylation is advanced and an analogy is drawn between the stress systems and positions of substitution in benzocyclobutene, biphenylene and bridged hydronaphthalenes.

WE HAVE recently shown[1] that acetylation, nitration and hydrobromination of benzocyclobutene (I) proceed with extensive dealkylation, the electrophile taking up a position on the benzene nucleus previously occupied by a methylene group. Because of this the maximum yields of substituted benzocyclobutenes obtained were about 35%; only 4-substitution was observed. This paper examines the relative variation of dealkylation and 4-substitution with variation in reagent and provides an estimate of the relative reactivities of the 3- and 4-positions.

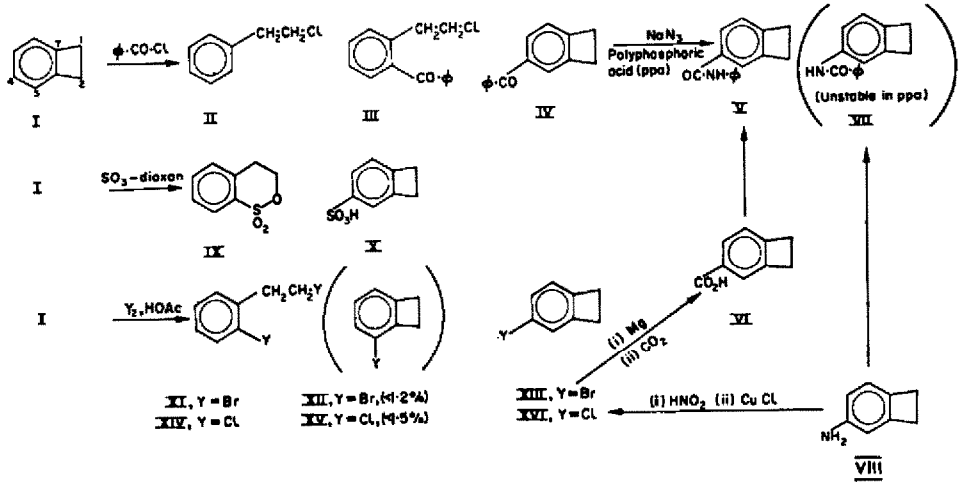
Friedel-Crafts benzoylation. The aluminium chloride and stannic chloride catalysed reactions in ethylene chloride (0–25°) and nitromethane (−35°) yield mixtures containing varying quantities of β-phenethyl chloride (II) most of which is removed by distillation; the other products, after distillation, are readily separated into two ketones, $C_{15}H_{13}ClO$ (III) and $C_{15}H_{12}O$ (IV).

Compound III contains mono- and 1,2-disubstituted benzene rings (IR), two adjacent methylene groups (NMR) and is oxidized by permanganate to *o*-benzoylbenzoic acid; as no reaction is observed with Brady's reagent the keto group is probably sterically hindered. We formulate III as 2′-(2-chloroethyl)-benzophenone.

Compound IV is a nuclear substituted benzocyclobutene containing mono- and 1,2,4-trisubstituted benzene nuclei (IR); the NMR spectrum shows a two to one ratio of aryl to methylenic protons, the latter as a singlet; thus IV is 4-benzoylbenzocyclobutene. This is confirmed by the Schmidt azide rearrangement in polyphosphoric

[1] J. B. F. Lloyd and P. A. Ongley, *Tetrahedron* **20**, 2185 (1964).

acid[2] of IV to benzocyclobutene-4-carboxanilide (V) in about 40% yield which relates IV to the known benzocyclobutene-4-carboxylic acid (VI). This reaction also produces a material identical (IR, phosphate ester) with that obtained when 4-benzocyclobutenylbenzamide (VII), prepared from 4-aminobenzocyclobutene (VIII), is treated with polyphosphoric acid; which suggests that both amides are formed in the rearrangement. The instability of VII in acid is expected since the substituted amino substituent should facilitate a protodealkylation, just as it does in 4-acetamidobenzocyclobutene.[1,3]



The presence of β-phenethyl chloride in the reaction mixtures suggests that benzoylation of this rather than of benzocyclobutene could be producing III, though *para*-orientation would be more probable if this were so. However, when β-phenethyl chloride is benzoylated in ethylene chloride, a solvent in which benzocyclobutene gives predominantly III, we find a polymeric material is the sole product. The IR

TABLE 1. BENZOYLATION OF BENZOCYCLOBUTENE

Catalyst and solvent	Products isolated (%)		
	II	III	IV
$AlCl_3$, $(CH_2)_2Cl_2$	32*	42	18
$AlCl_3$, CH_3NO_2	37	trace	54
$SnCl_4$, CH_3NO_2	3	trace	84

II is β-phenethyl chloride; III, 2′-(2-chlorethyl)-benzophenone; IV, 4-benzoylbenzocyclobutene. * Includes product of further reaction.

spectrum of this material is comparable with a residue obtained under the same conditions from benzocyclobutene hence, though further benzoylation of II undoubtedly occurs, III must be an acyldealkylation product of benzocyclobutene.

The variation of product yields with reaction conditions is given in Table 1.

Sulphonation. In concentrated sulphuric acid benzocyclobutene gives a polystyrene-like material,[4] presumably through a series of protodealkylations. We find that

[1] R. T. Conley, *J. Org. Chem.* **23**, 1330 (1958).
[3] L. Horner, H.-G. Schmelzer and B. Thompson, *Chem. Ber.* **93**, 1774 (1960).
[4] M. P. Cava and D. R. Napier, *J. Amer. Chem. Soc.* **80**, 2255 (1958).

such reactions can be completely avoided by the use of dioxan-sulphur trioxide complex in ethylene chloride.[5] Under these conditions, at 0–20°, benzocyclobutene gives a neutral product, $C_8H_8SO_3$ (IX), and a sulphonic acid (X) in approximately equal amounts.

Product IX is a sulphonate ester containing normal and 'active' methylene groups (IR). Equal numbers of aromatic and methylenic protons are present, the latter as an A_2X_2 sextet (NMR). Permanganate oxidation gives *o*-sulphobenzoic acid hence IX is *β*-hydroxyethylbenzene-*o*-sulphonic acid sultone.

The acid X is separated as its barium salt, which, after purification by Soxhlet extraction in methanol, analyses for barium as $Ba(C_8H_7O_3S)_2$. Fusion with potassium hydroxide and oxidation with permanganate result in almost complete degradation and no significant quantities of material useful for structural assignment can be isolated; in our experience extensive over-oxidation is typical of nuclear substituted benzocyclobutenes. We formulate X as benzocyclobutene-4-sulphonic acid on the basis of physical data (Experimental section) which, for the barium and sodium salts, indicate a 1,2,4-trisubstituted benzene nucleus bearing a sulphonate and two methylene groups as substituents.

Bromination. This is carried out in the presence of iodine using 95% acetic acid aq as solvent. VPC shows the presence of three products (peak areas) as XII (1·2), XIII (86), XI (13); the retention volumes of XII and XIII are nearly equal, that of XI is considerably greater than the other two. Solid–liquid chromatography of the mixture gives two well separated fractions. The first, C_8H_7Br, possesses a 1,2,4-trisubstituted benzene nucleus (IR), a three to four ratio of aryl to methylenic protons, the latter as a singlet (NMR), and can be converted, through the Grignard derivative, to benzocyclobutene-4-carboxilic acid (VI) in over 90% yield, hence characterizing 4-bromo-benzocyclobutene (XIII). VPC shows that XIII is still contaminated by XII however. As XII has a retention volume different from *β*-phenethyl bromide, is unaffected by refluxing alkali and has a volatility comparable with XIII, it is apparently not a ring-opening or side-chain halogenation product.

The second chromatography fraction is pure XI, (VPC) analysing as $C_8H_8Br_2$. The presence of a 1,2-disubstituted nucleus (IR), two adjacent methylene groups (NMR) and permanganate oxidation to *o*-bromobenzoic acid define XI as *o*-bromo-*β*-phenethyl bromide.

As these results leave only 1·2% of volatile product uncharacterized then no more than this amount of 3-bromobenzocyclobutene is being formed. What little can be inferred concerning the nature of XII is not inconsistent with what is expected for the 3-bromo compound. The quantities of XI and XIII isolated correspond in yield to 11% and 78% respectively; which, in view of the volatility of these compounds and consequent losses during recovery from the chromatography elutes, is considered in reasonable agreement with the VPC result.

Chlorination. The reaction conditions and separation procedures used for the chlorination are essentially the same as in the bromination. Four products are found by VPC: XV (1·5), XVI (75), XIV (19), XVII (4). Components XV and XVI have nearly equal retention volumes; component XVII is particularly slow moving and diffuse. Solid–liquid chromatography gives three well separated fractions.

[5] C. M. Suter, P. B. Evans and J. M. Kiefer, *J. Amer. Chem. Soc.* **60**, 538 (1938).

The first fraction is XVI, still contaminated by XV (VPC). Analysis gives C_8H_7Cl, NMR and IR data compare closely with 4-bromobenzocyclobutene (XIII) and the formation of the same compound in 66% yield by a Sandmeyer reaction from VIII confirms XVI as 4-chlorobenzocyclobutene. The contaminant XV is apparently not a ring-opening product and it is not present in the sample of XVI prepared by the Sandmeyer reaction. Comparison of the IR spectra of the two samples suggests XV contains a 1,2,3-trisubstituted nucleus, as would 3-chlorobenzocyclobutene; even so an upper limit of about 1·5% is placed on the extent of 3-chlorination.

The second solid–liquid chromatography fraction is shown by IR and NMR data, and by oxidation to *o*-chlorobenzoic acid, to be *o*-chloro-*β*-phenethyl chloride (XIV). Finally the third fraction, obtained by stripping the column with methylene chloride, contains a small amount of acetate (XVII) together with residues of the other chlorination products.

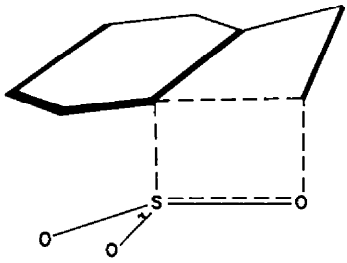
The yields of isolated XVI and XIV are 69% and 13% respectively, which is considered to be in satisfactory agreement with the VPC result.

DISCUSSION

The constitutions of the ring-opening products isolated from the reactions reported here and in earlier studies,[1,3] in particular their completely *ortho*-orientation, indicates that electrophilic dealkylation must be taking place. Whereas there is considerable evidence[6–8] which suggests that dealkylations on tertiary-alkylated substrates pass through a transition state analogous in structure to the benzeneonium intermediate involved in deprotonation,[8] the formation of such an intermediate, and the related transition state, involving the 7-position of benzocyclobutene would probably be precluded by strain effects.[9] Furthermore this would require generation either of an *o*-substituted *β*-phenethyl carbonium ion, which is energetically improbable, or of a substituted styrene (by synchronous proton loss from the *α*-methylene group), both of which would result in substituted *α*-phenethyl products by rearrangement or addition processes; in no case have we been able to detect such compounds. Benzocyclobutene dealkylations tend to predominate when the reagents used have, in their ground states, a high asymmetry of charge distribution (sulphonation, nitration and acylation, excepting nitro-methane benzoylation). This generalization is not applicable to de-tertiary alkylation reactions but agrees well with what is observed when primary alkyl or methyl groups are displaced: for example, under conditions appropriate to aromatic electrophilic substitutions, hexamethylbenzene undergoes demethylation on nitration[10] and acylation[11] whereas bromination[12] and chlorination,[13] under heterolytic conditions, occur only on the methyl substituents; the behaviour of this compound on sulphonation is as yet not properly characterized.[14] These observations suggest that dealkylations on primary-alkylated nuclei require a reagent capable of dispersing

[6] H. E. Albert and W. C. Sears, *J. Amer. Chem. Soc.* **76**, 4979 (1954).
[7] F. Bell, *J. Chem. Soc.* 120 (1958).
[8] P. B. D. de la Mare and E. A. Johnson, *J. Chem. Soc.* 4076 (1963).
[9] We are indebted to Dr. A. W. P. Jarvie for this observation.
[10] L. Moore and T. B. Johnson, *J. Amer. Chem. Soc.* **57**, 1287 (1935).
[11] H. Hopff and A. K. Wick, *Helv. Chim. Acta* **43**, 1473 (1960).
[12] R. Josephson, R. M. Keefer and L. J. Andrews, *J. Amer. Chem. Soc.* **83**, 3562 (1961).
[13] E. Baciocchi and G. Illuminati, *Tetrahedron Letters* 637 (1962).
[14] N. C. Deno, P. T. Groves and G. Saines, *J. Amer. Chem. Soc.* **81**, 5790 (1959).

any positive charge developing on the leaving group during reaction, possibly by bond-formation as in the multicentre transition states which have been invoked for displacements on organometallic compounds[15] and some aromatic deprotonations.[16] For instance we would represent the sulphonation of benzocyclobutene as proceeding through a four-centre transition state:



thus minimizing unfavourable strain effects and stabilizing the leaving-group. On this basis the lower levels of dealkylation effected by the halogens is attributable to their decreased ability to disperse a positive charge. Analogous arguments can be advanced concerning the other reagents examined, though with less precision in some cases because of the ill-defined nature of the reactants involved.

The benzoylation results allow some clarification of the kinetic study by Jensen and Maciel,[17] which gives the rates of benzoylation (in ethylene chloride catalyzed by $AlCl_3$, disappearance of reagent measured) of benzocyclobutene, indane and tetralin, relative to *o*-xylene, as 2·8, 1·9 and 2·3 respectively. Under these conditions, however, we find that benzocyclobutene undergoes extensive proto- and acyl-dealkylation giving *β*-phenethyl chloride and 2′-(2-chloroethyl)-benzophenone, the extent of acyldeprotonation being only about 20%. If the kinetic results are modified to allow for this then the relative rates of acyl-deprotonation in this series become approximately 1, 1·9 and 2·3. This is precisely the order expected from a consideration of the inductive effects exerted by the cycloalkene substituents.[18] The position of *o*-xylene is slightly anomalous though in view of the uncertainty about the products obtained in the kinetic study this is probably not significant; obviously more data are required here.

Finally we wish to make some observations concerning the reactivity of the 3-position in benzocyclobutene. By analogy with *o*-xylene, indane and tetralin,[19–26] extensive 4- relative to 3-substitution of benzocyclobutene should, and does, occur on

[15] R. E. Dessy and F. Paulik, *J. Chem. Ed.* **40**, 185 (1963).
[16] P. B. D. de la Mare, I. C. Hilton and S. Varma, *J. Chem. Soc.* 4044 (1960).
[17] F. R. Jensen and G. Maciel, *J. Org. Chem.* **25**, 640 (1960).
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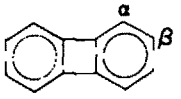
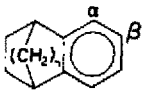
[23] W. Borsche and M. Pommer, *Ber. Dtsch. Chem. Ges.* **54**, 102 (1921).
[24] W. Scharwin, *Ber. Dtsch. Chem. Ges.* **35**, 2511 (1902).
[25] A. R. F. Hesse, *Ber. Dtsch. Chem. Ges.* **53**, 1645 (1920).
[26] G. Schroeter, Svanoe, H. Einbeck, H. Geller and E. R. Riebensahm, *Liebig's Ann.* **426**, 83 (1922).

sulphonation, acetylation and benzoylation. Such information as is available for halogenations and nitrations in this series[27–32] tends to be somewhat disparate but certainly indicates a considerable reactivity for the nuclear positions α with respect to the alkyl substituents; also from the additivity relationship[33] and the partial rate factors for chlorination of toluene in acetic acid[34] the proportion of α-relative to β-chlorination of *o*-xylene under these conditions may be calculated as about 1·3; and on the basis of electronic and steric effects little difference should be observed in benzocyclobutene: the observed proportion is certainly not less than 40. There is a remarkably close analogy here with diphenylene (XVIII) and the bridged hydronaphthalenes (XIX, XX). With electrophilic reagents only β-substitution of biphenylene is observed;[35] which has been described as an impressive agreement with Huckel



XVIII



XIX n=1
XX n=2

molecular orbital predictions.[36] However, the reactivity of the β- relative to α-position in biphenylene is estimated from the kinetics of tritiodeprotonation as 64, whereas molecular orbital delocalization energies require a ratio of about 4.[37] In the bridged hydronaphthalenes β:α substitution ratios for nitration have been recently reported[38] to be 13·5 and 29·3 for XIX and XX respectively and interpreted in terms of steric hindrance at the α-position; however, such an interpretation is at odds with the increased rates of nitration reported[38] for these compounds, relative to less rigid molecules.

The stress system set up in the benzene nuclei of biphenylene by the deformed bond angles of the C_4 ring is entirely analogous to what has been invoked for benzocyclobutene.[1] Similarly, the angle of 60° subtended by the aralkyl bonds in unrestricted *ortho*-alkylated benzenes will be compressed in the bridged hydronaphthalenes and stress the benzene nuclei analogously to the C_4-ring containing compounds. We submit that the high selectivity of electrophilic substitutions on these three types of compound may well have a common origin, in stress effects.

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[28] W. Davis, J. L. Everett and W. C. J. Ross, *J. Chem. Soc.* 1331 (1950).
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[34] H. C. Brown and L. M. Stock, *J. Amer. Chem. Soc.* **79**, 5175 (1957).
[35] Wilson Baker and J. F. W. McOmie, in *Non-Benzenoid Aromatic Compounds* (Edited by D. Ginsberg) p. 80, Interscience, New York (1959).
[36] A. Streitweiser, *Molecular Orbital Theory for Organic Chemists* p. 345. Wiley, New York (1961).
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EXPERIMENTAL

M.ps are uncorrected. UV spectra were plotted manually using a Hilger and Watts Uvispek H-700. NMR and IR spectra were obtained using Perkin Elmer R10 (60 MC) and Infracord-237 instruments respectively. VPC was carried out on an Aerograph Autoprep A-700.

Benzoylation of benzocyclobutene

(A) *Catalysed by* $AlCl_3$ *in* $(CH_2)_2Cl_2$. To a cooled (0°) stirred solution of 7·0 g (52·5 mM) $AlCl_3$ and 7·9 g (56 mM) benzoyl chloride in 50 ml $(CH_2)_2Cl_2$ was added, over 1 hr, 5 g (48 mM) benzocyclobutene in 15 ml $(CH_2)_2Cl_2$. The mixture was kept at 0–5° for a further hr, then quenched in water (250 ml). The organic phase was collected, washed with 10% NaOH aq and then with water, dried ($MgSO_4$) and the solvent evaporated off. The residue was vacuum distilled to give: (a) 1·20 g β-phenethyl chloride b.p. 105–106°/20 mm, n_D^{20} 1·5279 (lit. 105°/20 mm, n_D^{20} 1·5279); IR (neat liquid) identical with the known compound; VPC (5 ft column 20% silicone-SE 30 on Chromosorb -P, at 150°)—homogeneous; (Found: Cl, 25·45. Calc. for C_8H_9Cl: Cl, 25·22%); (b) 7·16 g mixture b.p. 144–146°/0·2 mm; (c) 0·99 g residual brown viscous liquid; IR, neat liquid, maxima (cm^{-1}) at 1665 s 1600 m 1580m 1270 s ($Ar_2C{=}O$), 765 m 755 m 710 s 700 s (mono- and (?) *o*-disubstituted benzene nuclei), bands exhibited by (b) were also present. The mixture (b; 3 g) was separated by chromatography on a column containing 100 g silica gel, using CH_2Cl_2 as solvent, into: (i) 0·095 g (with a, 21%) β-phenethyl chloride (IR identical with known compound) (ii) 2·03 g (42%) **2′-(2-chloroethyl)-benzophenone** b.p. 140–141°/0·19 mm, n_D^{20} 1·5989; IR, neat liquid, maxima (cm^{-1}) at 1665 s 1600 m 1585 m 1290–1270 s ($Ar_2C{=}O$), 765 m 710 m (mono- and (?) *o*-di-substituted benzene nuclei); NMR, in CCl_4, – nine aryl protons (2·1–2·9τ) and four side-chain protons giving an A_2B_2 spectrum centred at 6·64τ (two adjacent methylene groups). (Found: C, 73·54, 73·79; H, 5·49, 5·35; Cl, 14·65, 14·30. $C_{15}H_{13}ClO$ requires: C, 73·62; H, 5·35; Cl, 14·48%); (iii) 0·74 g (18%) *4-benzoylbenzocyclobutene* as a colourless oil, IR identical with that of the main product from benzoylation in CH_3NO_2 (below), which formed an oxime, m 170–172° undepressed on admixture with *4-benzoylbenzocyclobuteneoxime* (below). A benzoylation at 25° gave a similar result. The chloroethylbenzophenone did not form a 2,4- dinitrophenylhydrazone even after prolonged (24 hr r.t. also 2 hr at reflux) contact with Brady's reagent, the benzoylbenzocyclobutene reacted readily.

(B) *Catalyzed by* $AlCl_3$ *in* CH_3NO_2. In 30 ml CH_3NO_2 was dissolved 6·8 g (48·5 mM) benzoyl chloride and 6·67 g (50 mM) $AlCl_3$. The solution was cooled to −40° and a mixture of 4·75 g (45·7 mM) benzocyclobutene and 5 ml CH_3NO_2 added, with stirring, at such a rate that the temp of the reaction mixture did not exceed −35° (15 min). At 5½ hr the mixture was removed from the cooling bath, warmed to 10° (20 min), and poured into water. The product was extracted into CH_2Cl_2 (100 ml), CH_3NO_2 removed from it by shaking with 100 ml 10% NaOH aq, washed with water, dried ($MgSO_4$), and the solvent removed leaving a brown coloured oil. Distillation gave: (a) 2·05 g β-phenethyl chloride b.p. 105–106°/20 mm, n_D^{20} 1·5285; IR and VPC (conditions as above) identical with the known compound; (b) 5·76 g yellow oil b.p. 134–137°/0·15 mm; (c) a negligible quantity of involatile black residue. Fraction b (2g) was chromatographed on the silica gel column used in (A) to give 0·115 g β-phenethyl chloride (with a, 37%) and 1·78 g (54%) 4-benzoylbenzocyclobutene, m 35–39°, which crystallized from light petroleum–diethyl ether mixtures as colourless leaflets m 38–39°; IR, KBr disc and in CS_2, maxima (cm^{-1}) at 1660 s 1600 m 1580 m 1290 s 1280 s ($Ar_2C{=}O$), 1210 m (benzocyclobutene methylenes), 865–860 m (doublet) 840 m (1,2,4-trisubstituted nucleus), 750 m 695 s (mono-substituted nucleus); NMR in CCl_4—two to one ratio of aryl to methylene protons as a complex band (2·2–3·1τ) and a singlet (6·81τ) respectively; UV in ethanol, maxima (mμ) at 344 (ε = 151), 253 (19,100). (Found: C, 86·70, 86·44; H, 5·77, 5·52. $C_{15}H_{12}O$ requires: C, 86·60; H, 5·81%). Oxime: colourless needles from MeOH aq, m 170–172°, (Found: C, 80·57; H, 6·04; N, 6·54. $C_{15}H_{13}NO$ requires: C, 80·65; H, 5·87; N, 6·28%). The mother liquors from the recrystallization of 4-benzoylbenzocyclobutene were returned to the chromatography column; CH_2Cl_2 eluted 250 mg of oil indicated by IR to be mainly 4-benzoylbenzocyclobutene containing a small quantity of the chloroethylbenzophenone. The oil gave a weak reaction for labile Cl (methanolic $AgNO_3$).

(C) *Catalysed by* $SnCl_4$ *in* CH_3NO_2. Benzocyclobutene (45·7 mM) in 5 ml CH_3NO_2 was added to 8·45 g (60 mM) benzoyl chloride and 15·9 g (61 mM) $SnCl_4$ dissolved in 30 ml CH_3NO_2 under the same conditions as in (B) except that the reaction mixture was allowed to warm up slowly, to −8°, overnight. The products were separated essentially as in (B) to yield (on reacted benzocyclobutene) (a) 7·05 g (33·8 mM, 84%) 4-benzoylbenzocyclobutene, m 36–38°, (b) 0·77 g mixture of about two

to one (IR) in 4-benzoylbenzocyclobutene to 2'-(2-chloroethyl)-benzophenone and (c) a mixture estimated by IR and VPC to contain 5·4 M benzocyclobutene and 1·4 mM (3%) β-phenethyl chloride.

Benzoylation of β-phenethyl chloride

β-Phenethyl chloride (6·75 g, 48 mM) was subjected to the same reaction conditions described under (A) for benzocyclobutene. The product was 9·30 g vitreous solid which gave highly viscous and slightly opalescent solutions in chlorohydrocarbon solvents. The IR spectrum of the product was comparable with that of the residue (c) obtained from benzocyclobutene under the same conditions.

Oxidation of 2'-(2-chloroethyl)-benzophenone

The ketone (58 mg, 0·24 mM) was refluxed with $KMnO_4$ (200 mg, 1·3 mM) in 10 ml 1% Na_2CO_3 aq for 2 hr. After cooling MnO_2 was filtered off and SO_2 passed through the solution until it was strongly acid. The precipitated product was filtered off, recrystallized and dried (110°) to yield 41 mg (75%) *o*-benzoylbenzoic acid m 128–129°, undepressed, (lit. 128°), IR identical with the known compound; hydrate: m 92–94°, undepressed, (lit. 94°).

Schmidt azide rearrangement of 4-benzoylbenzocyclobutene

To a mixture of the ketone (216 mg, 1·04 mM) and polyphosphoric acid (3 g) at 50° was added, over 2½ hr, 165 mg (2·5 mM) NaN_3. Heating was continued for 1½ hr when N_2 evolution ceased. The mixture was cooled, treated with water (20 ml) and the product extracted with $CHCl_3$. The extract was concentrated and chromatographed on silica gel yielding to $CHCl_3$, (a) 105 mg colourless solid and (b) 20 mg yellowish oil. The solid (a) was recrystallized from EtOH aq to yield 91 mg (39%) *benzocyclobutene-4-carboxanilide* m 160–161°. The same compound (m 160–161°, undepressed, IR identical) was obtained in 89% yield when benzocyclobutene-4-carbonyl chloride[1] was treated with a solution of aniline and an equivalent quantity of pyridine in acetone. (Found: C, 80·45, 80·43; H, 5·93, 6·00; N, 6·02, 6·12. $C_{15}H_{13}NO$ requires: C, 80·65; H, 5·87; N, 6·28%). When 20 mg 4-*benzocyclobutenylbenzamide*, (m 158–159°, 86% yield from benzoylchloride and 4-aminobenzocyclobutene in acetone–pyridine; (Found: C, 80·58, 80·55; H, 5·98, 6·00; N, 6·08, 6·20. $C_{15}H_{13}NO$ requires: C, 80·65; H, 5·87; N, 6·28%) was treated with polyphosphoric acid, as in the azide rearrangement, there was recovered 4 mg oil the IR spectrum of which (1265 s 1100 s 1020 s, phosphate ester) compared identically with (b). Under the same conditions benzocyclobutene-4-carboxanilide was quite stable (93% recovered).

Sulphonation of benzocyclobutene

Benzocyclobutene (4·75 g, 45·7 mM) in 5 ml $(CH_2)_2Cl_2$ was added dropwise to a cooled (0°), stirred mixture of SO_3 (4·4 g, 55 mM) and dioxan (4·85 g, 55 mM) in 70 ml $(CH_2)_2Cl_2$. When addition was complete (20 min) the mixture was warmed to r.t., poured into water (100 ml) and the organic and aqueous phases separated. The organic phase was washed with water and dried ($MgSO_4$); removal of the solvent left 4·35 g (23·6 mM, 52%) *β-hydroxyethylbenzene-o-sulphonic acid sultone* as a colourless solid, m 62–74°, crystallizing from CCl_4–EtOEt as leaflets m 82–83° (3·66 g); IR, in CS_2 and CCl_4, maxima (cm^{-1}) at 1480 m (CH_2), 1425 m ("active" CH_2), 1375 vs 1365 vs 1195 vs (sulphonate), 885 m 800 m 755 s (either one, three or four adjacent aryl hydrogen atoms, the 2000–1650 absorption pattern was characteristic of an *o*-disubstituted benzene); NMR, 1M solution in CH_2Cl_2—equal numbers of aromatic and side chain protons, the latter giving an A_2X_2 spectrum, approaching 1st order, resulting in two unsymmetrical triplets centred at 5·16 and 6·85τ (two adjacent methylene groups). (Found: C, 51·71, 51·98; H, 4·57, 4·58; S, 17·39, 17·51; $C_8H_8SO_3$ requires: C, 52·16; H, 4·38; S, 17·40%). The aqueous phase was neutralized to phenolphthalein with saturated $Ba(OH)_2$ aq, $BaSO_4$ removed, the solution concentrated to 10 ml and treated with 400 ml acetone to precipitate the crude product which was filtered off and dried (110°). Soxhlet extraction yielded, to EtOH, 400 mg solid containing Cl^-, which was rejected, and, to MeOH, 4·77 g (9·5 mM, 42%) *barium di-(benzocyclobutene-4-sulphonate)*. IR, nujol and hexachlorobutadiene mulls, maxima (cm^{-1}) at 1610 m 895 m 835 s (1,2,4-trisubstituted benzene), 1220–1180 several strong bands, 1070 s ($-SO_3^-$); UV in water, maxima (mμ) at 275 (ε = 1,560), 268(1,550), 262(1080), 220(7,240); NMR, Na salt in water three aryl protons as an ABX system, the AB part forming a multiplet around −3 ppm (wr. H_2O)

and the X part a doublet centred at −2·4 ppm, only one *ortho*-coupling was apparent (1,2,4-trisubstituted nucleus); and four methylenic protons as a singlet at 1·65 ppm (benzocyclobutene CH_2s); a weak resonance around −2·7 ppm suggested some impurity was present. (Found: Ba; 27·5; $C_{16}H_{14}BaO_6S_2$ requires Ba, 27·3%). In alkaline $KMnO_4$ and fused KOH this compound was completely degraded.

Oxidation of β-hydroxyethylbenzene-o-sulphonic acid sultone

The sultone (276 mg, 1·5 mM) was oxidized by $KMnO_4$ (1·16 g, 7·3 mM) in refluxing 1% Na_2CO_3 aq (1½ hr) and the mixture worked up in a conventional way.[39] The product was *o*-sulphobenzoic acid (1·08 mM) isolated as its S-benzylthiuronium salt, m 214–215°, undepressed on admixture with the salt (m 214–215°) prepared directly from genuine *o*-sulphobenzoic acid; the IR spectra of the two products were identical. (Found: N, 10·62, 10·55. Calc. for $C_{23}H_{26}N_4O_5S_2$: N, 10·48%). The generally quoted literature value for the salt, 206°, is evidently incorrect.

Bromination of benzocyclobutene

In 40 ml 95% HOAc aq was dissolved benzocyclobutene (4·75 g, 45·7 mM) and I_2 (100 mg, 0·4 mM). The solution was cooled to 0° and Br_2 (8 g, 50 mM) in 5 ml HOAc slowly added (20 min). After standing 48 hr the mixture was poured into water, the product collected in light petroleum (b 30–40°), washed in turn with Na_2SO_3 aq, Na_2CO_3 aq and water, dried (Na_2SO_4) and the solvent removed leaving 8·21 g colourless oil. VPC (20 ft column, 20% glycerol on Chromosorb-W, 100°, and on a 5 ft column, 20% silicone-SE 30 on Chromosorb-P at 150° and 180°) showed, apart from a small quantity of solvent and unreacted benzocyclobutene, three components having peak areas in proportion (a) 1·2, (b) 86, (c) 13 (order of emergence); (a) and (b) were not completely separated by the silicone column. Chromatography of the mixture (2·0 g) on 100 g silica gel in light petroleum (40–60°) yielded two well separated fractions; the first was *4-bromobenzocyclobutene* (1·59 g, 78%), colourless liquid, b 118–119°/20 min; after distillation: n_D^{20} 1·5872; IR, neat liquid, maxima (cm^{-1}) at 1570 m 864 s 811 s (1,2,4-trisubstituted benzene nucleus), 1200 m (benzocyclobutene methylenes); NMR in CCl_4—three aryl protons (2·5–3·3 τ) and four methylene protons as a singlet at 6·96 τ; UV in ethanol, maxima, mμ (ε) at 267 (1,620), 273(2,200), 280·5(2,020). (Found: C, 52·59, 52·59; H, 3·88, 4·07; Br, 43·56. C_8H_7Br requires: C, 52·49; H, 3·85; Br, 43·66%). VPC showed this compound was component (b), still accompanied by (a). (a) was shown not to be β-phenethyl bromide and was unaffected by refluxing aqueous alkali. The second fraction was *o-bromo-β-phenethyl bromide* (0·33 g, 11%), b 135–137°/10 mm; after distillation: n_D^{20} 1·5953; IR, neat liquid, maxima (cm^{-1}) at 1570 m 755 s (1,2-disubstituted benzene), 1470 s 1440 s (two > CH_2s); NMR in CCl_4—equal numbers of aryl (2·3–3·2 τ) and side-chain protons, the latter giving an A_2B_2 spectrum centred at 6·63 (two adjacent methylene groups). (Found: C, 36·44; H, 3·28; Br, 60·58. $C_8H_8Br_2$ requires: C, 36·40; H, 3·05; Br, 60·55%).

Benzocyclobutene-4-carboxilic acid from 4-bromobenzocyclobutene

An etherial solution *4-benzocyclobutenylmagnesium bromide*, from 4-bromobenzocyclobutene (1·0 g, 5·46 mM) and Mg (132 mg, 5·43 mM) in 20 ml Et_2O, was poured onto 25 g powdered solid CO_2. After warming to r.t. the mixture was acidified (HCl aq) and the product extracted into Et_2O. The combined extracts (50 ml) were shaken with 5% Na_2CO_3 aq (10 ml, ×3), the aqueous extracts acidified (HCl aq) and the precipitated product filtered off. It was recrystallized from EtOH aq as 744 mg (92%) benzocyclobutene-4-carboxilic acid, m 140–141°, undepressed, (lit. 139–140°), IR identical with the known compound.

Oxidation of o-bromo-β-phenethyl bromide

The bromide (90 mg, 0·34 mM) was oxidized by $KMnO_4$ (374 mg, 2·37 mM) in 2% KOH aq (5 ml), overnight, under reflux. A conventional work-up[39] yielded *o*-bromobenzoic acid (37 mg, 54%) m 146–147°, undepressed, (lit. values between 145–150° have been given), IR identical with the known compound.

Chlorination of benzocyclobutene

Chlorine (3·4 g, 48 mM) was passed into a cooled (0°), stirred solution of benzocyclobutene (4·75 g, 45·7 mM) and I_2 (100 mg, 0·4 mM) in 25 ml 95% HOAc aq. The solution was refrigerated (0°) overnight and a product mixture (7·11 g colourless oil) obtained as in the bromination; VPC showed four

[39] A. I. Vogel, *Practical Organic Chemistry*, p. 672; Longmans, Green; London (1956).

components having peak areas as (d) 1·5, (e) 75, (f) 19, (g) 4, (g) was particularly slow running and diffuse; IR showed the presence of a small amount of acetate (1745, 1235 cm^{-1}). Chromatography of the mixture (6·97 g) on silica gel yielded, to light petroleum (40–60°), two well separated fractions; the first was 4-chlorobenzocyclobutene (4·26 g, 69%), colourless liquid, b 94–96°/10 mm; after distillation: n_D^{20} 1·5612; IR, neat liquid, maxima (cm^{-1}) at 1595 s 875 s 820 s (1,2,4-trisubstituted benzene nucleus), 1205 m (benzocyclobutene methylenes) m 780 w (presence of 3-chlorobenzocyclobutene?); NMR in CCl_4—three aryl protons (2·8–3·4 τ) and four methylenic protons, singlet 6·95τ; UV in EtOH, maxima, mμ (ε), at 267(1,470), 274(1,980), 281(2,000). (Found: C, 69·44; H, 5·05; Cl, 25·00. C_8H_7Cl requires: C, 69·38; H, 5·09; Cl, 25·59%). VPC showed this compound was component (e), still accompanied by (d). (d) was unaffected by refluxing aqueous alkali. The second fraction from the silica gel column was *o*-chloro-β-phenethyl chloride (1·03 g, 13%), b 118–120°/9 mm, 61°/0·3 mm (lit. 58–60°/0·4 mm); after distillation: n_D^{20} 1·5498, IR, neat liquid, maxima (cm^{-1}) at 1580 m 745 s (1,2-disubstituted benzene), 1475 s 1445 s (two $>CH_2$s); NMR in CCl_4—equal numbers of aryl (2·4–3·1τ) and side-chain protons, the latter as an A_2B_2 system centred at 6·6τ); VPC—identical with (f). (Found: Cl, 41·6. Calc. for $C_8H_8Cl_2$: Cl, 40·5% possibly a small amount of polyhalogenated material was present here): with refluxing alkaline $KMnO_4$ this compound was shown to give *o*-chlorobenzoic acid, (34%) m 140°, undepressed, (lit. 140°), IR identical with genuine *o*-chlorobenzoic acid; and an ether [IR: 1055 cm^{-1}(C—O—C), 750 cm^{-1} (1,2-disubstituted benzene)] that was not further oxidized under these conditions. When the silica gel column was stripped with CH_2Cl_2 an oil (0·54 g) containing acetate (1745 and 1230 cm^{-1}) and further quantities of the other halogenation products (IR) was obtained.

4-Chlorobenzocyclobutene from 4-aminobenzocyclobutene

To a suspension of di-(benzocyclobutene-4-ammonium) sulphate in 1 ml 2N HCl aq at 0° was added, with shaking, $NaNO_2$ (62 mg). The solution obtained was transferred, under N_2, to CuCl (from 275 mg $CuSO_4.5H_2O$) dissolved in conc. HCl (0·5 ml), and the mixture warmed to 60° when N_2 evolution ceased. After making alkaline (NaOH) the product was steam distilled out, collected in light petroleum (3 ml, b 30–40°), washed with 0·5N HCl aq, dried ($MgSO_4$), and the solvent removed in a stream of N_2 leaving 4-chlorobenzocyclobutene (82 mg, 66%); IR (neat liquid) and VPC (glycerol column)—identical with the compound obtained from the chlorination of benzocyclobutene except that contaminant (d) and the IR band at 780 cm^{-1} were now absent.

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