Tetrahedron Letters No. 43, pp 3895 - 3898, 1976. Pergamon Press. Printed in Great Britain.

BAEYER-VILLIGER OXIDATION VIA CARBOCATIONS IN A STRAINED CAGE SYSTEM

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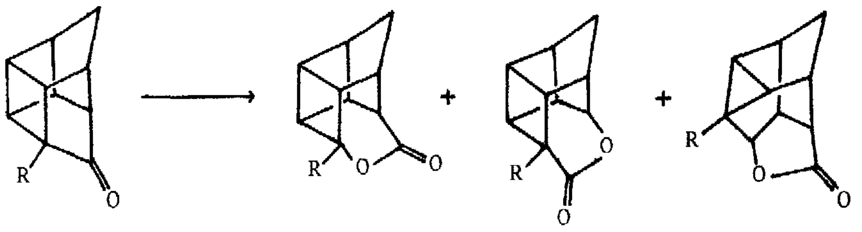
(Received in Japan 6 August 1976; received in UK for publication 9 September 1976)

Pentacyclic cage compounds with bicyclo[2.2.0]hexane, which were easily synthesized photochemically from the corresponding Diels-Alder dimers,[1] undergo remarkable reactions releasing most or some of their strain energies, e.g., rearrangement to a bisnordiamantane,[2] hydrogenolysis to ditwistane and bisnorditwistane,[3] reversion to Diels-Alder dimers,[1a] and ring expansion with diazomethane.[1b] We now report Baeyer-Villiger oxidation of a cage compound (1)[4] as an extension of our work for examination of the reactivity of cage compounds and on their synthetic applications. Compound 1 gave mainly a six-membered lactone (2) and a rearranged five-membered lactone (4), which were probably formed through a mechanism other than the ordinary one.[6]



1: R=H
1a: R=D

2: R=H
2a: R=D

3: R=H
3a: R=D

4: R=H
4a: R=D

A solution of 1 (0.7 g) and m-chloroperbenzoic acid (1.5 eq) in chloroform (30 ml) was allowed to stand at room temperature for 1 hr to give quite rapidly three lactones, 10-oxapentacyclo-[5.4.0.0^{2,5}.0^{3,9}.0^{4,8}]undecan-11-one (2) [50%; mp 145.5-147° (hexane); ν (CCl_4) 1761, 1368, 1071 cm^{-1}; δ (CCl_4) 4.70 (1H, t, J = 6 Hz); m/e 162 (M^+, 1), 118 (3), 117 (10), 105 (10), 97 (55), 91 (13), 66 (100%)], 11-oxapentacyclo[5.4.0.0^{2,5}.0^{3,9}.0^{4,8}]undecan-10-one (3) [1.1%; mp 127-128.5° (hexane); ν (CCl_4) 1753, 1372, 1060 cm^{-1}; δ (CCl_4) 4.64 (1H, m); m/e 162 (M^+, 2), 118 (3), 117

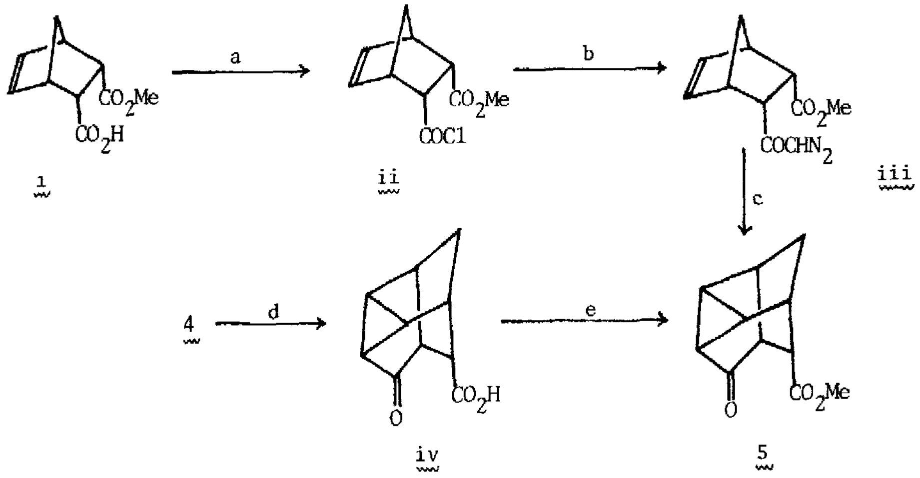
(8), 105 (5), 97 (36), 91 (9), 66 (100%)] and 11-oxapentacyclo[6.3.0.0^{2,4}.0^{3,7}.0^{5,9}]undecan-10-one (4) [13%; mp 135-136° (hexane); ν (CCl_4) 1781, 1348, 1176, 1008 cm^{-1}; δ ($CDCl_3$) 5.06 (1H, q, J = 3 and 7 Hz); *m/e* 162 (M^+, 3), 118 (23), 117 (34), 91 (14), 84 (40), 79 (100), 66 (6%)].[7] Results of this reaction in various solvents are shown in Table I.

Table I. Oxidation of 1 (0.35 g) in various solvents (16 ml) with *m*-chloroperbenzoic acid (1.5 eq) at room temperature.

solvent	time (min)	yield,%[a] 4	2	4/2 ratio
benzene	15	12	56	0.21
dioxane	15	14	55	0.25
chloroform	3	10	35	0.29
	7	13	49	0.27
	15	15	55	0.27
	30	16	57	0.28
dioxane:H_2O (9:1)	60	15	45	0.33
dioxane:H_2O (1:1)	60	31	46	0.67

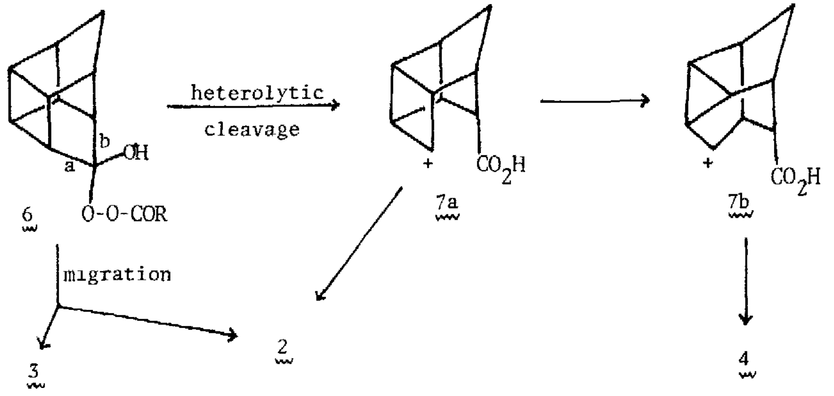
[a] Calculated by using the NMR integration data at 4.70 ppm for 2 and at 5.06 ppm for 4. The yield of 3 was almost nil.

Both 2 and 3 have a six-membered lactone (IR) and a similar fragmentation pattern (mass). The distinction between 2 and 3 was provided by NMR spectra of 2a and 3a derived from a deuterated starting material (1a).[1b] In 2a, the original signal at 4.70 ppm disappeared, whereas that at 4.64 ppm remained unchanged in 3a. Compound 4 has a five-membered lactone (IR 1781 cm^{-1}) and a fragmentation pattern (mass) clearly different from those of 2 and 3, though all three products have the same molecular ion peak at 162. The quartet signal at 5.06 ppm in 4 changed to a doublet (J = 7 Hz) in a deuterated product (4a). These data and mechanistic consideration revealed the structure of 4, which was confirmed by an unequivocal synthesis of 7-methoxycarbonyl tetracyclo[4.3.0.0^{2,4}.0^{3,8}]nonan-5-one (5) [mp 45-46° (benzene-hexane); ν (CCl_4) 1730, 1200 cm^{-1}; δ (CCl_4) 1.56-1.80 (1H, m), 1.86-2.5 (4H, m), 2.52-2.96 (4H, m), 3.58 (3H, s); *m/e* 192 (M^+, 4), 164 (7), 149 (20), 114 (95), 99 (48), 79 (100%)] from the known half ester (i) as shown in the following scheme.



ii, oil; iii, crude mp ~70° (dec); iv, mp 128-129° (benzene);
a, $SOCl_2$, pyridine, 30-35°, 4 hr; b, CH_2N_2, Et_2O; c, CuI, THF, 40-45°;
d, $KMnO_4$, NaOH; e, CH_2N_2.

These data and following discussions suggest a mechanism other than the ordinary one. First, 4 is the primary product, not the secondary one formed from 2 by an acid-catalyzed rearrangement.[9] Treatment of 2 with m-chloroperbenzoic acid and m-chlorobenzoic acid at room temperature for 24 hr or with acetic acid at 50° for 12 hr gave no trace of 4.[12] Progress of the oxidation in chloroform was followed by NMR analysis, and the ratio of 4:2 was found to remain almost constant throughout the oxidation. Compound 4 cannot be apparently formed by the migration of bond a or b in an intermediate (6). Second, the ratio of 4:2 changes with increasing solvent polarity (Table I). This solvent effect suggests that 2 is formed by a mechanism different from that for the formation of 4. The migration mechansim is conceivable. However, since there seems to be no significant difference in migratory aptitude between bonds a and b in 6,[1b] the large



difference between the yields of 2 and 3 is difficult to be interpreted by the migration mechanism. A short-lived carbocation (7a) may be an intermediate from 6 to 2.

In conclusion, the mechanism of the oxidation of 1 involves mainly a carbocation (7b) and probably another cation (7a) as intermediates[13] formed by a heterolytic cleavage of bond a in 6 rather than the migration of the same bond. This cleavage can be assisted by the most strained central bond in the bicyclo[2.2.0]hexane system.

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(3) K. Hirao, T. Iwakuma, M. Taniguchi, E. Abe, O. Yonemitsu, T. Date, and K. Kotera, J. Chem. Soc. Chem. Commun., 691 (1974).

(4) Very recently, Mehta et al.[5] reported that oxidation of 1 with ceric ion furnished 3 as a single product, while that with m-chloroperbenzoic acid gave a mixture of 2 and 3. Mechanistic considerations for these reactions were also presented.[5] This work prompted us to report our preliminary results concerning the oxidation of 1 which makes it difficult to accept most of Mehta's discussions and conclusions.

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(7) Oxidation of 1 with ceric ammonium sulfate under Mehta's conditions[5] gave only 4, and not 3.

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(9) Similar rearranged lactones from strained compounds with bicyclo[2.2.0]hex-2-yl ketones[10] and with a cyclobutyl ketone[11] have been obtained. A mechanism involving a cyclobutyl-cyclopropylcarbinyl rearrangement of the first formed ordinary oxidation products have been proposed in these cases.

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(12) On treatment with a stronger acid (trifluoroacetic acid or p-toluenesulfonic acid) in chloroform at room temperature for 15 min or with acetic acid under reflux for 48 hr, 2 changed completely, of course, into 4.

(13) A non-classical cation intermediate has been proposed in the oxidation of tricyclo[3.2.1.$0^{3,6}$]octan-7-one,[14] but an additional resonance stabilization owing to the cyclopropylcarbinyl-cyclobutyl system[15] may be hardly expected in the case of 1 with a highly strained and rather rigid ring system.

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