Intramolecular Cyclisation Catalysed by Silver(I) Ion; a Convenient Synthesis of Aurones

Ting-Ting Jong* and Shang-Jen Leu
Department of Applied Chemistry, Providence University, Shalu, Taichung Hsien, Taiwan, Republic of China

Silver(I) ion catalysed intramolecular cyclisation of $R'C_6H_4C{\equiv}CCOC_6H_3(OH)R$ (**1a–d**) at room temperature gives the corresponding aurone (**2a–d**) as the major product with a trace amount of the flavone; compounds (**1a–d**) could be prepared by the addition of the corresponding lithium acetylide (**4a–b**) to the substituted salicyl aldehyde (**5a–c**), followed by MnO_2 oxidation.

It has been reported that aurone type flavonoids have analgesic activity,[1] and recently M. Anf'mkolk *et al.* have shown that aurone derivatives of plant extracts produce potent, dose-dependent, and ultimately complete inhibition of iodothyronine deiodinases.[2] Many flavonoids also showed anti-platelet aggregation and other biological activity; a convenient and efficient synthetic method of aurone type flavonoids is therefore desirable.

We report here an efficient and high yield route to aurone by intramolecular cyclisation of 3-aryl-1-[2(4)-hydroxyaryl]prop-2-yn-1-ones (**1a–d**) in the presence of a catalytic amount of $AgNO_3$† in methanol (Scheme 1).

A few aurones (**2a–d**)‡ were successfully synthesised by the above method and were found to have the *Z*-configuration by comparison with the reported data.[4,5] Although the five-member ring product should not be the electronically favoured product in this cyclisation, the aurones (**2a–d**) were obtained in high yields (~90%) with only a trace of the flavones (**3a–d**). A possible explanation is that the Ag(I) ion is co-ordinated both to the triple bond and the adjacent benzene ring, causing a partial positive charge at the α-carbon (next to the carbonyl carbon) which favours nucleophilic attack of the oxygen atom at that carbon atom.

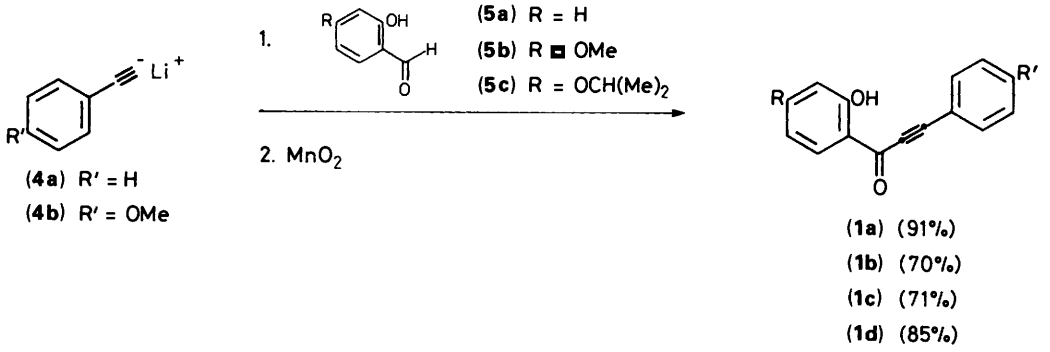
The key compounds (**1a–d**) in this synthetic strategy were synthesised by the addition of a substituted lithium acetylide (**4a–b**) to a 2-hydroxybenzaldehyde (**5a–c**) at −78 °C, followed by MnO_2 oxidation (Scheme 2). The overall yield of the aurones in three steps is *ca.* 60%.

Experimental

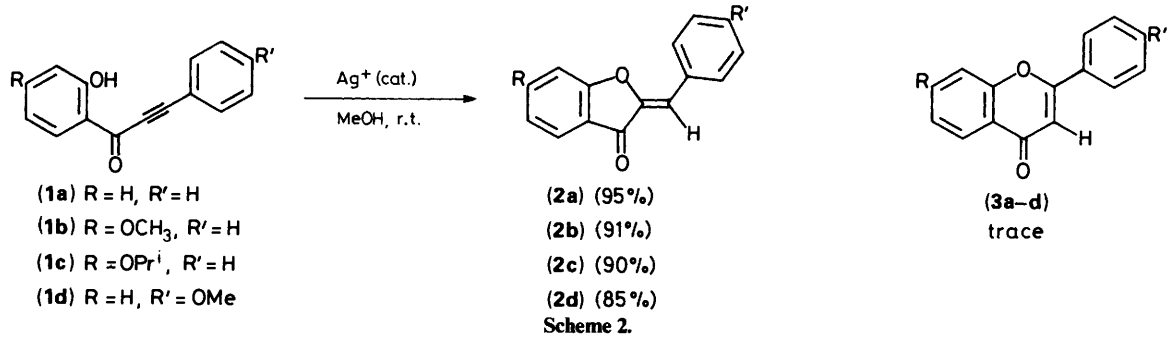
General Procedure.—A solution of (**1a**) (0.5 mmol) and $AgNO_3$ (0.15 mmol) in methanol (5 ml) was stirred at room temperature until the starting material was consumed. Methanol was removed under reduced pressure, water was added, and the mixture was extracted with diethyl ether. The crude product was chromatographed on silica gel (EtOAc–Hex, 1:5) to yield the aurone (**2a**) (90%, R_F = 0.4) and the flavone (**3a**) (5%, R_F = 0.2).

Compound (**1a**): *m/z* 222 (M^+, 100%), 221 (36), 120 (14); ν_{max} 3 066, 2 204, 1 626, 1 598 cm^{-1}; δ_H 6.96–7.03 (2 H, m, 3′-H, 5′-H), 7.40–7.56 (4 H, m), 7.70 (2 H, dd, *J* 1.5 and 8.0 Hz, 2-H, 6-H), 8.13 (1 H, dd, *J* 1.6 and 8.2 Hz, 6′-H), 11.77 (1 H, s, OH).

† Ag(I) ion catalysed intramolecular cyclisation has been successfully achieved in the total synthesis of cyanobacterin in our previous work.[3]
‡ NMR and IR data for aurones (**2a,b,d**) are in excellent agreement with the reported data.[4,5]



Scheme 1.



Scheme 2.

Compound (**1c**): *m/z* 280 (M^+, 54%), 238 (64), 237 (100), 137 (82), 136 (82); ν_{max} 2 980, 2 204, 1 628, 1 588 cm^{-1}; δ_H 1.38 (6 H, d, *J* 6.1 Hz, OMe), 4.64 (1 H, m), 6.41 (1 H, d, *J* 2.4 Hz, 3′-H), 6.49 (1 H, dd, *J* 2.4 and 8.8 Hz, 5′-H), 7.38–7.52 (3 H, m, 3-, 4-, and 5-H), 7.68 (2 H, dd, *J* 1.6 and 6.5 Hz, 2-H, 6-H), 7.98 (1 H, d, *J* 8.8 Hz, 6′-H), 12.23 (1 H, s, OH).

Compound (**2c**): *m/z* 280 (M^+, 100%), 238 (30), 237 (35); ν_{max} 1 698, 1 653, 1 605. $\delta_H(CDCl_3)$ 1.42 (6 H, d, *J* 6.0 Hz, 2 × Me), 4.68 (1 H, m), 6.72 (1 H, dd, *J* 2.1 Hz and 8.5 Hz, 5-H), 6.74 (1 H, d, *J* 2.1 Hz, 7-H), 6.81 (1 H, s, C=CH), 7.38–7.47 (3 H, m, 3′-, 4′-, and 5′-H), 7.69 (1 H, d, *J* 8.3 Hz, 4-H), 7.90 (2 H, dd, *J* 1.4 and 8.0 Hz, 2′-H and 6′-H); δ_C 183.6, 169.3, 166.6, 148.5, 133.1, 131.9, 130.5, 129.4, 126.5, 114.9, 114.0, 112.3, 98.3, 71.7, 22.4.

Acknowledgements

The authors wish to thank the National Science Council of the Republic of China (NSC77-0208-M126-08) for financial support.

References

1 O. Flandre, M. Damon, R. Darmanaden, H. Castel, J. Orzalesi, *C. R. Seances, Soc. Biol. Ses Fil.*, 1977, **171**, 146.
2 M. Auf'mkolk, J. Koehrle, R.-D. Hesch, and V. Cody, *J. Biol. Chem.*, 1987, **261**, 11623.
3 T.-T. Jong and P. Williard, *J. Org. Chem.*, 1984, **49**, 735.
4 J. S. Hastings and H. B. Heller, *J. Chem. Soc., Perkin Trans. 1*, 1972, 2128.
5 A. Pelter and R. S. Ward, *J. Chem. Soc., Perkin Trans. 1*, 1979, 328.

Paper 9/04287C
Received 26*th July* 1989
Accepted 6*th October* 1989