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A ($_{\pi}2$ + $_{\pi}2$) PHOTOCYCLOADDITION REACTION AS A FACILE ROUTE TO ANGULARLY SUBSTITUTED CIS-HYDRINDANES AND CIS-DECALANES

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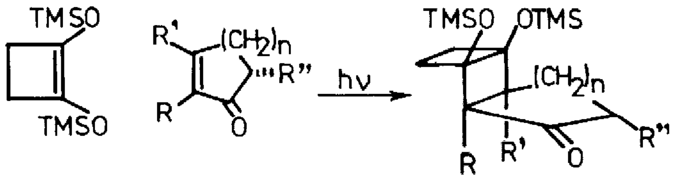
SUMMARY

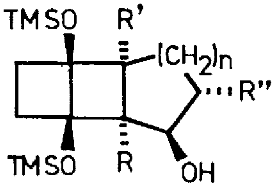
The photochemical addition of 1,2-bis(trimethylsiloxy)cyclobutene to, respectively, 2-cyclopentenones and 2-cyclohexenones represents a novel and facile entry into angularly substituted bicyclo[4.3.0]nona-2,5-diones and bicyclo-[4.4.0]deca-2,5-diones.

The ($_{\pi}2$ + $_{\pi}2$) photocycloaddition reaction between enones and alkenes has been applied as a key step in the synthesis of many natural products. Our own work in this field dealt with short and efficient preparations of synthons for hydroazulenes[2] and prostaglandins[3]. We now report a facile route to angularly substituted cis-bicyclo[4.3.0]nona-2,5-diones (cis-hydrindane skeleton) and cis-bicyclo[4.4.0]deca-2,5-diones (cis-decalane skeleton).

The construction of the carbon frameworks requires a ($_{\pi}2$ + $_{\pi}2$)photoreaction between the easily accessible 1,2-bis(trimethylsiloxy)cyclobutene[4] (1) and 2- and/or 3-methyl substituted 2-cyclopentenones (2) or 2-cyclohexenones (3). Selective irradiation in the region of the $n\rightarrow\pi^*$ band of the enones was achieved at 350 nm (RUL-lamps) in a Rayonet reactor with a 4-fold excess of the cyclobutene in n-pentane or benzene solution at room temperature. The reactions were monitored by TLC and UV spectroscopy. The pure cycloadducts 4 and 5 (only the anti-isomers are shown in the scheme) were obtained upon distillation (0.1 mm Hg). The yields were good (75-80 %) when starting from the enones 2a, 2c, 3b and 3d; lower efficiencies (40-50 %) were noted with the enones 2b and 3c[5]. On the other hand, 2-methyl-2-cyclohexenone (3a) afforded only a trace of photoadduct; the abnormal behaviour of this particular enone in photocycloaddition reactions has already been noted in the literature[6].



1 2,3 4,5



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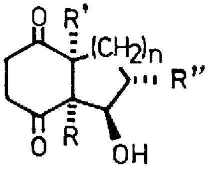

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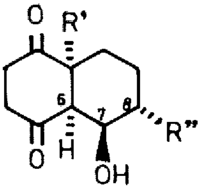
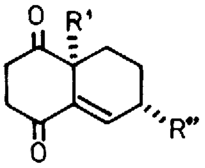


9 b,d



10 b,d

2,4,6,8 ; n = 1
3,5,7,9 ; n = 2

	R	R'	R"
a	Me	H	H
b	H	Me	H
c	Me	Me	H
d	H	Me	i Prop

Structure identification was performed by combined GC-CIMS techniques; chemical ionization mass spectrometry allows differentiation to be made between the cis-anti-cis (4,5) and the cis-syn-cis photoadducts[7]. The photocycloaddition proceeds with very high stereoselectivity as the cis-anti-cis isomers 4 and 5 were present for > 99.9 %, except for the reactions with 2b and 3d, where 10 % of the cis-syn-cis isomer was found. This selectivity is of no importance for further synthetic work as the stereochemical feature, which differentiates both isomers, is lost during the oxidative ring cleavage. More important is the observation that the photoaddition with (-)piperitone (3d) leads to 5d with the relative cis configuration[8] of the methyl(R') and isopropyl(R") groups; indeed, this particular stereochemistry is found in most eudesmane sesquiterpenes (see also structures 9d and 10d).

Reduction of 4 and 5 with LiAlH$_4$ gave the endo alcohols due to hydride attack from the least hindered exo face of the molecule. Treatment of the alcohols 6 and 7 with methanol for 24 h at r.t. (without exclusion of oxygen) to bring about the silyl ether cleavage, surprisingly gave directly subsequent oxidation[9] to the desired cis-hydrindanes 8 and cis-decalanes 9. The overall yields, starting from 4 and 5, were between 50 % and 70 % after column chromatography (silica gel; ethyl acetate-isooctane 2:8). The spectral data are in accordance with the proposed structures; the data for 9d are given as an example.

9d : $M^{+\cdot}$ at m/z 238; IR : 3600, 1705 cm^{-1}; ^1H NMR : δ : (360 MHz, $CDCl_3$) : 0.87 (3H, d, 6.8 Hz), 0.94 (3H, d, J = 6.8 Hz); 1.23 (3H, s); 1.30-1.70 (5H, m), 2.09 (1H, m), 2.60-2.90 (4H, m), 2.91 (1H, d, J = 4.0 Hz), 3.07 (1H, s), 3.89 (1H, 2 x d, J = 8.6 Hz and 4.0 Hz). The δ-value of 1.23 for the angular methyl protons proves the cis-fused structure[10], while the large (8.4 Hz) and small (4.0 Hz)[11] coupling constants for H-6 establish the relative configuration at the carbon atoms 5, 6 and 7 and the conformation with both the hydroxyl function and the isopropyl group in equatorial position.

Treatment of 9b and 9d with TsOH in refluxing benzene affords the corresponding α,β-unsaturated ketones 10b and 10d in an almost quantitative yield after column chromatography (silica gel, ethyl acetate-isooctane 1:4) : 10b : $M^{+\cdot}$ at m/z 178; IR : 1710, 1690, 1620 cm^{-1}; ^1H NMR : δ (90 MHz, $CDCl_3$) : 1.3 (3H, s), 1.6-1.9 (4H, m), 2.28 (2H, m), 2.76 (4H, m), 6.96 (1H, t, J = 4.2 Hz).

10d : $[\alpha]_D^{20}$ in $CHCl_3$ (C:0.05) : +158,6°; $M^{+\cdot}$ at m/z 220; UV : 255 nm; IR : 1705, 1680, 1610 cm^{-1}; ^1H NMR : δ (90 MHz, $CDCl_3$) : 0.93 (3H, d, J = 6.8 Hz), 1.25 (3H, s), 1.45-1.98 (5H, m), 2.13 (1H, m), 2.59-2.89 (4H, m), 6.96 (1H, 2 x d, J = 2.4 Hz and 1.2 Hz).

Further work exploiting the efficient route to the hydrindane and decalane skeletons and the typical structural array of compounds 8, 9 and 10 is in progress.

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b. "Bevoegdverklaard Navorser" of the NFWO-FNRS.

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5. As the TLC and GC analyses of the crude photoadducts gave satisfactory results, the lower yields are most probably due to thermal unstability upon distillation. Also 2-cyclopentenone and 2-cyclohexenone gave lower yields (40-50 %) of the photoadducts.
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8. This cis configuration is proven by ^{1}H NMR analysis of the subsequent product 9d. For analogous results, see P.A. Wender and J.C. Lechleiter; J. Am. Chem. Soc., 99, 207 (1977) and G.L. Lange and F.C. McCarthy; Tetrahedron Letters, 4749 (1978).
9. Addition of $NaIO_4$ speeds up the reaction with, however, substantially the same yields.
10. F.P. Boer, J.J. Flynn, H.H. Freedman, S.V. Mehinley and V.R. Sandel; J. Am. Chem. Soc., 89, 5067 (1967). Slow chromatographic separation on untreated silica gel causes partial isomerisation to the trans fused compound, the δ value then being 1.01.
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