UNEXPECTED REGIOSPECIFICITY IN PHOTOCHEMICAL
α-CLEAVAGE OF HYDRINDANONES.

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ABSTRACT. *Triterpene derived trans-hydrindanones 1 of the hopane and lupane series undergo highly regiospecific photochemical α-cleavage; they are cleaved in high yields on the least substituted side of the ketone. The more stable cis-hydrindanones 1' exclusively cleave on the more substituted side as expected.*

The major products of the photolysis of cycloalkanones usually correspond to a pre-ferred cleavage adjacent to the more highly substituted α-carbon[1], although low yields of reaction products resulting from the cleavage on the less favored side have occasionnaly been observed[2]. Exceptions are cyclic α-cyclopropyl and α-cyclobutyl ketones which often cleave on the side of the carbonyl removed from the three or four membered ring, a fact which may be partially explained by the reduced stability of the cyclopropyl or cyclobutyl radicals[1a,3a]. Relatively few of these reactions have become of real preparative value in organic synthesis, mainly due to the obtention of mixtures and the difficulty of predicting the reactions path-ways followed by the intermediate biradicals[1a,3].

During the synthesis of a novel series of tetracyclic terpene hydrocarbons of geo-chemical significance[4] from pentacyclic hopane precursors[5], we have discovered an unexpected highly regiospecific Norrish type I reaction undergone by triterpene derived trans-hydrindano-nes of type 1, which are cleaved in high yields on the least substituted side (a) of the car-bonyl function. Furthermore we could show that the site of cleavage was strictly stereochemis-try dependent, since the more stable cis-hydrindanones 1' exclusively cleaved on the higher substituted side (b) giving rise to the more stable biradicals as expected (Figure 1).

In the hopane series the C_{27} trans-ketone, 22,29,30-trinorhopan-21-one 2[6,7] (27 mg) was irradiated in degased anhydrous methanol (120 ml) in a Pyrex vessel with a high pressure mercury lamp (125 W) for 3 hrs at room temperature.

The reaction mixture was analysed by capillary gas chromatography (GC) and coupled GC-mass spectrometry[8], which showed the presence of only four compounds. Silica gel TLC yiel-ded 7 mg of separable ketones comprising essentially the starting material 2 and a small amount (< 1 mg) of the epimeric ketone 3. In the reaction products 4 and 5 (19 mg) the unex-pected unsaturated aldehyde 4 was highly predominant (97%)[9], implying a photochemical cleava-ge on the least substituted side of the ketone followed by a hydrogen abstraction at C-19,in which a transfer of the more readily accessible 19β(H) could be favored.

The more stable C_{27} cis-ketone, 22,29,30-trinor-(17αH)-hopan-21-one 3 (26 mg) obtained by quantitative isomerization of 2 and easily separable from 2 by silica gel TLC[6,7], was photolysed under the same conditions as above. The reaction mixture contained 9 mg of starting material 3, with a trace of 2, and 15 mg of transformed products 4 and 5 which were in this case dominated by the methyl ester 5 (97%)[10]. The latter results from the expected cleavage on the more highly substituted side of the carbonyl function, as illustrated recently in the case of another triterpene cis-hydrindanone[11], with a subsequent hydrogen abstraction at C-20 leading to the formation of the ketene which was trapped as the methyl ester.

Very similar results were obtained in the lupane series, in which the ketones 6 and 7 were prepared from lupanol as a starting material[12]. As in the case of the hopane series the more stable cis-ketone 7 could be obtained quantitatively from 6 by isomerisation with base, both compounds being separable on silica gel TLC.

Irradiation of the trans-ketone 6 under the same conditions as above yielded again the unsaturated aldehyde 8 as the very major transformation product[13], whereas the cis-ketone 7 almost exclusively led to the expected methyl ester 9[14].

These results show that pure compounds can be obtained in high yields by photoinduced cleavage of hydrindanones of type 1 and 1', an aspect which may be useful for synthetic purposes. The regiospecificity of the cleavages is exclusively conditioned in this case by the stereochemistry of the ring juncture of the hydrindanones. Unlike the cis-hydrindanones for which more conformational possibilities exist, the trans-hydrindanones 1 are more strained and rather rigid molecules[15,16]. Molecular models do not show however any obvious explanation for the "abnormal" α-cleavage of the trans-hydrindanones which is unexpected in terms of stability of the intermediate biradicals. The high yields of aldehydes 4 and 8 indicate that photochemical epimerization[17,18] of the starting ketones does not occur to a great extent. This could either mean that α-cleavage on the more substituted side of the carbonyl function is not significant, or that reclosure to the starting ketone by a reversible singlet state α-cleavage[18,1a] takes place faster than epimerization or than abstraction of the readily accessible hydrogens at C-20 in compound 2 (respectively C-2 in compound 6). In the latter case less efficient cleavage on the least substituted side of the ketone followed by abstraction of a C-19 hydrogen could become product determining. A quasi-concerted mechanism implying a rapid transfer of the favorably located 19β hydrogen into a biradical in formation between C-20 and C-21 (respectively the 1α hydrogen and the C-2 and C-3 positions in 6) could also explain the observed products (Figure 1, bottom). However no conclusive evidence has been reported yet for such a process, suggested in particular for the cleavage of α-cyclobutyl ketones[19,20], and in a few cases arguments in its disfavor have been advanced[3a,21]. A careful study of the kinetic aspects and of the quantum efficiencies of these photochemical reactions may eventually help to elucidate some of these points.

Further work on sterical and conformational aspects of the photolytic cleavage of hydrindanones related to type 1 is in progress.
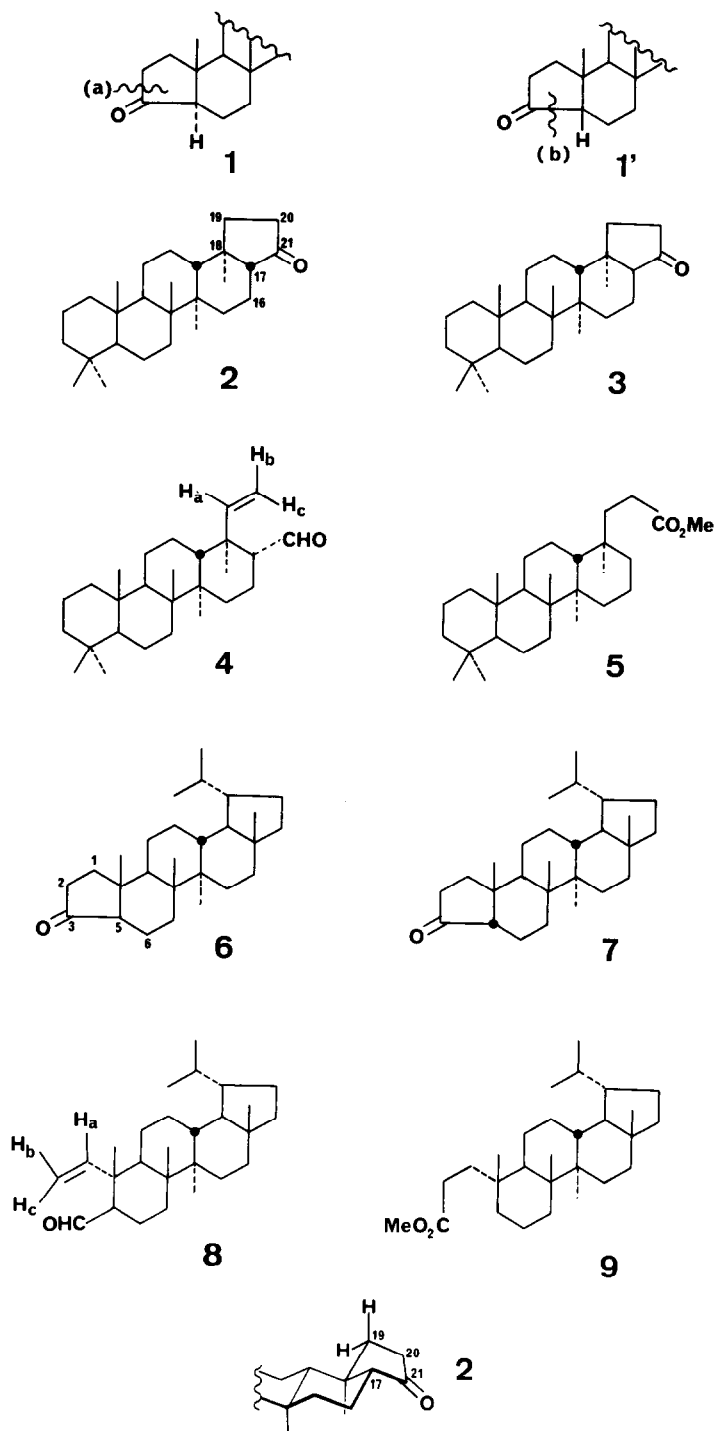
FIGURE 1. Trans- and cis-hydrindanones of types 1 and 1' from the hopane (2, 3) and lupane (6, 7) series and products of their photolysis.

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8. Conditions : OV 73, 25m x 0.25mm. GC-MS : SE 30, 25m x 0.25mm, LKB 9000 S.

9. Analytical data of 4 : ^{1}H nmr (250 MHz,CDCl$_3$): 9.62(1H,s broad, H-21); 5.77(1H,dd,$J_{Ha,Hb}$= 10.5Hz, $J_{Ha,Hc}$=17.5Hz,H-19); 5.19(1H,dd,$J_{Hb,Hc}$=1Hz, $J_{Hb,Ha}$=10.5Hz,Hb-20); 4.98(1H,dd,$J_{Hc,Hb}$ =1Hz, $J_{Hc,Ha}$=17.5Hz,Hc-20); 2.08(1H,dd,$J_{17\beta,16\alpha}$=11.5Hz, $J_{17\beta,16\beta}$=4Hz, H-17); 1.00, 0.98, 0.94, 0.85, 0.82, 0.79(3H each,s).
MS (70eV) m/z=384(M$^+$,5%); 369(5); 366(2); 231(22); 191(100). Exact mass : M$^+$=384,3388; C$_{27}$H$_{44}$O : 384, 3392. F = 164-166°C; IR(CHCl$_3$, cm^{-1}) : 3090, 2740, 1715, 1635.
The identification was further confirmed by decarbonylation of 4 with tris(triphenyl phosphine) rhodium chloride in benzonitrile, which led to the corresponding C$_{26}$ olefin known from previous studies (4).

10. Analytical data of 5 : ^{1}H nmr (250 MHz,CDCl$_3$) : 3.66(3H,s,-OC$\underline{H}_3$); 2.22(2H,m,H-20); 0.99, 0.95, 0.84(3H each,s); 0.81(6H,s); 0.79(3H,s).
MS (70eV) m/z=416(M$^+$,14%); 401(14); 385(1); 329(M$^+$-side chain,15); 191(100).Exact mass : M$^+$=416, 3656; C$_{28}$H$_{48}$O$_2$: 416, 3654. F = 131-132.5°C; IR(CHCl$_3$, cm^{-1}) : 1730.

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13. Analytical data of 8 : ^{1}H nmr (200 MHz,CDCl$_3$): 9.62(1H,s broad,H-3); 5.76(1H,dd,$J_{Ha,Hb}$=10.7 Hz, $J_{Ha,Hc}$=17.5Hz,H-1); 5.19(1H,d,$J_{Hb,Ha}$=10.7Hz,Hb-2); 4.99(1H,d,$J_{Hc,Ha}$=17.5Hz,Hc-2); 2.09 (1H,dd,$J_{5\alpha,6\beta}$=10.6Hz, $J_{5\alpha,6\alpha}$=4.7Hz,H-5); 1.08, 0.97, 0.96, 0.77(3H each,s); 0.84, 0.75 (3H each, d,J=6.8Hz).
MS (70eV) m/z=384(M$^+$,6%); 369(9); 366(2); 351(2); 341(14); 259(8); 231(66); 81(100).
Exact mass : M$^+$=384, 3384; C$_{27}$H$_{44}$O = 384, 3392. IR(CHCl$_3$,cm^{-1}): 3090, 2740, 1715, 1635.

14. Analytical data of 9 : ^{1}H nmr (200 MHz,CDCl$_3$): 3.67(3H,s,-OC$\underline{H}_3$); 2.23(2H,m,H-2); 1.07, 0.93, 0.85, 0.76(3H each,s); 0.84, 0.76 (3H each,d,J=6.7Hz).
MS (70eV) m/z=416(M$^+$,21%); 401(12); 385(2); 373(29); 329(M$^+$-(CH$_2$)$_2$ CO$_2$CH$_3$,42); 123(100).
Exact mass : M$^+$=416, 3653; C$_{28}$H$_{48}$O$_2$=416, 3654. IR(CHCl$_3$,cm^{-1}) : 1730.

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