Reaction of 2-Iodocyclohepta-2,4,6-trien-1-one with 1-Azabicyclo[2,2,2]octane. An Unusually Easy Nucleophilic Opening of a Bicyclo[2,2,2]octane Skeleton

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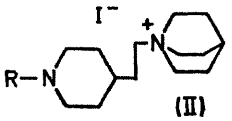
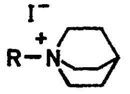
Summary 1-Azabicyclo[2,2,2]octane (I) reacts with 2-iodocyclohepta-2,4,6-trien-1-one in benzene to give either 2-(4-β-1-azoniabicyclo[2,2,2]octane-ethylpiperidino)-cyclohepta-2,4,6-trien-1-one iodide (II) or 2-(1-azoniabicyclo[2,2,2]octane)cyclohepta-2,4,6-trien-1-one iodide (III), or a mixture of both according to reaction conditions; (III) is readily rearranged to 2-(4-β-iodoethylpiperidino)cyclohepta-2,4,6-trien-1-one (IV).

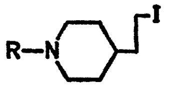
THE chemistry of 1-azabicyclo[2,2,2]octane (I) is characterised by (*a*) the ready availability of the nitrogen electron lone-pair even towards sterically hindered electrophilic sites and (*b*) the great stability of the bicyclic skeleton of either the free base or of its quaternary salts towards both heat and a variety of reagents.[1] Such stability has been attributed to a lack of severe strain in the bicyclic system[1] and, in fact, the retro-Menshutkin reaction proves to be a very easy process in the case of strained cycles.[2]

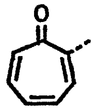
We report here a case where the normal behaviour (*b*) breaks down under extremely mild conditions. In fact, while investigating the base catalysis behaviour[3] of (I) over the piperidinodehalogenation of 2-halogenocyclohepta-2,4,6-trien-1-one[4] we found that (I) in a great excess (*ca.* 10^5) reacts with 2-iodocyclohepta-2,4,6-trien-1-one in benzene at room temperature affording 2-(4-β-1-azoniabicyclo[2,2,2]-octane-ethylpiperidino)cyclohepta-2,4,6-trien-1-one iodide (II), m.p. 200—202°, which precipitates in excellent yield.†

There is some hint that (II) comes from 2-(1-azoniabicyclo[2,2,2]octane)cyclohepta-2,4,6-trien-1-one iodide (III) as an intermediate through nucleophilic attack by (I) at the saturated carbon α to the quaternary nitrogen. Thus, when equimolar (I) and 2-iodocyclohepta-2,4,6-trien-1-one are left in benzene at room temperature, (III), m.p. 176—177°, precipitates in a good yield whereas, at reflux, a mixture of both (II) and (III) is obtained in a moderate yield. Moreover, when recrystallisation of (III) with boiling 95% ethanol is attempted, only the first small crop of crystals are of pure (III) while concentration of the mother-liquor affords 2-(4-β-iodoethylpiperidino)cyclohepta-2,4,6-trien-1-one (IV), m.p. 80·5—81·5°.‡


(II)


(III)


(IV)

R =


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† Spectral analysis showed that (II) is the primary product and that it did not arise during work-up.

‡ Structural assignments of (II), (III), and (IV), which analyse correctly, are supported by ^{1}H n.m.r. and i.r. spectra and by the fact that (III) lacks the intense u.v. long-wavelength absorption band which is characteristic of (II), (IV), and 2-piperidinocyclohepta-2,4,6-trien-1-one,[4] and which is certainly related to the availability of an unshared electron pair from nitrogen, present only in the latter compounds.

Owing to the previously known great stability of quaternised (I),[1] most of the driving force for the easy ring opening observed in the case of (III) should arise from the possibility of delocalising on the cyclohepta-2,4,6-trien-1-one moiety the couple of electrons acquired by the nitrogen during the process.[5] Such an interpretation demands a product-like transition state for our retro-Menshutkin reaction in accordance with recent ideas from a detailed examination of solvent effects on the rate of quaternisation of trimethylamine by alkyl halides.[6] This contrasts with the suggestion of a reactant-like transition state for the iodo-debenzylation of benzylphenyldimethylammonium iodide as previously suggested[7] from the examination of the rate effect of *para*-substitutents at the benzyl group.

The present results also reveal an important limitation on the use of (I) as a catalyst.

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[3] For references as to the scope of such studies, see F. Pietra, *Quart. Rev.*, 1969, **23**, 504; S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.

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