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SYNTHESIS AND REARRANGEMENTS OF ALKYL-QUADRICYCLANONES

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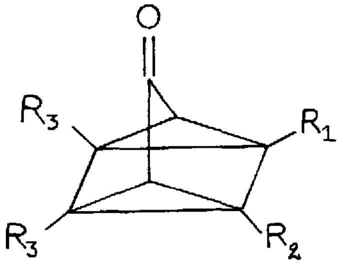
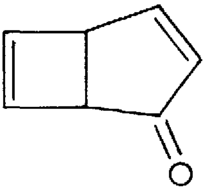
Summary : Both 1-isopropyl-6- and 7-methoxycarbonyl-quadricyclanones, the first alkyl-substituted molecules of this type, have been synthesized. Cycloaddition reactions with methylpropiolate failed. Their different behaviour in rearrangement and degradation reactions is discussed.

Up to now only a few quadricyclanones (I) has been described in the literature and their chemistry remains relatively unexplored. The unsubstituted ketone I_a (1) was first reported by Story and Fahrenholtz in 1964 and shown to isomerise under Oppenhauer oxidation conditions or by treatment with alumina to the bicycloheptadienone II (4). More recently, it was shown by Prinzbach (5) that thermolysis of I_a in pyridine solution at 130° mainly yielded, besides some benzene (3-5%) and II (5-6%), the intringuing tricyclo$[4.1.0.0^{2,7}]$hept-4-en-3-one (III) (30-35%); II appears to be the thermal rearrangement product of III. The four substituted quadricyclanones I_{b-e} described up to now on the other hand are known to isomerise thermally exclusively to the corresponding benzene

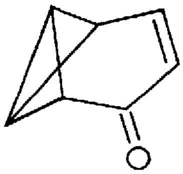


(I)

	R_1	R_2	R_3	Ref.
a)	H	H	H	(1)
b)	$COOCH_3$	H	H	(2,3)
c)	$COOCH_3$	$COOCH_3$	H	(2)
d)	$COOCH_3$	$COOCH_3$	$COOCH_3$	(2)
e)	CN	H	H	(3)



(II)



(III)

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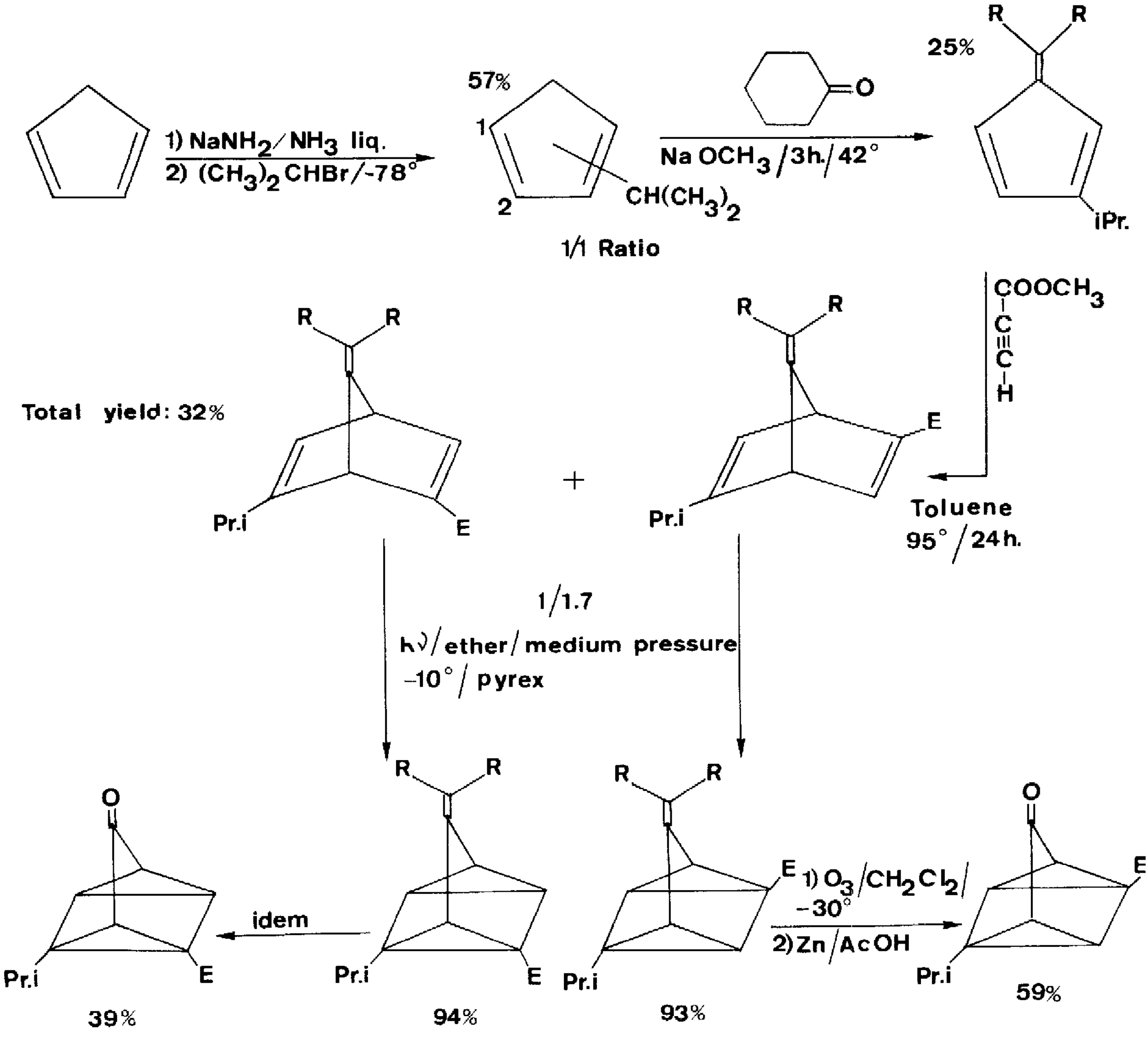
derivatives with loss of carbon monoxyde(2,3).

We now wish to report the synthesis of the two first alkyl-quadricyclanones by the reaction sequence(6) shown in Figure I, as well as their rearrangements; relevant NMR-data are given in Table I. Cyclopentadiene is transformed according to Alder(7) to a 1/1 mixture of 1- and 2-isopropyl-cyclopentadienes, which is then engaged in a Knoevenagel-type condensation with cyclohexanone; under the reaction conditions used, <u>only</u> the 2-isopropyl-6,6′-pentamethylenefulvene is obtained(8).



$R,R = -(CH_2)_5-$; $E = -COOCH_3$

<u>FIGURE I</u>

Diels-Alder reaction between this molecule and methyl propiolate gives a mixture of the two isomeric methylene-norbornadienes, the "pseudo-para" adduct being predominant as expected on the basis of known rules(9). NMR-identification of these isomers (separated by dry column chromatography : SiO_2, CCl_4/C_6H_6 6:4) is easily done on the number of olefinic to adjacent and opposite bridgehead hydrogen coupling constants appearing in the pattern of H_1 and H_4. *Intramolecular photocyclisation of these compounds followed by ozonolysis lead* to the corresponding quadricyclanones in rather good yields(10).

TABLE I : ^{1}H-NMR data of the relevant new compounds.

(All δ- en J-values are apparant and are given in ppm. and Hz. respectively)

2-isopropyl-6,6'-pentamethylene-fulvene ($CDCl_3$, 60 MHz) : 1.17(d,6H,J=6.8Hz), 1.70(m,6H), 2.61(m,5H), 6.19(m,δH_1), 6.52(m,2H).

7-cyclohexylidene-2-isopropyl-5-methoxycarbonyl-bicyclo[2.2.1]hepta-2,5-diene ($CDCl_3$,100 MHz) : 0.99(d,3H), 1.03(d,3H), 1.44(m,6H), 1.93(m,4H), 2.49(m,1H), 3.72(s,3H), 4.02(H_1,m), 4.32(H_4,m), 6.34(H_3,m), 7.67(H_6,m); $J_{1,3}$=1.1; $J_{1,6}$=3.5; $J_{3,4}$=3.4; $J_{4,6}$=1.2; $J_{3,isopr.H}$=1.65; $J_{1,4}$=2.4.

7-cyclohexylidene-2-isopropyl-6-methoxycarbonyl-bicyclo[2.2.1.]hepta-2,5-diene ($CDCl_3$, 100 MHz) : 1.01(d,3H), 1.04(d,3H), 1.44(m,6H), 1.94(m,4H), 2.56(m,1H), 3.72(s,3H), 4.10(H_4,m), 4.26(H_1,m), 6.17(H_3,m), 7.70(H_5,m); $J_{1,3}$=1.2; $J_{1,4}$=2.4; $J_{1,5}$=1.2; $J_{3,4}$=3.4; $J_{4,5}$=3.4; $J_{3,isopr.H}$=1.6.

1-isopropyl-6-methoxycarbonyl-tetracyclo[$3.2.0.0^{2,7}.0^{4,6}$]heptan-3-one ($CDCl_3$, 100 MHz) : 0.87(d,3H), 0.94(d,3H), 1.30(H_2,m), 2.01(H_4,m), 2.01(m,1H), 2.66 (H_7,m), 2.82(H_5,m), 3.71(s,3H); $J_{2,4}$=1.6; $J_{2,7}$=5.1; $J_{4,5}$=5.0; $J_{5,7}$=1.8.

1-isopropyl-7-methoxycarbonyl-tetracyclo[$3.2.0.0^{2,7}.0^{4,6}$]heptan-3-one ($CDCl_3$, 100 MHz) : 1.02(d,3H), 1.14(d,3H), 1.43(H_4,m), 1.88(H_2,m), 1.96(m,1H), 2.31(H_5, m), 2.66(H_6,m), 3.73(s,3H); $J_{2,4}$=1.5; $J_{4,5}$=4.9; $J_{4,6}$=4.9; $J_{5,6}$=5.8.

When these molecules were refluxed for 18h. in methylpropiolate as the solvent, no $[{}_{\sigma}2_s + {}_{\sigma}2_s + {}_{\pi}2_s]$ cycloadduct could be isolated; this desactivation of the quadricyclanone nucleus may be ascribed, when compared to earlier results(2,3), to steric effects due to the presence of a substituent on each side of the four-membered ring. In each case, the corresponding disubstituted benzene derivative, probably produced by a thermally forbidden ring-opening and subsequent symmetry-allowed loss of carbon monoxyde (2,3), could be isolated (m-methoxycarbonyl- and p-methoxycarbonyl-cumene, 21% and 14% respectively). In the case of the 1-isopropyl-6-methoxycarbonyl-quadricyclanone however, a new compound appeared (yield : 6%) which could be identified as being the 6-isopropyl-7-methoxycarbonyl-tricyclo[$4.1.0.0^{2,7}$]hept-4-en-3-one (M^+=206, ^{1}H NMR ($CDCl_3$, 100 MHz, δ in ppm and J in Hz, apparent values) : 1.05(d,3H), 1.20(d,3H), 2.03(m,1H), 3.39(dd,H_2), 3.53(d,H_1), 3.72(s,3H), 5.63(dd,H_4), 7.00 (d,H_5); $J_{1,2}$=2.8; $J_{2,4}$=1.8Hz; $J_{4,5}$=10.0). This is the first example of a substituted quadricyclanone which rearranges thermally to a tricycloheptenone derivative; no analogously rearranged compound could be detected in the case of the isomeric 1-isopropyl-7-methoxycarbonyl-quadricyclanone. This difference in behaviour could well be explained by the particularly efficient stabilisation of the zwitterionic intermediate(5) shown in Figure II produced by the (simultaneous or subsequent) C_1C_2- and C_6C_7-bond breaking in the 1,6-disubstituted quadricyclanone derivative, and which could then cyclize to the final product; no such stabilisation can occur for the 1,7-isomer.

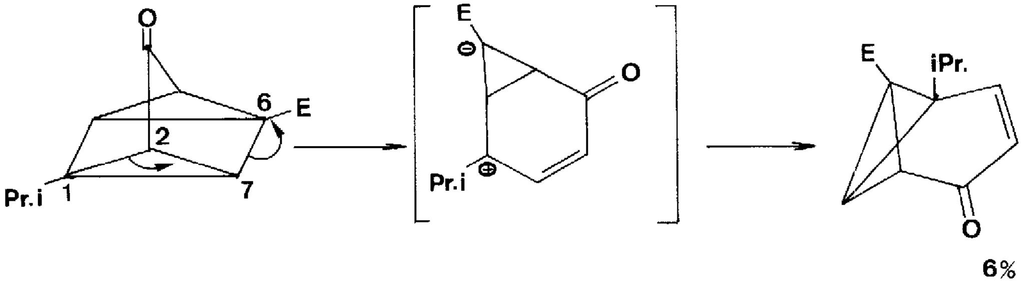


FIGURE II

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