

spectrum was superimposable with the IR spectrum of an authentic sample. The mixed melting point obtained showed no depression.

*Anal.*—Calc. for  $C_{15}H_{20}O_3$ : C, 72.17; H, 8.06; mol. wt. 248. Found: C, 72.38; H, 8.26; *m/e* 248.

**Isolation of Costunolide**—Costunolide was isolated from the chloroform fraction of *M. champaca* by crystallization from hexane–benzene, and the crude crystals from *T. ovata* were purified by recrystallization from hexane–benzene to give 352 mg of colorless spears, mp 106–107° [lit. (4) mp 106–107°]. The IR and PMR spectra were identical to the authentic spectra.

*Anal.*—Calc. for  $C_{15}H_{20}O_2$ : C, 77.54; H, 8.67; mol. wt. 232. Found: C, 77.32; H, 8.84; *m/e* 232.

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\* To whom inquiries should be directed.

# NMR Solvent Shift Data for Methoxylated Xanthenes

R. A. FINNEGAN\* and K. E. MERKEL

**Abstract** □ The NMR spectra of 1-, 2-, 3-, and 4-hydroxyxanthenes, 1,3-, 1,5-, 1,6-, 1,7-, 1,8-, 2,5-, 3,4-, 3,5-, 3,6-, and 4,5-dihydroxyxanthenes, 1,3,6- and 1,3,8-trihydroxyxanthenes, and 1,3,6,8-tetrahydroxyxanthone, as well as those of the corresponding methyl ethers and acetates, were recorded. The spectra of the methyl ethers were measured in deuteriochloroform, benzene, trifluoroacetic acid, and 3% trifluoroacetic acid in benzene. The solvent shift parameters for the methoxyl resonances are tabulated and discussed.

**Keyphrases** □ Methoxyxanthenes, various—NMR spectra and solvent shift data □ NMR—spectra and solvent shift data, various methoxyxanthenes □ Xanthenes, methoxy substituted—NMR spectra and solvent shift data

Recently, the isolation of four simple hydroxylated xanthenes from seed extracts of *Mammea americana* L. was reported (1). They were identified as the 2- and 4-mono-hydroxy derivatives and the 1,7- and 1,5-dihydroxy derivatives by a combination of spectroscopic studies and syntheses of authentic materials (1). The last substance, in fact, was prepared for the first time. The 2,5- and 4,5-dihydroxy isomers were also prepared (2). During this work, other hydroxylated xanthenes (3, 4) were prepared, not only for comparison purposes but also for inclusion in a preliminary antitumor screen (5).

The chemical shifts of methoxy resonances in some methoxyxanthone derivatives were dependent on the position of substitution (3). The magnitude of the benzene-induced solvent shift for the methyl group in substituted anisoles was dependent on the nature and orientation of the substituents (6). These facts suggested that benzene-induced shifts of methoxyl resonances in methoxyxanthenes also might be position dependent and, therefore, might be helpful in elucidating the structures of naturally occurring hydroxyxanthenes and methoxyxanthenes.

While this work was in progress, benzene-induced shifts

**Table I—Chemical Shifts (Parts per Million) for Methoxyl Resonances of Various Methoxyxanthenes in Various Solvents**

Xanthone	Trifluoroacetic Acid	Deuteriochloroform	Benzene	Benzene-Trifluoroacetic Acid
1-Methoxy	4.50	4.05	3.43	3.39
2-Methoxy	4.12	3.94	3.29	3.43
3-Methoxy	4.18	3.95	3.18	3.16
4-Methoxy	4.27	4.05	3.33	3.32
1,8-Dimethoxy	4.37	3.99	3.42	3.40
3,6-Dimethoxy	4.18	3.95	3.19	3.20
4,5-Dimethoxy	4.22	4.08	3.34	3.30
1,3-Dimethoxy	4.42	4.00	3.38	3.37
	4.23	3.92	3.22	3.22
1,5-Dimethoxy	4.50	4.03	3.41	3.36
	4.28	4.03	3.34	3.30
1,6-Dimethoxy	4.44	4.03	3.45	3.45
	4.20	3.92	3.16	3.15
1,7-Dimethoxy	4.48	4.04	3.44	3.41
	4.13	3.92	3.27	3.33
2,5-Dimethoxy	4.27	4.05	3.38	3.40
	4.12	3.95	3.29	3.33
3,4-Dimethoxy	4.30	4.05	3.84	3.75
	4.22	4.03	3.25	3.22
3,5-Dimethoxy	4.29	4.06	3.38	3.35
	4.17	3.94	3.11	3.12
1,3,6-Trimethoxy	4.38	3.99	3.44	3.42
	4.18	3.91	3.28	3.33
	4.18	3.91	3.22	3.25
1,3,8-Trimethoxy	4.34	3.98	3.43	3.45
	4.25	3.95	3.37	3.38
	4.17	3.89	3.22	3.26
1,3,6,8-Tetramethoxy	4.26	3.94	3.42	3.38
	4.15	3.88	3.26	3.38

of methoxyl resonances in flavonoids (7–11) and substituted xanthenes (12, 13) were reported and, indeed, found to be of use in structure determination. Useful solvent shift correlations were previously derived for steroidal ketones (14, 15) and substituted coumarins (16). In addition, trifluoroacetic acid (I) was found to be a useful adjunct to the

**Table II—Solvent Shift Data for Monomethoxyxanthenes and Selected Dimethoxyxanthenes**

Xanthone	Methoxyl Position	$\Delta$ Deuteriochloroform- Benzene	$\Delta$ Trifluoroacetic Acid- Benzene	$\Delta$ Trifluoroacetic Acid- Deuteriochloroform
1-Methoxy	1	0.62	1.07	0.45
2-Methoxy	2	0.65	0.83	0.18
3-Methoxy	3	0.77	1.00	0.23
4-Methoxy	4	0.72	0.94	0.22
1,8-Dimethoxy	1(8)	0.57	0.95	0.38
3,6-Dimethoxy	3(6)	0.76	0.99	0.23
4,5-Dimethoxy	4(5)	0.74	0.88	0.14
1,5-Dimethoxy	1	0.62	1.09	0.47
	5	0.69	0.94	0.25
1,6-Dimethoxy	1	0.58	1.04	0.41
	6	0.76	0.99	0.28
1,7-Dimethoxy	1	0.60	1.04	0.44
	7	0.65	0.86	0.21
2,5-Dimethoxy	2	0.66	0.83	0.17
	5	0.67	0.89	0.22
3,5-Dimethoxy	3	0.83	1.06	0.23
	5	0.68	0.91	0.23

**Table III—Average Solvent Shift Values for Each Position of the Xanthone Ring**

Position	Average $\Delta$ Deuteriochloroform- Benzene	Average $\Delta$ Trifluoroacetic Acid- Benzene	Average $\Delta$ Trifluoroacetic Acid- Deuteriochloroform
1(8)	0.59 (0.57–0.62)	1.02 (0.95–1.09)	0.42 (0.38–0.47)
2(7)	0.65 (0.65–0.66)	0.84 (0.83–0.86)	0.20 (0.18–0.22)
3(6)	0.78 (0.76–0.83)	1.01 (0.99–1.06)	0.24 (0.23–0.28)
4(5)	0.71 (0.67–0.74)	0.91 (0.88–0.94)	0.20 (0.14–0.25)

use of benzene (II) and deuteriochloroform (III) as shift-inducing solvents (9, 10, 17) and was included in the present study.

**EXPERIMENTAL**

The preparation of the compounds used (1–4) and their complete NMR, IR, and UV data and those of their related phenols and corresponding acetates were presented previously (4). All spectra were determined using a 60-mHz spectrometer. Tetramethylsilane (2%) was employed as the internal reference in all solvents. The concentration of the solute was not greater than 3% (w/v), and the benzene-trifluoroacetic acid solvent contained 3% (v/v) of the latter. The chemical shifts for the methyl groups in the various methoxyxanthenes are listed in Table I.

**RESULTS AND DISCUSSION**

Table II lists the  $\Delta$  values ( $\Delta = \delta_{\text{Solvent 1}} - \delta_{\text{Solvent 2}}$ ) for the four monomethoxyxanthenes and for eight (of the 10 possible) dimethoxyxanthenes that do not have the methoxyl groups in the same ring. For Table III, the data from Table II were retabulated and averaged according to

the methoxyl positions on the xanthone nucleus. (For the purposes of averaging, the symmetrical xanthenes were counted twice. The range of values found is also included in the table.)

Since the 3(6)-position is *para* to the electron-withdrawing carbonyl group, it showed the largest benzene-induced shift,  $\Delta$  (III–II), in line with the indications of Bowie *et al.* (6) for simple anisole derivatives. The magnitude of  $\Delta$  (III–II) decreased in the order of C-3(6) > C-4(5) > C-2(7) > C-1(8), and the differences in magnitudes were large enough to distinguish among the closely related isomeric pairs listed in Table II. The introduction of the second methoxyl group into the unsubstituted ring of monomethoxyxanthone seemed to have little effect on the  $\Delta$  (III–II) value for the first methoxyl. A possible exception was seen for 3,5-dimethoxyxanthone, where the shift for the 3-methoxyl group was somewhat enhanced. This exception could have been a reflection of the fact that the 5-methoxyl group, being *meta* to the carbonyl group, increased its electron-withdrawing power.

Methoxyl resonances appeared at relatively low field in trifluoroacetic acid, so relatively large solvent shifts were obtained in combination with benzene. These shifts again showed a dependence on the position of substitution; their magnitude decreased in the order C-1(8)  $\approx$  C-3(6) > C-4(5) > C-2(7). The 1(8)- and 3(6)-positions (*ortho* and *para* to the

**Table IV—Solvent Shift Data for Some Methoxyxanthenes Having More than One Methoxyl Group on the Same Ring**

Xanthone	Methoxyl Position	$\Delta$ Deuteriochloroform- Benzene	$\Delta$ Trifluoroacetic Acid-Benzene	$\Delta$ Trifluoroacetic Acid- Deuteriochloroform
1,3-Dimethoxy	1	0.62	1.04	0.42
	3	0.70	1.01	0.31
3,4-Dimethoxy	3	0.78	0.97	0.25
	4	0.21	0.46	0.19
1,3,6-Trimethoxy	1	0.55	0.94	0.39
	3(6)	0.63	0.90	0.27
	6(3)	0.69	0.96	0.27
1,3,8-Trimethoxy	1(8)	0.55	0.91	0.36
	3	0.67	0.88	0.28
	8(1)	0.58	0.95	0.30
1,3,6,8-Tetramethoxy	1(8)	0.52	0.84	0.32
	3(6)	0.62	0.89	0.27
Average	1(8)	0.56	0.90	0.35
	3(6)	0.68	0.93	0.27
Average (12, 13)	2(7)	0.55		
	3(6)	0.64		
	4(5)	0.67		

carbonyl group) were those from which the electron pairs on the methoxyl groups were most efficiently delocalized and, therefore, were the least basic positions. The fact that they showed enhanced rather than reduced values for  $\Delta$  (I-II) suggests that protonation occurred on the carbonyl oxygen rather than on the ether oxygens.

Tables II and III also list the  $\Delta$  (I-III) values, which also showed positional dependence, in this case mainly for the 1(8)-position where the shift was about twice that for the other three positions. This pattern was similar to that found (9) for methoxyflavones, where the shift for the 5-methoxyl (*ortho* to the carbonyl) was larger and easily distinguished from those for methoxyls at the 6-, 7-, or 8-position. Values of 0.37 and 0.15 ppm were reported (10) for the 1- and 7-methoxyls of 1,7-dimethoxyxanthone, and the deviations from the presently reported measurements of 0.44 and 0.21 ppm probably resulted from the slightly different experimental conditions.

Table IV gives shift data for a few xanthenes having two methoxyls in the same ring. The abnormally low value of  $\Delta$  (III-II) for the 4-methoxyl in 3,4-dimethoxyxanthone is consistent with values reported for similarly situated methoxyls flanked by two *ortho*-substituents (6, 12, 13, 16, 18). This apparent decrease in the ability of the benzene solvent to shield the methoxyl group in question has been ascribed to steric hindrance. This effect is also apparent in the corresponding value of  $\Delta$  (I-II) for the 4-methoxyl in this compound. The  $\Delta$  (I-III) value (0.19 ppm), however, is quite normal for a methoxyl in this position (*cf.*, the value 0.20 ppm in Table III), although it was suggested (9, 17) that such a methoxyl ought to show an enhanced shift because of its increased basicity.

Although the data in Table IV are limited, they suggest that polyoxygenation tends to increase the  $\Delta$  values by a small amount. This decrease can also be noted in the values reported (12, 13) for a series of 1,3,5,6- and 1,3,6,7-tetraoxygenated xanthenes (further substituted by saturated or unsaturated alkyl groups), which are included (as average values) in Table IV.

Finally, the trifluoroacetic acid addition shifts,  $\Delta$  (II-II/I), were extremely small (*cf.*, Table I), mostly within the experimental error of 1-2 Hz. Therefore, they are of little help in distinguishing the positions of methoxylation, at least in these simple xanthenes. This finding is in contrast to their potential usefulness in the methoxyflavone series (9).

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\* To whom inquiries should be directed.