tertiary (τ 9.02; 3H; *s*) and one secondary C-methyl group (τ 9.11; 3H; *d*; J = 6 cps). The oily methyl ester (IX) of A, $C_{21}H_{30}O_3$, $[\alpha]_D$ −67.5°, ν_{max} 1728 cm^{-1}, was readily converted by reduction with lithium aluminium hydride into the corresponding alcohol (X), $C_{20}H_{30}O_2$, $[\alpha]_D$ −37.5°, ν_{max} 3630 cm^{-1}, which also failed to crystallise. In this latter compound and the derived aldehyde (III), which also occurs naturally, the $-CH_2OH$ (τ 6.37, *d*; 6.51, *d*; 1H each; J = 11 cps) and $-CHO$ (τ 0.54; *s*) resonances respectively show no vicinal spin-spin coupling. Further, the presence of a $\beta\gamma$-unsaturated acid grouping in A was shown by its smooth conversion at 280°C/0.1 mm into the nor-olefin (XI), $C_{19}H_{28}O$, $[\alpha]_D$ −32.5°, which showed three $C-CH_3$ resonances at τ 9.13 (3H; *s*; *tert.*), 8.95 (3H; *d*; J = 7 cps; *sec.*), and 8.35 (3H; broadened *s*; vinyl) and, significantly, no vinyl proton signals.

This evidence bearing in mind that the labdane-related diterpenoid, solidagenone [1] (XII) occurs in *S. canadensis* L., would appear to indicate a rearranged labdane skeleton [2] for solidagoic acid A and thus the constitution (I).

The marked similarity of the NMR spectra of solidagoic acids B (II) and A (I) suggests that the former differs solely in that the vinyl methyl has been replaced by an allylic primary alcohol present as its angelate ester. Thus there are resonances in the NMR spectrum of acid B, λ_{max}^{EtOH} 221 mμ (log ε 3.78), at τ 5.50 (2H; *s*; $-CH_2O-$) and 3.96, 7.95−8.15 (1H and 6H, respectively; typical [3] angelate pattern). Moreover, pyrolysis of acid B at 320°C/0.01 mm afforded angelic acid, m.p. 45°C (also identified by GLC; 10 % FFAP, 125°C) and the oily γ-lactone (XIII), $C_{20}H_{26}O_3$, λ_{max} 1778 cm^{-1}.

The formation of this lactone provides further support for the proposed structure of acid A which has been correlated with B as follows. Reduction of the oily methyl ester (XIV) of B, $C_{26}H_{38}O_5$, $[\alpha]_D$ −25°, ν_{max} 1728 cm^{-1}, with lithium aluminium hydride led to the diol (IV) which also occurs naturally. The derived diacetate (XV), $C_{24}H_{34}O_5$, $[\alpha]_D$ −44°, on hydrogenolysis (H_2/Pd/EtOH/NEt_3) gave the monoacetate (XVI), $C_{22}H_{32}O_3$, $[\alpha]_D$ −50°, which has also been obtained by direct acetylation of alcohol (X).

Tentative structures for the hemiacetal (V) and dialdehyde (VI) follow from their conversion with lithium aluminium hydride into the diol (IV), while the chemical and spectroscopic evidence is compatible with structures (VII) and (VIII) for the remaining two diterpenoids of natural provenance.

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1. Anthonsen, T., McCabe, P. H., McCrindle, R. and Murray, R. D. H. *Chem. Commun.* **1966** 740; *Acta Chem. Scand.* **21** (1967) 2289.
2. Misra, R., Pandey, R. C. and Sukh Dev. *Tetrahedron Letters* **1964** 3751; Cocker, W., Moore, A. L. and Pratt, A. C. *Tetrahedron Letters* **1965** 1983; Pinhey, J. T. and Simpson, R. F. *Chem. Commun.* **1967** 9; Jefferies, P. R. and Payne, T. G. *Tetrahedron Letters* **1967** 4777.
3. Fraser, R. R. *Can. J. Chem.* **38** (1960) 549.

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Benzene-induced Solvent Shifts in the NMR-spectra of Acetophenones and Acetyl Chromenes

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In the work with chromenes from *Eupatorium* species,[1] we were faced with the problem of differentiating between the structures *1a* and *2* for a new chromene isolated from *Eupatorium riparium* Regel, isomeric with evodionol (*3a*) [2] and allo-evodionol (*4*).[3] In the following the new chromene is designated ripariochromene.

In a recent communication Scheinmann [4] has reported that a methoxyl group in xanthones is shifted 0.6 ppm when going from deuterochloroform to benzene as solvent. However, the Δ-value [$\Delta = \tau$ (benzene) − τ ($CDCl_3$)] is 0.4 ppm lower

when the methoxyl group is flanked by two α-substituents [two ether groups (*cf.* also Ref. 7), a hydroxyl and an ether group, an alkyl and an ether group or by a carbonyl and an alkyl group].

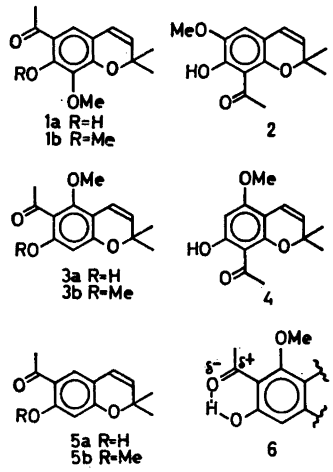
Benzene-induced solvent shifts have their origin in collision complexes between benzene and solute [5] and may take place at any electron deficient site of a local dipole. Regardless of the correctness of this picture it is obvious that two *ortho* substituents must influence the interaction between solvent and a substituent on a benzene ring.

It will be shown here that for *ortho* hydroxy acetophenones there are some exceptions from the rules for xanthones. The methoxyl group in evodionol (*3a*) is shifted 0.66 ppm, while the expected Δ-value [4] is 0.2—0.3 ppm. When the hydroxyl group is methylated the Δ-value decreases to the normal value 0.10 ppm.

The high Δ-value for the methoxyl group in evodionol is obviously caused by the

Table 1. The Δ-values for acetyl-methyl, methoxyl, methyl, and hydroxyl groups in 2-hydroxy acetophenones and *o*-hydroxy acetyl chromenes (acetophenone numbering) in deuterochloroform and benzene. $\Delta = \tau$ (benzene)$-\tau$ ($CDCl_3$).

Compound		1	2	3	4	5	6
Acetophenone							
2-hydroxy	$CDCl_3$	7.43	−2.30				
	C_6H_6	8.00	−2.65				
	Δ	0.57	−0.35				
2-hydroxy-4-methyl	$CDCl_3$	7.46	−2.30		7.68		
	C_6H_6	7.97	−2.77		8.02		
	Δ	0.51	−0.47		0.34		
2-hydroxy-5-methyl	$CDCl_3$	7.43	−2.07			7.71	
	C_6H_6	7.97	−2.60			8.00	
	Δ	0.54	−0.53			0.29	
2-hydroxy-3,4-dimethoxy	$CDCl_3$	7.43	−2.90	6.05	6.08		
	C_6H_6	7.92	−2.93	6.19	6.71		
	Δ	0.49	−0.03	0.14	0.63		
2-hydroxy-4,5-dimethoxy	$CDCl_3$	7.46	−3.22		6.11	6.16	
	C_6H_6	7.97	−3.85		6.57	6.80	
	Δ	0.51	−0.63		0.46	0.64	
2-hydroxy-4,6-dimethoxy	$CDCl_3$	7.39	−3.98		6.18		6.13
	C_6H_6	7.60	−4.68		6.78		6.91
	Δ	0.21	−0.70		0.60		0.78
Evodionol (*3a*)	$CDCl_3$	7.32	−3.40				6.18
	C_6H_6	7.62	−4.00				6.84
	Δ	0.30	−0.60				0.66
Eupatoriochromene [6] (*5a*)	$CDCl_3$	7.49	−2.68				
	C_6H_6	8.01	−3.28				
	Δ	0.52	−0.60				
Ripariochromene (*1a*)	$CDCl_3$	7.46	−2.80	6.11			
	C_6H_6	8.00	−3.40	6.12			
	Δ	0.54	−0.60	0.01			



planar and fixed structure of the strongly hydrogen-bonded system (*6*). The high Δ-value is also in accordance with the empirical rule of Conolly and McCrindle.[6]

On the contrary the Δ-value for the acetyl-methyl group in evodionol and 2-hydroxy-4,6-dimethoxy acetophenone is 0.30 and 0.21, respectively, while the Δ-value for the corresponding methyl group in 2-hydroxy-acetophenones without 6-substituent is 0.5—0.6 ppm. On methylation of the 2-hydroxyl group the acetyl-methyl group is hardly shifted at all in benzene solution (Δ = 0—0.1 ppm). This is in accordance with earlier findings [7] which state that the shift of the acetyl-methyl group is decreased from 0.44 ppm in acetophenone to 0.01 ppm in 2-methoxy-acetophenone and to —0.06 in 2,6-dimethoxy-acetophenone.

Table 2. The Δ-values for acetyl-methyl, methoxyl, and methyl groups in 2-methoxy acetophenones and *o*-methoxy acetyl chromenes (acetophenone numbering) in deuterochloroform and benzene. $\Delta = \tau$ (benzene) $- \tau$ ($CDCl_3$).

Compound		1	2	3	4	5	6
Acetophenone							
2-methoxy-5-methyl	$CDCl_3$	7.41	6.13			7.71	
	C_6H_6	7.61	6.67			7.80	
	Δ	0.20	0.54			0.09	
2,5-dimethoxy	$CDCl_3$	7.40	6.13			6.22	
	C_6H_6	7.49	6.60			6.57	
	Δ	0.09	0.47			0.35	
2,3,4-trimethoxy	$CDCl_3$	7.41	6.03	6.11	6.13		
	C_6H_6	7.49	6.30	6.30	6.65		
	Δ	0.08	0.27	0.19	0.42		
2,4,5-trimethoxy	$CDCl_3$	7.42	6.08		6.14	6.15	
	C_6H_6	7.40	6.63		6.70	6.73	
	Δ	−0.02	0.55		0.56	0.58	
2,4,6-trimethoxy	$CDCl_3$	7.56	6.21		6.10		6.21
	C_6H_6	7.57	6.70		6.59		6.70
	Δ	0.01	0.49		0.49		0.49
Methyl evodionol (*3b*)	$CDCl_3$	7.52	6.22				6.24
	C_6H_6	7.61	6.86				6.34
	Δ	0.09	0.64				0.10
Methyl eupatoriochromene (*5b*)	$CDCl_3$	7.46	6.13				
	C_6H_6	7.49	6.83				
	Δ	0.03	0.70				
Methyl ripariochromene (*1b*)	$CDCl_3$	7.42	6.02	6.10			
	C_6H_6	7.49	6.29	6.33			
	Δ	0.07	0.27	0.23			

On the basis of Tables 1 and 2 it seems reasonable to postulate the following rules for the benzene-induced solvent shifts in the NMR-spectra of 2-hydroxy and 2-methoxy acetophenones and related chromenes:

2-Hydroxy-acetophenones:

1. Hydroxyl group; $\Delta = -0.5$ to -0.6 ppm (2-hydroxy-4,6-dimethoxy acetophenone shows an unexplainable high Δ-value).
2. Acetyl-methyl group:
   a. Free 6-position; $\Delta = 0.5-0.6$ ppm.
   b. Methoxyl, ether, or alkyl group in 6-position; $\Delta = 0.2-0.3$ ppm
3. Methoxyl groups:
   a. In 6-position; $\Delta = 0.6-0.8$ ppm.
   b. Others; $\Delta = 0.4-0.6$ ppm.

When there are two *ortho* substituents to the methoxyl group the shift is decreased by 0.2–0.4 ppm, according to the findings of Scheinmann.[4]

2-Methoxy-acetophenones:

1. Acetyl-methyl group; $\Delta = 0-0.1$ ppm.
2. Methoxyl groups:
   a. In 2- or 6-position; $\Delta = 0.5-0.7$ ppm.
   b. Others; $\Delta = 0.4-0.5$ ppm.

Where there are two *ortho* substituents to the methoxyl group the shift is decreased by 0.2–0.4 ppm according to the findings of Scheinmann.[4]

On the basis of these rules the structure *1a* was chosen for riparіochromene. The Δ-value for the acetyl-methyl group is 0.54 ppm which indicates a free 6-position. The lack of shift for the methoxyl group shows that both *ortho* positions are substituted.

The spectra were recorded on a Varian A-60-A spectrometer and solvents used were $CDCl_3$ and benzene p.a. from E. Merck.

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1. Anthonsen, T. *Acta Chem. Scand.* **22** (1968). *In press.*
2. Lahey, F. A. *Univ. Queensland Papers, Dep. Chem.* **1941** No. 17 and **1942** Nos. 20, 21.
3. Sutherland, M. D. *Univ. Queensland Papers, Dep. Chem.* **1949** No. 35.
4. Scheinmann, F. *Chem. Commun.* **1967** 1015.
5. Ronayne, J. and Williams, D. H. *J. Chem. Soc.* **B 1967** 540.
6. Connolly, J. D. and McCrindle, R. *Chem. Ind. (London)* **1965** 379.
7. Bowie, J. H., Ronayne, J. and Williams, D. H. *J. Chem. Soc.* **B 1967** 535.
8. Sørensen, N. A. *IUPAC Symposium, Section H-73,* Melbourne 1960.

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Developmental Changes in Lactate Dehydrogenase Isoenzyme Patterns of Rabbit Tissues

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Lactate dehydrogenase (LDH) exists in multiple forms, isoenzymes, separable by electrophoresis and by chromatography. It was postulated and later proved that the five commonly encountered LDH isoenzymes are composed of two polypeptide subunits, H and M, in various combinations of four: LDH–1 = H_4, LDH–2 = H_3M *etc.* Various tissues possess distinct patterns; cardiac and skeletal muscle tissues have mainly H_4 and M_4, respectively. The synthesis of H and M subunits is regulated by separate genes, the activities of which probably determine the LDH pattern. A given cell type can synthesize both H and M subunits, and these chains associate randomly *in vitro* to form the five isoenzymes in amounts corresponding to binomial distributions. The LDH pattern of tissues with high aerobic metabolism generally has a predominance of H subunits, whereas preferentially anaerobic tissues have a dominance of M subunits. The mechanisms for the regulation of synthesis and catabolism of H and M subunits are unknown.

Developmental changes in LDH patterns have been described in a number of species

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