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RING-CHAIN ISOMERIC TRANSFORMATIONS.
THE CYCLOHEMIKETAL STRUCTURE OF
4,4,4-TRIFLUORO-1-(2-HYDROXYPHENYL)-1,3-BUTANEDIONES

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Abstract: Compounds 4-8 exist only in the cyclohemiketal form both in the solid state and in solution, in contrast with earlier assumptions on their enolic structure.

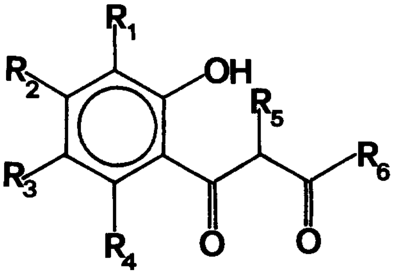
Although ring-chain isomeric transformations involving hydroxycarbonyl compounds are well established,[1] scanty attention has been paid in this respect to the products obtained by Claisen condensation of 2-hydroxyaryl alkyl ketones with esters or by Baker-Venkataraman rearrangement of 2-acyloxyaryl alkyl ketones.[2]

Indeed, most of them have been generically described as 1,3-diketones (form A), and the formation of 2-hydroxy-4-chromanones (form B) has been rather regarded as an anomaly than correctly interpreted in terms of prevalent ring form stability.[3]

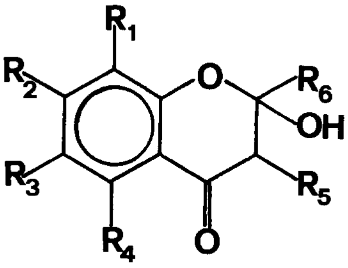
In a study on multiple hydrogen bonds, 1-(2-hydroxyphenyl)-1,3-butanediones 1 and 2 have been found to exist in solution mainly in the enol form C,[4] while the 4,6-dimethoxy derivative 3 has been reported to be a 3:1 keto-enol mixture in $CDCl_3$.[2c,5]

In agreement with the general expectation that an enhancement of the electrophilic properties of the carbonyl group would stabilize the ring form and displace the equilibrium towards it,[1] and in contrast with earlier assumptions on their enolic structure,[6] we produce here spectroscopic evidence that 4,4,4-trifluoro-1-(2-hydroxyphenyl)-1,3-butanediones 4-8 exist only in the cyclohemiketal form B both in the solid state and in solution.

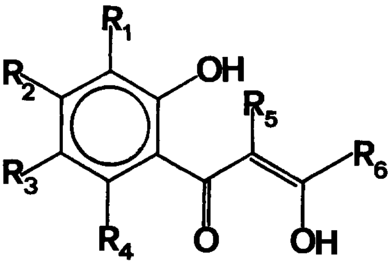
The IR spectra as KBr discs show a broad band for OH stretching in the 3280-3240 cm^{-1} region and a single, strong carbonyl absorption in the 1675-1650 cm^{-1}



A



B



C

1, $R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = Me$

2, $R_1 = R_2 = R_4 = R_5 = H$; $R_3 = Me$; $R_6 = Me$

3, $R_1 = R_3 = R_5 = H$; $R_2 = R_4 = OMe$; $R_6 = Me$

4, $R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = CF_3$

5, $R_1 = R_2 = R_4 = R_5 = H$; $R_3 = Me$; $R_6 = CF_3$

6, $R_1 = R_3 = R_5 = H$; $R_2 = R_4 = Me$; $R_6 = CF_3$

7, $R_1 = R_3 = R_4 = R_5 = H$; $R_2 = OMe$; $R_6 = CF_3$

8, $R_1 = R_3 = R_5 = H$; $R_2 = R_4 = OMe$; $R_6 = CF_3$

region. In chloroform solution, the corresponding bands appear at about 3200 and 1690-1670 cm^{-1}, respectively.

There are no carbonyl bands below 1650 cm^{-1}, which would be expected if an open-chain form were present. In fact, 2 and 3 present a chelated C=O group at 1611 and 1600 cm^{-1}, respectively,[2c,4] while ß-diketones of the general form $ArCOCH_2COCF_3$ possess carbonyl bands below 1650 cm^{-1}.[7]

The ^1H NMR spectra in $CDCl_3$ exhibit at about δ 3 a two-protons signal as a singlet or AB quartet, for the methylene protons. The OH proton resonates in the δ 3.8-4.5 region. In acetone-d_6 the OH absorption is found in the δ 7.2-7.5 region. The other signals are not remarkably shifted.

In either solvent, no signals are observed downfield of δ 10 and in the olefin region (aromatic protons excluded) as is, on the contrary, reported for 1, 2, and 3.[2c,4]

No variations in IR and ^1H NMR spectra are observed with the lapse of time.

Spectral data of compounds 4-8 are summarized on Table I.

The little information so far available on the argument does not allow significant conclusions to be drawn on the substituent effects on multiple equilibria in 1-(2-hydroxyphenyl)-1,3-butanedione derivatives, although a marked influence of the aromatic substitution is evident in the case of $R_6 = Me$.[2c]

Table I. ^{1}H NMR and IR Data of 4,4,4-Trifluoro Derivatives 4-8[8]

compd	^{1}H NMR, δ (J, Hz)				IR, cm^{-1}	
	-COCH_2-	OH	aromatic protons	other signals	CO	OH
4	3.05(s)^{a} 2.93 and 3.30^{b} (ABq, J=16.5)	3.87(br)^{a} 7.45(br)^{b}	7.03-8.00^{a} 7.06-7.93^{b}		1675^{c} 1690^{d}	3260^{c} 3180^{d}
5	3.02(s)^{a} 2.88 and 3.25^{b} (ABq, J=16.5)	3.80(br)^{a} 7.33(br)^{b}	6.91-7.73^{a} 6.93-7.67^{b}	2.31(s, 5-Me)^{a} 2.30^{b}	1680^{c} 1695^{d}	3270^{c} 3200^{d}
6	2.88 and 3.07^{a} (ABq, J=16.5) 2.82 and 3.22^{b} (ABq, J=16.5)	4.10(br)^{a} 7.27(br)^{b}	6.73(s)^{a} 6.78(s)^{b}	2.28(s, 4-Me)^{a} 2.30^{b} 2.57(s, 6-Me)^{a} 2.53^{b}	1665^{c} 1680^{d}	3280^{c} 3205^{d}
7	2.90 and 3.10^{a} (ABq, J=16.5) 2.85 and 3.22^{b} (ABq, J=16.5)	4.45(br)^{a} 7.45(br)^{b}	6.50-7.90^{a} 6.58-7.87^{b}	3.83(s, 4-OMe)^{a} 3.90^{b}	1665^{c} 1685^{d}	3240^{c} 3200^{d}
8	2.72 and 3.02^{e} (ABq, J=16.5)	8.34(br)^{e}	6.18(s)^{e}	3.85(s, 4- and 6-OMe)^{e}	1650^{c} 1670^{d}	3280^{c} 3200^{d}

[a] Measured in $CDCl_3$. [b] Measured in acetone-d_6. [c] Measured in KBr discs. [d] Measured in $CHCl_3$. [e] Measured in $CDCl_3$- DMSO-d_6= 5:1 because of the very poor solubility of 8 in $CDCl_3$ alone and in acetone-d_6.

However, the results obtained for $R_6 = CF_3$ indicate unambiguously the powerful inductive control by this group since only the ring forms are present, irrespective of aromatic substitution.[9]

A study of the substituent effects in a series of 4- and/or 5-substituted 1-(2-hydroxyphenyl)-1,3-butanediones is in preparation.

REFERENCES AND NOTES

(1) R. Valters, Russ. Chem. Rev., 43, 665 (1974).

(2) (a) G. P. Ellis in "Chromenes, Chromanones, and Chromones", G. P. Ellis, Ed., Wiley-Interscience, New York, 1977, Chapter 9; (b) V. K. Ahluwalia, D. Kumar, N. Rani, and Sunita, *Indian J. Chem., Sect. B*, **15B**, 328 (1977); (c) V. K. Ahluwalia and D. Kumar, *ibid.*, 514 (1977); (d) H. Obara and J. Onodera, *Bull. Chem. Soc. Jpn.*, **41**, 2798 (1968); (e) H. Obara and J. Onodera, *ibid.*, **42**, 3345 (1969).

(3) N. Narasimhachari, D. Rajagopalan, and T. R. Seshadri, *J. Sci. Ind. Res. (India)*, **11B**, 347 (1952); N. Narasimhachari, D. Rajagopalan, and T. R. Seshadri, *ibid.*, **12**, 287 (1953); F. Eiden and W. Luft, *Arch. Pharm.(Weinheim)*, **306**, 634 (1973).

(4) G. Dudek and E. P. Dudek, *Tetrahedron*, **23**, 3245 (1967).

(5) 3 is reported to enolise in the direction opposite to that depicted in the form C, but spectral data do not seem to support unambiguously this statement. In particular, the enolic OH shift is not quoted (cfr. ref. 4).

(6) W. B. Whalley, *J. Chem. Soc.*, 3235 (1951).

(7) K. C. Joshi, V. N. Pathak, and S. Bhargava, *J. Inorg. Nucl. Chem.*, **39**, 803 (1977).

(8) Compounds 5, 6, and 7 have been prepared according to ref. 6. Compounds 4 and 8 have been obtained in an analogous fashion from 2-hydroxyacetophenone and 4,6-dimethoxy-2-hydroxyacetophenone, respectively.
4: mp 153-154 °C (from benzene); 8: mp 198-200 °C (from acetone). Both compounds gave satisfactory elemental analyses.

(9) For similar conclusions, see: H. Alper, *J. Chem. Soc., Chem. Commun.*, 383 (1970); H. Alper, E. C. H. Keung, and R. A. Partis, *J. Org. Chem.*, **36**, 1352 (1971).

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