SYNTHESIS AND CHARACTARIZATIONS OF NEW COUMARIN DERIVATIVES AS ULTRAVIOLET ABSORBERS

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Coumarins, Phnols, Ultraviolet absorber, Dimethyl acetylenedicarboxylate

Abstract

Novel coumarines having an ester groups in position 4, have been prepared via new methedology utilizing yeilds. The new method make it posiple to prepare new class of bis coumarines. The new coumarines derivative showed good uv absorbtion properties making them a good UV absorbers in the range of 250- 410 nm.

INTRODUCTION

Coumarins are simple molecules, with most of the derivatives having been known for more than a century. Coumarins constitute an important class of natural products, many of which exhibit useful drug activity (Gregory *et al.*, 2002; Kirkiacharian *et al.*, 2002). Moreover coumarins are a group of compounds that have important roles as food constituents, antioxidants, stabilizers, and immunodualatory substances, such as fluorescent markers for use in analysis, learns, and in clinical use (O'Kennedy and Douglas, 1997; Murry *et al.*, 1982; Hurry *et al.* 1988; Ziegler et al., 1987; Wells and Morrison, 1975; Lafitte et al., 2002). To date, naturally occurring coumarins have been isolated from

over 800 species of plants and microorganisms, and more than 1,000 coumarin derivatives have been described (Lovell et al. 1999).

In view of the natural occurrence and useful range of biological activity associated with these coumarins, various methods have been developed for their synthesis. The history of coumarins, synthesis began in the mid-19th century with Perkin's discovery of the famous synthesis, which now bears his name (Johnson, 1942).

A variant of the Perkin reaction, in which a coumarin is formed under much milder conditions, utilizes malonic acid. Another variant, the Kostanecki-Robinson reaction, can be used to prepare 3- and 4-substituted coumarins (Wawzonek, 1951).

Fifteen years after Perkin discovered his coumarin synthesis, von Pechmann reported an alternative method (Sethna, S. and Phadke, 1953). We now report a new synthetic approach to coumarin derivatives, which is a one-pot reaction, facile, and convenient.

Recently, a direct, efficient, and operationally convenient approach to the synthesis of some 4-carboxymethyl coumarins based on the aromatic electrophilic substitution reaction between the conjugated base of substituted phenols **1** and a vinyl triphenylphosphnium salt has been reported (Scheme 1) (Cobridge, 1995).

In this report we will investigate the scope and limitations of the later procedure to the synthesis of poly fanctunal coumarins and to qulitativelly assest the new coumarines as ultraviolet absorber to be used in cosmatic ingredents and sunscreens.

Expermintal

Melting points were recorded on a Thomas-Hoover capillary melting apparatus without correction. Microanalyses were carried out using a Perkin Elmer 240B Analyzer IR spectra were taken as KBr disk on a Nicolet Magna 520 FTIR spectrometer, ^{1}H-NMR were recorded in $CDCl_3$ on a Brucker DPX 400 MHz spectrometer using TMS as internal standard. ^{13}C-NMR were recorded in $CDCl_3$ on a Brucker DPX 100 MHz. UV-visible spectra were recorded on a Shimadzu 260 spectrometer for solutions.

Materials

Dimethylacetylenedicarboxylate, triphenyl phosphine, were obtaind from Aldrich chemicals, All the phenols and naphtholes were obtaind from Acros Organics (Belgium).

General Procedure

One mole of phenol derivatives and one mole of triphenylphosphine was dissolved in CH_2Cl_2. The reaction mixture was cooled in ice bath to –5 °C, and mixture of CH_2Cl_2 & dimethylacetylenedicarboxylate was added dropwise within 10 min with stirring. The reaction mixture was then refluxed for 4-5 hours the solvent was removed under reduced pressure and the solid mass was purified by recrystalization from ethanol.

Result and Discussion

Synthesis of coumarines

The reaction of phenols **1** with dimethyl acetylenedicarboxylate (DMAD) **2** in the presence of triphenylphosphine leads to the corresponding coumarins **3** (Scheme 1). Different substituted phenols were used to studies the scope and limitations of the procedure and are summariezed in scheme 1. Also, it has been found that different dialkyl acetelen dicarboxylates are also undergo the same reaction and gave 3-alkyl subistituted cumarines carboxylates such as ethyl 6-formyl-8-methoxy-2-oxo-2*H*-chromene-4-carboxylate **4**. The structure of compounds **3a-f** were deduced from their elemental analysis and their IR, ^1H and ^{13}C NMR data Table 1, 2, 3, 4 and 5.

The reaction was also applied for the preparation of benzo annalated coumarines, from the correspounding naphthols. 1-Naphtol gave under the same conditions used for phenol the coumarine derivative **5**. On the other hand, 2-Naphthol gave exclusivelly coumarine **6** and not the coumarine derivative **7**. This was confermed from the H-NMR Spectrum, which showed the absence of the two aromatic protons singlets which are expected for compounds **7**. It was also of great interest to examine the posibility of the synthesis of di-coumarine fanctionality from some dihydroxy naphthalene. Thus, when 2,3-dihydroxynaphthalene were treated with two molar equivilents of dimethyl acetylenedicarboxylate (DMAD) in the presence of axcees triphenylphosphine, the di-coumarin compound **7** was obtaind. In the same maner, when 2,7-dihydroxynaphthalene was subjected to the same reaction condition, the dihydroxy coumarine **9** was obtaind exclusively and not the di-coumarine derivatives **10**. this was follwed from the H-NMR spectrum which showed two dublets for the aromatic protons at 7.41 and 7.60 ppm.

2-Hydroxy naphthaldehydes when reacted with dimethyl acetylenedicarboxylate (DMAD) gave only dimethyl 3*H*-benzo[*f*]chromene-2,3-dicarboxylate **11**.

Ultraviolet absorption properties

The UV- Visible spectra of the new coumarines are given in Figures 1-4. In general, coumarins derived from phenol derivatives usually showed absorbtion bands in the region of 325-360 nm and a vally between 315-420 nm. On the other hand coumarins derived from 1 and 2-hydroxy naphthalens, gave a a broud and intens bands covering a wide range of uv spectrum, rendering them as excellent uv absorber in the range of 300-415 nm. Where coumarines derived from di-hydroxy naphthalene gave the same trend shown by coumarins derived from mono hydroxy naphthalene. The dimethyl 3*H*-benzo[*f*]chromene-2,3-dicarboxylate **11** showed a broad band covering the uv spectrum between 320 nm and 420 nm. Finally the coumarins derived from phenols are good candedates to be used as ultraviolet absorber for the UVA in the range between 200-300 nm. where as coumarins derived from mono and di hydroxy naphthalens are excelent UV absorber in UVB rang lying between 300-400 nm.

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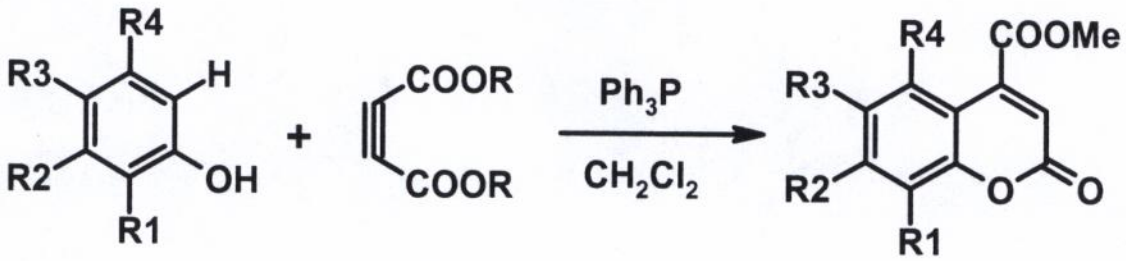
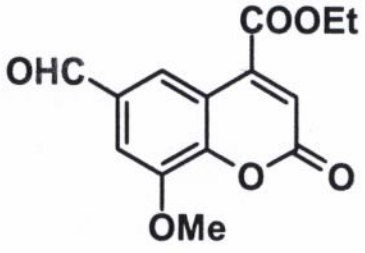


1 2 3

Entry No.	R1	R2	R3	R4
a	MeO	H	CHO	H
b	H	H	COOH	H
c	$COCH_3$	H	H	H

Scheme 1



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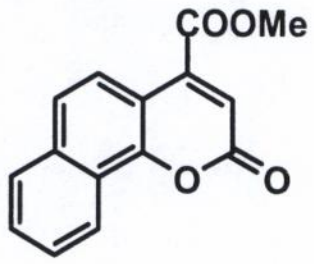

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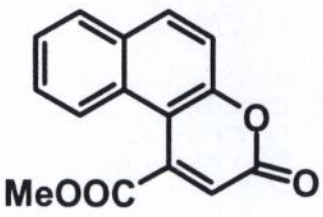

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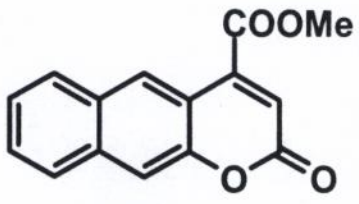

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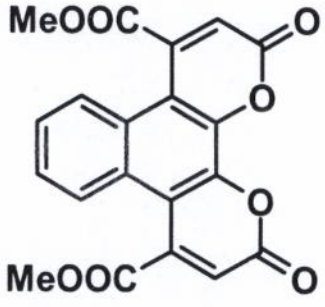

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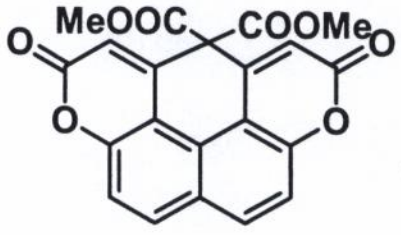

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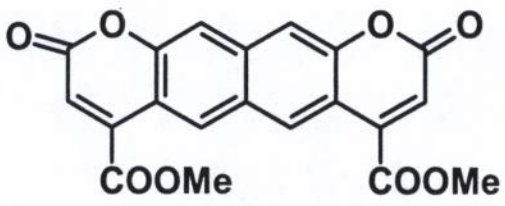

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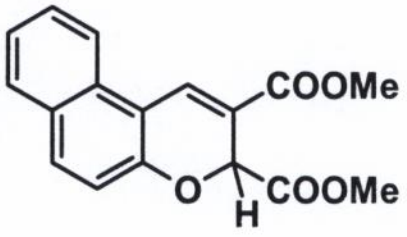

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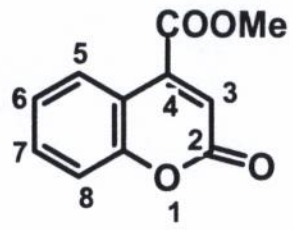
Table 1. Analytical Data of synthesied compounds 3a-c, 4, 5, 6, 8, 9 and 11

Compd No.	M.P. (C)	Yield (%)	MF	Calculated		Found	
				C	H	C	H
3a	182	20	$C_{13}H_{10}O_5$	59.55	3.61	59.23	3.72
3b	140	44	$C_{12}H_8O_6$	58.07	3.25	58.21	3.12
3c	40	23	$C_{13}H_{10}O_5$	63.42	4.09	63.22	4.21
4	118	50	$C_{14}H_{12}O_6$	60.87	4.38	60.69	4.21
5	110	40	$C_{15}H_{10}O_4$	70.86	3.96	70.91	4.01
6	58	58	$C_{15}H_{10}O_4$	70.86	3.96	70.76	3.87
8	50	90	$C_{20}H_{12}O_8$	63.16	3.18	63.01	2.98
9	Oil	56	$C_{15}H_{10}O_4$	63.16	3.18	63.31	3.21
11	58	61	$C_{17}H_{14}O_5$	68.45	4.73	68.51	4.88

Table 2. IR spectral data of synthesized cumarines 3a-c, 4, 5, 6, 8, 9 and 11

Compd No	ν/cm^{-1}
3a	1724.8, 1032.7, 1144.1, 1599.2
3b	2361.4, 2685.2, 1016.6, 1098.7, 1165.6, 1552.3, 1671.9
3c	1731.7, 1024, 1092, 1117.7, 1195.2, 1586.8
4	1712.4, 1012.1, 1158.4, 1593.8, 1712.4
5	1550.9, 1589.3, 1001.6, 1100.3, 1181.9, 1731.7
6	1009.5, 1094, 1585.1, 1738.5
8	1119.7, 1169.9, 1245, 1623, 1731.5
9	1022, 1106, 1250.7, 1591, 1724
11	1116.5, 1185.2, 1710.4, 1577,1630.4

Table 3. H^1-NMR Data of coumarines 3a-c and 4



Compd no	H-3	H-5	H-6	H-7	H-8	OTHER
3a	7.33	7.70	7.40	7.5		2.21 (s, 3H, $COOCH_3$), 4.2 (s, 3H, CH_3O), 10.18 (s, 1H, CHO)
3b	6.86	7.66		7.56	7.48	3.81 (s, 3H, $COOCH_3$)
3c	7.33	7.70	7.4	7.5		2.21 (s, 3H, CH_3CO), 3.80 (s, 3H, $COOCH_3$)
4	7.07	8.44		7.62		1.47 (t, 3H, CH_3), 4.02 (s, 3H, CH_3O), 4.5 (q, 2H, CH_2O), 9.99 (s, 1H, CHO)

Table 4. ^{1}H-NMR Data of Coumarine derivatives 5, 6, 8, 9 and 11

Protones	**5**	**6**	**8**	**9**
H-3	7.13	7.30	7.39	7.13
H-4	7.78		8.1	
H-5	7.83	8.05	7.46	7.60
H-6	7.44	7.59		7.41
H-7	8.31	7.78		
H-8	8.70	7.97		
H-9		7.79		
H-10	8.0	7.48		
Others	4.17 (s, 3H, $COOCH_3$)	3.64 (s, 3H, $COOCH_3$)	4.18 (s, 3H, $COOCH_3$)	3.71 (s, 3H, $COOCH_3$)

Table 5. ^{13}C-NMR Data of synthesized cumarines 3a-c, 4, 5, 6, 9 and 11

Compd No.	δ (ppm)
3a	53, 56 , 110.6, 111.8, 116.5, 120.7, 123.6, 132.1, 132.7, 141.6, 148.4, 158.5, 190.5
3b	52.18, 115.03, 121.54, 128.34, 128.50, 1319, 132.6, 133.20 , 161.53, 165.14
3c	52.18, 115.03, 121.54, 128.34, 128.5, 131.54,131.8, 132.6, 133.19, 161.53, 165.14
4	13.85, 56.22, 62.67, 110.33 , 116.29, 120.26, 123.33, 128.19, 131.71, 132.44, 141.67, 147.83, 158.31, 163.02, 190.31
5	53.22, 111.49, 118.23, 121.74, 122.95, 124.57, 127.25, 127.6, 128.4, 12932, 132.0, 133.7, 143.36 , 151.82 , 160.08, 164.52
6	53.52, 115.50, 117.31, 123.21, 126.08, 128.6, 129.4, 132.1, 133.8, 134.56 , 137.16, 145.85, 154.84 , 159.47, 167.73
9	58.31, 111.76, 128.44, 128.6, 129.0, 130.9, 131.99, 132.6, 133.7, 134.14, 160.1, 168.3
11	52.23, 52.66, 71.33, 113.17, 117.55, 118.59, 121.46, 124.48, 124.61, 127.77, 128.5, 128.7, 129.11, 129.86 , 130.6, 131.94, 133.39

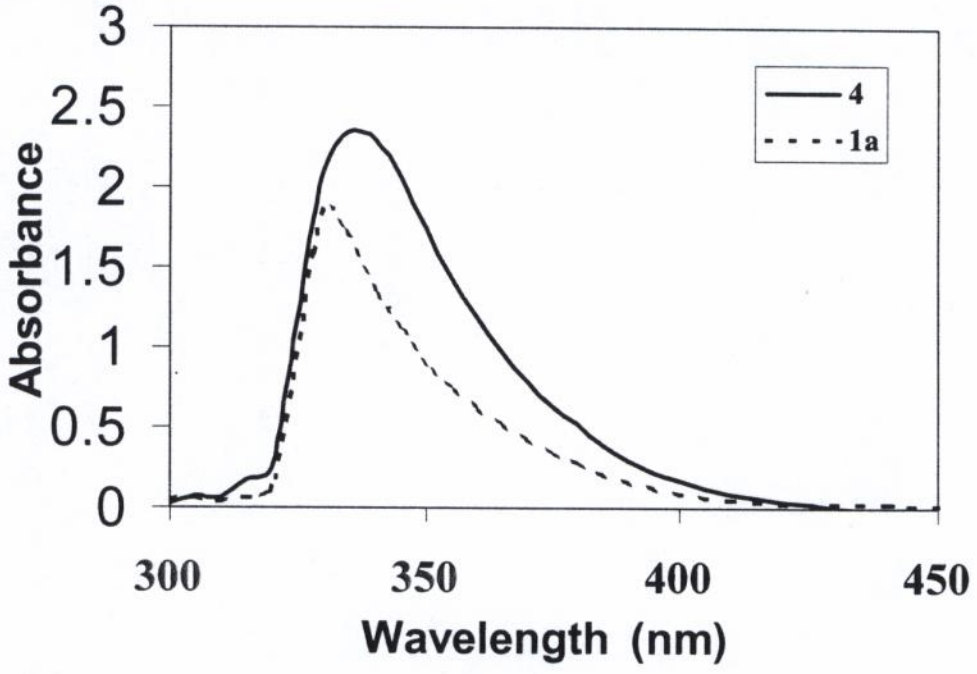


Figure 1. Absorption spectra of coumarine 1a and 4 in chloroform solutions

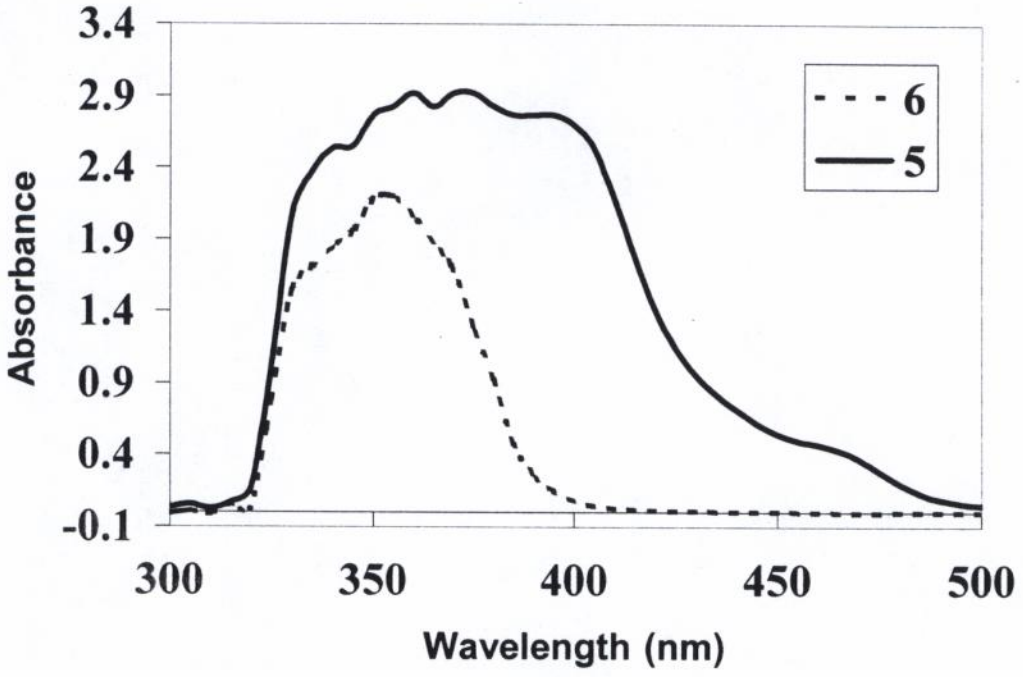


Figure 2. Absorption spectra of coumarine 5 and 6 in chloroform solutions

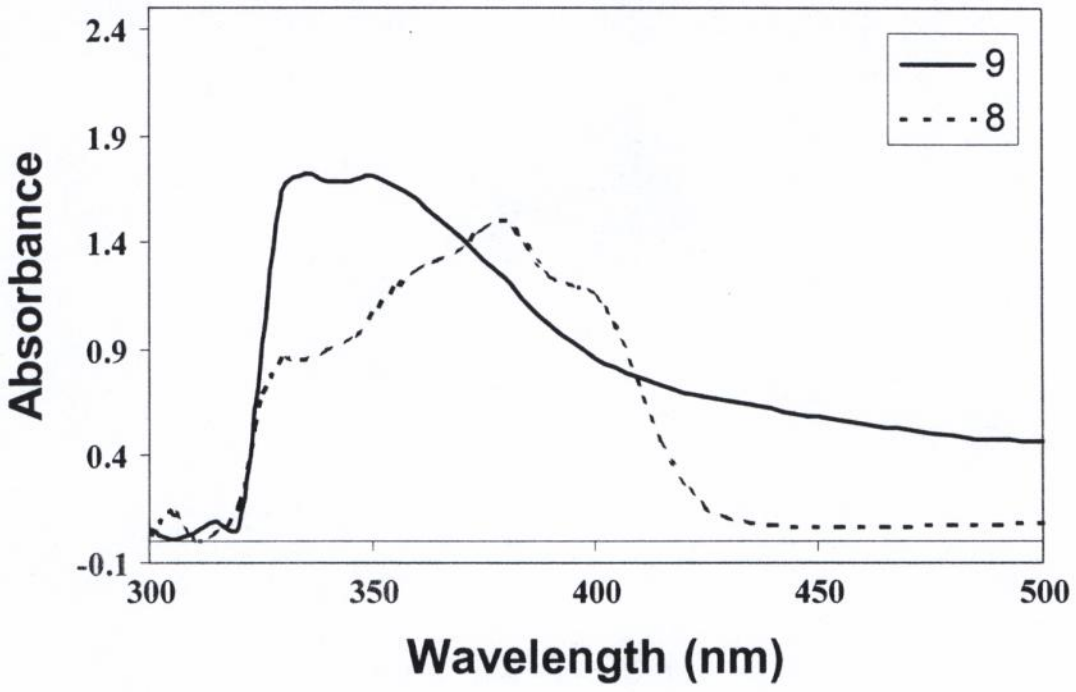


Figure 3. Absorption spectra of coumarine 8 and 9 in chloroform solutions

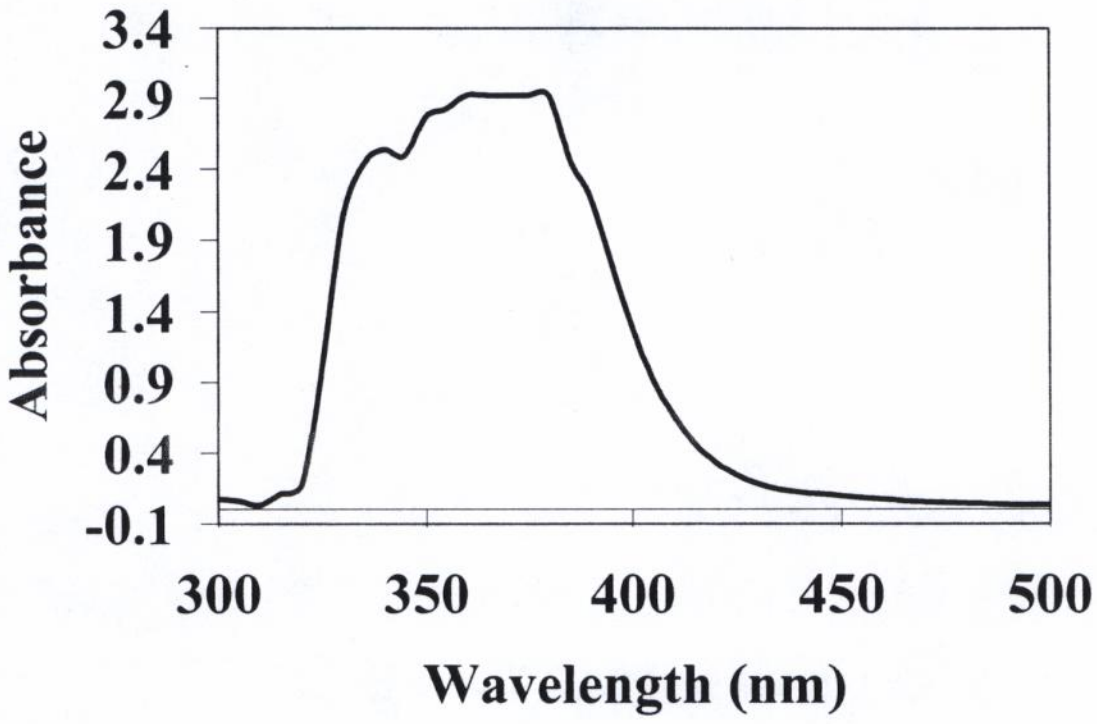


Figure 4. Absorption spectra of Pyran 11 in chloroform solution