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Note

Lewis acid promoted synthesis of 2(3*H*)-benzofuranones

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A Lewis acid promoted one-step synthesis of 2(3*H*)-benzofuranones *via* an intramolecular rearrangement of the corresponding substituted O-methoxyacetylbenzenes and coumarins is described.

Keywords: O-Methoxyacetylbenzenes, intramolecular rearrangement, 2(3*H*)-benzofuranones, furano-benzopyran-2-ones

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Introduction

During the Lewis acid mediated reaction of O-methoxyacetyl derivatives of substituted benzenes and coumarins, a new one-step method for the synthesis of 2(3*H*)-benzofuranones (**Scheme I**) has been discovered. Benzofuranones are reported to show a wide spectrum of biological activity[1-4] such as analgesic, hypnotic, blood platelet aggregation and edema-inhibiting, anticonvulsant and anti-inflammatory. Thus, a new and convenient method for their synthesis would be useful in promoting the study of these biologically active compounds. Earlier 2(3*H*)-benzofuranones have been prepared by the lactonization of appropriately substituted *o*-hydroxyphenyl acetic acids[5]. This method has serious limitations due to the non-availibility of many *o*-hydroxyphenyl acetic acid analogues, although some can be prepared in three steps starting from the corresponding *o*-methoxybenzaldehydes[6]. Some other reported methods also either require inaccessible starting materials or involve multi-step procedures[7-12]. Moreover, the conversion is very low and the 2(3*H*)-benzofuranones are obtained in rather low yields.

Results and Discussion

The synthesis of 2(3*H*)-benzofuranones was achieved by an intramolecular cyclization of O-methoxyacetylbenzenes and coumarins in the presence of anhydrous aluminium trichloride under thermal conditions. The cyclized products were mainly identified by the presence of a strong absorption band at 1800-1820 cm^{-1}, characteristic for the lactone carbonyl of a five membered ring, in their IR spectrum and a two proton singlet in the region δ 3.7-4.5 in the ^1H NMR spectrum. The yield of the benzofuranones obtained by the present procedure varies with the nature of the substituent(s) present in the ring. O-Methoxyacetylbenzenes containing electron releasing substituents (Cl, CH_3, OCH_3) at the *para*-position gave fairly good yield of the products while the electron withdrawing substituents (R = CHO, $COCH_3$) gave benzofuranones in very low yields[13]. In case of 4-O-methoxyacetylanisole, cyclization and demethylation occurred simultaneously. Coumaryl esters also cyclized under similar conditions to give furano-benzopyran-2-ones (**4, 5** and **6**).

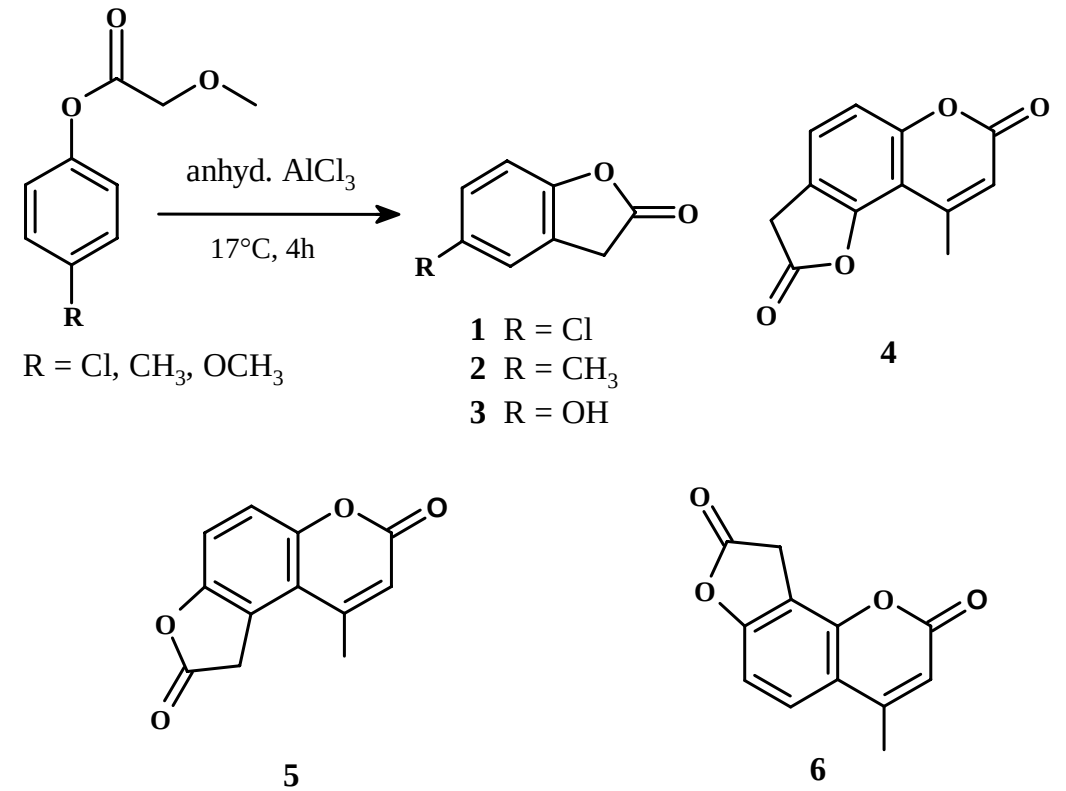
The pathway proposed for the formation of 2(3*H*)-benzofuranones involves an initial complexation of the Lewis acid $AlCl_3$ with the ether oxygen atom, followed by the intramolecular cyclization and subsequent aromatization. The low yields obtained in case of the compounds having electron withdrawing groups at the *para*-position may possibly be due to deactivation of the aromatic ring, thus effectively preventing a nucleophilic attack (**Scheme II**).

Experimental Section

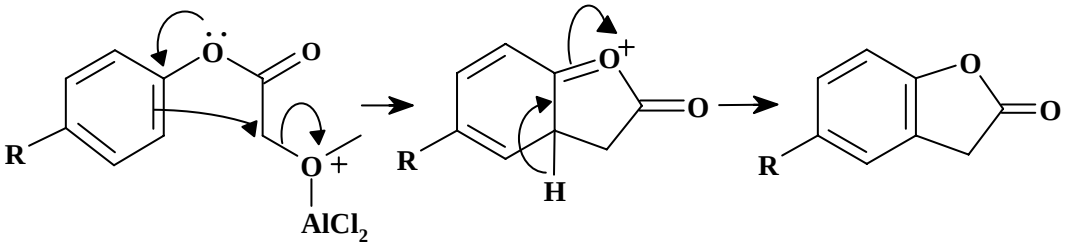
All the reactions were carried out at 170°C. The melting points were taken in open glass capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer IR spectrometer Model BX-II in KBr pellets and ^1H and ^{13}C NMR spectra were recorded on Bruker 300 MHz and 75.47 MHz model in $CDCl_3$, acetone-d_6 and DMSO-d_6. All chemical shifts are reported in δ (ppm) downfield from tetramethylsilane. Mass spectra were recorded on a Jeol-DX 303 instrument by using electron ionization at 70 eV and only major peaks are quoted.

General Procedure

O-Methoxyacetyl derivatives were prepared by acylation of phenols/hydroxycoumarins with



Scheme I



Scheme II

methoxyacetyl chloride in the presence of dry pyridine. A homogenous mixture of O-methoxyacetyl benzene/coumarin and anhyd. $AlCl_3$ was heated at 170°C for 4 h. The contents were then cooled and the reaction mixture quenched by adding ice-water mixture. Conc. HCl was then added and the aluminium complex decomposed by heating on a steam bath for 30 min. The contents were cooled and extracted with ether. The solvent free residue was preadsorbed on silica gel (60-120 mesh) and subjected to column chromatography. Elutions with $CHCl_3$ afforded **1** and **2**, while $CHCl_3$:MeOH (98:2) eluted **3, 4, 5** and 6.

5-Chloro-2(3*H*)-benzofuranone 1: m.p. 88-9°C. ^{1}H NMR ($CDCl_3$): δ 3.75 (2H, s, H-3), 7.04 (1H, d, *J* = 9.3 Hz, H-7), 7.27 (1H, dd, *J* = 2.0 and 9.3 Hz, H-6), 7.28 (1H, d, *J* = 2.0 Hz, H-4); ^{13}C NMR ($CDCl_3$): δ 45.4, 126.4, 127.4, 131.5, 145.7, 147.9, 155.9, 168.9; IR (KBr): 3088 (Ar), 2948, 2924 (-CH_2-), 1808 (C=O), 1059 cm^{-1} (Ar-Cl); EI-MS: m/z (%) 170 (M^+ +2, 34), 168 (M^+, 100), 142 (31), 140(93), 112(71).

5-Methyl-2(3*H*)-benzofuranone 2: m.p. 72-73°C (lit.[7] m.p. 74°C). ^{1}H NMR ($CDCl_3$): δ 2.39 (3H, s, -CH_3), 3.74 (2H, s, H-3), 7.08 (1H, d, *J* = 8.8 Hz, H-7), 7.14 (1H, dd, *J* = 1.9 and 8.8 Hz, H-6), 7.15 (1H, d, J

= 1.9 Hz, H-4); ^{13}C NMR ($CDCl_3$): δ 22.4, 46.3, 120.3, 126.9 127.8, 129.4, 134.6, 147.1, 169.7; IR (KBr): 3090 (Ar), 1820 cm^{-1} (C=O); EI-MS: m/z (%) 148 (M^+, 100), 147(62), 120(23).

5-Hydroxy-2(3*H*)-benzofuranone 3: m.p. 132-35°C. ^{1}H NMR (acetone-d_6): δ 3.78 (2H, s, CH-3), 5.67 (1H, brs, 5-OH), 6.82-7.15 (3H, m, Ar-H); ^{13}C NMR ($CDCl_3$): δ 46.4, 113.7, 114.5, 122.9, 132.4, 142.7, 151.8, 169.4; IR (KBr): 3400 and 1360 (O-H), 3050 (Ar), 1815 (C=O), 1225 cm^{-1} (C-O); EI-MS: m/z (%) 150 (M^+, 100), 149 (32), 122 (18).

Furan-2(3*H*)-one [5.4-*f*]-4-methyl-2*H*-1-benzopyran-2-one 4: m.p. 130-31°C. ^{1}H NMR (DMSO-d_6): δ 2.56 (3H, d, *J* = 1.1 Hz, -CH_3), 4.35 (2H, s, -CH_2CO-), 6.39 (1H, q, *J* = 1.1 Hz, H-3), 6.78 (1H, d, *J* = 8.3 Hz, H-8), 7.14 (1H, d, *J* = 8.3 Hz, H-7); ^{13}C NMR ($CDCl_3$): δ 22.1, 49.1, 114.8, 116.4, 119.6, 127.1, 131.5, 147.0, 150.9, 154.0, 158.7, 168.9; IR (KBr): 1810 (furan C=O), 1729 cm^{-1} (pyran C=O); EI-MS: m/z (%) 216 (M^+, 45), 215 (80), 187 (62), 160 (100), 132 (90).

Furan-2(3*H*)-one [4,5-*f*]-4-methyl-2*H*-1-benzopyran-2-one 5: m.p. 125-26°C. ^{1}H NMR (DMSO-d_6): δ 2.50 (3H, d, *J* = 1.0 Hz, -CH_3), 4.47(2H, s, -CH_2CO-), 6.45 (1H, q, *J* = 1.0 Hz, H-3), 7.43 (1H, d, *J* = 8.8 Hz, H-8), 7.50 (1H, d, *J* = 8.8 Hz, H-7); ^{13}C NMR ($CDCl_3$): δ 18.5, 48.7, 110.8, 116.9, 118.0, 125.0, 146.1, 146.2, 150.6, 152.1, 159.2, 169.9; IR (KBr): 1812 (furan C=O), 1716 cm^{-1} (pyran C=O); EI-MS: m/z (%) 216 (M^+, 60), 215 (90), 187 (89), 160 (86), 132 (100), 131 (83), 103 (58).

Furan-2(3*H*)-one [5,4-*h*]-4-methyl-2*H*-1-benzopyran-2-one 6: m.p. 126-27°C. ^{1}H NMR (DMSO-d_6): δ 2.49 (3H, s, -CH_3), 3.85 (2H, s, -CH_2CO-), 6.26(1H, s, H-3), 7.02(1H, d, *J* = 8.7 Hz, H-6), 7.66 (1H, d, *J* = 8.7 Hz, H-5); ^{13}C NMR ($CDCl_3$): δ 18.3, 51.8, 108.6, 110.1, 112.0, 125.0, 153.1, 154.0, 159.2, 160.1, 170.9; IR (KBr): 1803 (furan C=O), 1730 cm^{-1} (pyran C=O); EI-MS: m/z (%) 216 (M^+, 48), 215 (92), 187 (90), 160 (82), 132 (100), 131 (80), 103 (63).

Conclusion

An economical single-step synthesis of 2(3*H*)-benzofuranones using easily accessible reagents under thermal conditions has been developed successfully. This method can be used for the construction of furanone moiety on any aromatic or heterocyclic system in order to obtain novel biologically active pharmacophores of the future.

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References

1 Closse A, Haefliger W & Hauser D, *German Patent*, 2608697, 1976; *Chem Abstr*, 85, **1976**, 192536.

2 Closse A, Haefliger W & Hauser D, *US Patent*, 4252817, 1981; *Chem Abstr*, 95, **1981**, 7042.

3 Rathore H G S & Reddy V M, *J Indian Chem Soc*, 61, **1984**, 556.

4 Piccolo O, Filippini L, Tinucci L, Valoti E, Citterio A, Blaschim A & Peregallo L, *J Chem Res*, 8, **1985**, 258.

5 Aubert O, Augdahl A & Berner E, *Acta Chem Scandinavia*, 6, **1952**, 433.

6 Levine T E E & Fischbach H, *J Am Chem Soc*, 70, **1948**, 1930.

7 Holmquist H E, *J Org Chem*, 34, **1969**, 4164.

8 Ozaki Y, Quan Z, Watabe K & Kim S, *Heterocycles*, 51(4), **1999**, 727.

9 Hang H C, Drotleff E, Elliot G I, Ritsena T A & Konofelski J P, *Synthesis*, 3, **1999**, 398.

10 Magnus P & Kreisberg J D, *Tetrahedron Lett*, 40(3), **1999**, 451.

11 Setsune J, Ueda T, Shikata K, Matsukava K, Iida T & Kitao T, *Tetrahedron*, 42(10), **1986**, 2647.

12 Luo W, Yu Q S, Holloway H W, Parrish D, Greig N H & Bross A, *J Org Chem*, 70, **2005**, 6171.

13 Alongwith the 2(3*H*)-benzofuranones, other unidentified rearranged products were also obtained.