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ASPECTS OF ARYNE CHEMISTRY—I
A PHENANTHRENE SYNTHESIS[1]

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Abstract—Benzyne, generated by aprotic diazotization of anthranilic acid, has been found to add to isoeugenol methyl ether and to isosafrole to yield 9-methylphenanthrene derivatives. The reaction of benzyne with some other aromatic dienes was also investigated.

THE highly reactive arynes have attracted considerable attention,[2–5] especially as potentially useful synthetic intermediates. One of the simplest methods employed for the generation of arynes,[6,7] involves the diazotization of anthranilic acids in aprotic media. Evidence is available[8] to suggest that the decomposition of benzene diazonium-2-carboxylate (I), an isolated intermediate in one[6] procedure, occurs in a stepwise fashion via II to III. Other recent methods for the generation of arynes include (a) the diazotization and thermal decomposition of *o*-aminobenzene sulphinic acid,[9] (b) the pyrolysis of indanetrione,[10] (c) the thermal decomposition of 2-aryl-iodoniobenzoates[11] and (d) the oxidation of 1-aminobenztriazole with lead tetraacetate.[12]

By analogy with the reactions of acetylenes, arynes should act as dienophiles in the Diels-Alder reaction; this behaviour has been amply confirmed,[2] and the use of a reactive diene as a "benzyne trap" has been quite common for the detection of aryne intermediates. The existence of benzyne itself has been demonstrated by flash photolysis reactions[13] and also by mass spectrometry.[14] Heterocyclic arynes have

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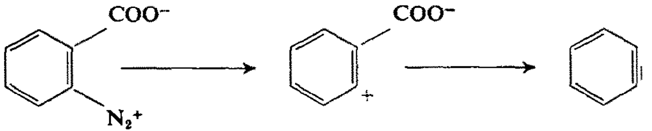
[1] A preliminary report of this work has been published: S. F. Dyke, A. R. Marshall and J. P. Watson, *Tetrahedron Letters* 3583 (1964).
[2] H. Heaney, *Chem. Rev.* **62**, 81 (1962).
[3] J. F. Bunnett, *J. Chem. Ed.* **38**, 278 (1961).
[4] R. Huisgen in *Organometallic Chemistry* (Edited by H. Zeiss) p. 36. Reinhold, New York (1960).
[5] G. Wittig, *Angew. Chem.* **69**, 245 (1957); **74**, 479 (1962).
[6] M. Stiles, R. G. Miller and U. Burckhardt, *J. Amer. Chem. Soc.* **85**, 1792 (1963).
[7] L. Friedman and F. M. Logullo, *J. Amer. Chem. Soc.* **85**, 1549 (1963).
[8] S. Yaroslavsky, *Chem. & Ind.* 765 (1965).
[9] G. Wittig and R. W. Hoffmann, *Angew. Chem.* **73**, 435 (1961).
[10] R. F. C. Brown and R. K. Solly, *Chem. & Ind.* 181 (1965).
[11] E. LeGoff, *J. Amer. Chem. Soc.* **84**, 3786 (1962): F. M. Beringer and S. J. Huang, *J. Org. Chem.* **29**, 445 (1964).
[12] C. D. Campbell and C. W. Rees, *Proc. Chem. Soc.* 296 (1964); *Chem. Comm.* 192 (1965).
[13] R. S. Berry, G. N. Spokes and R. M. Stiles, *J. Amer. Chem. Soc.* **82**, 5240 (1960).
[14] R. S. Berry, J. Clardy and M. E. Shafer, *J. Amer. Chem. Soc.* **86**, 2739 (1964).

also been generated and their reactions studied.[15] The Diels-Alder reaction[16] has always attracted considerable attention in synthesis, and the additions involving arynes and a variety of dienes have been quite intensively studied. Some examples described since the last review of the subject[2] include (a) the reaction of benzyne with benzene[17] to yield a mixture of diphenyl, benzocyclooctatetraene (IV) and benzobicyclo(2,2,2)octatriene (V), (b) the addition of benzyne to pyrroles of the type VI to form naphthalenes (VIII), presumably via (VII)[18] and (c) the production of phenanthrene (8%) and 9-methylphenanthrene (3·6%) from benzyne and phenylacetylene or 1-phenylpropyne respectively.[19]

Hudson and Robinson[20] reported a 1:1 adduct (X) between maleic anhydride



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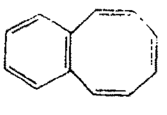
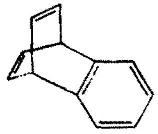
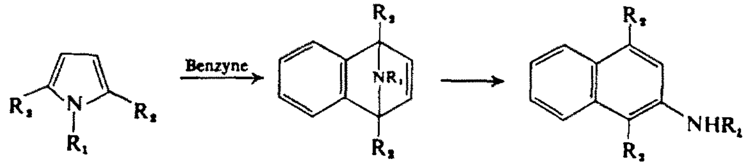


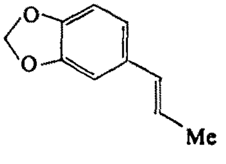
IV



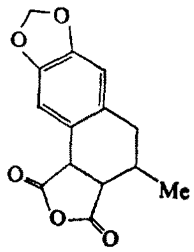
V



VI VII VIII



IX



X

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[15] T. H. Kaufmann, *Angew. Chem.* (Int. Ed.) **4**, 543 (1965).

[16] For some reviews see [a] B. S. Thyagarajan, *Chem. Rev.* **54**, 1038 (1954); [b] K. Alder, *Newer Methods of Preparative Organic Chemistry* p. 381. Interscience, New York (1948); [c] K. Alder and M. Schumacher, *Fortscher. Chem. Naturstoffe* **10**, 1 (1953); [d] A. S. Onishchenko, *Diene Synthesis*, S. Morison, Jerusalem, (1964); [e] J. G. Martin and R. K. Hill, *Chem. Rev.* **61**, 537 (1961); [f] Yu. A Titov, *Russ. Chem. Rev.* **31**, 267 (1962); [g] S. B. Needleman and M. C. Chang Kuo, *Chem. Rev* **62**, 405 (1962).

[17] R. G. Miller and M. Stiles, *J. Amer. Soc.* **85**, 1798 (1963).

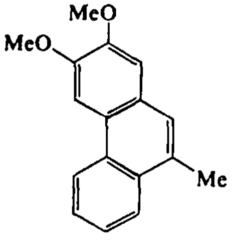
[18] E. Wolthius, D. V. Jagt, S. Mels and A. DeBoer, *J. Org. Chem.* **30**, 190 (1965).

[19] M. Stiles, U. Burckhardt and A. Haag, *J. Org. Chem.* **27**, 4715 (1962).

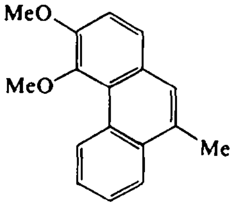
[20] B. J. F. Hudson and Sir R. Robinson, *J. Chem. Soc.* 715 (1941).

and isosafrole (IX); an analogous compound was formed from isoeugenol methyl ether and maleic anhydride. Isosafrole was also reported to form the expected dihydronaphthalene with ethyl acetylenedicarboxylate. Numerous examples have been reported[21] where styrenes have behaved as dienes in the Diels-Alder reaction.

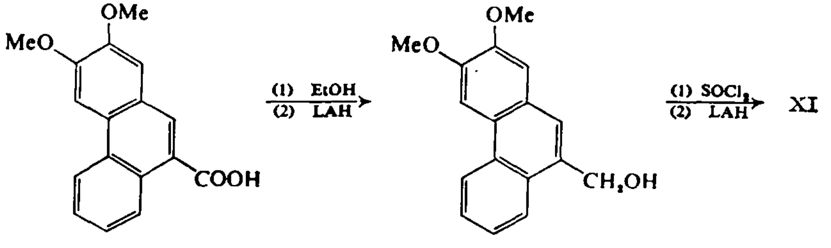
The reaction of benzyne with isosafrole and with isoeugenol methyl ether has been investigated. The aprotic diazotization of anthranilic acid[7] was the method selected for the generation of benzyne and the most satisfactory conditions were realised by adding concurrently solutions of anthranilic acid and amyl nitrite in acetonitrile to a refluxing solution of the styrene in the same solvent. With isoeugenol methyl ether two isomeric neutral compounds were isolated. Elemental analysis indicated an empirical formula of $C_{17}H_{16}O_2$, and their UV spectra, which were very similar, were suggestive of a phenanthrene system, rather than the expected 9,10-dihydrophenanthrene. Isoeugenol methyl ether (67%) was recovered from the reaction. The two phenanthrenes were identified as 2,3-dimethoxy-9-methylphenanthrene, m.p. 141–143° (XI; 21% yield, allowing for recovered styrene) and 3,4-dimethoxy-9-methylphenanthrene (XII). The NMR spectra were also compatible with these structures, but they were each confirmed by synthesis. The known[22] 2,3-dimethoxyphenanthrene-9-carboxylic acid (XIII), obtained in a normal Pschorr synthesis,[23] was esterified and reduced with LAH to the alcohol[24] (XIV). Conversion to the 9-chloromethyl derivative, and further reduction with LAH gave (XI), identical in all respects with the material obtained from isoeugenol methyl ether. Cook *et al.*,[25] who prepared



XI



XII



XIII XIV

[21] See Ref 16-*d* pp. 493–505.

[22] R. Pschorr and W. Buckow, *Ber. Dtsch. Chem. Ges.* 33, 1830 (1900).

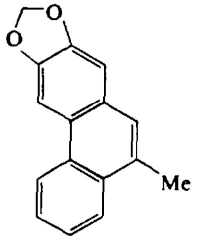
[23] DeLos F. DeTar, *Organic Reactions* 9, 409 (1957); W. A. Coudrey and D. S. Davies, *Quart. Rev.* 6, 367 (1952); P. H. Leake, *Chem. Rev.* 56, 27 (1956); D. H. Hey and J. M. Osbond, *J. Chem. Soc.* 3164 (1949).

[24] C. K. Bradsher and R. B. Destie, *Recueil* 83, 593 (1964).

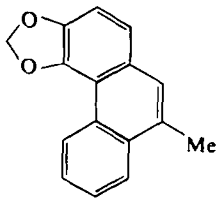
[25] J. W. Cook, J. D. Louden and R. K. Razdan, *J. Chem. Soc.* 4234 (1954).

XI from XIII via the sulphonylhydrazone, quote m.p. 131°. 3,4-Dimethoxy-9-methylphenanthrene (XII) has been described previously[26] as a white solid, m.p. 59–60° and was obtained from the known[27] 3,4-dimethoxyphenanthrene-9-carboxylic acid via the sulphonylhydrazide. In the present work an authentic sample of XII was obtained from the 9-carboxylic acid in manner similar to that described above for XI. The product so obtained was identical in every respect with the material obtained from isoeugenol methyl ether.

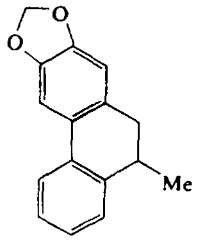
When isosafrole IX was allowed to react with diazotized anthranilic acid, two isomeric, neutral crystalline compounds were isolated and 49% of the isosafrole was recovered unchanged. The aromatic region of the NMR spectrum of the first compound, m.p. 140–141° (obtained in a nett yield of 22%) is very similar to that of XI so that structure XV was allocated to it. The spectral characteristics of the isomeric solid, m.p. 108–109° (4% yield) are so similar to those of XII that it was assigned structure XVI. Since 2,3-methylenedioxyphenanthrene-9-carboxylic acid is a known[28] compound, attempts were made to oxidize XV, but without success. Govindachari[29] has also reported failure in attempts to oxidize a 9-methylphenanthrene to the 9-carboxylic acid. 1,7-Dimethylphenanthrene has[30] been oxidized with potassium ferricyanide to a mixture of acids, which contained phenanthrene-1,7-dicarboxylic acid. Attempts were then made to convert XV to XI, but it was recovered unchanged when it was treated with phloroglucinol and conc sulphuric acid under the conditions described[31] for the scission of the methylenedioxy grouping in sanguarine.



XV



XVI



XVII

The nitrogen-containing byproduct (10% yield based upon anthranilic acid) m.p. >330°, mentioned in the preliminary note[1] was identified as acridone, arising presumably by cyclo-addition of benzyne to unchanged anthranilic acid. A small amount of N-phenylanthranilic acid was also recovered from the isosafrole reaction.

The diazotization of anthranilic acid, in the presence of isosafrole in solvents other than acetonitrile was then studied. With a mixture of acetone and methylene chloride a small amount of 2,3-methylenedioxy-9-methyl-9,10-dihydrophenanthrene

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[26] H. L. Holmes and C. C. Lee, *J. Amer. Chem. Soc.* **69**, 1996 (1947); H. L. Holmes, C. C. Lee and A. Mooradian, *Ibid.*, **69**, 1998 (1947).

[27] R. Pschorr and C. Sumuleanu, *Ber. Dtsch. Chem. Ges.* **33**, 1819 (1900).

[28] E. Mossetig and A. Burger, *J. Amer. Chem. Soc.* **52**, 2988 (1930); R. A. Konovalova, S. Yunusov and A. P. Ovekhov, *Bull. soc. Chim. Fr.* **53**, 1479 (1939); *J. Gen. Chem. USSR.* **9**, 1507 (1939), *Chem. Abstr.* **34**, 2852 (1940).

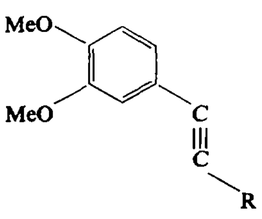
[29] T. R. Govindachari, *IUPAC International Symposium on the Chemistry of Natural Products* p. 428 Australia (1960); Butterworths, London (1961).

[30] L. Ruzicka, G. B. R. de Graaff and J. R. Hosking, *Helv. Chim. Acta* **14**, 233 (1931).

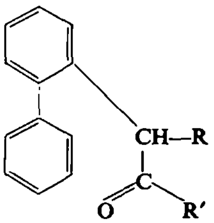
[31] E. Späth and F. Kuffner, *Ber, Dtsch. Chem. Ges.* **64**, 2036 (1931).

(XVII) was formed, and this yield rose to 14% by using the higher boiling toluene–methyl ethyl ketone mixture. Distillation of XVII, or heating under reflux in acetonitrile, or dehydrogenation with Pd–C yielded XV. Other solvents tried included diglyme, dimethylformamide and nitrobenzene. In all cases acridone and N-phenylanthranilic acid were isolated, but with nitrobenzene a 23% yield of XV was also realised. No improvement in yields was obtained in any of the solvents by using Diels-Alder catalysts[32,33] such as stannic chloride.

Attention was then turned to other potential dienes as starting materials to react with benzyne. With cinnamic acid, 3,4-dimethoxycinnamic acid, 3,4-dimethoxy-β-nitrostyrene, 3,4-dimethoxyphenylpropiolic acid[34] (XVIII, R = COOH), 3,4-dimethoxy-6-bromophenylacetylene[35] and benzonitrile only starting material, acridone and N-phenylanthranilic acid were identified among the products. When XVIII (R = H) was reacted with benzyne in acetonitrile, a 42% yield of the known[22] 2,3-dimethoxyphenanthrene was obtained (allowing for recovered acetylene). The UV and NMR spectra were also compatible with this structure. The phenylacetylene (XVIII, R = H) was prepared by Fulton and Robinson[34] by decarboxylation of XVIII (R = COOH) but we found that the application of the Villsmeir reaction, as described by Bodendorf and Kloss[36] to be more satisfactory.*



XVIII



XIX

9-Methylphenanthrenes have been reported sporadically in the literature. One of the most direct methods[37] for their preparation is probably that involving cyclodehydration of carbonyl compounds of the type XIX (R = H or alkyl; R^1 = H or alkyl). More recently it has been found[38] that substituted phenanthrenes can be obtained in good yield by the photolysis of suitable stilbenes, and in particular α-methylstilbenes lead to 9-methylphenanthrenes. A useful brief review of methods of preparation of stilbenes has recently appeared.[39] Older routes to 9-methyl-

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* We are indebted to Professor Bodendorf for supplying us with the full experimental details for this reaction.

[32] P. Yates and P. Eaton, *J. Amer. Chem. Soc.* **82**, 4436 (1960).

[33] R. Robinson and G. L. Fray, *J. Amer. Chem. Soc.* **83**, 249 (1961).

[34] J. D. Fulton and R. Robinson, *J. Chem. Soc.* 1463 (1933).

[35] K. W. Bentley, S. F. Dyke and A. R. Marshall, *J. Chem. Soc.* 3914 (1963).

[36] K. Bodendorf and P. Kloss, *Angew. Chem.* (Int. Ed.) **2**, 98 (1963).

[37] L. R. C. Barclay in *Friedel-Crafts and Related Reactions* (Edited by G. A. Olah) Vol. II; Part II; p. 889. Interscience, London (1964).

[38] F. B. Mallory, C. S. Wood and J. T. Gordon, *J. Amer. Chem. Soc.* **86**, 3094 (1964) and Refs therein cited; M. V. Sargent and C. J. Timmons, *J. Chem. Soc.* 5544 (1964); D. J. Collins and J. J. Hobbs, *Chem. & Ind.* 1725 (1965); C. S. Wood and F. B. Mallory, *J. Org. Chem.* **29**, 3375 (1964).

[39] O. H. Wheeler and H. N. Battle, *J. Org. Chem.* **30**, 1473 (1965); E. N. Morgan, P. J. Palmer, L. Kruszynska and W. R. N. Williamson, *J. Chem. Soc.* 3887 (1965).

phenanthrenes include the Haworth synthesis,[40] the Pschorr synthesis via the 9-phenanthrenecarboxylic acids, and methods of employing 9-halogeno or 9-hydroxyphenanthrenes.[41] The method described in this paper offers a simple, one-step synthesis of certain phenanthrenes.

EXPERIMENTAL

M.ps are not corrected.

Addition of benzyne to isoeugenol methyl ether. A solution of isoeugenol methyl ether (13·5 g) in MeCN (125 ml) was stirred and heated under reflux whilst solutions of anthranilic acid (10 g) in MeCN (150 ml) and n-amyl nitrite (10·6 ml) in MeCN (30 ml) were added concurrently during 1½ hr. After a further heating (1 hr), the mixture was evaporated to half bulk and cooled, when acridone (1·1 g) separated, as a crystalline solid m.p. 338–340°. (Lit[42] m.p. 348–350°). The filtrate from the acridone was evaporated to dryness under reduced press, and the residue was dissolved in ether. This solution was washed with 15% NaOHaq then with water, dried and evaporated. The residual brown oil was distilled under reduced press; unchanged isoeugenol methyl ether (9·0 g; 67%) b.p. 150–154°/5 mm was followed by a thick brown oil, b.p. 200–240°/2 mm. The latter fraction was triturated with ether/petrol (40–60°) and a yellow solid (0·88 g), m.p. 132–134° was collected. Recrystallization from EtOH gave white needles of XI, m.p. 141–143°. (Found: C, 81·3; H, 6·5; $C_{17}H_{16}O_2$ requires: C, 81·0; H, 6·35%.)

The residues from the above phenanthrene were chromatographed over alumina to yield XI (0·05 g), and XII was obtained as a yellow oil (0·4 g), which could not be solidified at room temp. The picrate was obtained as blood red needles from EtOH, m.p. 130–131°. (Found: C, 57·2; H, 4·1; N, 8·7. $C_{23}H_{19}N_3O_9$ requires: C, 57·4; H, 4·0; N, 8·7%.)

Compound XII has now been obtained as a white crystalline solid, m.p. 59–60° from petrol (40–60°). (Found: C, 80·6; H, 6·2. Calc. for $C_{17}H_{16}O_2$: C, 80·9; H, 6·4%.)

Addition of benzyne to isosafrole (IX). Benzyne was generated from anthranilic acid (20·0 g) and n-amyl nitrite (25 ml) and added to IX (20·25 ml) in MeCN as described for isoeugenol methyl ether. After removal of the MeCN, dissolving in ether, washing with NaOHaq, drying and evaporating as above, the dark residual oil was triturated with ether–petrol (40–60°) and a buff coloured solid, m.p. 138–140° (1·05 g) was collected. The residues were distilled under reduced press to yield IX (11·0 g; 49%) b.p. 80–100°/0·3 mm, then a dark orange oil b.p. 215–25°/0·3 mm, which when triturated with ether–petrol (40–60°) gave a yellow solid, m.p. 130° (1·0 g). The two solids, which were shown to be identical, were combined and crystallized from EtOH to give white blades, m.p. 140–141°, of XV. (Found: C, 80·9; H, 5·2. $C_{16}H_{12}O_2$ requires: C, 81·3; H, 5·1%.) From the filtrate was obtained XVI (0·4 g) as white needles, m.p. 108–109° from EtOH. (Found: C, 82·0; H, 5·6%.) The picrate was obtained as blood-red needles from EtOH, m.p. 185–186°. (Found: C, 56·9; H, 3·5. $C_{22}H_{15}N_3O_9$ requires: C, 56·8; H, 3·25%.)

2,3-*Methylenedioxy*-9-*methyl*-9,10-*dihydrophenanthrene* (XVII). A solution of IX (20·25 ml) in toluene (250 ml) was treated with anthranilic acid (20 g) in EtCOMe (80 ml) and n-amyl nitrite (21·3 ml) in toluene (75 ml) as described for the reaction in MeCN. After heating the mixture under reflux for 2 hr, maleic anhydride (10 g) was added and heating was continued for a further 30 min. The mixture was then evaporated to dryness under reduced press; the residual gum was taken up in ether (200 ml), the solution extracted with 15% NaOHaq (3 × 200 ml), then with water (2 × 200 ml), dried (Na_2SO_4) and evaporated. Distillation under reduced press yielded first a little unchanged IX, then XVII as an orange-yellow oil (5·0 g), b.p. 158–163°/0·15 mm. (Found: C, 80·6; H, 6·0. $C_{16}H_{14}O_2$ requires: C, 80·6; H, 5·9%.)

When XVII (4·0 g) was heated under reflux in xylene (20 ml) with PdC (1·0 g) for 24 hr, XV, m.p. 141–143° was isolated by standard methods.

[40] R. D. Haworth and C. R. Martin, *J. Chem. Soc.* 2720 (1932); W. E. Bachman, M. W. Cronyn and W. S. Sturve, *J. Org. Chem.* **12**, 596 (1947); N. P. Buu-Hoi and G. Saint Ruf, *C. R. Acad Sci., Paris* **254**, 2366 (1962).

[41] W. E. Bachman, *J. Amer. Chem. Soc.* **56**, 1363 (1934); G. Wittig, W. Uhlenbrock and P. Weinhold, *Chem. Ber.* **95**, 1692 (1962).

[42] C. F. H. Allen and G. H. W. McKee, *Organic Syntheses*, Coll. Vol. II, p. 15. Wiley, New York (1957).

2,3-*Dimethoxy-9-methylphenanthrene from the Pschorr reaction.* Compound XIII, m.p. 268–270° prepared as described by Pschorr and Buckow,[22] was esterified and reduced with LAH to XIV.[24] This alcohol (0·77 g) was suspended in dry benzene (40 ml), cooled in ice and stirred whilst $SOCl_2$ (1 ml) was added dropwise. The mixture was stirred at 0° for 2 hr, heated under reflux for 1 hr, poured into water and extracted with benzene. The benzene solution was washed, dried and evaporated to leave a pale orange gum (0·62 g) which crystallized on trituration with ether, m.p. 142–144°. This chloride (0·6 g), without further purification, was dissolved in benzene (20 ml) and added dropwise to a stirred suspension of LAH (0·35 g) in ether (40 ml). The mixture was heated under reflux for 4 hr, then left at room temp overnight. The excess of LAH was decomposed with AcOEt and dil H_2SO_4, and the mixture was extracted with benzene. The organic solution was washed with dil H_2SO_4, then with water, dried and evaporated to yield a white solid. Crystallization from EtOH gave white needles, m.p. 138–140°, undepressed upon admixture with the substance obtained from anthranilic acid and isoeugenol methyl ether.

3,4-*Dimethoxy-9-methylphenanthrene from the Pschorr reaction.* 3,4-Dimethoxyphenanthrene-9-carboxylic acid[27] was subjected to the reactions described above for XIII. The final product, XII was obtained as an oil, which could not be solidified at room temp. The picrate was obtained from EtOH as blood-red needles, m.p. 129–130°, undepressed on mixing with picrate of the product obtained from isoeugnol methyl ether.

Addition of benzyne to 3,4-*dimethoxyphenylacetylene.* A solution of 3,4-dimethoxyphenylacetylene (5·0 g) in MeCN (50 ml) was heated under reflux whilst solutions of anthranilic acid (4·06 g) in MeCN (70 ml) and n-amyl nitrite (4·4 ml) in MeCN (20 ml) were added concurrently during 2 hr. Heating was continued for a further 30 min and then solvent was removed under reduced press. The residue was dissolved in ether, washed with dil NaOHaq then with water, dried and evaporated. The residual brown solid (5·9 g) was chromatographed over silica gel and eluted with 10% $CHCl_3$ in petrol (40–60°) to yield recovered acetylene (4·05 g), Elution with 20% $CHCl_3$–petrol gave a mixed fraction followed by 2,3-dimethoxyphenanthrene (0·4 g), m.p. 130°. Recrystallization from EtOH gave white flakes m.p. 133–134°. (Lit.[22] m.p. 131°). (Found: C, 80·6; H, 5·8; OMe, 23·4. Calc. for $C_{16}H_{14}O_2$: C, 80·65; H, 5·9; OMe, 26·0%.)