

DIMERIZATION OF STRAINED POLYCYCLIC KETONES WITH DIAZOMETHANE

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Because of theoretical and synthetic interests, a number of studies on the diazomethane ring expansion of cyclic ketones have been reported and have recently been extensively reviewed.<sup>1)</sup> However, the reactivity toward constrained carbonyl groups having a strong electrophilic character<sup>2)</sup> has not been examined yet.<sup>3)</sup> In the course of our studies on strained molecules,<sup>5)</sup> we found an unusual dimer formation<sup>6)</sup> of some strained polycyclic ketones with diazomethane.<sup>8)</sup>

When bishomocubane (1)<sup>9)</sup> was allowed to react with a large excess of diazomethane in ether at 0-5° for 16 hr, ring expansion and dimerization occurred to yield a homologous ketone (2) [mp 53-55°;  $\nu$  (Nujol) 1710, 1699  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 1.37 (s, 2H,  $-\text{CH}_2-$ ), 2.18 (d, 2H,  $J = 3$  Hz), 2.42 (m, 2H), 2.66 (m, 2H), 2.99 (m, 3H), 3.17 (m, 1H); m/e 160 ( $\text{M}^+$ ), 117 ( $\text{M}^+ - \text{CH}_3\text{CO}$ ), 95 ( $\text{M}^+ - \text{C}_5\text{H}_6$ ), 66 ( $\text{C}_5\text{H}_6$ )] and a novel dimer (3)<sup>10)</sup> [mp 149-150°;  $\nu$  (Nujol) 3350, 1697  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 1.36 (s, 2H,  $-\text{CH}_2-$ ), 1.44 (t, 2H,  $J = 8$  Hz,  $-\text{CH}_2-$ ), 2.08 (d, 1H,  $J = 3$  Hz,  $-\text{CH}-\text{CO}-$ ); m/e 306 ( $\text{M}^+$ ), 240 ( $\text{M}^+ - \text{C}_5\text{H}_6$ ), 222 ( $\text{M}^+ - \text{H}_2\text{O}$ ,  $\text{C}_5\text{H}_6$ ), 156 ( $\text{M}^+ - \text{H}_2\text{O}$ ,  $2\text{C}_5\text{H}_6$ ), 66 ( $\text{C}_5\text{H}_6$ )], respectively. Since 2 did not react with 1 under both acidic and basic conditions, the dimer (3) must have been obtained directly from 1 and diazomethane. Ketones 4<sup>8)</sup> and 5<sup>12)</sup> also gave respective dimers under similar conditions and the results are summarized in Table I.

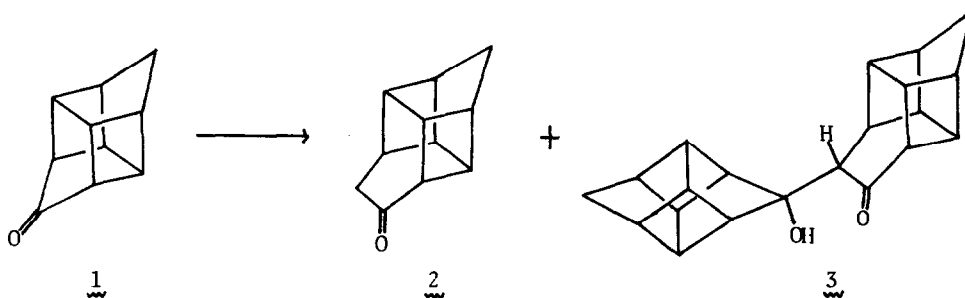
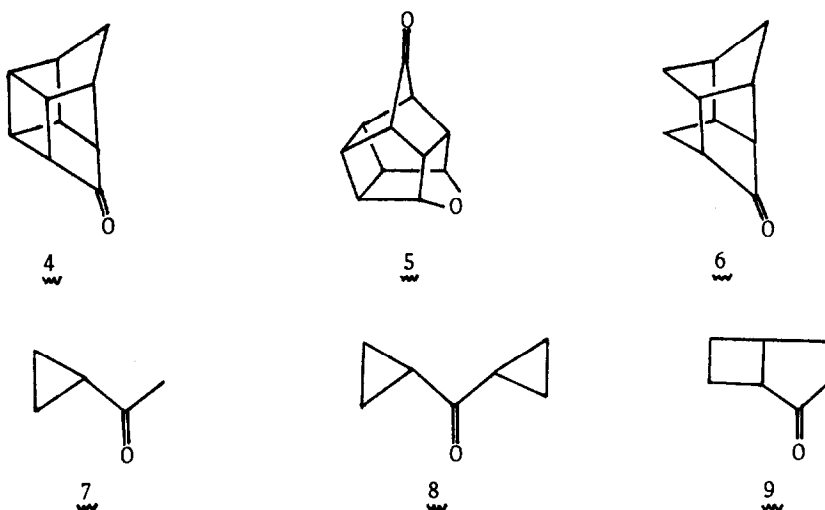


Table I. Reaction of Strained Polycyclic Ketones with Diazomethane

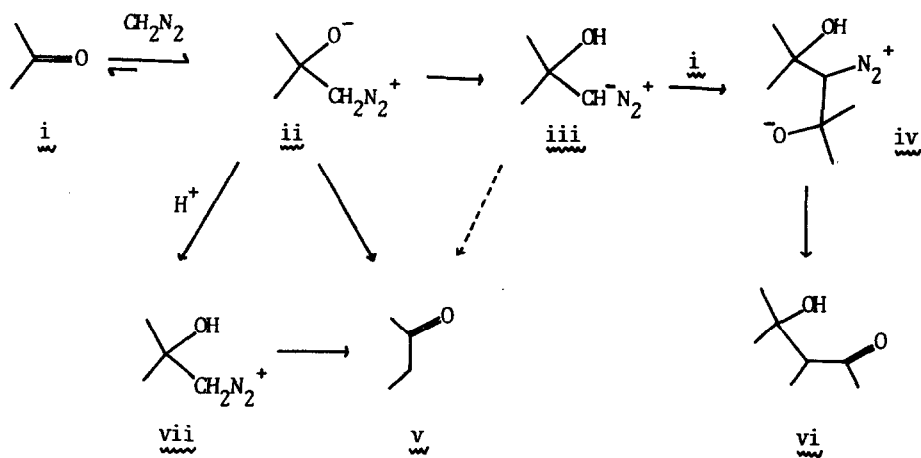
Ketone	Temp °C	Time hr	Product, % <sup>a)</sup>	
			Homoketone	Dimer
<u>1</u>	0-5	16	37	32
<u>4</u>	0-5	16	45 <sup>8)</sup>	44 <sup>14)</sup>
<u>5</u>	room temp	96	35 <sup>15)</sup>	35 <sup>15)</sup>

a) Isolation yield



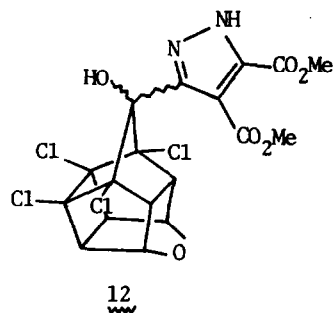
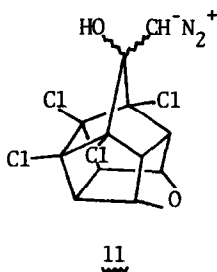
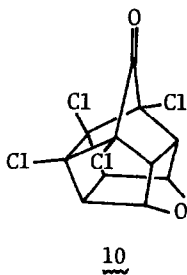
The most important factor directing a course of the reaction to the dimer formation must be a strain added to the carbonyl group in cage molecules, since the less strained ketone (5) was rather slow to react and compounds having a almost strain-free carbonyl group, 6,<sup>16)</sup> 7,<sup>17)</sup> 8,<sup>18)</sup> and 9,<sup>19)</sup> gave no traces of dimers under the same conditions. In the reaction of 1 with diazomethane, after 10 min, direct analysis of the whole reaction mixture by silica gel tlc revealed the formation of 2 together with only a trace of recovered 1.<sup>20)</sup> On the other hand, only the starting material (1) was detected when the diazomethane was removed from the above mixture before the tlc analysis.

These results show that the reaction may be described as illustrated in the following scheme. A constrained carbonyl group has a greater tendency to react with diazomethane than usual one has,<sup>2)</sup> and in a preliminary step gives quite rapidly a betain intermediate (ii), that is, the equilibrium between i and ii, which lies well over to the right, is rapidly established. Since the rearrangement of ii to a homoketone (v) is relatively slow in the absence of a proton donor,



an alternate reaction simultaneously takes place in the formation of a new diazo intermediate (**iii**) through an intramolecular proton transfer. The starting ketone (**i**) as a strong electrophile then attacks **iii** to form a dimer **vi** via **iv**.

Following experiments bear out the validity of the scheme. When methanol was present (5%) as a proton donor in the reaction medium of **1**, the yield of **2** increased (70%), whereas that of **3** decreased (3%). In the case of a ketone (**10**)<sup>13</sup> having electron-withdrawing chlorine atoms, the formation of both homoketone and dimer was expected to be retarded by electronic and steric effects. An intermediate (**11**) [ $\nu$  (neat)  $2080\text{ cm}^{-1}$ ], though rather unstable at room temperature, was actually isolated and characterized as a pyrazol derivative (**12**) [mp  $212\text{--}215^\circ$ ]<sup>15</sup> by 1,3-dipolar cycloaddition with dimethyl acetylenedicarboxylate. Further work on this reaction of more strained ketones is in progress and details will be reported in a subsequent publication.



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