# Unsymmetrically-substituted [2,2]Metacyclophanes *via* a Free-radical Substitution Reaction

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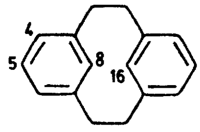
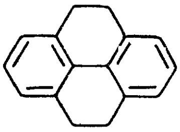
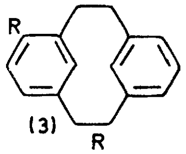
*Summary* Substitution of [2,2]metacyclophane (**1**) without transannular bonding has been performed using BzO·OBz–$CuCl_2$–MeCN, to produce the 4-benzoate (**3a**) and the 8-cyanomethyl derivative (**4**).



(**1**)

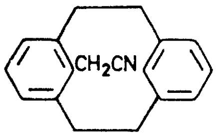


(**2**)

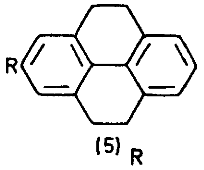


(**3**)

a; OBz
b; $OCOC_6H_4Cl$-*p*
c; OH
d; OMe

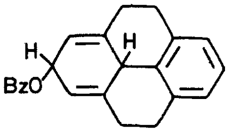


(**4**)



(**5**)

a; OBz
b; Ph



(**6**)

Derivatives of [2,2]metacyclophane (**1**), especially those which are unsymmetrically substituted, have been difficult to prepare.[1] A direct substitution route using various electrophiles failed since (**1**) was dehydrogenated to give the pyrene (**2**).[2] We hoped to achieve nuclear substitution of (**1**) *via* a free-radical reaction taking advantage of the inertness of the benzylic position and the low positional selectivity of the aromatic ring towards radical attack. Substituents were introduced at positions 4 or 8.

The reaction of (**1**) with BzO·OBz (3 equiv) and $CuCl_2$ (*ca.* 0·2 equiv) in acetonitrile at 80° for 42 h produced five compounds: (**2**) (4·5%) 4,5-dihydropyrene (5·8%), pyrene (1·6%), (**3a**) (5·2%), and (**4**) (1·6%).†

The benzoate (**3a**) was obtained as a viscous oil. On alkaline hydrolysis (**3a**) gave (**3c**) which was converted into the methyl ether (**3d**), m.p. 80—81°. With *pp′*-dichlorodibenzoyl peroxide the corresponding *p*-chlorobenzoate (**3b**) was obtained as a viscous oil.†

Appearance of 8- and 16-H resonances as a one-proton doublet (*J* 1—2 Hz) and a one-proton triplet (*J* 1·6—2 Hz), respectively, at an unusually high field supports the cyclo-

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† Satisfactory analytical figures, mass spectra, and i.r. data were obtained for these compounds.

phane structure and the substitution pattern (Table). Whereas the resonance due to the C-8 proton is similar to that of (**1**) and remains almost constant, that of the C-16 proton changes with the substituent in the benzene ring opposite.

TABLE. *Chemical shifts* ($\delta$) *of* 8- *and* 16-H *in* $CDCl_3$

| | 8-H | 16-H |
|---|---|---|
| (**1**) | 4·25 (t) | 4·25 (t) |
| (**3a**) | 4·30 (d) | 4·60 (t) |
| (**3b**) | 4·29 (d) | 4·55 (t) |
| (**3c**) | 4·20 (d) | 4·42 (t) |
| (**3d**) | 4·23 (d) | 4·36 (t) |

The cyanomethyl derivative (**4**), m.p. 181—182°, showed one-proton and two-proton resonances at $\delta$ 3·83 and 1·68, respectively. On irradiation at 716 Hz (100 MHz) the former signal became a sharp singlet and thus was assigned to the C-16 proton. The two-proton signal was assigned to $CH_2CN$ shifted to a high field (*cf.* $PhCH_2CN$, $\delta$ 3·44). [$^2H_{27}$]-Eu(fod)$_3$ caused a general downfield shift which was largest with $CH_2CN$ ($\Delta\nu$: $CH_2CN/ArH$ = *ca.* 5). The fact that all the external aryl protons shifted to a low field of similar magnitude indicated that $CH_2CN$ had been introduced in the central part of the molecule, not at position 4 or 5.

Positions 8 and 16 are overcrowded and less accessible although the electron density there is expected to be higher than at peripheral positions, due to transannular effects.[3] Attack at these positions appears to be possible only with less bulky electrophilic species such as $\cdot CH_2CN$. Release of strain energy (13 kcal) in the hexadienyl intermediate is also one of the driving forces.

Dehydrogenation and substitution reactions could be differentiated by selecting the reaction conditions: when $CuCl_2$ was absent neither (**3a**) nor (**4**) was formed and only a small amount of (**2**) (1%) resulted. Aeration appeared to be necessary for the formation of (**4**) since the deaerated mixture containing $CuCl_2$ did not produce (**4**). $CuCl_2$ (1 equiv) alone was found to dehydrogenate (**1**) to (**2**) (20%) as did $FeCl_3$ (8·5%) in MeCN.

Neither the 5- nor the 8-benzoate could be detected by g.l.c. Attack at C-5 could lead to the tetrahydropyrene derivative (**5a**) *via* the transannular benzoate (**6**).‡ The absence of (**5a**) was proved by comparison with an authentic sample (m.p. 162—163°). Also eliminated was the participation of a phenyl radical in the BzO·OBz reaction. With phenylazotriphenylmethane (in MeCN) no dehydrogenation or phenylation products were formed. The possible transannular product (**5b**), m.p. 126—126·5°, was not detected.

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‡ Another possible route from (**6**) is the formation of (**2**) by benzoic acid elimination. Even if (**6**) is the sole source of (**2**), it is only a minor reaction since (**2**) was formed only 1% when BzO·OBz alone was used.

[1] T. Hylton and V. Boekelheide, *J. Amer. Chem. Soc.*, 1968, **90**, 6887; V. Boekelheide, C. Ramey, E. Strum, T. Miyasaka, and B. A. Hess, jun., *J. Org. Chem.*, 1969, **34**, 1956; F. Vögtle, *Angew. Chem. Internat. Edn.*, 1969, **8**, 274; H. E. Zimmerman and G. Jones II, *J. Amer. Chem. Soc.*, 1970, **92**, 2753.

[2] For recent reviews on the reactions of [2,2]metacyclophanes see R. W. Griffin, jun., *Chem. Rev.*, 1963, **63**, 45; T. Sato, *Nippon Kagaku Zasshi*, 1971, **92**, 277; F. Vogtle and P. Neumann, *Angew. Chem. Internat. Edn.*, 1972, **11**, 73.

[3] Enhanced $\pi$-basicity was revealed by kinetic data from the (**1**)–TCNE complex, $\lambda_{max}$ 486 nm, $K$ = 17·5 l mol$^{-1}$ (S. Hayashi and T. Sato, *Nippon Kagaku Zasshi*, 1970, **91**, 950). $J_{C-H}$ found for C-8 (158 Hz) was larger than that for C-5 (150 Hz).