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# New reactions of fluorinated 2,4-dioxoesters with aromatic aldehydes

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**4-Polyfluoroalkyl 2,4-dioxobutanoates react with aromatic aldehydes to give 4-aryl-2,6-dihydroxy-2,6-di(fluoroalkyl)-3,5-diethoxalyltetrahydropyrans 3a,b, whereas the reaction of 4-pentafluorobenzoyl 2,4-dioxobutanoate with benzaldehyde gives 5,6,7,8-tetrafluoro-1-phenyl-1*H*-furo[3,4-*b*]chromene-3,9-dione 4.**

Reactions of non-fluorinated acylpyruvates[1,2] and aroylpyruvates[2,3] with aldehydes in the presence of bases (piperidine, $K_2CO_3$) typically result in 5-alkyl(aryl)-4-acyl(aroyl)-3-hydroxy-2,5-dihydrofuran-2-ones due to aldehyde addition to the activated methylene group (Knövenagel condensation) followed by lactonisation involving the alkoxycarbonyl fragment.

We found that the route of this reaction changes dramatically when a fluoroalkyl is introduced into 2,4-dioxoesters. 4-Polyfluoroalkyl-2,4-dioxobutanoates **1a**,**b** react with aromatic aldehydes to give 4-aryl-2,6-dihydroxy-2,6-di(fluoroalkyl)-3,5-diethoxalyltetrahydropyrans **3** instead of expected furanones **2**. The formation of pyrans **3** presumably occurs *via* intermediates **A**, **B**, **C** and **D**; this is typical of fluoroalkyl-containing 3-oxoesters[4] and due to the electron-withdrawing effect of the polyfluoroalkyl group determining the ability of these compounds to add a water molecule to the carbonyl group at the fluorinated substituent.[5]

As has been established by NMR spectroscopy,† compounds **3** have a tetrahydropyran structure rather than isomeric acyclic structure **D**. One set of signals from equivalent ester and fluoroalkyl groups in the $^1$H and $^{19}$F NMR spectra corresponds to the symmetric structure of **3**. A triplet signal ($^3J$ ~ 12 Hz) is observed for the H$^4$ proton, and a doublet signal ($^3J$ ~ 12 Hz) is observed for the H$^3$ and H$^5$ protons. The coupling constant ($^3J$ ~ 12 Hz) corresponds to the axial orientation of protons at C$^3$, C$^4$ and C$^5$. Obviously, the conformation of molecules **3a**,**b** is affixed by the *e*-orientation of bulky substituents R$^f$, Ar and $CO_2$Et.[6]

Apparently, the reaction of the 2,4-dioxoester that has a weaker electron-accepting pentafluorophenyl substituent with aldehydes still gives furanone **2**, but just as an intermediate, which undergoes cyclisation to 5,6,7,8-tetrafluoro-1-phenyl-1*H*-furo[3,4-*b*]-chromene-3,9-dione **4**. The cyclisation occurs due to intramolecular nucleophilic substitution of the *ortho*-fluorine atom with a hydroxyl group in the pentafluorophenyl substituent.

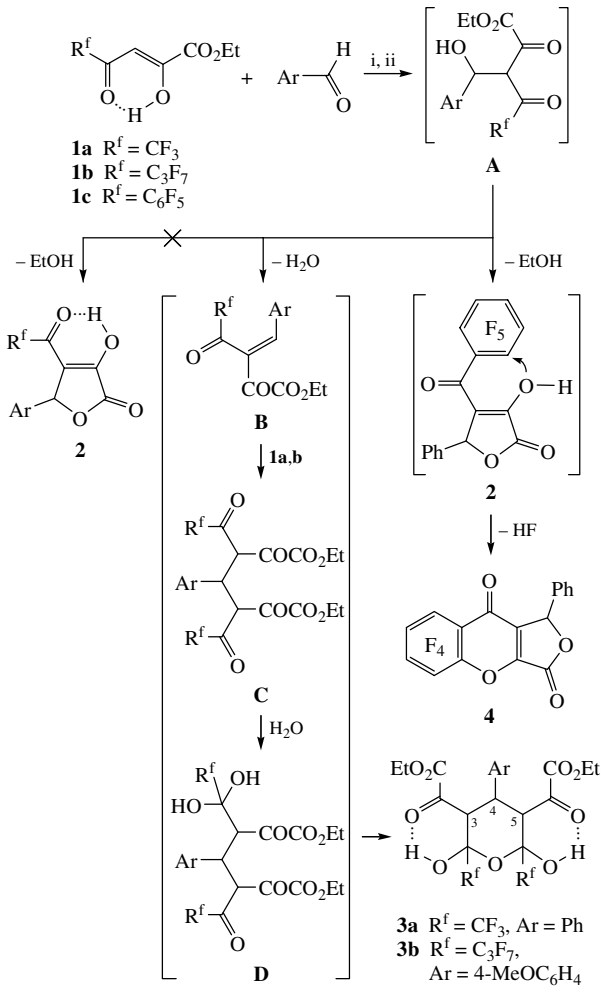
The suggested mechanism of formation of furochromone **4** is confirmed by the fact that it is impossible to obtain this product by the reaction of an aldehyde with 2-ethoxycarbonyl-5,6,7,8-tetrafluorochromone. The formation of the latter as an alternative intermediate is also possible in this reaction due to the easy self-cyclisation of pentafluorobenzoyl pyruvate **1c**.[7]

† New compounds **3a**,**b** and **4** were characterised by elemental analyses, IR and $^1$H (100 MHz and 400 MHz, $Me_4Si$), $^{19}$F (75.0 MHz and 400 MHz, $C_6F_6$) spectroscopy and mass spectrometry (EI, 70 eV).

*2,6-Dihydroxy-2,6-di(trifluoromethyl)-3,5-diethoxalyl-4-phenyltetrahydropyran* **3a** *(general procedure)*. A mixture of ester **1a** (2.12 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) in anhydrous diethyl ether containing a catalytic amount of piperidine was kept for five days at room temperature. The solvent was evaporated, and the precipitate formed was recrystallised from light petroleum to give 1.45 g (55%) of product **3a**, mp 128–130 °C. $^1$H NMR ([$^2H_6$]DMSO) $\delta$: 0.79 (t, 6H, 2OCH$_2$*Me*, *J* 7.1 Hz), 3.23 (d, 2H, H$^3$, H$^5$, *J* 12.3 Hz), 3.66–3.83 (m, 4H, 2O*CH*$_2$Me), 4.05 (t, 1H, H$^4$, *J* 12.3 Hz), 7.18–7.30 (m, 5H, Ph), 7.70 (br. s, 2H, 2OH). $^{19}$F NMR ([$^2H_6$]DMSO) $\delta$: 78.73 (s, $CF_3$). IR (Vaseline oil, $\nu$/cm$^{-1}$): 3340 (OH), 1715, 1690 (C=O), 1460 (C=C), 1200–1110 (C–F). Found (%): C, 47.52; H, 3.79; F, 21.37. Calc. for $C_{21}H_{20}F_6O_9$ (%): C, 47.56; H, 3.80; F, 21.49.

*2,6-Dihydroxy-2,6-di(heptafluoropropyl)-3,5-diethoxalyl-4-(4-methoxyphenyl)tetrahydropyran* **3b**. The procedure gave 2.59 g (68%) of product **3b**, mp 116–118 °C. $^1$H NMR ([$^2H_6$]DMSO) $\delta$: 0.81 (t, 6H, 2OCH$_2$*Me*, *J* 7.1 Hz), 3.29 (d, 2H, H$^3$, H$^5$, *J* 12.2 Hz), 3.71–3.78 (m, 4H, 2O*CH*$_2$Me), 3.75 (s, 3H, OMe), 4.06 (t, 1H, H$^4$, *J* 12.2 Hz), 6.80 (m, 2H, $C_6H_4$), 7.18 (br. s, 2H, 2OH), 7.52 (br. s, 2H, $C_6H_4$). $^{19}$F NMR ([$^2H_6$]DMSO) $\delta$: 38.98 (s, 2F, $CF_2$), 41.84 (m, 2F, $CF_2$), 81.42 (t, 3F, $CF_3$, $^3J_{F–F}$ 10.7 Hz). IR (Vaseline oil, $\nu$/cm$^{-1}$): 3430, 3300 (OH), 1710, 1700 (C=O), 1450 (C=C), 1250–1120 (C–F). Found (%): C, 40.29; H, 2.87; F, 35.17. Calc. for $C_{26}H_{22}F_{14}O_{10}$ (%): C, 40.07; H, 2.92; F, 34.97.

*5,6,7,8-Tetrafluoro-1-phenyl-1*H*-furo[3,4-b]chromene-3,9-dione* **4**. A mixture of ester **1c** (3.1 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) in ethanol containing two drops of hydrochloric acid (or piperidine) was refluxed for 6 h. The solvent was then evaporated, and the precipitate was washed with hot ethanol and chloroform to give 1.68 g (48%) of product **4**, mp 241–242 °C. $^1$H NMR ([$^2H_6$]DMSO) $\delta$: 6.67 (s, 1H, CH), 7.55–7.43 (m, 5H, Ph). $^{19}$F NMR ([$^2H_6$]DMSO) $\delta$: 2.96 (m, 1F), 4.89 (m, 1F), 16.59 (m, 1F), 18.71 (m, 1F). IR (Vaseline oil, $\nu$/cm$^{-1}$): 3020 (C–H val.), 1780 (OC=O), 1680 (C=O), 1660, 1650, 1485 (C=C), 990 (C–F). Found (%): C, 58.36; H, 1.56; F, 21.63. Calc. for $C_{17}H_6O_4F_4$ (%): C, 58.30; H, 1.73; F, 21.70.




**Scheme 1** *Reagents and conditions*: i, $Et_2O$, $HN(C_2H_4)_2CH_2$, 20 °C, 120 h; ii, EtOH, $HN(C_2H_4)_2CH_2$ (or HCl), reflux, 6 h.

Thus, we have observed an unusual behaviour of fluorinated 2,4-dioxoesters in reactions with aldehydes.

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## References

1 Z. Földi, G. Fodor and I. Demjén, *J. Chem. Soc*., 1948, 1295.
2 T. Kurihara, Ya. Sakamoto, T. Kobayashi and M. Mori, *J. Heterocycl. Chem*., 1978, **15**, 737.
3 V. L. Gein, L. F. Gein, E. N. Bezmaternykh and E. V. Voronina, *Pharm. Chem. J*., 2000, **34**, 254.
4 M. V. Pryadeina, O. G. Kuzueva, Ya. V. Burgart, V. I. Saloutin, K. A. Lyssenko and M. Yu. Antipin, *J. Fluorine Chem*., 2002, **117**, 1.
5 K. I. Pashkevich and V. I. Saloutin, *Usp. Khim*., 1985, **54**, 1997 (*Russ. Chem. Rev*., 1985, **54**, 1185).
6 (*a*) S. Hauptmann, J. Grafe and H. Remane, *Lehrbuch der Organischen Chemie*, VEB Deutscher Verlag für Grundstoffindustrie, Leipzig, 1976; (*b*) A. L. Terney, *Contemporary Organic Chemistry*, 2nd edn., Saunders Company, Philadelphia, 1980.
7 V. I. Saloutin, Z. E. Skryabina, I. T. Bazyl' and O. N. Chupakhin, *J. Fluorine Chem*., 1993, **65**, 37.

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