Synthesis of Annelated Oxetans *via* Cycloaddition Reactions of Quadricyclane under Thermal and High Pressure Conditions

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Annelated oxetans are synthesized *via* thermal or pressure assisted cycloaddition of quadricyclane with the appropriate carbonyl bond activated by electron withdrawing groups; the new compounds are very stable and do not undergo the usual cycloreversion of four membered rings.

The construction of the framework of annelated oxetans is often accomplished by the Paterno–Büchi reaction *via* the photochemical [2 + 2] cycloaddition reaction of cycloalkenes with aldehydes or ketones.[1] It would be of interest to find an easier procedure, since oxetans are useful intermediates in organic synthesis. Therefore the thermal reaction of C=O bonds with quadricyclane‡ (**1**) was investigated. Owing to its high strain (95 kcal/mol; 1 kcal = 4.184 kJ),[2] (**1**) reacts readily with common dienophiles *via* their C=C or C≡C bond at moderate temperatures.[3] This fact prompted us to examine whether the less active C=O bond would also undergo cycloaddition to (**1**).

In contrast to norbornadiene, its valence isomer, (**1**) undergoes cycloaddition in a ($2\pi + 2\sigma + 2\sigma$) fashion[5] to produce *exo*-tricyclo[4.2.1.0^{2,5}]non-7-enes. Tabushi has established that concerted *exo*-cycloaddition reactions are allowed.[4] If these reactions are fully concerted,§ they should be greatly enhanced by an increase in pressure. Careful selection of the temperature may permit the successful syntheses of oxetans which are otherwise extremely difficult to prepare (Scheme 1). The results of various syntheses are given in Table 1.

All experiments were carried out in 2.5 ml poly(tetrafluoroethylene) tubes with $CHCl_3$ as solvent. After the reaction was complete, the cycloadducts were recovered by evaporation of the solvent and purified by column chromatography.¶ The configurations of the adducts were confirmed by means of mass spectrometry and i.r. and ^1H n.m.r. spectroscopy. The assignments of the n.m.r. peaks were based on results obtained elsewhere[3,6] and were confirmed by double irradiation experiments. Mass spectra in each case exhibited characteristic

Table 1. Cycloaddition reactions of quadricyclane and carbonyl compounds.

		Conditions[a]			
R^1	R^2	Temperature/ °C	Pressure/ MPa	Yield (%)	$\alpha:\beta$[c]
CO_2Me	CO_2Me	100	0.1	95	—
CO_2Me	Ph	100	0.1	13	62:38[d]
		75	800	60	56:44
CO_2Et	Me	80	800[b]	90	50:50
COPh	Ph	80	850[b]	59	β only[d,e]
$CHCl_2$	Cl	80	850[b]	20	40:60[f]
Me	Ph	80	900	0	—
OMe	OMe	80	800	0	—
$-[CH_2]_4-$		80	850	0	—

[a] Reaction time (24 h). [b] At 0.1 MPa and 100 °C, the yield of cycloadduct is insignificant. [c] The ratio $\alpha:\beta$ was determined by g.l.c. and n.m.r. spectroscopy. [d] Assumed on the basis of the correlation between steric effects and deshielding of H-5. [e] Only one isomer is observed. [f] A third isomer is produced in this reaction representing about 15—20% of the total isomer mixture. In addition, the structure of adducts α and β can only be tentatively assigned since the coupling constant $J_{2,5}$ 8.1 Hz differs from the usual value of *ca.* 5.0 Hz even though the n.m.r. shifts are of the same order as those for the other adducts.

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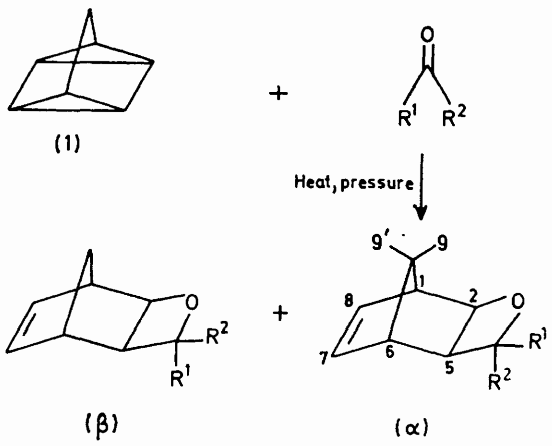
‡ Quadricyclane is commercially available (Aldrich) or can be easily prepared in high yield by $h\nu$ irradiation of bicyclo[2.2.1]-hepta-2,5-diene.

§ If establishment of the new bonds occurs simultaneously, one would expect a negative activation volume of about −25 to −30 ml/mol at room temperature, consequently the reaction rate should be increased by a factor of 100—300 between 1 and 800 MPa. The determination of $\Delta V^{\ddagger}$ for some ($2\pi + 2\sigma + 2\sigma$) reactions is currently under investigation.

¶ Experimental and spectroscopic details of each adduct are available upon request.



Scheme 1

fragment peaks resulting from opening of the oxetan ring[7] and retrocycloaddition at *m/z* 92 and 66. An example of adduct characterization is given for dimethyl *exo*-3-oxatricyclo-[4.2.1.0^{2,5}]non-7-ene-4-dicarboxylate.¶**

In conclusion, annelated oxetans can be synthesized *via* quadricyclane cycloaddition with appropriate carbonyl compounds. However, the carbonyl bond needs drastic activation by electron withdrawing groups. The presence of a π-system (aromatic ring) increases the reactivity at the C=O bond; phenylglyoxylate reacts even at 0.1 MPa (though moderately), while cycloaddition with ethyl pyruvate requires pressure assistance as does the reaction involving benzil. For the latter reaction, the remaining C=O bond in the oxetan ring is inactive toward further cycloaddition. Even the less active C=O bond substituted by Cl and $CHCl_2$ reacts under high pressure. The reactions shown here can easily be extended to further compounds provided that the C=O bond is sufficiently activated.[8]

Oxetans are cleaved, by rhodium catalysis under mild conditions, into π-bonded fragments.[9] The annelated oxetans synthesized in this work were subsequently subjected to temperatures from 25 to 125 °C in the presence of catalytic amounts of $[Rh(CO)_2Cl]_2$. However, the cycloreversion did not occur. It would therefore be interesting to take advantage of the stability of such compounds and convert them into useful derivatives retaining the oxetan ring.

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** Colourless liquid. G.l.c. (1 peak, room temp., 22 min). I.r. (3065, 2990, 2960, 2900, 1835, 1750, 1630, 1460, 1440, 1280, 1110, 1050, 955, and 915 cm^{-1}). ^{1}H N.m.r. ($CDCl_3$) δ 6.18 (br. dd, $^4J_{8,9}$ *ca.* 0.5 Hz, H-8), 5.88 (br. dd, $^3J_{7,8}$ 5.6 Hz, $^4J_{7,9}$ *ca.* 0.5 Hz, H-7), 4.61 (dt, $^3J_{2,5}$ 4.9 Hz, $^4J_{2,9}$ 1.4 Hz, H-2), 3.83 (OMe), 3.21 (dq, $^3J_{1,8}$ 3.0 Hz, $^3J_{1,9} = {}^3J_{1,9'} = {}^3J_{1,2}$ 1.4 Hz, H-1), 2.99 (dq, $^3J_{6,7}$ 3.0 Hz, $^3J_{6,9} = {}^3J_{6,9'}$ 1.4 Hz, H-6), 2.72 (dt, $^3J_{5,6} = {}^3J_{5,9'}$ 1.4 Hz, H-5), 1.86 (d quint, H-9′), and 1.54 (dt, $^2J_{9,9'}$ 10.2 Hz, H-9).

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