Mercury(II) Trifluoroacetate-mediated Transformation of 3-Bromo-1-phenylprop-2-ynyl Aryl Ethers; a Novel Synthesis of Flavanones

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The synthesis and mercury(II) trifluoroacetate mediated transformation of 3-bromo-1-phenylprop-2-ynyl aryl ethers to flavanones is reported.

Flavanones constitute one of the most important classes of the wide group of flavanoids. They are crucial substituents in a number of naturally occurring and pharmacologically important compounds, such as *C*-arylglycosides and *C*-glycosides. The chemistry of flavanones has been repeatedly reviewed in the literature.[1] The most widely adopted method for the construction of the 2-phenyl-2,3-dihydro-4*H*-1-benzo-pyran-4-one skeleton is the cyclisation of *o*-hydroxychalcones by acids,[2] bases,[3] silica,[4] light[5] or more recently by Co^{II} Schiff-base complexes.[6]

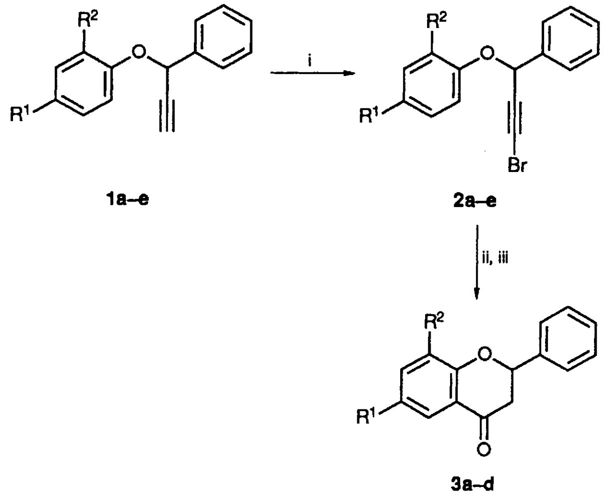
The ease with which the 1-arylprop-2-ynyl aryl ethers undergo the Claisen transformation,[7] as well as the success with the mercury(II)-mediated synthesis of chromanones[8] prompted us to look into the feasibility of a short, novel synthesis of flavanones by the above route. In this Communication we report such a route to flavanones.

The starting ethers **1a–c** were prepared by our recently reported[7,9] extension of the Mitsunobu coupling reaction of 1-phenylprop-2-yn-1-ol and the corresponding phenols. While these ethers failed to react with NaOBr (unlike the corresponding prop-2-ynyl aryl ethers[8]), the γ-bromo compounds **a–e** were prepared by the reaction of **1a–e** with *N*-bromosuccinimide (NBS) in the presence of a catalytic quantity of silver nitrate,[10] in yields of 86–92%.

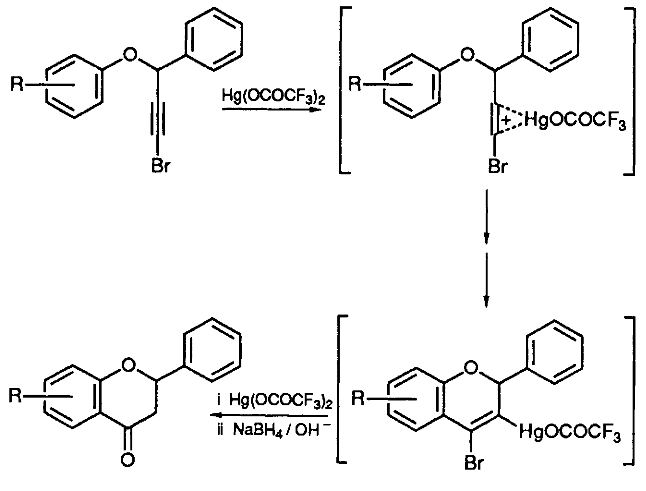
The ethers **2a–d** underwent a facile transformation to the flavanones **3a–d** in the presence of mercury(II) trifluoroacetate in dichloromethane, with yields of 90–92% after sodium borohydride work-up (Scheme 1).† The probable mechanism for this transformation is outlined in Scheme 2. There has been some controversy as to whether such transformations involve a sigmatropic process or a simpler electrophilic cyclisation.[11] The actual mechanism operating in this instance is currently under investigation with the use of aryl propargyl ethers with an optically active centre at the α-position.

Surprisingly, the ether **2e** failed to furnish the corresponding flavanone under the above conditions. This behaviour is in contrast to 3-bromoprop-2-ynyl-(4-methoxy)phenyl ether which is smoothly converted to 6-methoxychroman-4-one (84%) under identical conditions. However, the use of silver trifluoromethanesulphonate instead of mercury(II) trifluoroacetate furnished the highly unstable 4-bromoflavene **4** albeit in low yield (25%) Scheme 3. Attempts to convert **4** to the corresponding flavanone are in progress.

The cyclisation of *m*-substituted[12] γ-bromopropynyl aryl ethers showed no significant regioselectivity under the above



Scheme 1 *Reagents and conditions*: i, NBS, $AgNO_3$–acetone, 2 h; ii, Hg $(OCOCF_3)_2$–CH_2Cl_2, room temp.; iii, alkaline $NaBH_4$



Scheme 2

Table 1 Synthesis of flavanones by a Hg^{2+} mediated transformation

Entry	R¹	R²	Yield of **2** (%)	Yield of **3** (%)	M.p./°C (lit.)
a	H	H	88	92	74 (76)[4]
b	Me	H	91	90	104 (106–107)[15]
c	Cl	H	86	90	95 (98)[4,14]
d	H	Me	86	91	86
e	OMe	H	94	—	

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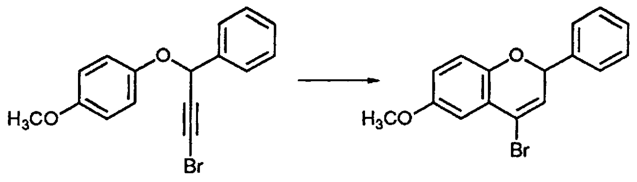
† *Experimental procedure*: To the 3-bromo-1-phenylprop-2-ynyl aryl ether **2a–e** (1 mM) dissolved in dry CH_2Cl_2 (7 ml) was added $Hg(OCOCF_3)_2$ (1 mM). The solution turned red after 5–10 mins. It was stirred for a period of 2 h at room temp., and a further portion of $Hg(OCOCF_3)_2$ (0.5–1.0 mM) was then added and stirring continued for a further period of 1 h. The mixture was cooled to 0 °C and an alkaline $NaBH_4$ solution (1.5–2.0 mM) was added slowly. After stirring for 1 h at room temp., the reaction mixture was filtered through celite, the filtrate was concentrated and purified by column chromatography to furnish the flavanones **3a–d** (Table 1).



2e **4**

Scheme 3 *Reagents and conditions*: Ag (OSO_2CF_3)-CH_2Cl_2, room temp., 15 min

conditions and a mixture of the regioisomers in a ratio of 3 : 2 was obtained. Under solution thermolysis conditions,[13] in ethylene glycol or in diethylaniline, neither the flavanone nor the 4-bromoflavene could be obtained with any of the ethers **2a–e**. In fact only a rapid and extensive decomposition resulted.

Thus, a short, novel and efficient synthesis of flavanones under neutral conditions has been effected.

One of the authors (R. S. S.) is grateful to CSIR for a fellowship. We are grateful to Professor G. Schröder and Dr H. Röttele, University of Karlsruhe, Germany for high resolution ^{1}H and ^{13}C NMR data; Dr K. Nagarajan, Searle (India) Ltd., Bombay, Professor T. R. Govindachari, SPIC Science Foundation, Madras and RSIC, IIT, Madras for mass spectral data and Professor A. Vasella, University of Zurich for a gift of $Hg(OCOCF_3)_2$.

Received, 9th May 1990; Com. 0/02050H

References

1 S. Wawzonek, in *Heterocyclic compounds*, ed. R. C. Elderfield, Wiley, New York, 1951, vol. 2, pp. 346–356; J. B. Harborne, T. J. Marby and H. Marby, *The Flavanoids*, Academic Press, New York, 1975, part 1, pp. 560–631; B. A. Bohm, in *The Flavanoids. Advances in research since 1980*, ed. J. B. Harborne, Chapman and Hall, New York, 1986, pp. 348–372.
2 T. A. Geissman and R. O. Clinton, *J. Am. Chem. Soc.*, 1946, **68**, 697.
3 J. J. P. Furlong and N. S. Nudelman, *J. Chem. Soc., Perkin Trans. 2*, 1985, 633.
4 N. K. Sangwan, B. S. Varma and K. S. Dhindsa, *Chem. Ind.*, 1984, 271.
5 A. Matsushima and H. Kageyama, *J. Chem. Soc., Perkin Trans. 2*, 1985, 743.
6 K. Maruyama, K. Tamanaka, A. Nishinaga, A. Inada and K. Nakanishi, *Tetrahedron Lett.*, 1989, **30**, 4145.
7 R. S. Subramanian and K. K. Balasubramanian, *Tetrahedron. Lett.*, 1988, **29**, 6797.
8 G. Ariamala and K. K. Balasubramanian, *J. Chem. Soc., Chem. Commun.*, 1988, 34.
9 R. S. Subramanian and K. K. Balasubramanian, *Synthetic Commun.*, 1989, **19**, 1255.
10 H. Hofmeister, K. Annen, H. Laurent and R. Wiechert, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 727.
11 D. K. Bates and M. C. Jones, *J. Org. Chem.*, 1978, **43**, 3856; R. P. Lutz, *Chem. Rev.*, 1984, **84**, 205, R. C. Larock and L. W. Harrison, *J. Am. Chem. Soc.*, 1984, **106**, 4218.
12 W. K. Anderson, E. J. LaVoie and P. G. Whitkop, *J. Org. Chem.*, 1974, **39**, 881.
13 G. Ariamala and K. K. Balasubramanian, *Tetrahedron*, 1989, **45**, 309.
14 C. T. Chang, F. C. Chen, T. S. Chen, K. K. Hsu, T. Ueng and M. Hung, *J. Chem. Soc.*, 1961, 3414.
15 O. Dann and G. Volz, *Ann. Chem.*, 1965, **685**, 167.