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AN NMR PROCEDURE FOR DETERMINING METHOXYL POSITIONS OF COUMARIN TRIMETHYLSILYL ETHERS USING THE BENZENE INDUCED SOLVENT SHIFT

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Abstract—The change in NMR chemical shift of methoxyl groups on coumarin trimethylsilyl ethers in benzene relative to chloroform or carbon tetrachloride correlates with the methoxyl position on the ring. The solvent shift is in the order 5, 7 > 6 > 8.

That benzene induces a change in the NMR chemical shifts ($\Delta\delta$) of flavonoid methoxyl groups at certain positions has been known for some time.[1] A recent report[2] indicates that similar data are available from flavonoid trimethylsilyl (TMS) ethers, which have the advantages of being more soluble in the NMR solvents used; furthermore, silylation has a minimal effect on the general nature of the spectra. We wish to report that a similar method can be used to determine the positions of methoxyl groups in naturally occurring coumarins.

The benzene induced change in chemical shift (relative to $CDCl_3$) of a number of methyl and methoxycoumarins has been reported.[3] It was shown that methoxyl groups in the 5- and 7-positions were shifted upfield in benzene (0·60–0·77 ppm) and an 8-methoxyl group was shifted only a relatively small amount (0·18 ppm). No data were reported on coumarins with 6-methoxyl groups or on coumarin glycosides.

Table 1 shows the benzene induced change in chemical shift (relative to CCl_4) of a number of coumarin TMS ethers and the solvent shift (relative to $CDCl_3$) of two fully methoxylated coumarins. The examples of Table 1 indicate solvent shifts similar to the above cited paper[3] for methoxyl groups in the 7-position (0·64–0·72 ppm). This suggests that TMS ethers do not affect the solvent induced shifts of methoxyl groups present in the same molecule. A similar finding for flavonoid TMS ethers[2] supports this conclusion. Additionally a significantly smaller solvent induced shift is noted for methoxyl groups in the 6-position (0·28–0·53 ppm), and the anomeric proton (Hα) in the 6-glucoside of Table 1 is almost unchanged in benzene.

In summary it seems possible to distinguish coumarin methoxyl groups in the 6- and 8-positions from those in the 5- or 7-positions by their smaller solvent induced change in

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[1] Wilson, R. G., Bowie, J. H. and Williams, D. H. (1968) *Tetrahedron* **24**, 1407.

[2] Rodriguez, E., Carmen, N. J. and Mabry, T. J. (1972) *Phytochemistry* **11**, 409.

[3] Grigg, R., Knight, J. A. and Roffey, P. (1966) *Tetrahedron* **22**, 3301.

chemical shift. The order of change in solvent induced chemical shift is 5- and 7-positions >6-position >8-position. The range of solvent shift changes are shown below:

Methoxyl positions	Ranges of Δ value (δCCl_4–δC_6D_6)
5,7	+0·60 to +0·77 ppm
6	+0·28 to +0·53 ppm
8	+0·18

Table 1. NMR chemical and solvent shifts of coumarin-TMS ethers

Compound*	Substituent position	δ ppm $CCl_4/CDCl_3$	δ ppm C_6H_6	Δ
7-Methylesculin	7	3·81	3·15	0·66
[6-hydroxy 7-methoxycoumarin 6-glucoside]	6 [Hα]	4·77	4·85	−0·08
Herniarin [7-methoxycoumarin]	7	3·78†	3·13	0·64
Scopoletin [6-methoxy-7-hydroxycoumarin]	6	3·75	3·47	0·28
Isocopoletin [6-hydroxy-7-methoxycoumarin]	7	3·80	3·08	0·72
Scoparon [6,7-dimethoxycoumarin]	6	3·85†	3·32	0·53
	7	3·88	3·16	0·72

* As the trimethylsilyl ethers.
† Data obtained in $CDCl_3$.

EXPERIMENTAL

All the coumarins used in this study were available commercially or easily prepared from them. The physical constants of all compounds were in agreement with the literature. TMS ethers were prepared by a standard flavonoid procedure[4] and NMR spectra (10–1 ppm) were recorded using a Varian HA100 spectrometer with tetramethylsilane as the internal standard.

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[4] Mabry, T. J., Markham, K. R. and Thomas, M. B. (1970) *The Systematic Identification of Flavonoids*, p. 255, Springer, New York.