A Simple Synthesis of [2.2.2.2]-Paracyclophane-1,9,17,25-tetraene by a Wittig Reaction

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Synthetic applications of the Wittig reaction are numerous, but only few deal with the synthesis of macrocyclic compounds, often by multistep sequences [1] or *via* low-yield reactions.[2,3] The major difficulty lies in the control of the *cis/trans* ratio at the double bonds formed in the Wittig reaction.

[2.2.2.2]Paracyclophanes can be prepared, together with smaller and larger paracyclophanes, from α,α′-dichloro-*p*-xylene and sodium.[4,5] A more general method enabling the introduction of a variety of substituents is desirable. Previous attempts to use a Wittig reaction gave only trace amounts of [2.2.2.2]-paracyclophanetetraenes.[3] We now wish to report a one-step synthesis of [2.2.2.2]paracyclophane-1,9,17,25-tetraene, or, systematically, pentacyclo[20.2.2.2$^{4-7}$.2$^{12-13}$.2$^{16-19}$]-dotriaconta-2,4,6,8,10,12,14,16,18,20,22,24,25,-27,29,31-hexadecaene, in a 15 % yield from terephthalaldehyde and the *bis*-triphenylphosphonium salt from α,α′-dibromo-*p*-xylene, Scheme 1.

Low reaction temperature favours ring formation, whereas high temperature favours polymerization. Addition of lithium iodide to the reaction mixture does not increase the yield.

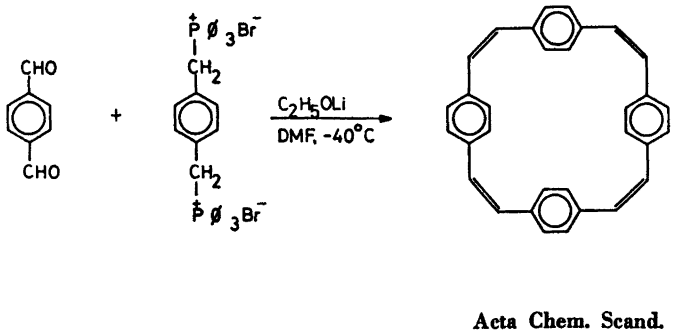
[2.2.2.2]Paracyclophane-1,9,17,25-tetraene is a yellow solid melting at 245 – 247 °C. Its NMR spectrum shows only two sharp singlets, demonstrating the equivalence of the aromatic hydrogens, as well as of the olefinic hydrogens. In contrast to [2.2.2.2]paracyclophane, the tetraene does not form any charge-transfer complex with tetracyanoethylene.

This new Wittig reaction makes it possible to study the chemistry of [2.2.2.2]paracyclophane-1,9,17,25-tetraene and substituted analogues, possible precursors for circulenes and new cage compounds.

Experimental. *[2.2.2.2]Paracyclophane-1,9,-17,25-tetraene.* To a solution of terephthalaldehyde (1.34 g, 10 mmol) and the *bis*-triphenylphosphonium salt from α,α′-dibromo-*p*-xylene (7.9 g, 10 mmol) [1] in dry dimethylformamide (200 ml) was added dropwise a solution of lithium (0.16 g, 22 mmol) in ethanol (50 ml). The mixture was vigorously stirred at −40 °C under nitrogen. The rate of addition was adjusted to maintain a faint red colour of the solution. The addition required 15 h. Water (200 ml) was added and the solution extracted with ether (3 × 150 ml). Evaporation of the solvent gave a yellowish oil which was purified by chromatography on silica gel with dichloromethane as solvent. The first fraction gave yellow needles (300 mg, 15 %), melting at 245 – 247 °C after recrystallization from carbon tetrachloride, identified as [2.2.2.2]paracyclophane-1,9,17,25-tetraene. (Found: C 93.7; H 5.90. Calc. for $C_{32}H_{24}$: C 94.1; H 5.92). MS: exact mass. found 408.1885, calc. 408.1878, *m/e*; 408 (M^+, 100 %), 204 (M^{++}, 5 %). NMR: sharp singlets at $\delta = 6.45$ (8 H) and $\delta = 7.32$ (16 H). UV: λ_{max} at 303 nm, log $\varepsilon = 4.76$. IR: 1603 m, 1507 m, 1424 m, 891 s, and 835 s cm^{-1}.

On gradient-sublimation of the crude product from the Wittig reaction, a small amount (total yield 1 %) of a less volatile product was obtained in addition to [2.2.2.2]paracyclophanetetraene. Its mass spectrum is consistent with a [2.2.2.2.2.2]paracyclophanehexaene; *m/e* 612 (M^+, 100 %) and 306 (M^{++}, 10 %). The IR spectrum indicates the presence of *trans*-double bonds, 970 cm^{-1} (s).

[2.2.2.2]Paracyclophane. [2.2.2.2]Paracyclophane-1,9,17,25-tetraene (408 mg, 1 mmol) was dissolved in benzene (100 ml) and hydrogenated at atmospheric pressure with palladium on charcoal as a catalyst. Four mmol of hydrogen was consumed in 120 min. Filtration and evaporation of the solvent gave, after recrystallization from acetic acid, [2.2.2.2]paracyclophane (366 mg, 90 %) melting at 180 – 181 °C (lit. 179 – 182 °C).[4,5] MS: exact mass,



Scheme 1.

found 416.248; calc. for $C_{32}H_{32}$, 416.250; *m/e* 416 (M^+, 58 %), 311 (14 %), 207 (72 %) and 104 (100 %). NMR: singlets at $\delta = 6.72$ (16 H) and $\delta = 2.85$ (16 H).

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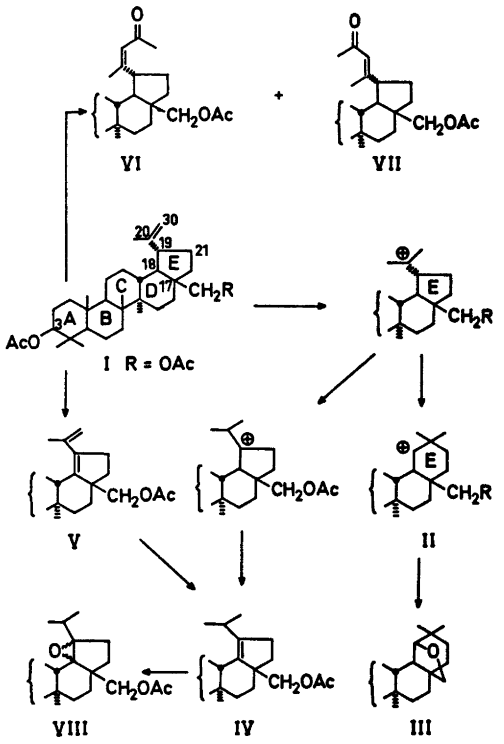

Triterpenes. A Novel Acid Catalysed Double Bond Migration in 3β,28-Diacetoxy-lup-20(30)-ene (Betulin Diacetate)

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The acid catalysed rearrangement of $\Delta^{20(30)}$-derivatives in the lupane series has been reported [1-3] to proceed *via* the secondary carbocation (II). Subsequent reactions are highly dependent on the reaction conditions and on the nature of the function R at C-28. The common feature of the end products is the enlargement of the five-membered ring E to six-membered.

The acid catalysed rearrangement of betulin diacetate (I) has been performed by Vystrčil *et al.*[2] in H_2SO_4-AcOH-benzene mixture and by Pettit *et al.*[3] in HCl-EtOH-$CHCl_3$ mixture. Both reactions lead to the allobetulin ring system (III) with a six-membered ring E.

When we carried out the isomerisation of betulin diacetate (I) with HBr in AcOH-Ac_2O-benzene solution, another reaction pathway was observed. Instead of breaking the bond between C-19 and C-21, the hydrogen at C-19 was shifted, and the double bond migration product, Δ^{18}-isomer (IV), was obtained. The Δ-[18]structure (IV) was confirmed by its identity (TLC, IR, ^{1}H NMR, MS, m.p., mixed m.p., $[\alpha]_D$) with an authentic sample prepared by PtO_2-catalysed hydrogenation [4] of the mercuric acetate dehydrogenation product (V) of betulin diacetate (I). In addition, compounds (IV), obtained either by hydrogenation of diene (V) or by isomerisation of betulin diacetate (I), gave identical epoxides (VIII) with *m*-chloroperbenzoic acid.

Increasing concentrations of both HBr and AcOH cause a more rapid reaction. Acetic anhydride addition gives a milder reaction but results in the formation of an *E/Z*-mixture of ketones (VI) and (VII), due to the addition of CH_3CO^+ to the double bond of betulin diacetate (I) followed by loss of a proton. Below 10 % HBr the reaction may demand months, while above 14 % HBr and 40 % AcOH all the starting material has reacted in a few hours or less and increasing amounts of less polar side products are formed. These side products were also obtained, when the Δ^{18}-isomer (IV) was treated with HBr in AcOH-Ac_2O-benzene solution. The ^{1}H NMR-spectrum of this mixture