

Synthesis of Some Medium- and Large-ring Cycloalk-2-ene-1,4-diones by Intramolecular Coupling of $\alpha\omega$ -Bis-diazoketones

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Summary In the presence of $\text{Cu}(\text{acac})_2$ (Hacac = acetylacetone) some $\alpha\omega$ -bis-diazoketones couple intramolecularly with loss of nitrogen giving cycloalk-2-ene-1,4-diones; the enediones can be converted into fused ring cyclopentenones by successive treatment with sodium dithionite and sodium hydroxide.

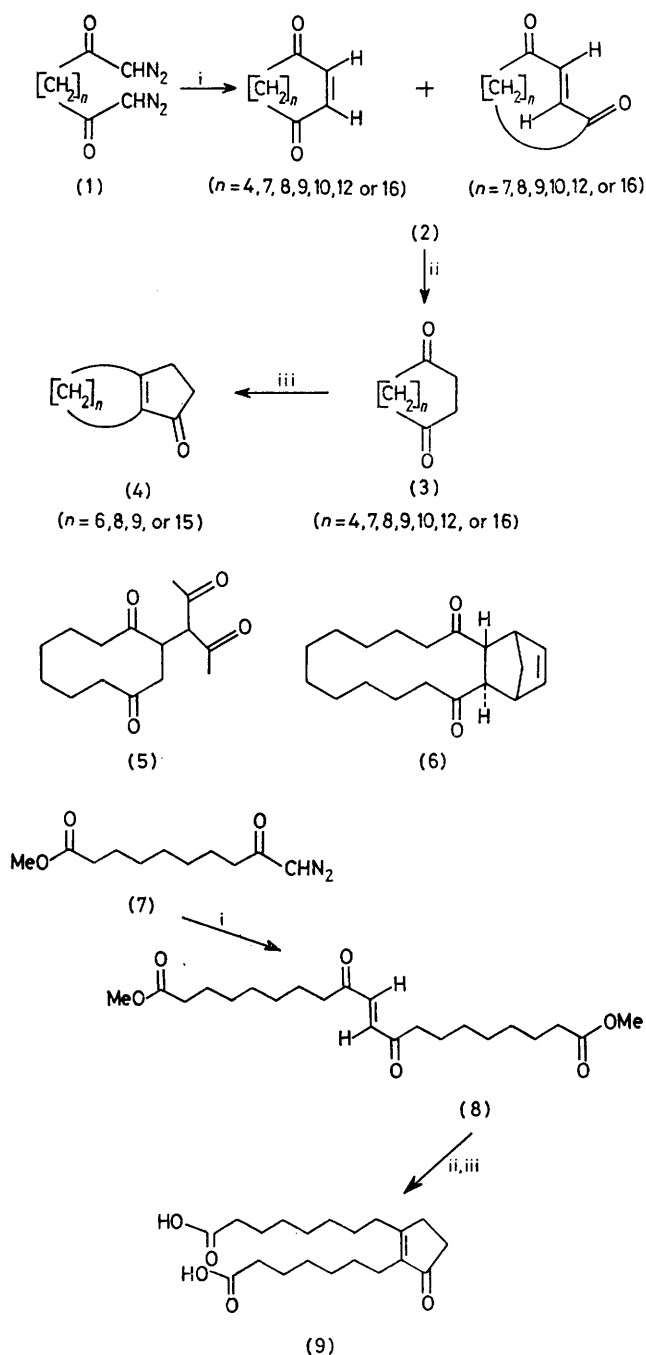
ALTHOUGH some diazoketones are known to undergo copper-catalysed intermolecular coupling with loss of nitrogen giving alk-2-ene-1,4-diones,¹ the reported yields are poor and the process has found little use in synthesis. As far as we are aware, there is only one published example of the intramolecular mode of this reaction in which the bis-diazoketone (**1**; $n = 3$) was treated with copper bronze to give a 30% yield of cyclohept-2-ene-1,4-dione (**2**; $n = 3$).² We report that intramolecular coupling of $\alpha\omega$ -bis-diazoketones is a quite general process, offering a direct route to a variety of medium- and large-ring cycloalk-2-ene-1,4-diones which are themselves versatile synthetic intermediates. Preliminary experiments showed that copper bronze, copper oxide, and copper powder are poor catalysts for this reaction; better results were obtained using bisacetylacetonatocopper.³

TABLE

Yield/%	n in compound (2)									
	4	5	6	7	8	9	10	12	16	
	30	<10	—	30	70	25	80	44	29	
<i>cis:trans</i> ratio	>20:1	—	—	1:3	1:10	1:10	1:9	1:3	1:7	

The results summarised in the Table were obtained by slow addition (*ca.* 5 h) of a dilute solution of the bis-diazoketone (**1**) (prepared from the appropriate diacid chloride and diazomethane) in dry benzene to a dilute solution of $\text{Cu}(\text{acac})_2$ (Hacac = acetylacetone) in dry benzene at 60 °C (Scheme). After *ca.* 24 h the products were isolated, purified by column and/or preparative layer chromatography on silica gel, and identified on the basis of i.r., n.m.r., and mass spectrometry; cyclo-oct-2-ene-1,4-dione (**2**; $n = 4$) was known already, having been synthesised from cyclo-octa-1,3-diene.⁴ This intramolecular coupling procedure works satisfactorily for the 8-, 11-, 12-, 13-, 14-, 16-, and 20-membered cycloalkenediones, but poorly for the 9-membered ring. In the 10-membered case coupling does apparently occur, though the product isolated (18%) was not the enedione; n.m.r. and mass spectrometric data suggested structure (**5**), presumed to have resulted from a subsequent reaction of the enedione with $\text{Cu}(\text{acac})_2$. Small amounts (6–11%) of similar products were also isolated in the 8-, 11-, and 13-membered cases.

With the exception of cyclo-oct-2-ene-1,4-dione (**2**; $n = 4$) which had *cis* geometry about the double bond, the cycloalkenediones were mixtures of *cis* and *trans* isomers with the latter predominating (see Table). This was clear from the n.m.r. chemical shifts [δ *ca.* 6.4 (s, *cis* vinylic H) and *ca.* 7.0 (s, *trans* vinylic H)], the relationship between geometry and chemical shift having been confirmed by combining the



SCHEME. i, $\text{Cu}(\text{acac})_2$; ii, $\text{Na}_2\text{S}_2\text{O}_4$; iii, NaOH .

major component of the 14-membered cycloalkenedione (**2**; $n = 10$) with cyclopentadiene in a crystalline Diels-Alder adduct (**6**) the n.m.r. spectrum of which clearly

showed the *trans* arrangement about the conjoining bonds. Whether the *trans*-cycloalkenediones were primary cyclisation products or the result of subsequent isomerisation was not established.

These cycloalkenediones are useful synthetic precursors to cycloalkane-1,4-diones and fused-ring cyclopentenones. Reduction of (**2**; $n = 4, 7, 8, 9, 10, 12,$ and **16**) with sodium dithionite⁵ in aqueous ethanol gave the saturated diones (**3**; $n = 4,$ ⁶ **7,**⁷ **8,**⁸ **9,**⁹ **10,** **12,**⁹ and **16**) in excellent yield. Exposure of the diones (**3**; $n = 7, 9, 10,$ and **16**) to sodium hydroxide in ethanol led to smooth conversion into the fused-ring cyclopentenones (**4**; $n = 6, 8, 9,$ and **15**).

Intermolecular coupling of a diazoketone can also be used to advantage. Thus the monomethyl ester of azelaic acid was converted into diazoketone (**7**), decomposition of which in the presence of $\text{Cu}(\text{acac})_2$ gave the crystalline *trans*-enedione (**8**) in 50% yield. Successive treatment of (**8**) with sodium dithionite in aqueous ethanol and sodium hydroxide in ethanol gave the diacid (**9**) in 90% yield.

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