

STERIODS AND ARYNES I.<sup>1</sup> REACTIONS OF BENZYNE AND  
TETRAFLUOROBENZYNE WITH 7-DEHYDROCHOLESTERYL METHYL ETHER

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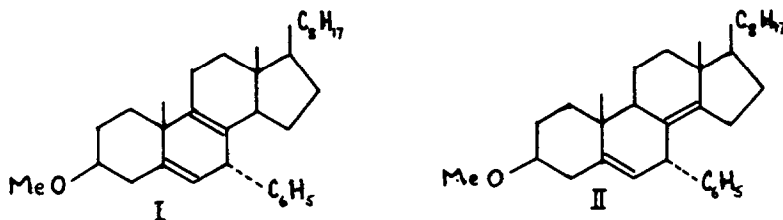
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The reactions of certain conjugated steroidal dienes in Diels-Alder additions,<sup>2</sup> and the reactions of steroidal olefins and dienes with carbene and dihalocarbenes<sup>3</sup> are well known. Surprisingly, no reactions of arynes in similar systems have been reported though many examples of the reactions of arynes with acyclic and cyclic olefins and dienes are in the literature.<sup>4</sup>

We find that the reaction of benzyne, generated from *o*-fluorophenylmagnesium bromide in tetrahydrofuran, with 7-dehydrocholesteryl methyl ether gives two products m.p. 133-134°C and 102-104°C identified as (I) and (II) respectively (combined yield 58% on steroid). The crude reaction product was chromatographed on alumina to remove biphenyls and triphenylene, and the crystalline mixture of (I) and (II) was separated by thin-layer chromatography on silica impregnated with silver nitrate.

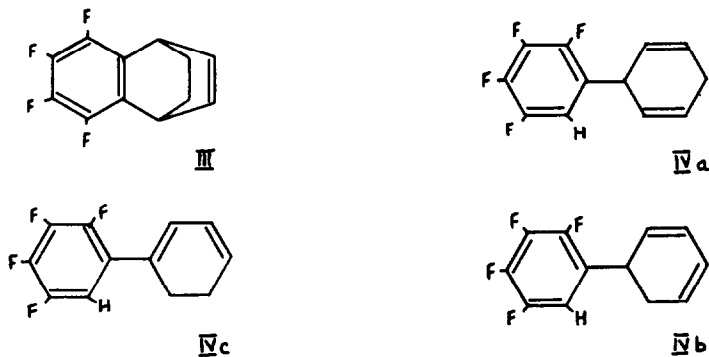


Elemental analyses and mass spectrometry showed (I) and (II) were isomeric and had a molecular formula  $C_{34}H_{50}O$ . The infrared spectra were almost identical, that of (I) possessing important bands at  $2850\text{cm}^{-1}$  ( $\text{O}-\text{CH}_3$ ),  $1100\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ),  $760\text{cm}^{-1}$  and  $702\text{cm}^{-1}$  (monosubstituted aromatic), and that of (II) at  $2850\text{cm}^{-1}$  ( $\text{O}-\text{CH}_3$ ),  $1100\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ),  $772\text{cm}^{-1}$  and  $702\text{cm}^{-1}$

(monosubstituted aromatic). The proton magnetic resonance spectrum of (I) showed multiplets at  $\tau$  2.8-3.1 (5 aromatic H),  $\tau$  4.7-4.9 (1 olefinic H),  $\tau$  6.1-6.4 (1 methine H:  $X_H^{OMe}$ ), and singlets at  $\tau$  8.74 ( $C_{19}$ -Me),  $\tau$  9.30 ( $C_{18}$ -Me) and  $\tau$  6.82 (OMe). The side chain methyl signals appeared as two partially superimposed doublets at  $\tau$  9.0-9.2. These data are compatible with structure (I) in which the  $C_{18}$ -methyl group is shielded while the  $C_{19}$ -methyl group is deshielded by the magnetic anisotropy of the 8,9-double bond.<sup>5</sup> The p.m.r. spectrum of (II) showed multiplets at  $\tau$  2.8-3.0 (5 aromatic H),  $\tau$  4.6-4.8 (1 olefinic H),  $\tau$  6.1-6.3 (1 methine H:  $X_H^{OMe}$ ), and a singlet at  $\tau$  6.78 (OMe). The  $C_{18}$ - and  $C_{19}$ -methyl groups and the side chain methyl groups appear as a close multiplet at  $\tau$  9.0-9.3. These data are compatible with the structure (II) in which the  $C_{18}$ -methyl group is deshielded and the  $C_{19}$ -methyl group is shielded by the magnetic anisotropy of the 8,14-double bond.<sup>5</sup>

The  $\alpha$ -configuration at  $C_7$  in both (I) and (II) is inferred from a plausible concerted insertion mechanism involving the allylic  $9\alpha$ -hydrogen and  $14\alpha$ -hydrogen atoms respectively in a six membered cyclic transition state.

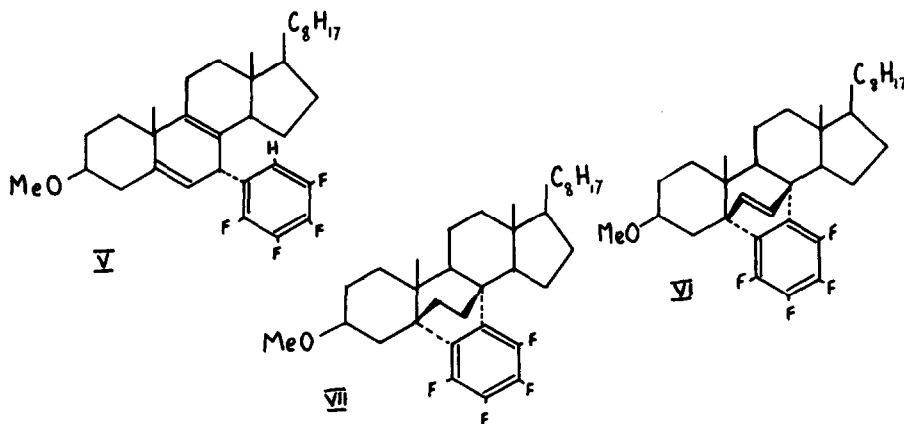
We have previously reported that tetrahalogenobenzenes have greater electrophilic properties than benzyne,<sup>6</sup> and this hypothesis was confirmed by reaction of tetrafluorobenzyne with 1,3-cyclohexadiene and 7-dehydrocholesteryl methyl ether. Reaction of the former gave a mixture (64% on Grignard) of adduct (III) (77%) and isomeric insertion products (possibly (IVa), (IVb), and (IVc), 11%).



Adduct (III) was separated by preparative gas-liquid chromatography and its structure was assigned on the following evidence. Elemental analysis indicated a molecular formula  $C_{12}H_8F_4$  and the p.m.r. spectrum showed multiplets at  $\tau$  3.3-3.7 (2 olefinic H),  $\tau$  5.4-5.9 (2 methine H) and  $\tau$  8.1-8.9 (4 methylene H). (III) absorbed 1 mole of hydrogen to give 5,6,7,8-tetrafluoro-

-1,4-ethanotetralin<sup>4e</sup> and on pyrolysis at 300°C gave 1,2,3,4-tetrafluoronaphthalene.<sup>4e</sup> The insertion product, separated by preparative gas-liquid chromatography, appeared to be a mixture of the isomers (IVa), (IVb), and (IVc) from p.m.r. data and the fact that it dehydrogenated, during chromatography, to give 1,2,3,4-tetrafluorobiphenyl.<sup>6</sup> The expected higher proportion of the 1,4-adduct versus insertion product and higher overall yield, compared to the reaction of benzyne with 1,3-cyclohexadiene reported by other workers,<sup>4b,c</sup> was thus obtained.

Reaction of 7-dehydrocholesteryl methyl ether with tetrafluorobenzyne, gave a mixture (80% on steroid) of two products identified as (V) (51%) and (VI) (22%) and a third component (27%), as yet unidentified and possibly a mixture.



The structure of (V) was assigned on the following evidence. Elemental analysis indicated a molecular formula C<sub>34</sub>H<sub>46</sub>F<sub>4</sub>O and the p.m.r. spectrum was very similar to that of (I) showing multiplets at  $\tau$  3.1-3.7 (1 aromatic H),  $\tau$  4.7-4.9 (1 olefinic H),  $\tau$  5.6-5.9 (1 methine H:  $\times_{\text{H}}^{\text{OMe}}$ ) and singlets at  $\tau$  6.76 (OMe),  $\tau$  8.63 (C<sub>19</sub>-Methyl) and  $\tau$  9.31 (C<sub>18</sub>-methyl). The side chain methyl signals appeared as two partially superimposed doublets at  $\tau$  9.0-9.2.

The structure of the 1,4-adduct (VI) was assigned from the following data. Elemental analysis indicated it was isomeric with (V) and the p.m.r. spectrum showed multiplets at  $\tau$  3.7-3.9 (2 olefinic H) and  $\tau$  8.95-9.2 (C<sub>18</sub>-, C<sub>19</sub>- and side chain methyl groups) and a singlet at  $\tau$  6.62 (OMe). The  $\alpha$ -configuration of the 1,2-disubstituted tetrafluorophenyl group is assigned from the p.m.r. spectrum of the dihydrocompound (VII) in which the C<sub>19</sub>-methyl group appears at  $\tau$  8.88. This shift downfield is compatible with the removal of the shielding effect of the  $\beta$ -bridging double bond.

The presence

of this 1,4-adduct indicates clearly the greater dienophilic properties of tetrafluorobenzene over benzene.

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