Remarkable Solvent Dependent Cyclisation of Methyl Vinyl Ketone across the 8,8a and 3,8a Positions of $\Delta^{1,8a}$-2-Octalone Dienamines. First Syntheses of the Tricyclo[8.4.0.0^{1,6}]tetradecane and Tricyclo[6.2.2.0^{1,6}]dodecane Ring Systems. Crystal Structures

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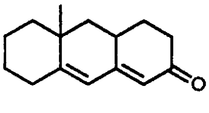
Reaction of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone with methyl vinyl ketone occurs primarily across the 8,8a-positions in methanol to provide the first synthesis of 10-methyltricyclo[8.4.0.0^{1,6}]tetradecane-3,13-dione (**5**), whereas in toluene reaction occurs across the 3,8a-positions to give 11-acetyl-6-methyltricyclo[6.2.2.0^{1,6}]dodecan-9-one (**6**), the stereochemistry of both structures being determined by *X*-ray analysis.

Recently we have reported that the alkylation of the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone with methyl propenoate and propenenitrile is solvent dependent;[1] in protic medium the reaction occurred at C-1 whereas in aprotic medium reaction occurred at C-4a. In an extension of this investigation we now report our preliminary observations on the reaction of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone with methyl vinyl ketone (MVK).

This reaction was expected to give either the linear (**1**) or angular (**2**) annulation product, as an extension of Stork's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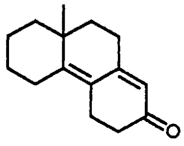
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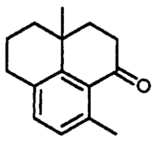
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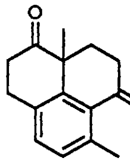
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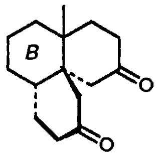
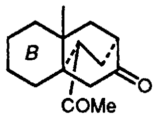
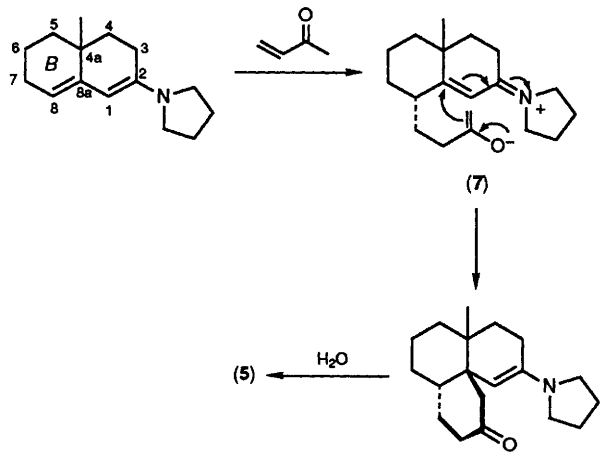


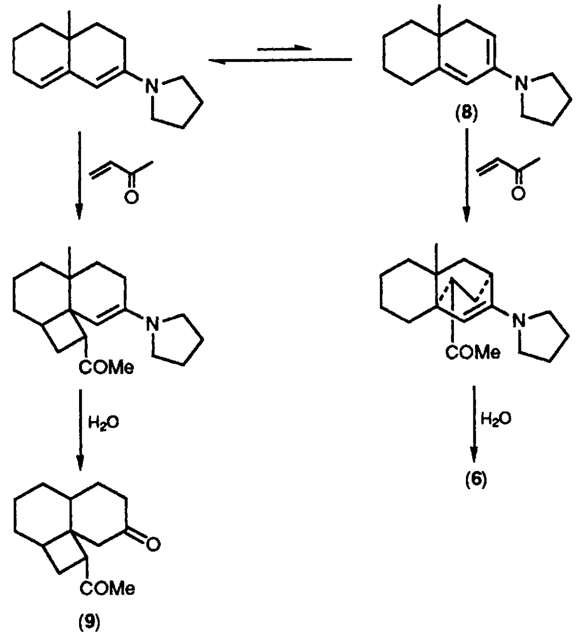
(5)



(6)



Scheme 1



Scheme 2

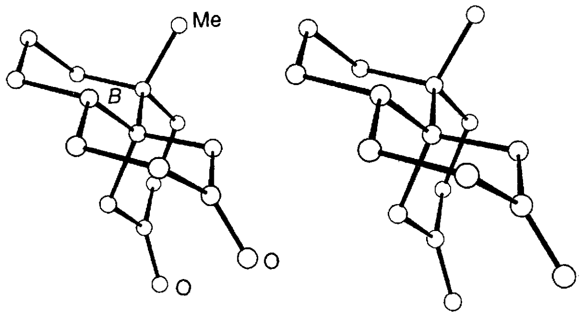


Figure 1

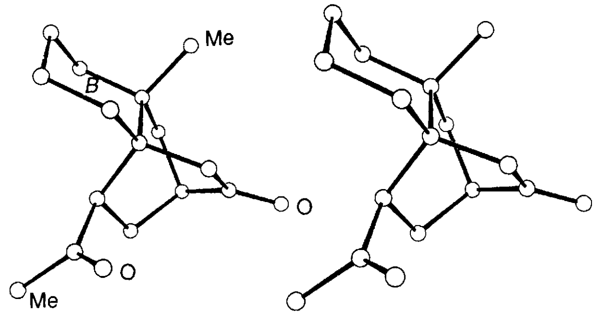


Figure 2

synthesis of $\Delta^{1,8a}$-2-octalones,[2] or (**3**) by analogy with the reported synthesis of (**4**) from the corresponding 5-oxodienamine.[3] In fact only compound (**1**) was produced in any detectable amount (by GC MS). The reaction was carried out initially in boiling methanol followed by hydrolytic work-up producing a complex mixture from which the 8,8a-cycloadduct [(**5**); 21%]† was isolated as the main component, and separated by flash chromatography into two stereoisomers. In boiling toluene the 3,8a-cycloadduct [(**6**); 28%]† was the main component of the complex mixture, together with a small amount (<5%) of the linear condensation product (**1**).

These results are remarkable and could not have been anticipated from previous work on related systems.[1,4] In methanol reaction occurs primarily at the less reactive δ-position[4b] of the dienamine, in stark contrast to the corresponding reaction with methyl propenoate and propenenitrile where reaction with this dienamine occurs at the more reactive β-position (C-1) in all solvents.[1] The mechanism of the subsequent cyclisation is not proved but probably involves a prototropic shift in the initially formed enolate anion to give (**7**), and subsequent cyclisation onto C-8a of the eniminium salt (Scheme 1) thus producing the quaternary centre. This provides access to the novel [8.4.0.0^{1,6}]tetradecane ring system for the first time.

The second result is also surprising, not only for the apparently inexplicable change in the regioselectivity of the reaction, but also as both products [(**1**) and (**6**)] must arise from the cross-conjugated dienamine [(**8**); Scheme 2] which we have shown previously[5] was not present in any detectable amount in the starting dienamine! To the best of our knowledge, this is the first synthesis of the tricyclo-[6.2.2.0^{1,6}]dodecane ring system. Formation of the alternative tricyclic structure [(**9**), Scheme 2] by [2 + 2]cycloaddition across the 8,8a-positions is mechanistically more plausible.

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† No attempts have yet been made to optimise yields. All new compounds gave the expected microanalytical, IR, NMR, and mass spectral data.

Cycloadduct (**9**) would give the same number of methine, methyl, methylene, and quaternary carbon signals in the ^{13}C NMR spectrum as (**6**) but has been ruled out from the *X*-ray crystal structure analysis.‡

The ^{13}C NMR spectrum of both isomers of (**5**) showed one methyl, two carbonyl, two quaternary carbon, one methine, nine methylene, and no alkenic signals. On this basis we assigned the tricyclo[8.4.0.0^{1,6}]tetradecane structure to both isomers. This was subsequently confirmed by a single crystal *X*-ray structure determination of the major isomer. The stereoscopic drawing of the enantiomer of (**5**)§ (Figure 1) shows that initial attack at C-8 occurred from the α-face of the dienamine, *anti* to the C-4a methyl group, as would be expected on steric grounds, but cyclisation at C-8a occurred *syn* to the angular methyl group. Both newly formed carbon–carbon bonds are therefore equatorial to ring *B* of the starting dienamine, and the original 1,8a-bond has become axial to ring *B*. The molecular framework is rigid with all three rings present as chairs with normal torsion angles.

The stereoscopic drawing of the enantiomer of (**6**)§ (Figure 2) shows that [4 + 2]cycloaddition to the dienamine (**7**) has again occurred from the less hindered α-face. The 'boats' in the tricyclo[2.2.2]octane residue are not ideal, but are all slightly twisted in the same sense through a mean torsion angle of 13°. This effectively reduces the volume of this part of the molecule while simultaneously relieving the non-bonded H ··· H and C ··· H repulsions caused by eclipsing.

The application of this reaction to this and other cyclic, acyclic, and heterocyclic dienamines is being actively pursued. The effect of experimental conditions and substituents on the yield and course of the reaction is also being determined.

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‡ However another as yet unidentified component (m.p. 80—82 °C; 13%) was isolated from this reaction which could be a stereoisomer of (**6**) or a regioisomer such as (**9**).

§ *Crystal data* for $C_{15}H_{22}O_2$ (**5**): white crystals, m.p. 139—141 °C (from hexane–ethyl acetate), $M = 234$, monoclinic, space group $P2_1/c$, $a = 7.171(1)$, $b = 15.610(1)$, $c = 11.481(1)$ Å, $\beta = 94.60°$, $U = 1281.2$ Å^3, $Z = 4$, $D_c = 1.21$ g cm^{-3}, 4027 reflections measured for $2.0 < \theta < 30.0°$, final residual $R = 0.063$ for 2753 observed reflections ($F > 2\sigma F$). *Crystal data* for $C_{15}H_{22}O_2$ (**6**): white crystals, m.p. 95—97 °C (from hexane–ethanol), $M = 234$, monoclinic, space group $P2_1/n$, $a = 6.702(2)$, $b = 13.074(2)$, $c = 14.505(2)$ Å, $\beta = 92.19°$, $U = 1270.1$ Å^3, $Z = 4$, $D_c = 1.22$ g cm^{-3}, 3990 reflections measured for $2.0 < \theta < 30.0°$; final residual $R = 0.067$ for 2816 observed reflections ($F > 2\sigma F$). All crystal data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo-K_α radiation ($\lambda = 0.7107$ Å). Both structures were solved by direct methods (MULTAN) and refined by block-diagonal least squares. The stereoscopic drawings were calculated with the ORTEP program. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.