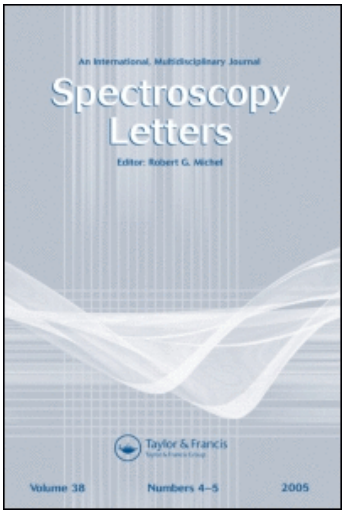

Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Structure and Conformation of Novel Derivatives of Chromanone: ^{1}H NMR, ^{13}C NMR and 1D-NOE Difference Spectroscopic Study of 8-(3'-Methyl - but - 2' - en -1' - oyl) - 7 - hydroxy - 2,2,5 -trimethyl chromanone

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To cite this Article Vijayalakshmi, C. S. , Prasad, K. Rajendra and Sur, Sandip K.(1991) 'Structure and Conformation of Novel Derivatives of Chromanone: ^{1}H NMR, ^{13}C NMR and 1D-NOE Difference Spectroscopic Study of 8-(3'-Methyl - but - 2' - en -1' - oyl) - 7 - hydroxy - 2,2,5 -trimethyl chromanone', Spectroscopy Letters, 24: 3, 389 — 396
To link to this Article: DOI: 10.1080/00387019108020664
URL: http://dx.doi.org/10.1080/00387019108020664

SPECTROSCOPY LETTERS, 24(3), 389-396 (1991)

STRUCTURE AND CONFORMATION OF NOVEL DERIVATIVES OF CHROMANONE : ^{1}H NMR, ^{13}C NMR AND 1D-NOE DIFFERENCE SPECTROSCOPIC STUDY OF 8-(3'-METHYL - BUT - 2' - EN - 1' - OYL) - 7 - HYDROXY - 2,2,5 - TRIMETHYL CHROMANONE

KEYWORDS : 8-(3'-Methyl - but - 2' - en - 1' - oyl) - 7 - hydroxy -2,2 - dimethyl-2H-chromanone, 8-(3'-Methyl - but - 2' - en - 1' - oyl) - 7 - hydroxy -2,2,5 - trimethyl-2H-chromanone, Structure elucidation, ^{1}H NMR, ^{13}C NMR, NOE, Molecular Mechanics.

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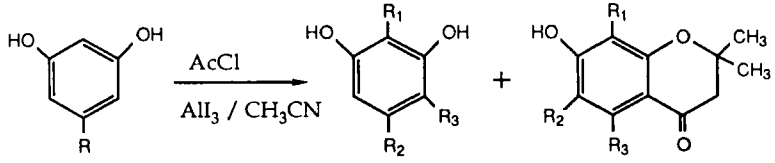
ABSTRACT

Elucidation of the structure and conformation of a hitherto unknown novel derivative of chromanone, 8-(3'-Methyl - but - 2' - en - 1' - oyl) - 7 - hydroxy - 2,2,5 - trimethyl-2H-chromanone, obtained as a byproduct in the Friedel-Crafts acylation of active phenolic compounds by NMR methods is reported. A combination of the 1D-NOE difference spectroscopy and Molecular Mechanics calculation was used to assign the conformation of the title compound.

INTRODUCTION

Taylor *et al* [1] isolated 3'-methyl-but-2'-en-1'-oyl derivative of chromone from plant material *Spathelia sorbifolia L* and it was shown that the existence of such compounds are possible biogenetically. Generally, Friedel-Crafts acylation of phenols with 3,3-dimethylacrylic acid or its chloride yield cyclized products, chromanones, rather than uncyclized products [2-4]. We have recently reported the synthesis of an uncyclized product namely, 1-(2',4'-dihydroxy phenyl)-3-methyl-but-2-en-1-one in 90% yield from the reaction of resorcinol with 3,3-dimethylacrylic acid in the presence of anhydrous aluminium chloride and phosphoryl oxy chloride [5]. However, the same reaction using orcinol and phloroglucinol instead of resorcinol resulted in cyclized product [5]. Much interest centers around these compounds because these are stable intermediates for the synthesis of 2,2-dimethyl-2H-chromenes [6,7], pyranoflavones [8,9] and pyranochromones [9,10]. Hence, it is apparent that there is no reagent hitherto known which is general and effective for the synthesis of 1-aryl-3-methyl-but-2-en-1-one derivatives. It was felt that anhydrous aluminium iodide could be utilized for this purpose and accordingly, resorcinol was reacted with 3,3-dimethyl acryloyl chloride in the presence of anhydrous aluminium iodide in acetonitrile. The products formed were identified as the 1-aryl-3-methyl-but-2-en-1-ones, **1** and **2**, and 8-(3'-methyl-but-2'-en-1'-oyl) derivative of 2,2-dimethyl-2H-chromanone **3**. A similar reaction of orcinol resulted in a mixture of 1-aryl-3-methyl-but-2-en-1-ones, **5** and **6**, and a trace of chromanone **8** (Scheme I).



Resorcinol R = H
Orcinol R = CH_3

Ac = -CO-CH=C(CH_3)$_2$

1 $R_1 = R_2 = H$, $R_3 = Ac$
2 $R_1 = Ac$, $R_2 = R_3 = H$
3 $R_1 = Ac$, $R_2 = R_3 = H$
4 $R_1 = R_3 = H$, $R_2 = Ac$
5 $R_1 = H$, $R_2 = CH_3$, $R_3 = Ac$
6 $R_1 = Ac$, $R_2 = H$, $R_3 = CH_3$
7 $R_1 = H$, $R_2 = Ac$, $R_3 = CH_3$
8 $R_1 = R_2 = H$, $R_3 = CH_3$

Scheme I

Nuclear Overhauser Effect (NOE), particularly the 1D-NOE difference spectroscopy has been used successfully to elucidate structure and conformation of a variety of synthetic and biosynthetic compounds [11]. The homonuclear cross-relaxation rates *via* dipolar coupling between two spins separated by a distance r are normally governed [11] by the sixth-power of the internuclear distances, r^6. In the present study, we report the study of the structure and conformation of 8-(3'-Methyl - but - 2' - en - 1' - oyl) - 7 - hydroxy - 2,2 - dimethyl-2H-chromanone, 3 and 8-(3'-Methyl - but - 2' - en - 1' - oyl) - 7 - hydroxy - 2,2,5 - trimethyl-2H-chromanone, 6, by proton 1D-NOE difference spectroscopy and Molecular Mechanics calculation [12]. The compound 6 has also been characterized by ^{13}C-NMR and IR spectroscopy.

EXPERIMENTAL

Reagent-grade resorcinol, orcinol and 3,3-dimethyl acrylic acid were purchased from SISCO, India and were used as received. Aluminium iodide was prepared according to a published procedure [13]. The solvents, acetonitrile and petroleum ether, were purified by standard procedure. The chloroform-d was obtained from Aldrich. All reactions were carried out under nitrogen atmosphere.

^{1}H-NMR spectra were recorded in $CDCl_3$ either at 100 MHz on a Varian XL-100 spectrometer or at 300 MHz on a General Electric QE-300 spectrometer using tetramethyl silane (TMS) as an internal standard. The ^{13}C-NMR and proton NOE experiments were conducted on a General Electric QE-300 spectrometer with TMS as an internal standard. For the NOE experiments, following parameters were used: proton 90^0 pulse-width 11 μs; 16 k data points; data acquisition time for each FID 1.36 sec and irradiation time 3 sec. The decoupler was turned off for 100 ms prior to the application of the rf pulse in order to avoid any decoupling and Bloch-Siegert shifts. A control spectrum with irradiation at a frequency far removed from the frequency of the peaks of interest was subtracted from the intensity enhanced spectrum in order to obtain the NOE difference spectrum [11]. The irrdiated peak appears inverted in the final spectrum. All measurements were done at room temperature (~ 295 K). Samples were excluded of oxygen by degassing thoroughly before NOE experiments were performed.

IR spectra were measured in nujol or as KBr wafer on a Perkin-Elmer 237 spectrophotometer or on a Nicolet 5DXB FT-IR spectrometer.

Molecular mechanics (MM2) calculations were carried out on a Tektronix 4211 graphic terminal attached to a Vax 8800 computer using the program MACROMODEL (version 1.5) obtained from the Columbia University, N. Y. The conformations with lowest

TABLE 1. ^1H NMR Spectral Data of Compounds 3 and 6.

Compound	$C_2(CH_3)_2$	C_3-2H	Chemical Shift, δ ppm (J, Hz) C_5-R	C_6-H	C_7-OH	$C_{2'}(CH_3)_2$	$C_{3'}$-H
3	1.50 s	2.80 s	7.90 (R =H) d, J =10	6.40 d, J=10	13.40 s	2.00 & 2.20 two s	6.80 s
6	1.45 s	2.72 s	1.94 (R=CH_3) s	6.39 s	12.07 s	2.21 & 2.25 two s	6.24 s

energy were obtained by iteratively minimizing the total steric energy of each conformation.

RESULTS AND DISCUSSION

The Friedel-Crafts acylation of resorcinol with 3,3-dimethyl acryloyl chloride in the presence of anhydrous aluminium iodide in acetonitrile afforded 3 as one of the by-products. A similar reaction using orcinol in place of resorcinol gave 6 as a by-product.

The compounds 3 and 6 have been characterized by ^1H and ^{13}C-NMR, IR and Mass spectroscopies. TABLE 1 lists the ^1H-NMR spectral data of 3 and 6 with the assignment of the chemical shifts. Figure 1 shows the broadband noise-decoupled ^{13}C-NMR of 6 in $CDCl_3$. The ^{13}C chemical shifts (δ, ppm) have been assigned as follows:

Carbonyl,	197.62 ;
α,β - Unsaturated carbonyl,	193.99 ;
Aryl,	160.02, 159.24, 155.72, 148.47, 126.36, 123.46 ;
Olefinic,	110.12, 105.05 ;
CH_2,	79.22 ;
Ar-CH_3,	47.98 ;
$C_{2'}(CH_3)_2$	27.98, 26.60 ;
$C_2(CH_3)_2$	22.76, 20.87

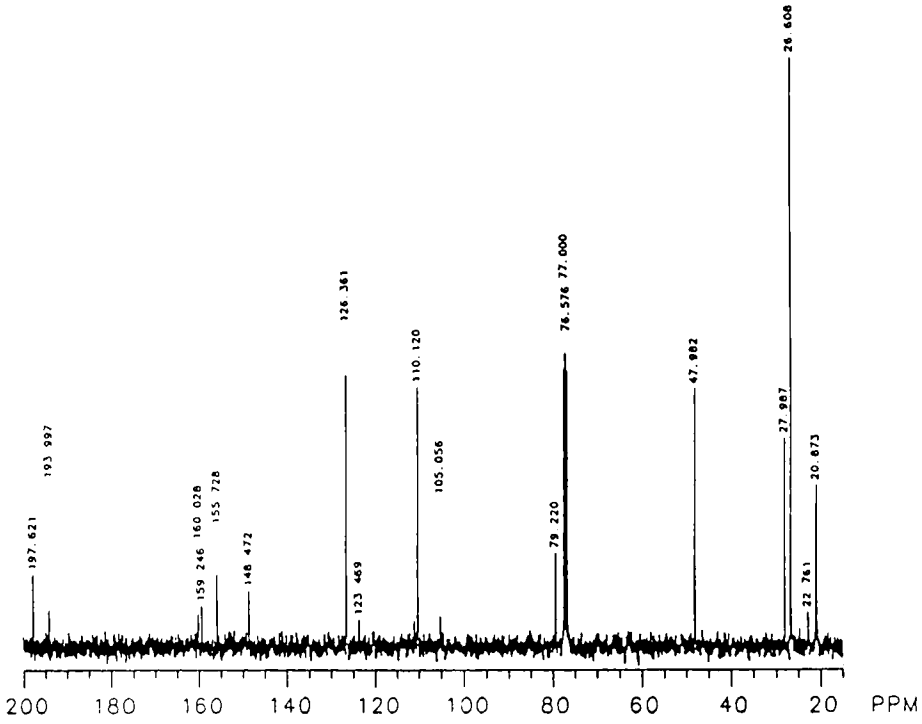


Figure 1. Broadband Proton Noise-decoupled ^{13}C NMR of 6.

The IR of 3 shows bands at 3350 (s, OH stretch), 1670 (s, free C=O) and 1630 cm^{-1} (s, α,β - unsaturated C=O). The corresponding IR bands of 6 appear at 3350 (s, OH stretch), 1666 (s, free C=O) and 1628 cm^{-1} (s, α,β - unsaturated C=O).

The structures of 3 and 6 were elucidated in the following way. It has been reported that the C-8 of flavanones and chromanones is more reactive than C-6 towards an electrophile [14]. The ^1H-NMR of 3'-methyl- but- 2'-en-1'-oyl derivative of chromanone shows an ortho coupling constant of $J_{5,6}$ = 10 Hz, providing evidence that the protons attached to C-5 and C-6 are probably adjacent to each other. On this basis, the alternative structure 4 for the product may be ruled out. We have, therefore, assigned the structure 3, 8-(3'- methyl- but-2'- en-1'-oyl)-2,2- dimethyl-2H-chromanone to the product obtained with resorcinol. In the case of compound 6, three-bond ortho-

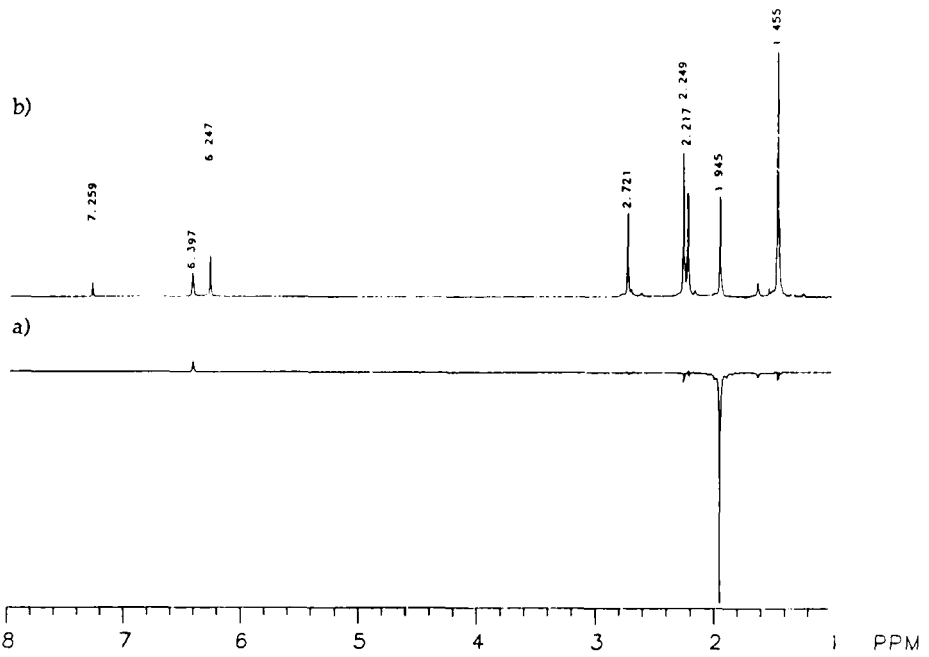
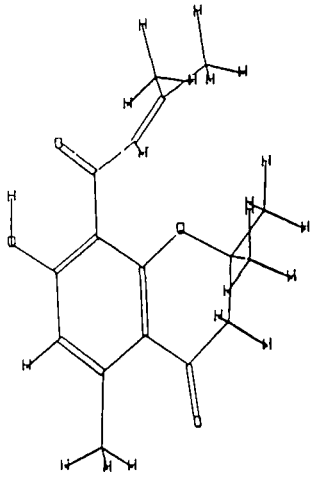


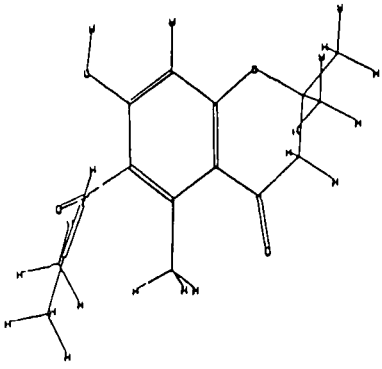
Figure 2. a) Proton 1D-NOE Difference Spectrum of **6**
b) Normal Proton NMR Spectrum of **6**

coupling would not arise since in this case C-5 is occupied by a methyl group. It is, therefore, difficult to differentiate between the two possible structures, **6** and **7**, from ^{1}H-NMR spectral evidence alone since both ring-protons (H_6 and H_8) will resonate more or less at the same frequency [6].

Figure 2 shows the homonuclear proton 1D-NOE difference spectrum of **6**, obtained by irradiating the C-5 methyl protons at 1.94 ppm. The ring-proton peak (δ 6.39) at C-6 is seen to enhance (4.8%) in intensity [15]. Irradiation of the peak at δ 6.39 produces an enhancement (5.0%) of the corressponding peak at 1.94 ppm. Further support to the structure **6** for the product has been obtained from the molecular mechanics (MM2) calculations. Figure 3 depicts the two possible structures, **6** and **7**, for the product. The MM2 calculations predict the structure **6** to be the one with lowest steric energy (E = 20.35 kcal mol^{-1}). The distance between the C-5 methyl protons and the ring-proton at C-6 has been estimated to be 2.31 A [16]. Structure **7**,



6



7

Figure 3. Lowest Energy Conformations of the Two Possible Structures of The 3'- methyl- but-2'- en-1'-oyl Derivative of Chromanone.

on the other hand is 5.56 kcal mol^{-1} higher in energy than the structure **6**. In structure **6**, the conformation with the C=O group of the acryloyl substituent facing the OH proton has lower energy as compared to the conformation in which the C=O group is close to the oxygen of the chromanone ring. This conformation of **6** has been supported by the observation of the H-bonding[17] of the OH proton with the C=O group in the IR (ν_{OH} = 3350 cm^{-1}) and ^{1}H-NMR (δ_{OH} = 12.07 ppm) spectra[6]. This H-bonding is expected because of the repulsive force that exists between the carbonyl oxygen and the oxygen of the chromanone ring in the alternative conformation. In the lowest-energy conformation of **7**, steric hindrance probably makes H-bonding difficult to form.

ACKNOWLEDGEMENT

We are thankful to CSIR, New Delhi, India for the award of a senior research fellowship to one of us (CSV).

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15. Irradiation at 6.24 ppm in the spectrm of **6** failed to show any enhancement in the intensity of the methyl protons at 1.94 ppm. This peak at 6.24 ppm has, therefore, been assigned to the olefinic proton.
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17. In **6**, the distance between the OH proton and the oxygen of the C=O group is ~2.03 A on the basis of the iterative MM2 calculation.

Date Received: 09/27/90
Date Accepted: 11/15/90