

TABLE I  
Influence of some metal ions on the inhibitory action of SDS on *Bacillus subtilis*

Metal ions used	Inhibition zone diameter (mm)	
	Without SDS	With SDS
Na	..	..
Ca	..	..
Mn	..	..
Zn	28	26
Ni	..	34
Mg	..	36
Cu	40	40
Cd	..	48
SDS alone		30

is the critical micelle concentration (CMC) for this detergent<sup>5,6</sup>. The antibacterial action of SDS may be due to its action on the membrane system of the bacterium, as detergents disorganise cell membrane and denature certain proteins essential for metabolism and growth<sup>1</sup>. Surfactants can also bring about inhibition by altering the surface structure of cells<sup>7</sup> and are also known to cause cytoplasmic shrinkage in bacteria<sup>8</sup>.

Among the metal studied, Cd<sup>++</sup> and Mg<sup>++</sup> enhanced inhibition by SDS though in the absence of the detergent they could not inhibit bacterial growth. The increased activity of SDS in the presence of these metals may be due to an increase in the number of micelles formed by the detergent, as salts are known to increase micelle number of surfactants<sup>9,10</sup>. Cu<sup>++</sup> inhibited bacterial growth even in the absence of the detergent and the addition of SDS had no effect. Surprisingly, SDS lost its activity completely in the presence of Ca<sup>++</sup>, Mn<sup>++</sup> or Na<sup>+</sup>. This may be due to these metals modifying the micelle structure<sup>11</sup>. Gupta *et al.*<sup>12</sup> reported a similar phenomenon with tetracycline hydrochloride. Addition of Ni<sup>++</sup> or Zn<sup>++</sup> had little influence on the inhibitory action of SDS. It is possible that these two metals alter the micelle structure in such a way that its bactericidal action was not affected.

Though Ni and Mg have similar effects, the inhibitory zone produced by Ni + SDS was not distinctly sharp and well defined.

The authors thank Prof. N. Venkatasubramanian, Principal, Vivekananda College, for his encouragement and valuable suggestions and Dr. S. Venugopalan, Professor of Botany, for facilities provided.

One of the authors (P. S. R.) thanks the C.S.I.R. for the award of a Junior Research Fellowship.

July 10, 1980.

1. Baker, Z., Harrison, R. W. and Miller, B. F., *J. Exp. Med.*, 1941, 74, 621.
2. Shafa, F. and Salton, M. R. J., *J. Gen. Microbiol.*, 1960, 22, 137.
3. Davis, J. G. *et al.*, *Proc. Soc. Gen. Microbiol.*, 1949, 3, communication.
4. Hans Bode, Robert Earnst and Joseph Arditti, *Environ. Pollution*, 1978, 17, 175.
5. James, W. McBain in *Colloid Science*, D.C. Heath and Co., U.S., New York, 1950, p. 253.
6. Mukerjee, P. and Mysels, K. J., in *Critical Micelle Concentrations of Aqueous Surfactant Systems*, U.S. Govt. Printing Office, Washington, D.C., 1971.
7. Mitchell, P. D. and Crowe, G. R., *J. Gen. Microbiol.*, 1947, 1, 85.
8. Salton, M. R. J., *Ibid.*, 1951, 5, 391.
9. Kratochvil, S. *et al.*, *J. Colloid. Int. Face Science*, 1979, 72, 106.
10. Shinoda, K., *Bull. Chem. Soc., Japan*, 1955, 28, 340.
11. Bunton, C. A., *Reaction Kinetics in Micelles*, ed. E. H. Cordes, Plenum Press, N.Y., London, 1973, p. 73.
12. Gupta, R. P., Yadav, B. N., Tiwari, O. P. and Srivastava, A. K., *Inorg. Chem. Acta*, 1979, 32, L95.

## GRIGNARD REACTION ON 3,4-CYCLOHEXENO- AND 3,4-CYCLOPENTENO-COUMARINS

J. R. MERCHANT AND K. M. BAKRE

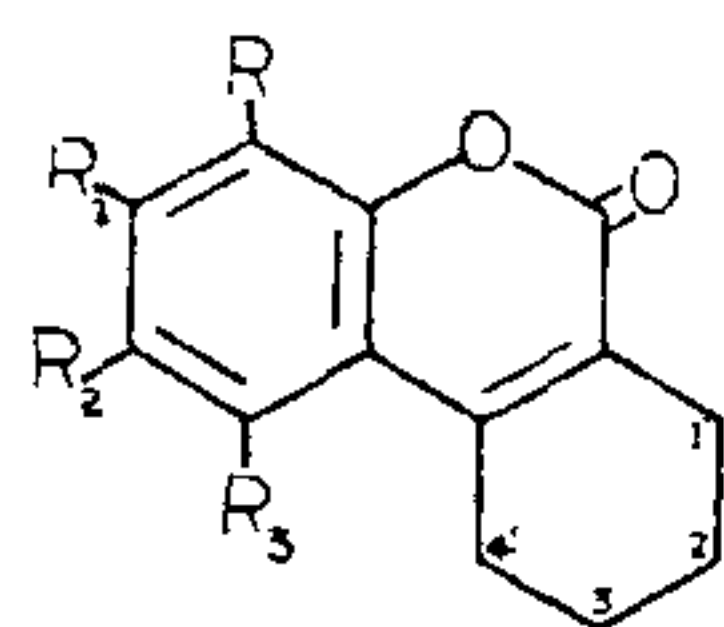
Department of Organic Chemistry  
Institute of Science, Bombay 400 032

In a project for the synthesis of compounds analogous to tetrahydrocannabinoids<sup>1,2</sup>, we studied the action of the Grignard reagent on 3,4-cyclohexeno- and 3,4-cyclopentenocoumarins. Not much work seems to have been done in this direction although the Grignard reaction on coumarins has been previously investigated to some extent<sup>3,4</sup>.

The starting materials, 3,4-cyclohexeno- and 3,4-cyclopenteno-coumarins were obtained by the Pechmann condensation of dimethylphenols with ethyl cyclohexanone- and ethyl cyclopentanone-2-carboxylates in the presence of sulphuric acid (80%). The 3,4-cyclohexenocoumarins and 3,4-cyclopenteno-coumarins so obtained had UV  $\lambda_{max}^{MeOH}$ : 220 nm (log  $\epsilon$  4.34), 275 nm (log  $\epsilon$  3.98) and 320 nm (log  $\epsilon$  3.99),

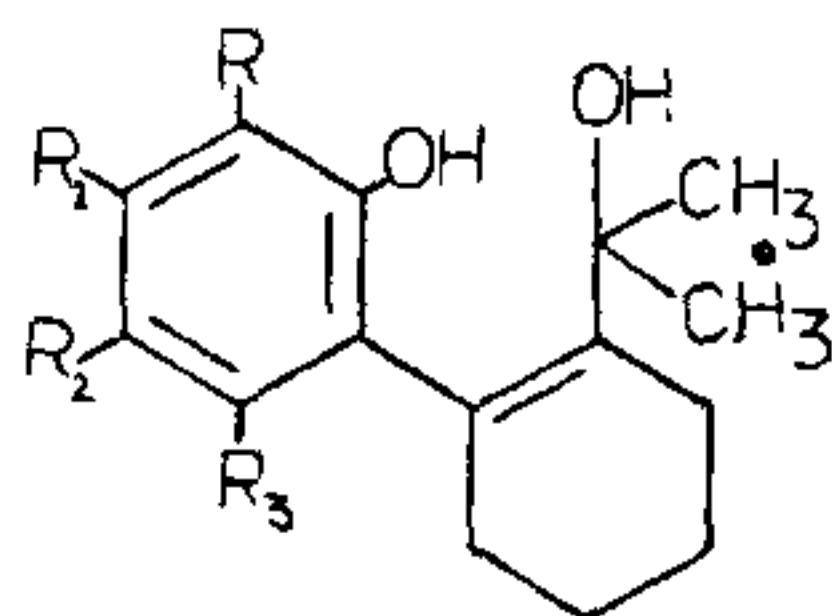
Whereas their IR showed the carbonyl frequency at around  $1700\text{ cm}^{-1}$ . The NMR spectrum ( $\text{CdCl}_2$ ,  $\delta$ ) of 6,7-dimethyl-3,4-cyclohexenocoumarin (Ic) integrated for sixteen protons and showed the following signals: 1.5 (m, 4H,  $-\text{CH}_2$  at  $\text{C}_3$  and  $\text{C}_4$ ), 2.2 (s, 6H, Ar- $\text{CH}_3$ ), 2.4 (m, 4H,  $-\text{CH}_2$  at  $\text{C}_1$  and  $\text{C}_2$ ) and 6.97-7.3 (d, 2H, aromatic).

The action of the Grignard reagent on the above coumarins was carried out as follows. The reagent [prepared from magnesium (0.166 mole) and methyl iodide (0.166 mole) in dry ether] was added to Ia in dry benzene and the mixture refluxed for 20 hr. On pouring the reaction mixture into ice and ammonium chloride, a colourless crystalline compound (IIa), m.p.  $104.05^\circ$ , was obtained in 30% yield. Its molecular composition was found to be  $\text{C}_{17}\text{H}_{24}\text{O}_2$  ( $M^+$  260). In the IR spectrum, the lactone band, which appeared at  $1700\text{--}1715\text{ cm}^{-1}$  in the coumarin was completely absent. Further, the spectrum showed an OH band at  $3512, 3385\text{ cm}^{-1}$ , whereas the



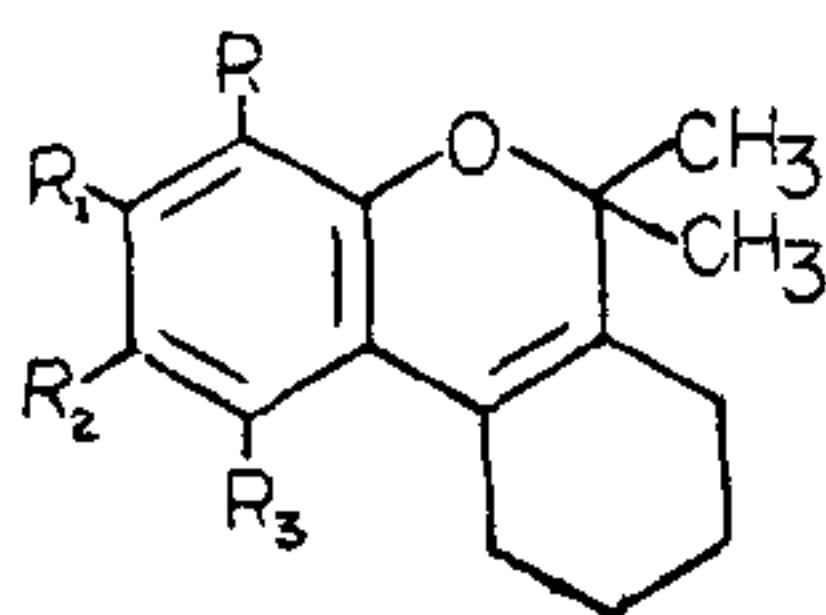
I

- (a)  $\text{R}=\text{R}_1=\text{CH}_3$ ;  
 $\text{R}_2=\text{R}_3=\text{H}$   
 (b)  $\text{R}=\text{R}_2=\text{CH}_3$ ;  
 $\text{R}_1=\text{R}_3=\text{H}$   
 (c)  $\text{R}_1=\text{R}_2=\text{CH}_3$ ;  
 $\text{R}=\text{R}_3=\text{H}$



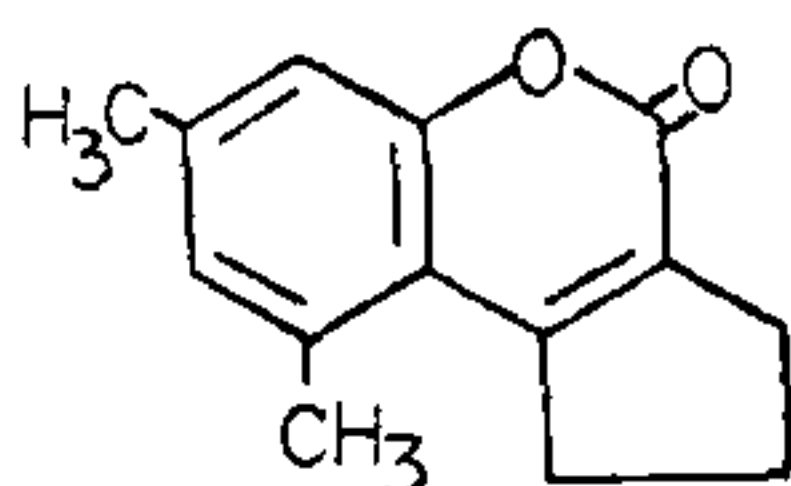
II

- (a)  $\text{R}=\text{R}_1=\text{CH}_3$ ;  
 $\text{R}_2=\text{R}_3=\text{H}$   
 (b)  $\text{R}=\text{R}_2=\text{CH}_3$ ;  
 $\text{R}_1=\text{R}_3=\text{H}$   
 (c)  $\text{R}_1=\text{R}_2=\text{CH}_3$ ;  
 $\text{R}=\text{R}_3=\text{H}$

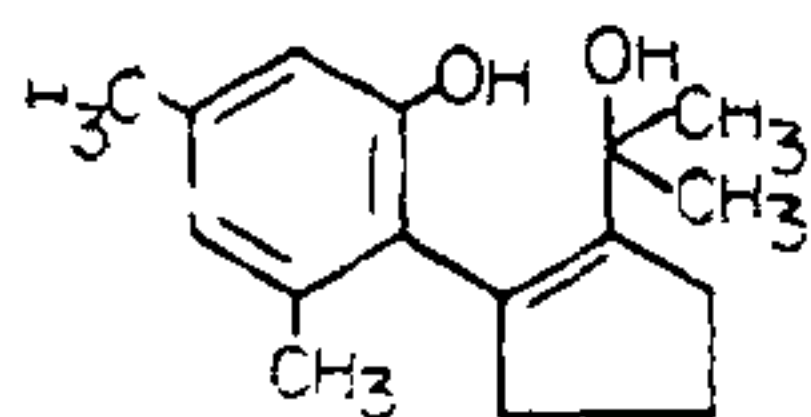


III

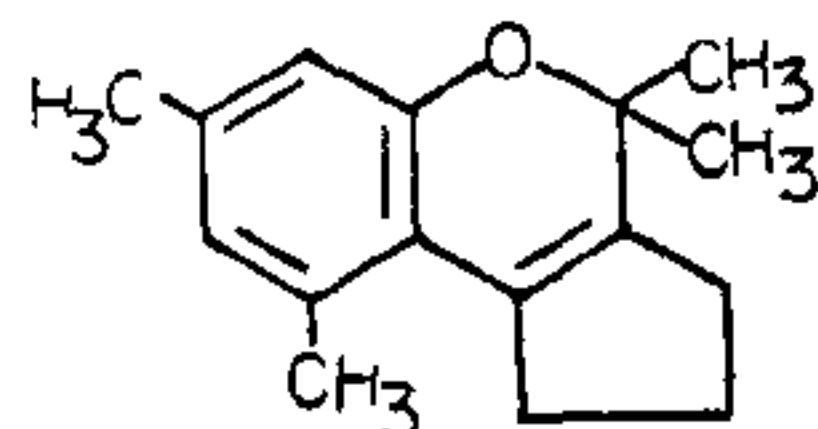
- (a)  $\text{R}=\text{R}_1=\text{CH}_3$ ;  $\text{R}_2=\text{R}_3=\text{H}$   
 (b)  $\text{R}=\text{R}_2=\text{CH}_3$ ;  $\text{R}_1=\text{R}_3=\text{H}$   
 (c)  $\text{R}_1=\text{R}_2=\text{CH}_3$ ;  $\text{R}=\text{R}_3=\text{H}$



IV



V



VI

$-\text{C}(\text{CH}_3)_2$  band appeared at  $1375$  and  $1360\text{ cm}^{-1}$  as a sharp doublet.

From the above spectral evidence, the compound was assigned the structure as 2-(3',4'-dimethyl-2'-hydroxyphenyl)-1-(1,1-dimethyl hydroxymethyl)-cyclohexene (IIa). This carbinol was found to be quite stable even after keeping for a long time at room temperature. On heating with phosphorous pentoxide in xylene it afforded a viscous oil (IIIa), b.p.  $195^\circ/5\text{ mm}$ . In the IR spectrum the hydroxyl band was found to be absent. Further, it showed bands at  $1605, 1440, 760$  (aromatic),  $1370$  and  $1350$  ( $-\text{C}(\text{CH}_3)_2$ )  $\text{cm}^{-1}$ . Its molecular composition was found to be  $\text{C}_{17}\text{H}_{22}\text{O}$  ( $M^+$  242). The compound was assigned structure as 3,4,6,6-tetramethyl-7,8,9,10-tetrahydro-6-dibenzopyran (IIIa).

The reaction also succeeds with 6,8-dimethyl- and 6,7-dimethyl-3,4-cyclohexeno-coumarins, to yield the carbinols (IIb, IIc) as oils, which were converted directly into 2,4,6,6-tetramethyl and 2,3,6,6-tetramethyl-7,8,9,10-tetrahydro-6-dibenzopyrans (IIIb, IIIc) with phosphorous pentoxide. The compound IIIb had b.p.  $205^\circ/5\text{ mm}$  and IIIc had b.p.  $215^\circ/5\text{ mm}$ .

The Grignard reaction also occurs with 5,7-dimethyl-3,4-cyclopentenocoumarin (IV) giving the carbinol (V) as an oil which without isolation was converted into 1,3,6,6-tetramethyl cyclopenta (C)-(1)-benzopyran (VI), b.p.  $185^\circ/5\text{ mm}$  in 30% yield.

It has been reported<sup>6</sup> that the Grignard reaction leads to 1,2- or 1,4-addition products depending upon the substituents on the coumarin ring, type of the Grignard reagent used and the reaction conditions employed. However, due to steric reasons, the 3,4-cyclohexeno- and 3,4-cyclopentenocoumarins undergo 1,2-addition only.

All compounds mentioned above gave satisfactory spectral and elemental data.

The authors are thankful to Unichem Research Laboratories Limited and Haffkine Institute, Bombay, for IR and NMR spectra.

August 18, 1980.

- Ghosh, R., Todd, A. R. and Wilkinson, S., *J. Chem. Soc.*, 1940, p. 1121.
- Adams, R. and Baker, B. R., *J. Am. Chem. Soc.*, 1940, **62**, 2405.
- Wawzonek, S., In *Heterocyclic Compounds*, eds. R. C. Elderfield, John Wiley and Sons, Inc., New York, 1951, **2**, 204.
- Heilbron, I. M. and Hill, D. W., *J. Chem. Soc.*, 1927, p. 2005.
- Barnes, C. S., Stroug, M. I. and Occolowitz, J. L., *Tetrahedron*, 1963, **19**, 839.