Synthesis of Fluorescent N-Acyl-p-Aminophenols

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Summary: Various N-acyl-p-aminophenol derivatives were synthesised by introducing cinnamyl, p-methoxy cinnamyl, (o- methoxycarbonyl)-o-coumaryl, o-coumaryl, m-coumaryl and ferulyl groups into p-aminophenol. N,N dicyclohexyl-carbodiimide was used as the condensing agent.

Introduction

4-aminophenol and N-acyl-p-aminophenol are reported to possess analgesic and antipyretic activities [1-4]. These observations prompted us to undertake the synthesis of several new N-acyl-p-aminophenol derivatives, by selecting cinnamyl, p-methoxy cinnamyl, (o-methoxycarbonyl)-o-coumaryl, o-coumaryl, m-coumaryl and ferulyl groups which were introduced at the amino function of the p-aminophenol. Some of these groups and their precursors like anisaldehyde and vanillin are commonly used as flavourants. These compounds are themselves least toxic and can be administered orally.

The substituted amides can be prepared by using various reagents such as acid chloride [5] mixed anhydride [6] 3-acyl-1,3- thiazolidine [7] and dicyclohexylcarbodiimide [8]. Out of these dicyclohexylcarbodiimide (DCCD) was successfully emplo-yed for introducing the cinnamyl and substituted cinnamyl groups in the amino function of p-aminophenol, using dioxan as a solvent. Other sol-

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vents like tetrahydrofuran, dichloromethane and dimethyl formamide did not give the desired results.

Experimental

All the chemicals were of reagent grade and used without further purification. Melting points are uncorrected. Ultraviolet spectra were recorded on Hitachi doluble beam spectrophotometer model- 220. Infra red spectra (KBr) were measured on Perkin Elmer IR- 1320. The mass spectra were run at low resolution mass spectra (6 Ei and 2 CI). The R_f values of all the compounds are given in Table-1.

Table 1: TLC on N-acyl-p-aminophenol derivative on silica Gel/Cellulose (1:1) Rf values x 10.

Deri-vatives	a	b	c	d	Fluorescence 366 nm
I	37	74	72	77	Brown
II	37	87	81	80	Yellow
III	26	73	74	74	Light brown
IV	26	70	73	90	Deep purple
V	75	82	86	75	Brown
VI	27	62	61	77	Deep purple

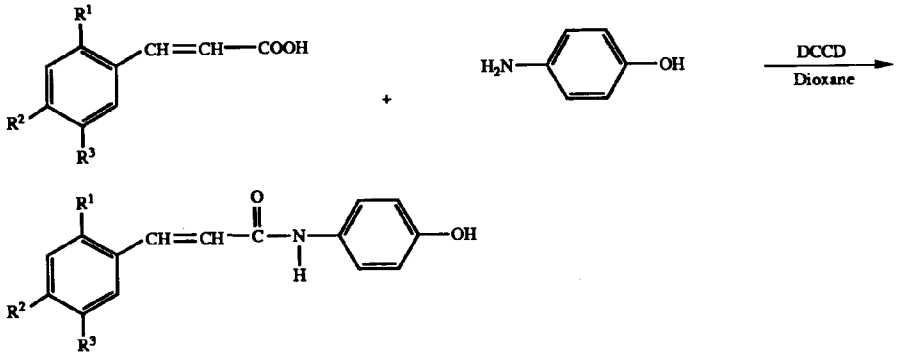
a Toluene-ethylacetate-formic acid (10:6:2)
b Ethyl acetate-acetone-acetic acid-water (10:4:2:1)
c Ethyl acetate-acetic acid-water (10:2:1)
d Butanol-water (8:1)

General Procedure

A solution of p-aminophenol (0.02 mole) in dioxan (70 ml) was prepared and corresponding acid (0.02 mole) was added, the reaction mixture was stirred for 30 minutes. N,N'- Dicyclohexylcarbodiimide (0.02 mole) dissolved in dioxan (25 ml) was added slowly to the stirring mixture at O°C. The reaction mixture was further stirred at room temperature for 24 hrs. The precipitated dicyclohexyl urea was filtered off. The solvent was evaporated in vacuo and the concentrate was dissolved in ethyl acetate. The organic layer was successively washed with cold 10% sodium carbonate, brine and dilute hydrochloric acid. The organic layer was dried over anhydrous sodium sulphate and ethyl acetate was distilled off under reduced pressure. The residue obtained was recrystallized from ethanol the physical and analytical data of the corresponding N-acyl-p-aminophenol derivatives are listed in Table 2.

N-(o-coumaryl)-p-aminophenol (VI)

A solution of N-[(methoxycarbonyl)-o-coumaryl]-p-aminophenol (2.5 mmole) in methanol (25 ml) and 1M aqueous sodium carbonate (2.5 mmole) was stirred overnight at room temperature.



(1) $R^1 = R^2 = R^3 = H$

(2) $R^1 = R^3 = H$; $R^2 = CH_3O$

(3) $R^2 = R^3 = H$; $R^1 = CH_3OCO$

(4) $R^1 = R^2 = H$; $R^3 = OH$

(5) $R^1 = H$: $R^2 = OH$; $R^3 = CH_3O$

(6) $R^2 = R^3 = H$; $R^1 = OH$

Scheme-1

Table 2: Physical characteristics and spectral data of N-acyl-p-aminophenols.

Compound	Molecular Formula (M.wt.)	Melting point °C	Yield %	$\lambda_{max\,(nm)}$ data	Mass spectral data	Infrared cm^{-1}
N-Cinnamyl-p-aminophenol(I)	$C_{15}H_{13}O_2N$ (239)	200	29.7	285	239,131(base peak,109 , 103,81,77 990,755	3300,3260 2850,1655 1556,1510,
N-(4-Methoxy -cinnamyl)-p-aminophenol (II)	$C_{16}H_{15}O_3N$ (269)	192-194	30	320	269,161(base peak), 109,90,77 950,760	3360,2850, 133,118, 1580,1540,
N-[(o-Methoxy carboxy)-o-coumaryl]-p-aminophenol(III)	$C_{17}H_{15}O_5N$ (313)	180-184	35.2	275	313,238,205, 3300,3100, 167,161(base peak),146,118 109,103	2900,1757, 1660,1550, 990, 760
N-(m-Coumaryl)-p-aminophenol(IV)	$C_{15}H_{13}O_3N$ (255)	165	60	285	255,245,162, 147 (base peak),119, 109,98,91	3470,3300, 2900,2835 1700,1650, 1570,995, 800
N-Ferulyl-p-aminophenol(V)	$C_{16}H_{14}O_4N$ (285)	172	59	330,332	285,224,196, 177,(base peak),149, 145,134,117, 109,89	3360,2920 1660,1570, 1510,970, 775
N-(o-coumaryl)-p-aminophenol(VI)	$C_{15}H_{13}O_3N$ (255)	166-168	64.4	275,325	255,245,161, 147(base peak),118 109,103,91	3320,2900, 1638,1570, 1540,992, 748

Methanol was distilled off, residue was treated with dilute sulphuric acid and extracted with ethyl acetate. Organic layer was washed twice with 5% sodium bicarbonate containing sodium chloride (1.0 g), then dried over anhydrous sodium sulphate. Ethyl acetate was distilled off under reduced pressure and the residue was dissolved in ethanol, the product was obtained as amorphours white powder.

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