The Reaction between αβ-Unsaturated Ketones and Ethylenediamine

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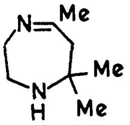
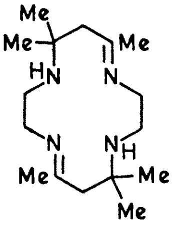
Summary Ethylenediamine reacts with different αβ-unsaturated ketones to give open chain adducts, or seven- or fourteen-membered rings.

THE reaction of ethylenediamine with αβ-unsaturated ketones, and in particular with mesityl oxide, has been variously reported to give rise to tetrahydro-1,4-diazepines (I)[1] or tarry polymeric material.[2] Curtis and Hay[2] also described the preparation of the diperchlorate of tetra-azacyclotetradecadiene (II) by using ethylenediamine monoperchlorate in place of the free amine. Both the seven- and fourteen-membered ring compounds have common structural features so that their differentiation is difficult save by molecular weight. Although the structure of compound (II) itself was not investigated, its conversion[2] into the well characterised nickel complex (III)[3] provided very strong evidence that it had the postulated structure.

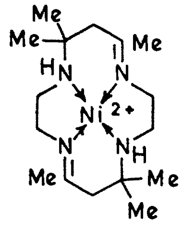
Further evidence for the surprisingly ready formation of this 14-membered heterocyclic ring system is now provided by the reaction products obtained when ethylenediamine itself is heated with a variety of benzylideneacetones in refluxing cyclohexane–ether in the presence of potassium carbonate. For example, benzylideneacetone itself gives a product with a molecular weight of 376·262865 ($C_{24}H_{32}N_4$ requires 376·262684) corresponding to the 14-membered-ring structure. The i.r. and n.m.r. spectra, presently being investigated in more detail, are also consistent with this formulation. Reduction of the imine groups is easily effected by sodium borohydride, to give products whose molecular weight and elemental analysis show them to be tetra-azacyclotetradecanes.[4]



(I)



(II)



(III)

BzCH$_2$·CHPh·NH·[CH$_2$]$_2$·NH·CHPh·CH$_2$Bz

(IV)

Condensation of mesityl oxide with ethylenediamine under identical conditions, however, gives a product whose molecular weight corresponds to the tetrahydrodiazepine (I).

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It has been shown[5] that *o*-phenylenediamine reacts with some $\alpha\beta$-unsaturated compounds to form dihydrobenzodiazepines but with others to give uncyclised adducts. Similarly ethylenediamine does not always give rise to heterocyclic derivatives and with, for example, benzylideneacetophenone gives a product which from elemental analysis appears to have structure (IV).

Thus ethylenediamine reacts with $\alpha\beta$-unsaturated ketones to form either tetra-azacyclotetradecadienes, tetrahydrodiazepines, or uncyclised adducts. This may be rationalised in terms of the following reaction scheme:

$$\begin{tikzcd}
R^1R^2C{=}CHCOR^3 \arrow[r, "A"] & H_2N\cdot[CH_2]_2\cdot NH\cdot CR^1R^2\cdot CH_2\cdot COR^3 \arrow[r, "B"] \arrow[dd, "C"] & \text{tetrahydrodiazepine} \\
+ & & \\
(CH_2NH_2)_2 & R^3CO\cdot CH_2\cdot CR^1R^2\cdot NH\cdot[CH_2]_2\cdot NH\cdot CR^1R^2\cdot CH_2\cdot COR^3 \arrow[d, "D"] & \\
& \text{tetra-azacyclotetradecadiene} &
\end{tikzcd}$$

Competition between reactions B and C will be a crucial factor in determining whether or not the tetrahydrodiazepine is formed. Reaction C (like reaction A) is a kinetically controlled conjugate addition and as such is strongly subject to steric influences. In the cases cited in this communication where $R^2 = H$, reaction C predominates, but when $R^1{=}R^2{=}Me$, the diazepine is formed. Whether or not reaction D will follow reaction C depends on the reactivity of the carbonyl groups; in accord with this, cyclisation occurred when $R^3{=}Me$ but not when $R^3{=}Ph$. It is noteworthy that cyclisation to a 14-membered ring occurs so readily and in good yield, without any of the special techniques normally required for the formation of large rings.

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