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Spectral Analysis of Some 3,6-Disubstituted-2 (3H)-Benzoxazolones

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Abstract: *A number of 6-acyl-3-substituted 2 (3H)-benzoxazolenes have been synthesized by Mannich reaction, using 6-(4-chlorobenzoyl)--2(3H) benzoxazolone and some substituted piperidine and their chemical structures have been identified by means of their IR, ^{13}C-NMR, Mass spectroscopic data and elementary analysis.*

Keywords : *^{13}C-NMR and Mass Spectra, Determination Mannich Bases of 2 (3H)-Benzoxazolones by using spectroscopic data.*

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Bazı 3,6-Disübstitüe 2 (3H)-Benzoksazolonların Spektral Analizleri

Özet: *6-(4-klorobenzoil)-2 (3H)-benzoksazolon ile sübstitüe piperidin türevlerinin Mannich reaksiyonu kullanılarak 6-açil-3,6-disübstitüte 2(3H)-benzoksazolon türevleri sentez edilmiş ve bileşiklerin kimyasal yapıları IR, ^{13}C-NMR, kütle spektrometrisi ve eleman analizleri ile kanıtlanmıştır.*

Anahtar Kelimeler : *^{13}C-NMR ve Kütle Spektrası, Spektroskopik veri kullanılarak 2(3H)-Benzoksazolon'un Mannich bazlarının tayini.*

Introduction

Antibacterial, antifungal, anticonvulsant, analgesic, antiinflammatory and hypnotic activities of benzoxazolones and their derivatives have been reported in the literature[1-5]. Different substituents on the N atom of benzoxazolone ring cause different biological activities[6,7]. In our previous work[8-11], some new Mannich bases of 6-acyl-2 (3H)-benzoxazolones were synthesized and their microbiological and pharmacological activities were tested. UV, IR and ^{1}H-NMR spectral methods were used for the determination of the chemical structures. In this study, four new 6-acyl-3-substituted 2 (3H)-benzoxazolone derivatives were prepared by using Mannich reaction and the structure of each product was determined by ^{13}C-NMR and Mass Spectrometer.

Material and Methods

Apparatus and Reagent: 2(3H)-benzoxazolone (Aldrich), piperidine(Merck), 3-methyl, 4-methyl and 3,4-dimethyl piperidine(Aldrich), polyphosphoric acid(Merck), p-chlorobenzoic acid(Aldrich) were purchased. Melting points were determined on a Thomas Hoover Apparatus and uncorrected. Mass spectra were recorded on a V6 16F Mass spectrometer with V6 data system 2000.

Chemistry

a) 6-(4-Chlorobenzoyl)-2(3H)-benzoxazolone

The title compound was prepared by treating 2 (3H)-benzoxazolone and p-chlorobenzoic acid in presence of polyphosphoric acid according to the method reported earlier[11].

b) General method of synthesis of Mannich bases

A mixture of 0.01 mole of substituted piperidine, 0.01 mole of 6-(4-chlorobenzoyl)-2(3H)-benzoxazolone and 0.012 mole of formalin in methanol was stirred on a steam bath for 30 minutes. The reaction mixture was then allowed to stand overnight in refrigerator. The precipitated solid was filtered, washed with cold water, dried and crystallized from n-hexane.

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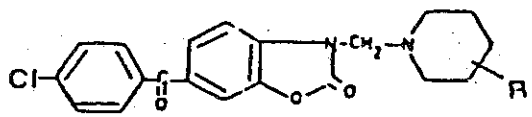
Results and Discussion

Derivatives of 3,6-disubstituted 2(3H)-benzoxazolone ring were synthesized from 6-(4-chlorobenzoyl)-2(3H)-benzoxazolone, formaldehyde and various piperidine derivatives. In our case, in spite of the fact that neither an acid nor a base catalyst was used, the yields of the reactions were quite high(Table 1).

The spectral data of the compounds (Table 2) are in accordance with literature values[4]. In the IR spectrum, C=0 streching (lactam and aromatic ketone), C=C bands were at expected values. N-H streching couldn't be observed around 3000-3200 cm^{-1}, because of binding the piperidine derivatives at 3 position of 2(3H)-benzoxazolone.

Noise decoupled spectra of the compounds were taken on a Bruker FT 200 spectrometer in $CDCl_3$.

Table 1. Physical properties and relative intensities(%) of the principal peak in the mass spectra of 3,6-disubstituted-2(3H)-benzoxazolones.



Comp. No	R	Yield %	mp* ℃	m/z 70 eV					
1	H	73.4	205	273.66 (53.06)	272.96(18.85)	162.96 (5.35)	161.97(61.67)	133.97(5.65)	98 (100)
2	3-CH_3	79.8	211	273.96(5.08)	272.94 (34.30)	162.96(9.09)	161.96(100)	133.98(8.37)	112.08 (89.83)
3	4-CH_3	81.2	213	273.94(5.11)	272.92 (33.30)	162.96 (7.92)	161.94(100)	133.98(6.73)	112.03(6.05)
4	3,5-$(CH_3)_2$	82	220	273.92 (4.87)	272.95 (32.77)	162.97 (8.79)	161.94 (100)	133.96 (7.80)	126.07 (26.44)

* Yields are obtained from first crystallisation.

Table 2. Results of IR and Microanalysis of 6-Acyl-3-disubstituted 2(3H)-benzoxazolone

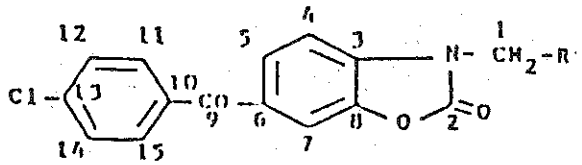
	IR cm^{-1}			Microanalysis(%)					
Comp. No.	Arom. Ketone	Lactam C=0	C-H Pip	C Calc.	C Found	H Calc.	H Found	N Calc.	N Found
1	1649	1782	2920	64.77	64.02	5.16	4.89	7.55	7.34
2	1645	1775	2920	65.53	65.41	5.50	5.38	7.28	6.98
3	1645	1780	2920	65.53	65.60	5.50	5.65	7.28	7.11
4	1650	1780	2920	66.24	66.48	5.81	5.80	7.02	7.28

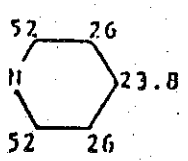
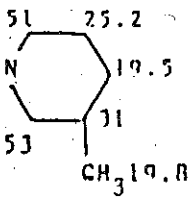
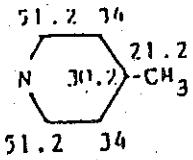
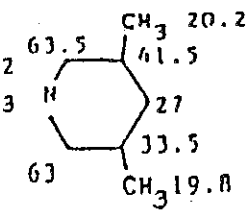
IR spectra were determined on a Perkin Elmer Model 457 IR in KBr. The microanalysis of C, H, N were performed by Butterworth Laboratories Ltd.

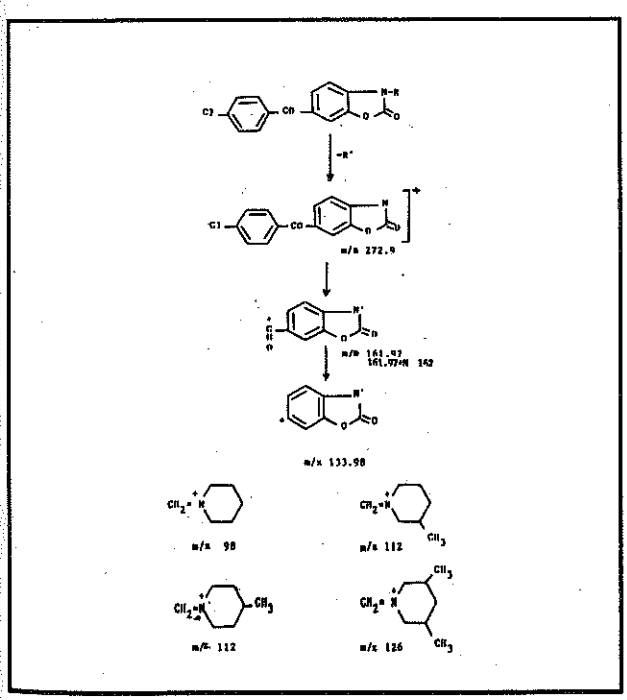
Chemical shifts are given in Table 3. TMS was used as internal standard. Ketone C=0 gave a peak at 194 ppm for all the compounds. The peaks at 139 and 136.5 ppm can be assigned to the substituted aromatic carbons. The remaining C atoms of the 4-chlorobenzene ring showed intense peaks at 128.8 and 131.2 ppm. Other small peaks at 132, 136, 142.5 ppm belonged to the C_6,-C_3- and C_8 - of the benzoxazolone ring respectively. The remaining carbons, namely C_7-,C_4 and C_5- appeared at 109.2, 111.2 and 127 ppm. Lactam carbonyl gave a peak at 155 ppm - CH_2- group between piperidine and benzoxazolone rings resonated at 66 ppm. R groups of the molecule showed different peaks according to the substituent on the piperidine ring. Data in earlier reports on ^{13}C studies of some benzoxazolone rings supported our ^{13}C assignments[12,13].

The mass spectroscopic fragmantation of 3,6-disubstituted 2 (3H)-benzoxazolone ring was also

Table 3. ^{13}C chemical shifts assignments of compounds.



Carbon Number	Comp. No. 1	2	3	4
1	66	66	65.5	65.5
2	155	155	155	155
3	136	136	136	136
4	111.5	111.2	111.5	111.3
5	127.2	127.2	126.3	127.2
6	132	132	132	132
7	109.1	109.1	109.1	109
8	142.5	142.5	142.5	142.5
9	194	193.7	193.7	194
10	136.5	136.1	136.1	136.1
11	128.8	128.8	128.8	128.8
12	131.2	131.2	131.2	131.2
13	139	139	139	138.9
14	131.2	131.2	131.2	131.2
15	128.8	128.8	128.8	128.5
R				



Scheme 1. Proposed fragmentation for the compounds

studied under positive ionization (Table 1). The mass spectroscopic behaviour of 3,6-disubtituted 2 (3H) - benzoxazolone ring was mainly characterized by the loss of the substituent at 3 position. For example, 3 - (4 - methylpiperidinomethyl) - 6 - (4 - chlorobenzoyl) - 2 (3H) benzoxazolone first lost 4-methylpiperidinomethyl-radical and gave a peak at m/z 272.94(see Scheme 1). The intensity of peak increased when the mass of the substituent increased at 3-position(Table 1). Second cleavage occured between C=0 and 4-chlorobenzene ring. As a result the remaining radical gave a peak at m/z 161. This fragment lost C=0 group and gave the base peak at m/z 133. For compounds 1 and 2, the base peaks were corresponding to the side chain radicals (CH_2=N(C_5H_{10}) and CH_2=N(C_6H_{12}) respectively. The overall process is outlined in Scheme 1. Unfortunately, M^+ couldn't be seen because of weak binding at 3 position.

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