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

John Mann,*[a] Philip D. Wilde,[a] and Mark W. Finch[b]

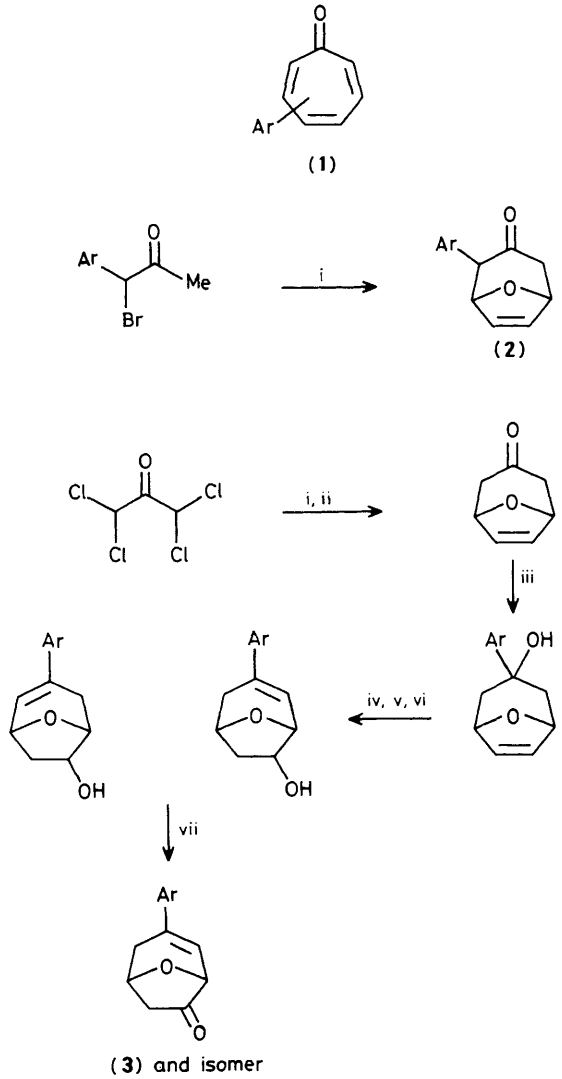
[a] *Department of Chemistry, University of Reading, Whiteknights, P.O. Box 224, Reading, Berkshire RG6 2AD, U.K.*
[b] *Lilly Research Centre Ltd., Eli Lilly and Company, Erl Wood Manor, Windlesham, Surrey GU20 6PH, U.K.*

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.

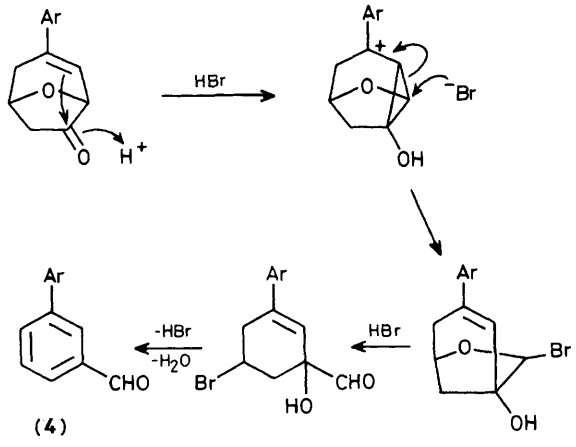
We required a route to aryl-tropones of general formula (**1**), and thought that these might be available through cleavage of the oxa-bridge of oxabicycles like (**2**) and (**3**). These are readily available using oxyallyl methodology,[1] and, in the case of (**3**), further functional group manipulation (Scheme 1). In the event, treatment of (**3**) [Ar = 2,3,4-$(MeO)_3C_6H_2$, mixture of isomers] with a variety of reagents known to cleave ether linkages (Me_3SiI,[2] AcCl–NaI,[3] $AlCl_3$–NaI,[4] and lithium hexamethyldisilazide[5]) resulted in formation of intractable mixtures. However, use of 48% aqueous HBr resulted in formation of one product in high yield (85%). This was shown to be the biaryl (**4**) [Ar = 2,3,4-$(MeO)_3C_6H_2$], and a possible mechanism for this interesting rearrangement is shown in Scheme 2.† The use of Me_2BBr[6] 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-$CF_3C_6H_4$) (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 Me_3SiBr, 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; δ(^{1}H, $CDCl_3$, 60 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, *J* 7 Hz, 1H, CHO) [nuclear Overhauser effect (n.O.e.) experiments at 400 MHz confirmed the structure shown]; $\nu_{max.}$ ($CDCl_3$ solution) 2850 and 1680 cm^{-1}. This product probably arises *via* intermediate (**7**), while the major cycloadduct 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 BBr_3–CH_2Cl_2 at −78 °C yielded the benzofuran (**9**) (R =

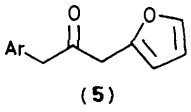


Scheme 1. *Reagents:* i, Et_3N, CF_3CH_2OH, furan; ii, Zn; iii, ArLi or ArMgBr; iv, BH_3·tetrahydrofuran; v, H_2O_2, NaOH; vi, H^+; vii, oxidation.



Scheme 2

† 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.



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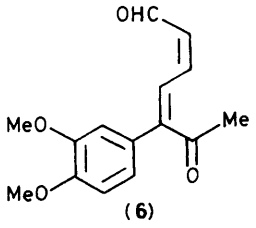

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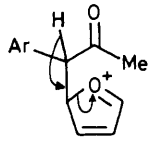

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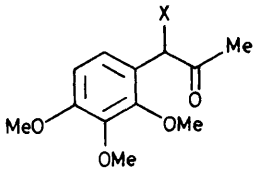

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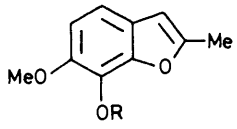

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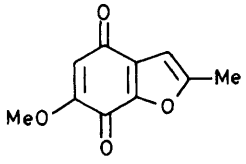

(10)

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 (^{1}H, $CDCl_3$, 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, *J* 9 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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