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REDUCTIVE CYCLISATION OF ALLENIC KETONES. A NEW APPROACH TO FUNCTIONALISED FIVE-MEMBERED RINGS.

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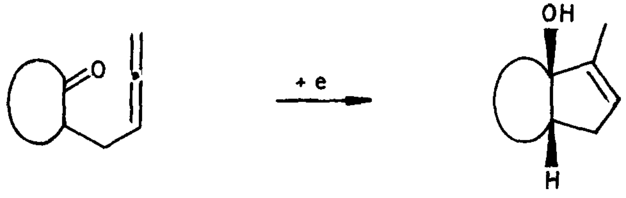
Summary: Electrolysis of a series of terminal allenic ketones, *e.g.* (4), (6), and (13) is shown to result in reductive cyclisation, through the *exo*-mode, producing five-membered rings, *viz*. (5), (7), and (14) incorporating a bridgehead hydroxyl group.

Illustrations of the use of radical initiated reductive cyclisations, leading to a range of carbo- and hetero-cyclic ring systems, have burgeoned in the past few years.[1] In connection with another synthetic problem, we required a method for the annulation of a five- (or six-) membered ring with concomitant introduction of unsaturation and a bridgehead hydroxyl group in the fused ring system. In this *Letter* we describe a solution to this problem based on electrochemical reductive cyclisation of a terminal allenic ketone, *viz*. (1) → (2).



(1) (2)

Alkylation of the anion (3) derived from iso-butylcyclopentyl imine (LDA, THF, HMPA; - 78°C) with 1-bromobuta-2,3-diene,[2] followed by mild hydrolysis (tartaric acid; - 78°C to 0°C) first gave the allene ketone (4; 50% overall), ν_{max} 1957, 1742 cm^{-1}; δ_c 219.7, 209.0, 87.7(d), 75.2(t), 48.7(d), 38.1(t), 29.2(t), 28.6(t), 20.7(t). Electrolysis of (4), in a conventional H-cell to 4F mol^{-1}, using a carbon rod cathode [-2.43 V (vs Ag-AgI), DMF, Et_4NOTs (∿0.7M)] resulted in smooth cyclisation (∿ 42%, isolated) to the cyclopentenol (5), ν_{max} 3340, 1657 cm^{-1}; δ 5.37(m, :C<u>H</u>), 2.87 - 1.05(m, 9H), 1.94(OH), 1.72(:CMe); δ_c 142.2, 126.7(d), 96.1, 50.1(d), 38.0(t), 37.8(t), 35.0(t), 25.6(t), 11.8(q).[3] The same cyclopentenol was also obtained (∿ 30%) when the allene ketone (4) was treated with sodium naphthalene radical anion (THF, 25°C). In a similar manner, electrolysis of the allene substituted cyclohexanone (6) led to the hydrindenol (7; 43%), δ5.49(m,:C*H*), 2.69 - 0.89(m,12H), 1.71(:CMe).

Although, to our knowledge, these are the first reports of reductive cyclisation of ω-allenic ketones, the formation of (5) from (4) [and (7) from (6)] complements the work of Stork,[4] and of Shono,[5] and of others[6] who have established that the corresponding acetylenic ketones (*viz*.8) undergo radical initiated cyclisation producing the (*exo*-) positional isomers (*viz*.9) of the (*endo*-) allylic alcohols (*viz*.2) obtained in this study. The regioselectivity of the radical initiated cyclisations of (4) and (8) leading to the formation of only a new five-membered ring through closure in the *exo*-mode is expected, and has ample precedent.[7]

We have also investigated the reductive cyclisation of the homologous allene ketone (13), which was produced from the acetylene ketone (10),[5] following reduction to the carbinol (11), chain extension to (12) (paraformaldehyde, Pr^i_2NH, CuBr, dioxan, heat), and oxidation of (12) using barium manganate.[8] Electrolysis of (13), using the same conditions as those used for (4), led (23%) to a single, isomerically pure, bicyclic alcohol whose spectral data ν_{max} 3380, 1640 cm^{-1}; δ5.88(ddd,*J* 17.4, 10.4, 10.2, C*H*:CH$_2$), 5.07(m,:CH$_2$), 2.47(m,C*H*CH:), 2.5 - 1.02 (m, 12H), δ_c 138.2 (d), 115.5 (t), 92.8, 55.6(d), 51.5(d), 37.7(t), 34.8(t), 30.1(t), 29.9(t), 25.9(t) were consistent with the vinyl substituted bicyclooctanol (14). The stereochemistry at the ring juncture in (14) is assigned *cis*- since the corresponding *trans*-bicyclo[3.3.0]octane is highly strained, and the *trans*-relationship between the vinyl group and the bridgehead hydroxyl group in the bicycle followed from inspection and comparison of n.m.r. shift data with those of related systems. Like (4) and (6), the allene ketone (13) was therefore found to cyclise in only the *exo*-mode producing only the five-membered ring. Furthermore, the cyclisation yields the more thermodynamically favoured *trans*-(1,2- and 1,5-) substituted product. In a similar manner, electrolysis of the δ-ketoallene (15) led (56%) to the homoallylic alcohol (16) ν_{max} 3370, 1640 cm^{-1}; δ5.84(ddd,*J* 14.7, 12.2, 7.6, C*H*:CH$_2$), 5.08(m, :CH$_2$), 2.69(m,C*H*.CH:), 2.20 - 0.7(m,5H), 1.16(Me), 1.14(Me), 1.06(Me); δ_c 138.1(d), 115.6(t), 81.0, 56.0(t), 55.0(d), 45.4(t), 37.8, 32.1(q), 31.6(q), 25.1(q).

Further work is now in progress to extend and expand the scope of these novel reductive cyclisations in natural product synthesis.

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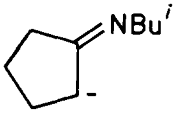

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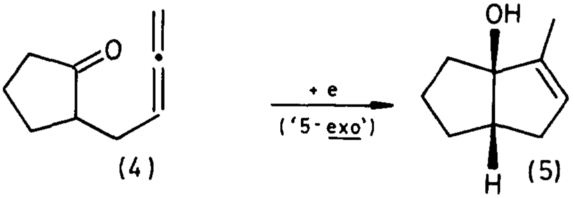

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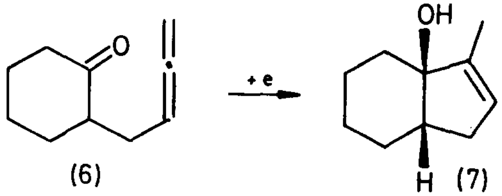

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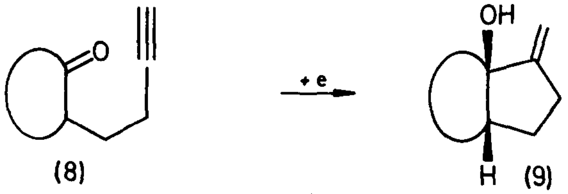

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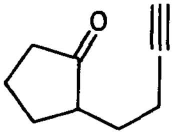

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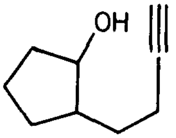

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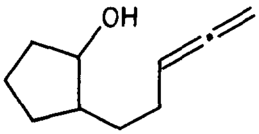

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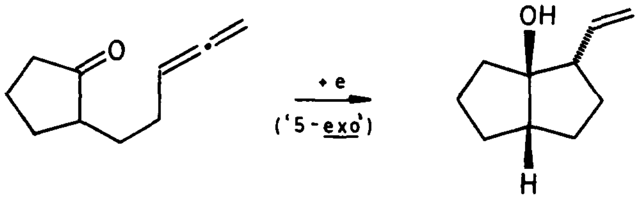

(13) (14)

(15) (16)

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