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REARRANGEMENT OF 1,3,5,8-TETRAOXYGENATED XANTHONES IN HOT AQUEOUS MORPHOLINE

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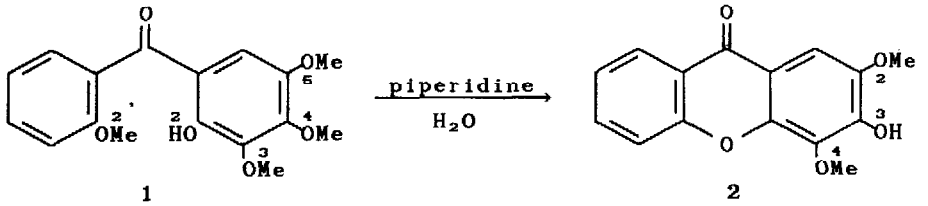
Summary: Aqueous morpholine demethylation of 2-prenyl-1-hydroxy-3,5,8-trimethoxyxanthone leads to a mixture of 1,3,5,8- and 1,3,7,8-tetraoxygenated xanthones.

Aqueous piperidine or morpholine at reflux temperature have been used to effect cyclisation of 2,2'-dioxygenated benzophenones to xanthones[1] as well as in the selective demethylation of polymethoxybenzophenones and polymethoxyxanthones.[1-3] An interesting case, where both reactions occur concurrently is in the conversion of 2-hydroxy-2',3,4,5-tetramethoxybenzophenone (1) to 3-hydroxy-2,4-dimethoxyxanthone (2).[1] The reverse process, in which demethylation of a polymethoxyxanthone is accompanied by ring-opening to a benzophenone, has not been reported.



1 2

In the course of the synthesis of two minor xanthones (**3** & **4**)[4,5] from *Garcinia mangostana*, we observed a novel rearrangement during the demethylation of 2-prenyl-1-hydroxy-3,5,8-trimethoxyxanthone (**5**) with aqueous morpholine.

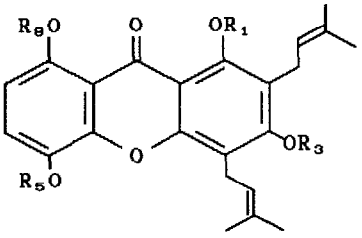
Reaction of 2,3,6-trimethoxybenzoic acid with phloroglucinol in the presence of phosphorous pentoxide and methanesulphonic acid[6] afforded, as the major product, 1,3-dihydroxy-5,8-dimethoxyxanthone.[7,8] Prenylation of this xanthone by the usual method[11] and methylation of the products gave the 2-prenyl and 2,4-diprenyl derivatives (5 & 6).

Treatment of xanthone 5 (650 mg) with morpholine-water (9:1, 20 ml) in a sealed tube at 145°C for seven days gave a mixture which was separated by centrifugal chromatography on silica gel to give two tetrahydroxyxanthones (7 & 8) and two monomethoxyxanthones (9 & 10) (M^+, ^1H NMR).[12] All four products exhibited two *ortho*-coupled protons and two chelated hydroxyls in their ^1H NMR spectra. Examination of their UV[13] and ^{13}C NMR spectra suggested that two of the products (7 & 9) were 1,3,7,8-tetraoxygenated, while the other two had the expected 1,3,5,8-tetraoxygenation. Complete methylation converted both 7 and 9 to the same tetramethyl ether (11) confirming their identical oxygenation. The ^{13}C NMR spectrum of 11 showed four methoxyl resonances at δ 55.8, 57.3, 61.7 and 62.1. The presence of two deshielded methoxyl signals is consistent with structure 11, as both the 1- and 8-methoxyls are di-*ortho*-substituted.[14] Methylation of xanthone 8 gave the natural product (3), identified by spectral comparison of its diacetate with that of an authentic sample.[15]

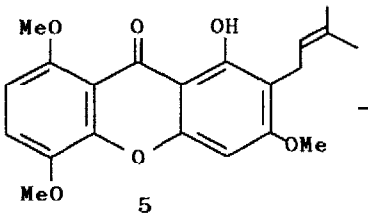
Demethylation of 6 with aqueous morpholine yielded gartanin (4) (30%) (mmp, UV, ^1H and ^{13}C NMR), and 5-O-methylgartanin (12). Methylation of either product gave tetra-O-methylgartanin, mp. 87-89° (lit.[4] 85°). No 1,3,7,8-tetraoxygenated products were detected.

The isolation of xanthones 7 and 9 from the reaction of 5 with aqueous morpholine may be explained if ring-opening to a benzophenone intermediate (13) had occurred in the course of dealkylation. Subsequent ring-closure could lead to both 1,3,7,8- and 1,3,5,8-tetraoxygenated xanthones. This observation prompted us to investigate the behaviour of the parent tetramethoxyxanthones under similar conditions. Treatment of 1,3,5,8-tetramethoxyxanthone with aqueous morpholine and methylation of the product gave mainly 1,3,7,8-tetramethoxyxanthone and only a trace of the starting material, while similar treatment of 1,3,7,8-tetramethoxyxanthone gave mainly starting material and a trace of 1,3,5,8-tetramethoxyxanthone.

Our results suggest that the well-known base-catalysed ring-closure of 2,2'-dioxygenated benzophenones is a reversible process and consequently 1,2-(≡7,8-) and 1,4-(≡5,8-) dioxygenated xanthones may undergo rearrangement in hot alkaline media.



4 $R_1=R_3=R_5=R_8=H$
6 $R_1=H$; $R_3=R_5=R_8=Me$
12 $R_1=R_3=R_8=H$; $R_5=Me$



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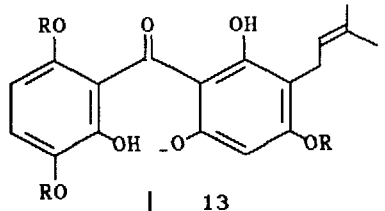

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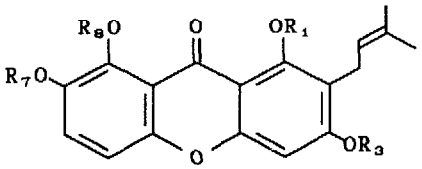
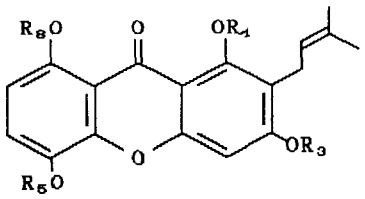


7 $R_1=R_3=R_7=R_8=H$
9 $R_1=R_3=R_8=H$; $R_7=Me$
11 $R_1=R_3=R_7=R_8=Me$



3 $R_1=R_5=R_8=H$; $R_3=Me$
8 $R_1=R_3=R_5=R_8=H$
10 $R_1=R_3=R_8=H$; $R_5=Me$

References and Notes

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7. The xanthone obtained had mp. 292-295° decomp.(lit.[8] 192-194°); methylation gave 1,3,5,8-tetramethoxyxanthone, mp. 209-210° (lit.[9] 210°; lit.[10] 209-210°).
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11. S. Amand and A.C. Jain, *Aust. J. Chem.*, 1974, 27, 1515.
12. Yields: 7, 80 mg; 8, 135 mg; 9, 85 mg; 10, 55 mg. Satisfactory analytical and spectral data (UV, ^{1}H and ^{13}C NMR) were obtained for compounds 3-12 and will be reported in a subsequent paper.
13. UV spectra: λ max/EtOH (logϵ) (7): 385(3.60), 327(4.20), 271(4.41), 264(4.39), 240(4.41); NaOAc: 372(4.25), 271, 263, 239; (8): 346(4.18), 317sh, 282(4.39), 255sh, 239sh, 228sh; NaOAc: 370(4.25), 278; (9): 392(3.73), 324(4.25), 271(4.45), 266(4.43), 240(4.43); NaOAc: 369(4.11), 343, 272, 265, 238; (10): 375sh, 343(4.03), 330sh, 279(4.21), 250sh, 240(4.30), 229(4.27); NaOAc: 372(4.10), 278, 238.
14. R.K. Chaudhuri, F. Zymalkowski and A.W. Frahm, *Tetrahedron*, 1978, 34, 1837.
15. We are grateful to Dr. N.U. Khan for a gift of the diacetate of 3.

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