

BRIDGED BICYCLIC RING SYSTEMS FROM 3-(2'-OXOCYCLOALKYL) PROPANALS PRODUCED VIA ENAMINES

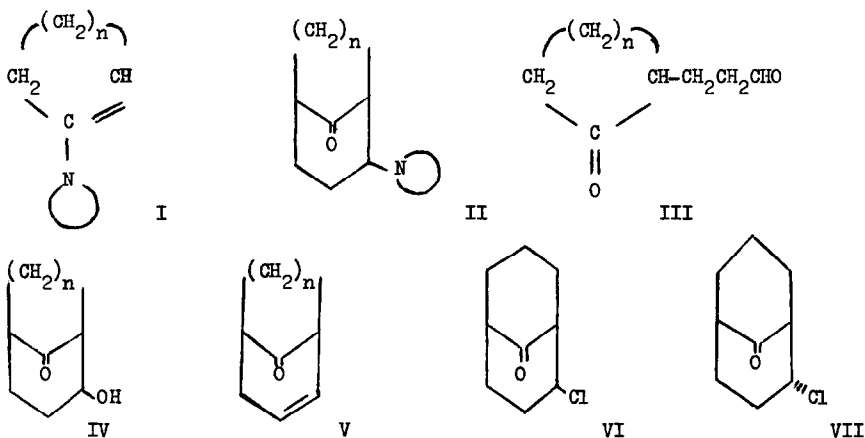
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Enamines derived from cycloalkanones (I) react with acrolein to give 2-amino $[n:3:1]$ bicycloalkanones (II) in moderate yield⁽¹⁾. The only reported method of obtaining the intermediate 3-(2'-oxocycloalkyl) propanals (III) from an enamine reaction is that of Cope and co-workers who, by reaction of 1-pyrrolidinocyclohexene with acrolein at 0°, obtained a 28% yield of 3-(2'-oxocyclohexyl) propanal (III, n = 3).⁽²⁾ This compound could be cyclised with 7N hydrochloric acid to $[3:3:1]$ bicyclononan-2-ol-9-one (IV, n = 3) in 60% yield.⁽²⁾



Compounds of the type (IV) are attractive intermediates for a range of substituted $[n:3:1]$ bicycloalkanes required in this laboratory and we have investigated the sequence $I \rightarrow III \rightarrow IV$ with a view to obtaining increased yields in each stage.

It has been found that treatment of 1-morpholinocyclohexene with one mole of acrolein in ether at room temperature for two hours followed by treatment of the enamine intermediate with 2N hydrochloric acid (1.1 mole) gives the aldehyde (III, n = 3) in 60-65% yield. Cyclisation of the enamine intermediate to the aminobicycloalkanone (II, n = 3) seems to be slow (ca. 12 hours in benzene at 80°, by I.R. spectroscopy), and the surprising observation that the initial enamine intermediate shows very little carbonyl absorption in the I.R. places doubt

on the suggested mechanism for the formation of II.^(1c) The high yield of III (n = 3) obtained in this reaction led us to study the general utility of this synthetic method. Reaction of 1-morpholinocycloheptene with acrolein in ether at room temperature for 12 hours followed by acid hydrolysis gave 3-(2'-oxocycloheptyl) propanal (III, n = 4) in 70% yield but 1-morpholinocyclopentene gave only 5% of the required aldehyde (III, n = 2). When the reaction was conducted at -15° the keto-aldehyde (III, n = 2) was obtained in 35% yield together with 5% [3:2:1] bicyclooctan-2-ol-8-one (IV, n = 2).

Attempted cyclisations of the keto-aldehydes (III, n = 2 - 4) to the bicycloalkenones (V, n = 2 - 4) with concentrated sulphuric acid proceeded in low yields (4%, n = 2; 10%, n = 3 & 4).

However, the bicycloalkanol-ones (IV, n = 3 & 4) were obtained in 90-95% yield by refluxing the keto-aldehyde with Amberlite I.R. 120 resin in water until a homogeneous solution of the cyclic hydroxyketone was produced (ca. 1 hour). In the case n = 2 a 65% yield of [3:2:1] bicyclooctan-2-ol-8-one was obtained.

Dehydration of the hydroxyketones IV (n = 3 & 4) was effected smoothly by sulphuric acid (ca. 70% yield) or by pyrolysis of the benzoate esters (70% yield). In the case n = 2, sulphuric acid dehydration gave very low yields of [3:2:1] bicyclooct-2-en-8-one. Attempted dehydration of [3:3:1] bicyclononan-2-ol-9-one with POCl₃/pyridine resulted in the formation of the enone together with endo- and exo-2-chloro [3:3:1] bicyclononan-9-one. (VI & VII).⁽³⁾

Studies on the scope of this entry into [n:3:1] bicyclic ring systems are now in progress and preliminary results indicate that, at present, this method is the best general entry into systems of type (V) where n > 2.

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