A PHOTOCHEMICAL PARACYCLOPHANE SYNTHESIS: INTRAMOLECULAR OXETANE FORMATION

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We wish to report a novel paracyclophane synthesis based upon the remote oxi-
dation concept developed by Breslow.[1] The cyclophanes II and III we report are
not candidates for the smallest or most strained cyclophanes.[2] Rather, the high
yield of the one step stereospecific synthesis of II and of its conversion to
III recommend this photochemical approach to the more general problem of macrolide
ring formation. Intramolecular oxetane formation has previously been used to gen-
erate small rings.[3]

Treatment of benzophenone-4-carboxylic acid chloride with ω‑undecylenyl alco-
hol in refluxing benzene containing pyridine gave, after work-up and elution from
a silica gel column, the ketoester I, which yielded white crystals from ethanol at
$-20°$ with m.p. ~ $15°$; $\lambda_{max}^{CCl_4}$ 5.77, 5.96, 11μ; $\delta_{TMS}^{CDCl_3}$ 8.2 (2H,d,J=8), 7.3-7.9
(7H,m), 5.5-6.2 (1H,m), 5.1 (1H,bd,J=5), 4.9 (1H,m), 4.4 (2H,t,J=6), 1.2-2.2
(16H,m); m/e 378.2195 (calc. 378.2195).

A carbon tetrachloride solution 1.1×10^{-3}M in I was irradiated with a mercury lamp through a uranium glass filter until the bands at 5.96 (ketone) and 11 μ (olefin) disappeared (4 hours). Evaporation of solvent gave an oil which was placed on florisil. Elution with benzene followed by benzene-1% ethyl acetate gave the oxetane II in 83% yield as an oil which crystalized from ethanol as a white solid with m.p. 93-94°; $\lambda_{max}^{CCl_4}$ 5.83 μ; λ_{max}^{MeOH} 246 nm (ε16,200); m/e 378.2195 (calc. 378.2195).

In order to separate the NMR signals due to the hydrogens on carbon bearing oxygen, the oxetane II was hydrolyzed with base to afford the hydroxy acid IV. The NMR spectrum of IV contains a triplet (2H,J=6) at δ3.6 which is assigned to the methylene hydrogens next to the hydroxyl. Also present were one-proton signals at δ4.7 (dd,J=6,1.5) and 4.3 (t,J=6); these are assigned to the oxetane methylene hydrogens which are expected to couple with each other (J=6) and, to different extents, with the oxetane methine hydrogen (J=6,1.5). Since the aliphatic chain in IV is no longer held in close proximity to the benzene ring, the aliphatic hydrogen signal takes up the region δ1.0-1.7 compared to the value of δ0.5-1.9 for II.

Treatment of II with silica gel in hexane effected loss of formaldehyde and afforded the olefin III in 90% yield. White crystals obtained from ethanol had m.p. 85-86°, $\lambda_{max}^{CCl_4}$ 5.82 μ, λ_{max}^{MeOH} 243 mm (ε22,800), m/e 348.2085 (calc. 348.2089). The single olefinic hydrogen in III gave rise to a triplet (J=8) at δ6.4 in the NMR spectrum which also contained signals at δ8.1 (2H,d,J=8, aromatic H ortho to carbonyl), 7.2 (7H,m,other aromatic H), 4.4 (2H,t,J=5,methylene H next to oxygen), and δ0.5-1.9 (m,16H,aliphatic).

Further structural proof was afforded by the degradation of III in base with sodium periodate/catalytic potassium permanganate[4] to a mixture of benzophenone-4-carboxylic acid (V) and 10-hydroxydecanoic acid (VI) which were separated by

$$III \xrightarrow[\cdot \quad OH^-]{MnO_4^-/IO_4^-} \qquad V \qquad \xleftarrow[OH^-]{MnO_4^-/IO_4^-} I$$

+

$$HO(CH_2)_9CO_2H$$

VI
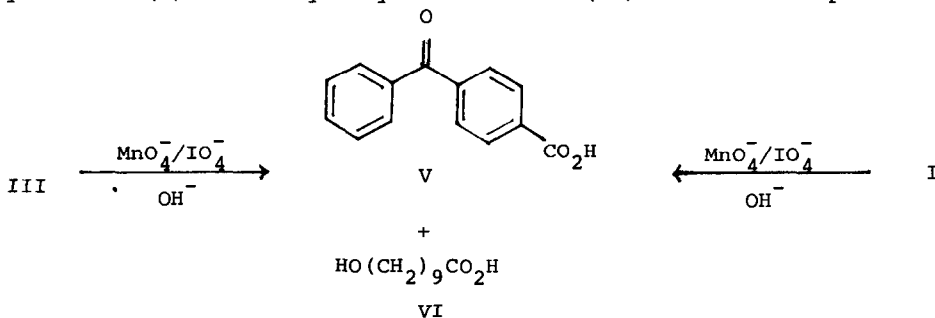
virtue of the greater solubility of VI in water. V and VI were shown spectroscopically and by m.p. and mixed m.p. to be identical with authentic samples;

authentic VI was obtained by periodate/permanganate treatment of ω-undecylenyl
alcohol and found to have m.p. 73-74° (lit.[5] m.p. 75°) after recrystallization
from hexane/acetone.

The nmr spectrum of II contains some unusual features. While the monosub-
stituted benzene ring gives a singlet at δ7.4, the disubstituted benzene ring
gives three discrete signals: a broadened 2-proton singlet at δ8.2, and coupled
(J=8) doublets centered at δ7.8 and 6.8. The magnitude of the coupling constant
reveals that the hydrogens at δ7.8 and 6.8 are ortho to one another. The other
two hydrogens, also adjacent, accidentally have similar chemical shifts.

Since the i.r. spectra of II and III indicate significant conjugation of
the ester carbonyl with the benzene ring, we visualize the structures of these
cyclophanes as shown in Figure 1. Rocking motion of the benzene ring about the
axis defined by the para substituents interconverts protons d and d', and e and
e' in IIIa.

FIGURE 1

	H	δ	J(Hz)
	a,a'	8.2	-
IIa	b	7.8	8
	c	6.8	8
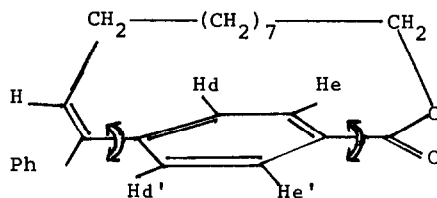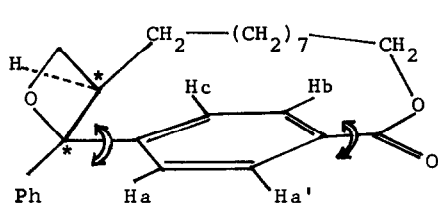
	H	δ	J(Hz)
IIIa	d,d'	7.2	8
	e,e'	8.1	8

The non-equivalence of the two pairs (Ha and Hc; Ha' and Hb) of aromatic
hydrogens occupying ostensibly similar positions in IIa must be related to the
presence of two chiral centers in the oxetane ring. These pairs of hydrogens
would become equivalent if the benzene ring in II could rotate through the
ring of the cyclophane. Molecular models indicate that it cannot. That proton
a (Figure 1) is shifted so far down field suggests that it experiences strong
deshielding from either the other phenyl ring or the C-O bond.

ACKNOWLEDGEMENT

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