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Physical Sciences Section

Pakistan J. Sci. Ind. Res., Vol. 14, Nos. 1-2, February-April 1971

COMPARATIVE STUDIES OF PROTON MAGNETIC RESONANCE OF SOME ISOCOUMARINS AND ISOCARBOSTYRYL-4-CARBOXYLIC ACID. PART I

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(Received October 23, 1970)

The PMR studies of isocoumarin-4-carboxylic acid (I), methyl isocoumarin-4-carboxylate (II), 7-methoxy-isocoumarin-4-carboxylic acid (III), methyl 7-methoxy isocoumarin-4-carboxylate (IV), 7-methoxy-3,4-dihydro-isocoumarin (V), 6,8-dimethoxy isocoumarin (VI) and isocarbostyryl-4-carboxylic acid (VII) have been described.

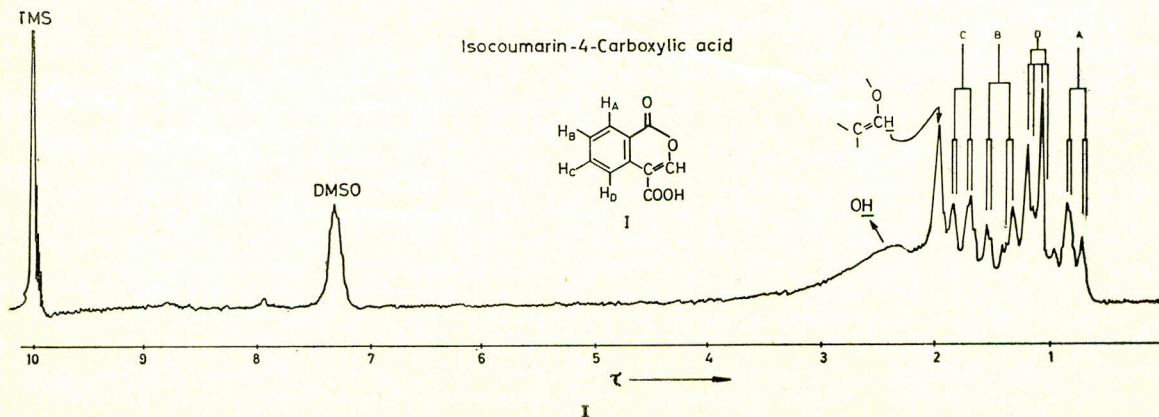
The general methods of syntheses of isocoumarins have been well established by different workers.¹ However, there is no data available to date on their proton magnetic resonance. As quite a few of the isocoumarins prepared by one of us were available, it was felt of interest to undertake their PMR studies, particularly of the coupling constants in the benzenoid region and to record their UV and IR absorption. All the compounds were recorded in DMSO (d₆), except in one case where the use of CDCl₃ could not be avoided to study the solvent effect of such a polar and strongly hydrogen bonded solvent.

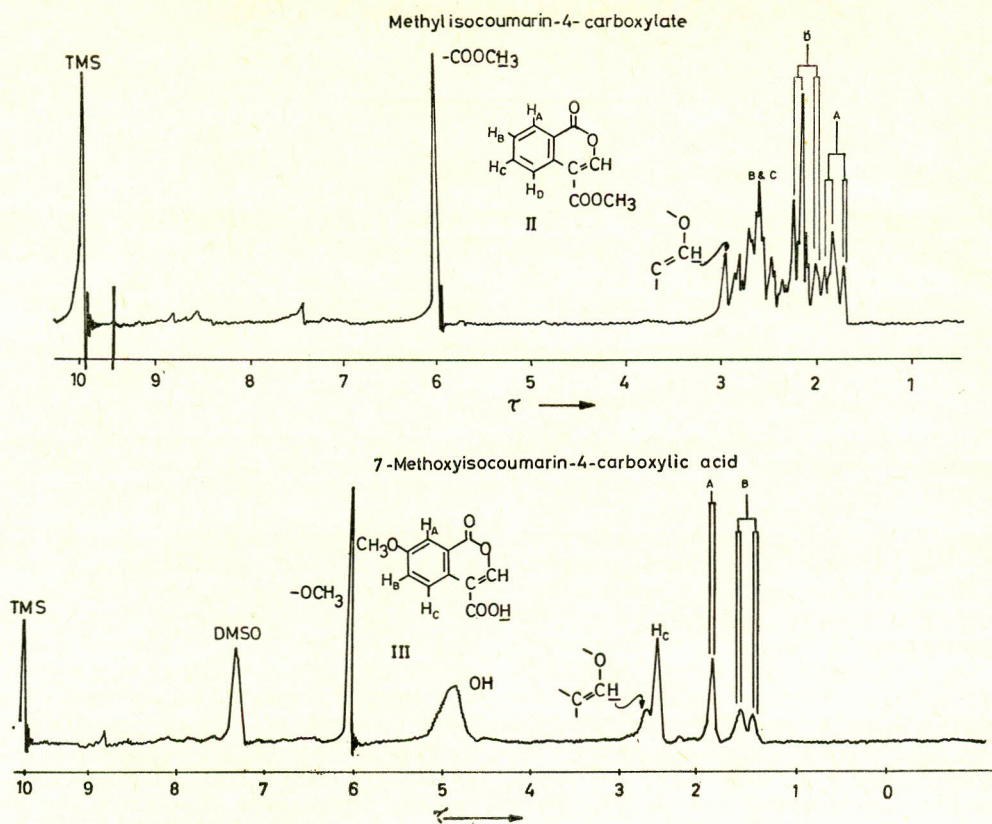
The PMR spectra of isocoumarin-4-carboxylic acid (I) (in DMSO d₆) showed very fine splitting between the aromatic protons H_A, H_B, H_C and H_D. The H_A proton showed a double doublet at τ 0.76 with *ortho* and *meta* coupling (J 8 c/s and 2 c/s respectively) with H_B and H_C. As expected the chemical shift of H_A appeared at a low value due to the presence of the carbonyl group in the vicinity. The proton H_D appeared at τ 1.11 as an ill-defined double doublet with its *ortho* coupling with H_C well established (J 8 c/s).

The remaining two protons H_B and H_C showed a double doublet centred at τ 1.40 and τ 1.76 with the coupling constant of 8 and 2 c/s for *ortho* and *meta* orientations of these protons. The olefinic proton in ring B showed a sharp singlet appearing at τ 1.9 and finally the hydroxyl proton of the carboxyl group which showed up as a broad hump centred at τ 2.48 completed the PMR picture of isocoumarin-4-carboxylic acid (I).

The UV absorption band appeared at λ_{max} 320 nm (ϵ 5648) with shoulders at 270 nm (ϵ 7949) and 244 nm (ϵ 13380). With a drop of base it showed a slight bathochromic shift with bands at λ_{max} 324 nm (ϵ 4273) and 265 nm (ϵ 6134). The original spectrum was regained with a drop of acid. Its IR spectrum Nujol showed strong absorption bands at 3356 OH cm⁻¹, 3077 cm⁻¹, 2778 cm⁻¹, and 1686 cm⁻¹ carboxyl >CO. The rest of the supporting bands appeared at 1634, 1493, 1473, 1387, 1350, 1316, 1277, 1181, 1161, 1064, 1036, 1009, 894.5, 802.6, 788, 751.9 and 689.7 cm⁻¹.

The PMR spectrum of methyl isocoumarin-4-carboxylate (II) showed a sharp singlet at τ 6.2





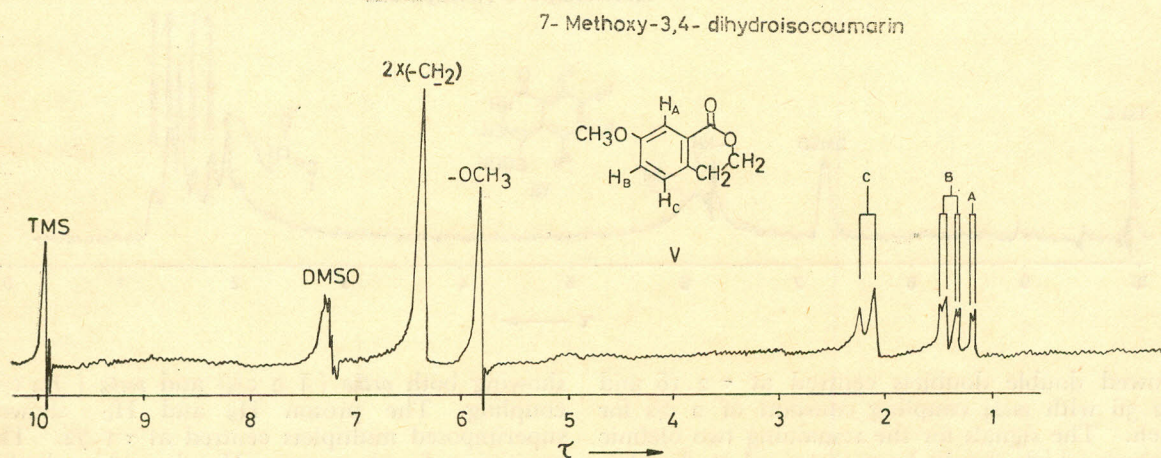
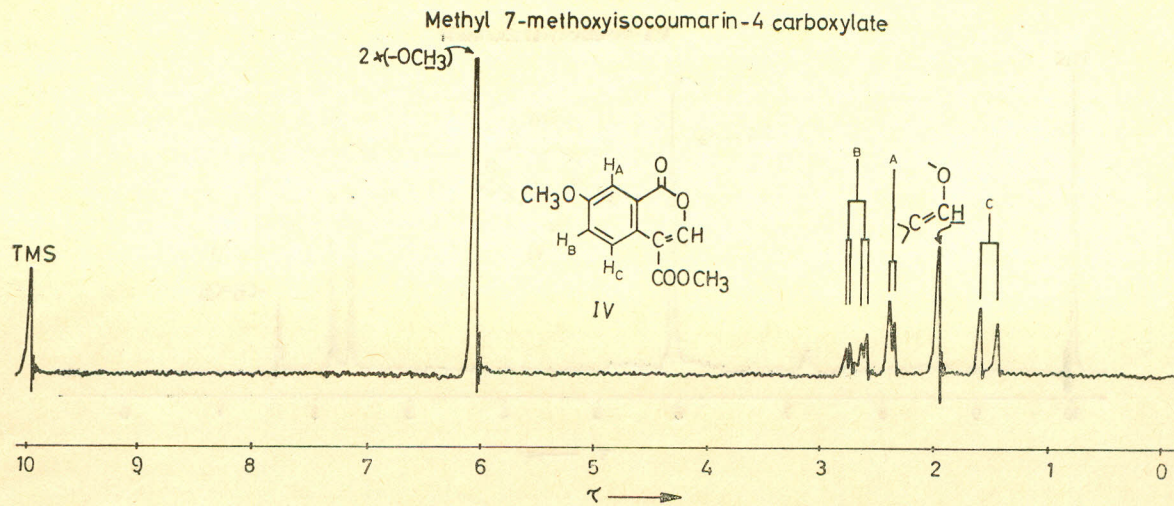
(3H) for $-\text{OCH}_3$ of the ester group. The olefinic proton appeared at $\tau 3.0$ (1H). The rest of the benzenoid protons appeared between the region $\tau 1.65$ and $\tau 2.85$. The H_A proton showed a double doublet centred at $\tau 1.82$ with *ortho* and *meta* coupling ($J 8$ c/s and 2 c/s respectively). The proton H_D also showed a double doublet centred at $\tau 2.2$ with the same coupling constants ($J 8$ and 2 c/s) as was observed for proton H_A . Proton H_B and H_C showed complex multiplets centred at $\tau 2.55$ for the two protons. This region was not very well resolved.

The UV absorption band showed λ_{max} at 310 nm ($\epsilon 3396$), 272 nm ($\epsilon 5568$), 264 nm ($\epsilon 4929$) and shoulder at 238 nm ($\epsilon 9982$). With a drop of base it showed a sharp band at 268 nm ($\epsilon 7527$). Its IR spectrum (Nujol) showed a strong absorption band (for ester) at 1748 cm^{-1} . The rest of the bands appeared at 1623 , 1502 , 1490 , 1468 , 1431 , 1342 , 1314 , 1290 , 1248 , 1138 , 1052 , 1026 , 1000 , 888.9 , 850.3 , 816 , 789 and 689.7 cm^{-1} .

The PMR spectrum of 7-methoxy isocoumarin-4-carboxylic acid (III) in DMSO showed a sharp singlet at $\tau 6.1$ (3H) for the $-\text{OCH}_3$. Then there was a broad hump centred at $\tau 4.8$ for the hydroxyl proton of the carboxyl group. In the lower region there was an ill-defined double doublet centred at $\tau 1.56$ for H_B proton of the benzene ring showing

ortho and *meta* coupling ($J 7$ and 2 c/s respectively). The proton H_A showed a weak coupling ($J 1.5$ c/s) due to *meta* orientation centred at $\tau 1.98$. The proton H_C and the olefinic proton of the ring B although overlapped could be distinguished at $\tau 2.6$ and $\tau 2.64$ respectively. Its UV showed λ_{max} 335 nm ($\epsilon 4494$), 276 nm ($\epsilon 6662$), 267 nm ($\epsilon 7256$) which showed a bathochromic shift with a drop of base at 339 nm ($\epsilon 4484$), 275 nm ($\epsilon 4502$), and 267 nm ($\epsilon 4586$). The original spectrum was regained on the addition of a drop of acid absorption bands. IR spectrum (Nujol) showed at 3356 , 2941 , 2632 and 1709 cm^{-1} (acid carbonyl). The benzenoid ring stretching bands appeared at 1600 and 1580 cm^{-1} . The rest of the out-of-plane bands appeared at 1504 , 1445 , 1404 , 1342 , 1285 , 1274 , 1250 , 1212 , 1190 , 1136 , 1062 , 1029 , 1012 , 889 , 845 , 803 and 778 cm^{-1} .

The PMR spectrum of methyl 7-methoxyisocoumarin-4-carboxylate (IV) in DMSO showed a singlet appearing at $\tau 6.05$ (3H) accounting for the protons of *O*-methyl ether. Then there was a double doublet for H_B centred at $\tau 2.75$ with *ortho* and *meta* coupling with protons H_C and H_A ($J 7$ and 2.2 c/s respectively). A double doublet centred at $\tau 2.38$ with the coupling constant of 2 c/s accounted for H_A . There was a sharp singlet appearing at $\tau 2.0$ for the olefinic proton of the



ring B. The proton H_C of the benzene ring showed a doublet centred at $\tau 1.54$ showing *ortho* coupling with proton H_B ($J 8$ c/s).

The UV absorption spectra showed λ_{\max} 275 nm ($\epsilon 8482$) and 250 nm ($\epsilon 9988$). With a drop of base it showed one sharp band λ_{\max} at 270 nm ($\epsilon 18270$) which regained the original absorption bands by a drop of acid. Its IR spectrum (Nujol) showed a sharp band at 1739 cm^{-1} for the carbonyl of ester group. The benzenoid stretching bands appeared at 1610 and 1575 cm^{-1} . The rest of the bands appeared at 1511 , 1471 , 1379 , 1351 , 1307 , 1284 , 1272 , 1250 , 1232 , 1220 , 1183 , 1139 , 1062 , 1029 , 909 , 897 , 875 , 853 , 818 and 790 cm^{-1} .

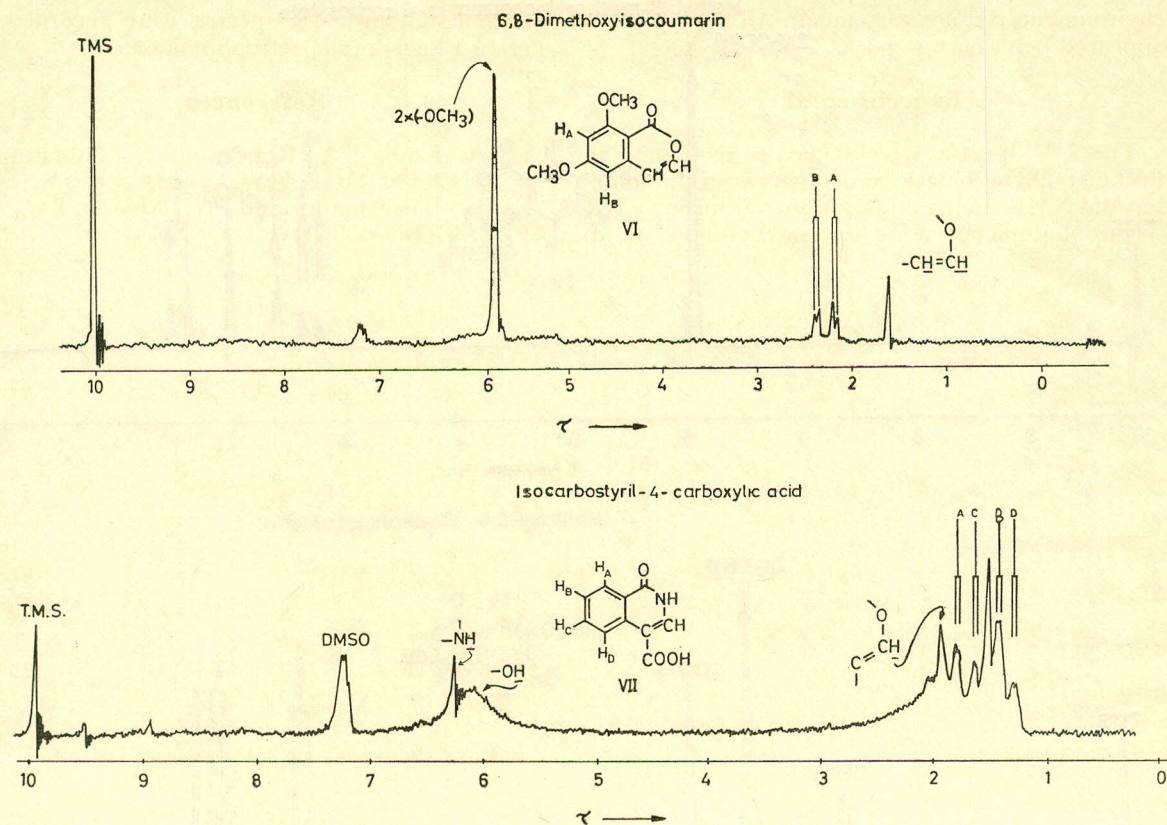
The PMR spectra of 7-methoxy-3,4-dihydroisocoumarin (V) in DMSO showed unexpectedly a sharp singlet at $\tau 6.34$ for 4 protons due to two methylene groups although they should have shown double triplets. The signals for the protons of $-\text{OCH}_3$ appeared at $\tau 5.9$ (3H).

The benzenoid region showed very fine splitting for protons H_A , H_B and H_C . The signal for the

proton H_A appeared as a doublet centred at $\tau 1.32$ with coupling constant of 2 c/s due to its coupling with the proton H_B . The signal for proton H_B *meta* to H_A and *ortho* to H_C appeared as a double doublet centred at $\tau 1.5$ with coupling constants of 2 and 8 c/s respectively. The signal for the proton H_C showed up at $\tau 2.25$ as a doublet with coupling constant of 8 c/s for its *ortho* coupling with the proton H_B .

The UV absorption spectrum showed λ_{\max} 276 nm ($\epsilon 1352$) and 248 nm ($\epsilon 1495$) which showed a hypsochromic shift with a drop of base and λ_{\max} 270 nm ($\epsilon 2030$). Its IR spectrum (Nujol) showed absorption band at 1718 cm^{-1} ($\text{C}=\text{O}$), 1618 and 1587 cm^{-1} (for benzenoid stretching) and the supporting bands appeared at 1504 , 1471 , 1377 , 1337 , 1295 , 1266 , 1250 , 1190 , 1142 , 1053 , 1035 , 1018 , 1010 , 906 , 893 , 885 , 875 , 870 , 840 , 790 and 940 cm^{-1} .

The PMR spectrum of 6,8-dimethoxyisocoumarin (VI) DMSO showed a sharp singlet centred at $\tau 5.92$ (6H) for the protons of the two OCH_3 groups. The benzenoid protons H_A and H_B



showed double doublets centred at τ 2.16 and τ 2.36 with *meta* coupling constant of 2 c/s for each. The signals for the remaining two olefinic protons which should have appeared as doublets appeared as a singlet at τ 1.6 (2H). This was quite parallel to the case of 7-methoxy-3,4-dihydroisocoumarin (V), in which the signals for the four protons on carbons 3 and 4, appeared as a singlet at τ 6.34 (4H) instead of appearing as two triplets.

The UV absorption spectrum showed λ_{\max} 278 nm (ϵ 6612), 268 nm (ϵ 8108), 255 nm (ϵ 10220) and 234 nm (ϵ 17230). All these fine maximas collapsed with a drop of base and showed one band at λ_{\max} at 270 nm (ϵ 12900). Its IR spectrum (Nujol) showed absorption bands at 1724 cm^{-1} for carbonyl group of the isocoumarin ring. The benzenoid ring stretching bands appeared at 1618 and 1577 cm^{-1} . The rest of the supporting bands for CH and C—CH₃ appeared at 1504 , 1385 , 1386 , 1307 , 1253 , 1235 , 1217 , 1170 , 1111 , 1070 , 1031 , 945 , 883 , 865 , 847 and 791 cm^{-1} .

The PMR spectrum of isocarbostyryl-4-carboxylic acid² (VII) in DMSO showed a broad hump at τ 6.3 (1H) and τ 6.1 (1H) for the two protons in CONH— and COOH groups. The olefinic proton appeared at τ 2.1. The benzenoid proton H_A showed a double doublet centred at τ 1.76,

showing both *ortho* (J 9 c/s) and *meta* (J 2 c/s) coupling. The proton H_B and H_C showed superimposed multiplets centred at τ 1.72. The remaining fourth proton H_D showed a double doublet at τ 1.6, showing both *ortho* and *meta* coupling (J 9 and 2 c/s respectively).

The UV absorption showed λ_{\max} 308 nm (ϵ 3309), 267 nm (ϵ 3445) and 258 nm (ϵ 4619). The sharp band at 308 nm was due to the presence of imido system in the molecule. It showed a sharp band at λ_{\max} at 277 nm (ϵ 20240) indicating the collapse of all the four bands as observed in the compounds reported earlier. It had hardly any effect with drop of an acid. Its IR absorption (Nujol) bands showed a band at 1723 cm^{-1} for $>\text{CO}$ of —CONH. The other carbonyl vibrations appeared at 1650 cm^{-1} . The benzenoid stretching bands appeared at 1608 and 1585 cm^{-1} . At higher wave numbers there were sharp bands at 3360 and 3095 cm^{-1} for —NH group.

The above study has clearly demonstrated that, in DMSO as a solvent, the PMR spectra of the isocoumarins in the benzenoid region were nicely resolved and show up the *ortho* and *meta* coupling constants unambiguously. It was not possible to record the coupling between *para* protons. However, the chemical shift of these protons in different

environments did not vary much. All these protons appeared between τ 1-3.

Experimental

The UV spectra were taken in methanol on Beckman DB automatic recording spectrophotometer and NMR on high resolution varian 60 NMR spectrophotometer, using tetramethylsilane as an

internal standard. IR spectra were recorded on Perkin-Elmer 137 spectrophotometer.

References

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