Rearrangements of Aryl-8-oxabicyclo[3.2.1]octenones: Synthesis of Novel Biaryls and 1-Aryl-3-furylpropanones

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The formation of 3-arylbenzaldehydes through rearrangement of 3-aryl-8-oxabicyclo[3.2.1]oct-2-en-7-ones is reported, together with various rearrangement reactions of 2-aryl-8-oxabicyclo[3.2.1]oct-6-en-3-ones, and a novel approach to the natural product acamelin.

We required a route to aryl-tropones of general formula (1), and thought that these might be available through cleavage of the oxa-bridge of oxabicycles like (2) and (3). These are readily available using oxyallyl methodology,¹ and, in the case of (3), further functional group manipulation (Scheme 1). In the event, treatment of (3) [Ar = 2,3,4-(MeO)₃C₆H₂, mixture of isomers] with a variety of reagents known to cleave ether linkages (Me₃SiI,² AcCl-NaI,³ AlCl₃-NaI,⁴ and lithium hexamethyldisilazide⁵) resulted in formation of intractable mixtures. However, use of 48% aqueous HBr resulted in



(3) and isomer

oxidation.

Scheme 1. Reagents: i, Et₃N, CF₃CH₂OH, furan; ii, Zn; iii, ArLi or

ArMgBr; iv, BH₃ · tetrahydrofuran; v, H₂O₂, NaOH; vi, H⁺; vii,

formation of one product in high yield (85%). This was shown to be the biaryl (4) [Ar = 2,3,4-(MeO)₃C₆H₂], and a possible mechanism for this interesting rearrangement is shown in Scheme 2.† The use of Me₂BBr⁶ also provided this biaryl, albeit with two of the three methoxy groups cleaved (49– 58%). Analogous chemistry was possible with the oxabicycle (3) (Ar = 3-CF₃C₆H₄) (64% yield); although further investigations are clearly necessary, this route has potential for the production of novel biaryls.

When oxabicycles like (2) $[Ar = 2-MeOC_6H_4, 3, 4-(MeO)_2C_6H_3, and 3, 4-(MeO)_2, 6-BrC_6H_2]$ were treated with Me₃SiBr, ring cleavage occurred to yield furans (5) in excellent yields (81, 70, and 84% respectively). Interestingly, during the cycloaddition to produce the cycloadduct (2) $[Ar = 3, 4-(MeO)_2C_6H_3]$, yellow crystalline side-product (6) was always obtained, m.p. 90-93 °C; $\delta(^{1}H, CDCl_3, 60 \text{ MHz}) 2.4$ (s, 3H, MeCO), 3.8 (s, 3H, OMe), 3.9 (s, 3H, OMe), 6.2-7.4 (complex m, 6H, 3 aryl-H and 3 olefinic-H), and 9.5 (d, J7 Hz, 1H, CHO) [nuclear Overhauser effect (n.O.e.) experiments at 400 MHz confirmed the structure shown]; v_{max} . (CDCl₃ solution) 2850 and 1680 cm⁻¹. This product probably arises *via* initial bonding between the methyl carbon and the furan ring (*cf.* ref. 1a).

Finally, problems with ring bromination were encountered during attempts to prepare the oxyallyl precursor (8) (X = Br). In consequence, an attempt was made to replace the methoxy groups with acetoxy, with the aim of reducing the reactivity of the ring. Treatment of the aryl ketone (8) (X = H) with BBr₃-CH₂Cl₂ at -78 °C yielded the benzofuran (9) (R =



[†] Other complex molecular rearrangements of oxabicyclo[3.2.1]octenones have been reported recently: V. Sampath and N. E. Schore, J. Org. Chem., 1983, 48, 4882; B. Föhlisch and O. Herrscher, Tetrahedron, 1985, 41, 1979.



H) rather than the desired phenol (36% yield, not optimised), and this was characterised as its acetate (9) (R = MeCO), m.p. 64-65 °C (lit.⁷ 67.5-69 °C); δ (¹H, CDCl₃, 220 MHz) 2.39 (d, J 1 Hz, 3H, Me), 2.40 (s, 3H, OCOMe), 3.85 (s, 3H, OMe), 6.27 (q, J 1 Hz, 1H, olefinic-H), 6.85 (d, J 9 Hz, 1H,

5-H), 7.19 (d, J9 Hz, 1H, 4-H); these data are identical to data reported in ref. 7. This compound (9) (R = H) was the last intermediate in a seven-step synthesis of acamelin (10), an allergen from Australian blackwood (Acacia melanoxylon **R**. Br.) and the present route thus constitutes a formal total synthesis of this natural product. Other naturally occurring benzofurans may also be accessible using this methodology.

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