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An efficient one-pot synthesis of spiro dihydrofuran fluorene and spiro 2-hydroxytetrahydrofuran fluorene derivatives via [3+2] oxidative cycloaddition mediated by CAN

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ABSTRACT

Spiro dihydrofuran fluorene derivatives were prepared via [3+2] oxidative cycloaddition of 1,3-dicarbonyl compounds to 9-benzylidene-9*H*-fluorene and 2-(9*H*-fluorene-9-ylidene)-1-phenylethanone derivatives mediated by ceric ammonium nitrate. In the case of the reaction of 9-benzylidene-9*H*-fluorene with acyclic 1,3-dicarbonyl compounds, spiro 2-hydroxytetrahydrofuran fluorene derivatives were obtained.

Fluorene-based derivatives have been extensively investigated for electronic and photonic applications, such as light emitting diodes, charge-transfer agents, field effect transistors, sensors, and more recently, two-photon absorbing materials.[1]

When compared to unsubstituted fluorene, 9,9-disubstituted fluorene building blocks containing oligomers and polymers have higher solubility and thermal stability.[2] Also the optical, thermal, and electrochemical properties of oligofluorenes are known to be changed by varying the substitution patterns or by introducing a spiro-configured structure at the C-9 position of the fluorenyl ring.[3]

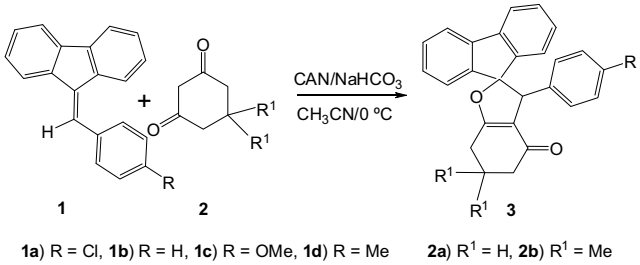
Spiro-functionalization at the C-9 position of a fluorene unit not only improves the emission spectral quality but also prevents the aggregation of the polymer at the ground state, and thereby minimizes excimer formation in solid films.[4] One such spiro-configured fluorene system is spiro bi-fluorene, which was introduced by Tour and co-workers.[5] Since then, there has been a continuous exploitation of spiro bi-fluorene building blocks in the construction of oligomers and polymers.[6] Also, research continues in the structural modification of the spiro-bifluorene unit either by introducing a heteroatom in the structural frame or by linking the spiro unit to a heteroaromatic ring in order to improve and extend its applications.[7]

Incorporating heteroaryl groups, for example, thiophene, pyridine, and carbazole into spiro compounds will be a useful strategy to expand the application of spiro compounds. Recently, Xie et al. synthesized novel thiophene-containing ter [9,9′-spiro bifluorene] analogue.[8]

To contribute to this area of research, herein, we describe an efficient one-pot synthesis of novel spiro dihydrofuran fluorene derivatives by the [3+2] oxidative cycloaddition of cyclic and acyclic 1,3-dicarbonyl compounds to 9-benzylidene-9*H*-fluorene and 2-(9*H*-fluorene-9-ylidene)-1-phenylethanone derivatives mediated by ceric ammonium nitrate, in which a substituted dihydrofuran unit is spirally attached to the C-9 position of the fluorene ring.

Initially, the reaction was explored by treating 1,3-dicarbonyl compound **2a** with 1 equiv of **1a** at 0 °C in the presence of 2.5 equiv of CAN and 3 equiv of $NaHCO_3$ in acetonitrile (Scheme 1, Table 1). The reaction proceeded smoothly within 15 min to afford **3a** as a single regioisomer in 80% yield after purification by column chromatography. No other isomer could be detected.

In the ^{1}H NMR spectrum of **3a** the benzylic proton appeared as a singlet at δ 4.85 ppm, and in the ^{13}C NMR spectrum a signal due to the spiro carbon at δ 98.7 ppm confirmed the formation of **3a**.[9] The structure of **3a** was also confirmed by X-ray diffraction studies (Fig. 1). In the ortep diagram of compound **3a** the, C-6 atom is disordered over two positions with occupancy factors of 0.3



1 2 3

1a) R = Cl, **1b**) R = H, **1c**) R = OMe, **1d**) R = Me **2a**) R^1 = H, **2b**) R^1 = Me

Scheme 1.

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Table 1
Synthesis of spiro dihydrofuran fluorene derivatives from 9-benzylidene-9*H*-fluorene derivatives

Entry	9-Benzylidene-9*H*-fluorene derivative **1**	1,3-Dicarbonyl compound **2**	Products[a] **3**			Yield (%)
				R	R^1	
1	**1a**	**2a**	**3a**	Cl	H	80
2	**1a**	**2b**	**3b**	Cl	Me	82
3	**1b**	**2a**	**3c**	H	H	83
4	**1c**	**2b**	**3d**	OMe	Me	78
5	**1c**	**2a**	**3e**	OMe	H	79
6	**1d**	**2a**	**3f**	Me	H	83

[a] All the reactions were complete in 15 min.

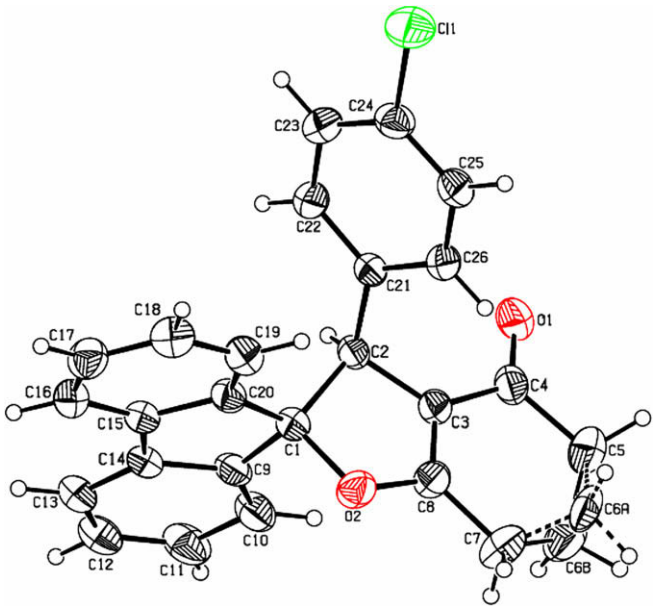


Figure 1. Ortep diagram of **3a**.

(C6A) and 0.7 (C6B) because of large thermal vibration of this atom.[10] Similar products were obtained in good yields using a variety of substituted (9-benzylidene-9*H*-fluorene) derivatives under similar conditions. The results are summarized in Table 1.

Treating **1b** with acyclic 1,3-dicarbonyl compound **4a** under similar reaction conditions gave the corresponding expected spiro [dihydrofuran-fluorene] derivative (**5b**) in a 1:1 ratio with a compound whose molecular weight exceeded by 18 units that of the expected product (Scheme 2). In the IR spectrum, the appearance of a peak at 3435 cm^{-1} confirmed the presence of an OH group. The OH proton could not be detected in the ^1H NMR spectrum, but an additional proton in the aliphatic region was observed. Instead of a singlet, two doublets at δ 3.99 ppm and 4.87 ppm corresponding to one proton each with coupling constants of *J* 13.75 Hz were found which confirmed that these protons were located adjacent to one another with trans stereochemistry.

Based on these results and further information from the ^{13}C NMR spectrum, the structure of the product was assigned as spiro 2-hydroxytetrahydrofuran fluorene derivative **6b**.[11] Further, the molecular formula was confirmed from mass spectrometer. The relative stereochemistry of the substituents on the tetrahydrofuran ring was assigned based on NOE experiments. In the ^1H NMR spectrum of **6b**, a singlet at δ 1.87 ppm was attributed to methyl group attached to the tetrahydrofuran ring, and the two doublets at δ 4.87 ppm and δ 3.99 ppm were attributed to Ha and Hb, respectively (Fig. 2). While irradiating the proton Hb, a little enhancement was observed in the signal at δ 1.87 ppm and no such enhancement was observed in the signal at δ 4.87 ppm, which suggests a trans relationship between the protons Ha and Hb and a cis relationship between the proton Hb and the methyl group (Fig. 2). To further confirm this, single crystals of compound **6e** were obtained by recrystallisation, and the stereochemistry was confirmed unambiguously by X-ray diffraction studies (Fig. 3).[12]

Similar products were obtained while treating other (9-benzylidene-9*H*-fluorene) derivatives with acyclic 1,3-dicarbonyl compounds. The results are summarized in Table 2. A plausible mechanism for the formation of **5** and **6** is given in Scheme 3.

As the first step, Ce^{4+} ion abstracts an electron from the 1,3-dicarbonyl compound (**4**), generating radical (i) which in turn reacts with 9-benzylidene-9*H*-fluorene derivative to form the radical (ii). Again another Ce^{4+} ion abstracts an electron from radical (ii) affording carbocation (iii). The carbocation (iii) thus formed can undergo reaction following two different path ways namely A and B to furnish the products **5** and **6**, respectively. In path A, the expected product **5** is formed from carbocation (iii) via deprotonation. In path B, the product **6** is formed from carbocation (iii) by the attack of water molecule on the carbonyl carbon followed by cyclization.

The formation of **3** as the only product in the reaction of cyclic 1,3-dicarbonyl compound **2** with **1** (Scheme 1) clearly supports the mechanistic pathways. In the case of cyclic 1,3-dicarbonyl compound, the water molecule could not easily approach the carbonyl carbon to afford the 2-hydroxy tetrahydrofuran derivative (Path B) due to steric factors, thereby the competing deprotonation reaction (Path A) takes place rapidly to give the expected spiro dihydrofuran fluorene derivative **3** as the only product (Scheme 1). Whereas in

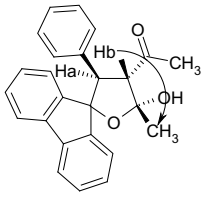
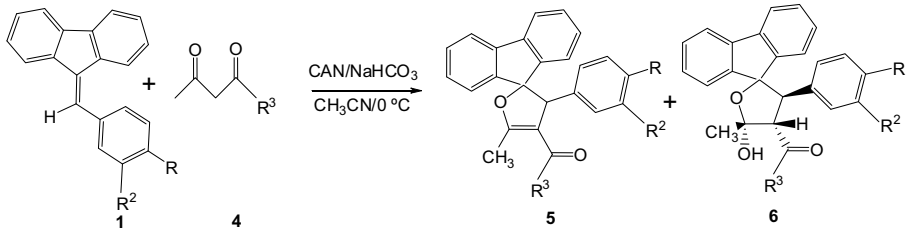


Figure 2. Characteristic nOe of compound **6b**.



1a) R = Cl,R^2 = H, **1b**) R = H, R^2 = H, **1e**) R = Cl, R^2 = Cl **4a**) R^3 = Me, **4b**) R^3 = OEt

Scheme 2.

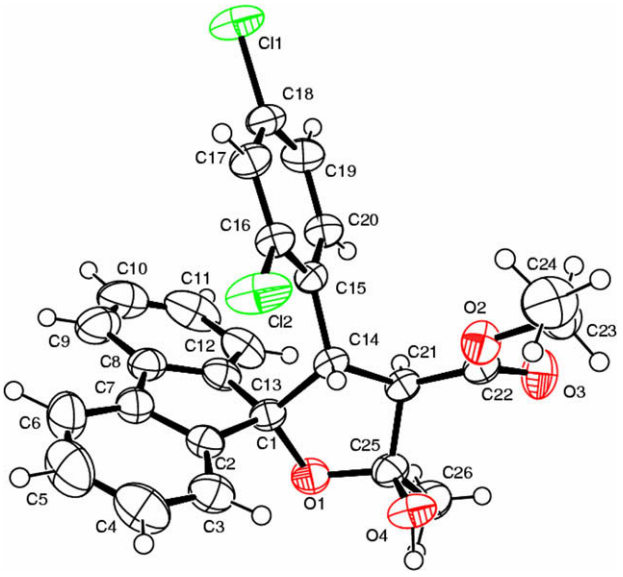


Figure 3. Ortep diagram of **6e**.

Table 2
Synthesis of spiro dihydrofuran fluorene and spiro 2-hydroxytetrahydrofuran fluorene derivatives from 9-benzylidene-9*H*-fluorene derivatives

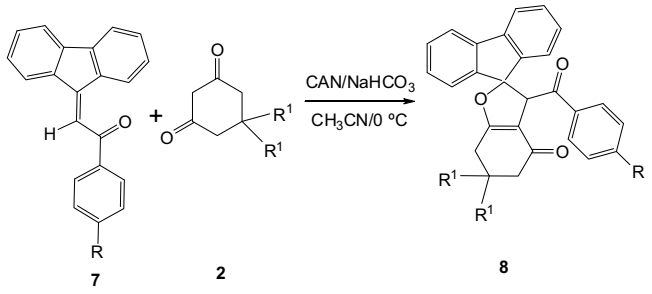
Entry	9-Benzylidene-9*H*-fluorene derivative **1**	1,3-Dicarbonyl compound **4**	Products[a,b] **5, 6**				Yield[c] (%)
				R	R^2	R^3	
1	**1a**	**4a**	**5a, 6a**	Cl	H	Me	81
2	**1b**	**4a**	**5b, 6b**	H	H	Me	80
3	**1b**	**4b**	**5c, 6c**	H	H	OEt	83
4	**1e**	**4a**	**5d, 6d**	Cl	Cl	Me	78
5	**1e**	**4b**	**5e, 6e**	Cl	Cl	OEt	79

[a] All the reactions were completed within 15 min.
[b] Products **5** and **6** were obtained in 1:1 ratio.
[c] Isolated overall yield.

the case of acyclic 1,3-dicarbonyl compound, both the competing reaction pathways A and B (deprotonation and attack of the water molecule on the carbonyl carbon followed by cyclization) takes place, resulting in the formation of products 5 and 6 in (1:1) ratio (Scheme 2).

In the case of the reaction of dimedone (**2b**) with 1 equiv of **7b** in the presence of 2.5 equiv of CAN and 3 equiv of $NaHCO_3$ at 0 °C in acetonitrile (Scheme 4, Table 3), **8d** was obtained as a single isomer in 82% yield after purification through column chromatography. In the ^1H NMR spectrum, the proton of the dihydrofuran ring appeared as a singlet at δ 5.26 ppm, and in the ^{13}C NMR spectrum the spiro carbon appeared at δ 95.9 ppm which confirmed the formation of the product.[13] Similar products were obtained with other 2-(9*H*-fluorene-9-ylidene)-1-phenylethanone derivatives. The results are summarized in Table 3.

In conclusion, we have successfully prepared the spiro-configured fluorene derivatives in which a functionalized furan is spirally attached to the C-9 position of the fluorene ring. Further utilization of this spiro unit as a building block to prepare oligomers and polymers and the investigation of its photoluminescence properties are underway.

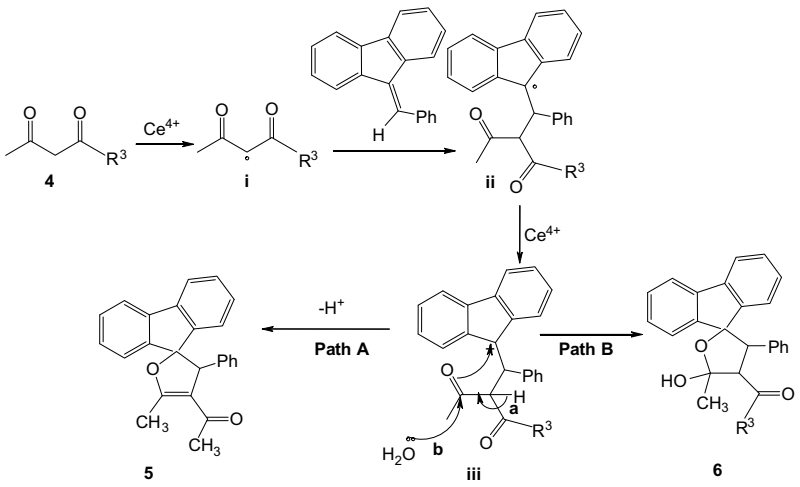


Scheme 4.

Table 3
Synthesis of spiro dihydrofuran fluorene derivatives from 2-(9*H*-fluorene-9-ylidene)-1-phenylethanone derivatives

Entry	2-(9*H*-Fluoren-9-ylidene) -1-phenylethanone **7**	1,3-Dicarbonyl compound **2**	Products[a] **8**			Yield (%)
				R	R^1	
1	**7a**	**2a**	**8a**	H	H	85
2	**7a**	**2b**	**8b**	H	Me	84
3	**7b**	**2a**	**8c**	Cl	H	80
4	**7b**	**2b**	**8d**	Cl	Me	82

[a] All the reactions were complete within 15 min.



Scheme 3.

Acknowledgment

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9. *General procedure for* **3a**: To a stirred mixture of 9-(4-chlorobenzylidene)-9*H*-fluorene (**1a)** (1.03 mmol, 0.3 g), 1,3-dicarbonyl compound **2a** (1.03 mmol, 0.115 g, 1 equiv), and $NaHCO_3$ (3.09 mmol, 0.260, 3 equiv) in acetonitrile (10 mL), ceric ammonium nitrate (2.58 mmol, 1.412 g, 2.5 equiv) dissolved in acetonitrile (5 mL) was added dropwise at 0 °C under N_2. The reaction mixture was stirred until completion of the reaction as monitored by TLC. Water was added to the mixture and the product was extracted into ethyl acetate (2×20 mL) and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave a crude product, which was purified by column chromatography on silica gel, with ethyl acetate–hexane (4:6) as eluent to afford the 0.328 g pure product (80%) as a white crystalline solid. Single crystals of **3a** were obtained by recrystallization from ethyl acetate.
Spectral data for compound **3a** (Table 1): mp = 150 °C. IR: ν_{max} = 1390, 1483, 1630, 1716, 2923, 3040 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.61(d, 1H, J = 7.65 Hz), 7.53 (d, 1H, J = 7.65 Hz), 7.51 (d, 1H, J = 7.65 Hz), 7.43 (t, 1H, J = 6.85 Hz), 7.32 (t, 1H, J = 6.85 Hz), 7.21 (t, 1H, J = 7.6 Hz), 7.06 (d, 2H, J = 8.4 Hz), 6.89 (t, 1H, J = 7.65 Hz), 6.72 (d, 2H, J = 8.4 Hz), 6.54 (d, 1H, J = 7.65 Hz), 4.85 (s, 1H), 2.55–2.76 (m, 4 H), 2.23–2.29 (m, 2H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 179.7, 147.5, 141.2, 140.5, 139.5, 136.3, 132.9, 130.3, 129.7, 129.5, 128.8, 128.3, 127.4, 126.5, 122.9, 120.2, 119.9, 115.4, 98.7, 53.1, 37.2, 24.8, 22.0. MS (EI) m/z = 398 (M^+), 400 (M^++2). Anal. Calcd for $C_{26}H_{19}ClO_2$: C, 78.29; H, 4.80. Found: C, 77.89; H, 4.68.
10. Crystallographic data for the compound **3a** in this Letter have been deposited with the Cambridge Crystallographic Data centre as Supplemental Publication No. CCDC 702989. Copies of the data can be obtained, free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 01223 336033 or email: deposit@ccdc.cam.ac.uk).
11. *General procedure for* **5b** *and* **6b**: Following the general procedure as described above, **5b** and **6b** were obtained from 9-benzylidene-9*H*-fluorene (**1b**) (1.18 mmol, 0.3 g), acetyl acetone (**4a**) (1.18 mmol, 0.118 g, 1 equiv), and $NaHCO_3$ (3.54 mmol, 0.297 g, 3 equiv) in the presence of ceric ammonium nitrate (2.95 mmol, 1.62 g, 2.5 equiv) as a crude mixture, which was purified and separated by column chromatography on silica gel, with ethyl acetate–hexane (3:7) as eluent to afford the product **5b** 0.166 g and **6b** 0.175 g.
Spectral data for compound **5b** (Table 2): mp = 146 °C. IR: ν_{max} = 1374, 1450, 1595, 1664, 1715, 2929, 3061 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, 1H, J = 7.65 Hz), 7.61–7.66 (m, 1H), 7.41–7.52 (m, 3 H), 7.27–7.33 (m, 2H), 7.17–7.20 (m, 3H), 6.79–7.02 (m, 2H), 6.44 (d, 1H, J = 7.65 Hz), 4.78 (s, 1H), 2.56 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.5, 171.1, 148.5, 141.4, 140.6, 139.5, 139.1, 134.8, 130.1, 129.5, 128.7, 128.5, 127.6, 127.2, 126.7, 122.5, 120.2, 119.7, 115.3, 96.4, 57.5, 29.8, 15.6. MS (EI) m/z = 352 (M^+). Anal. Calcd for $C_{25}H_{20}O_2$: C, 85.20; H, 5.72. Found: C, 84.78; H, 5.50.
Spectral data for compound **6b** (Table 2): mp = 102 °C. IR: ν_{max} = 1354, 1450, 1494, 1601, 1693, 2922, 3033, 3435 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, 1H, J = 7.65 Hz), 7.46–7.47 (m, 1H), 7.37–7.41 (m, 2H), 7.28–7.32 (m, 2H), 7.07–7.12 (m, 2H), 6.88–6.93 (m, 3H), 6.60 (d, 2H, J = 6.9 Hz), 4.87 (d, 1H, J = 13.75 Hz), 3.99 (d, 1H, J = 13.75 Hz), 2.25 (s, 3H), 1.89 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 206.9, 147.4, 145.2, 140.6, 139.8, 134.7, 129.5, 129.3, 128.9, 128.3, 127.9, 127.2, 127.1, 125.0, 124.6, 119.8, 119.7, 104.2, 93.5, 63.7, 56.3, 30.3, 27.6. MS (EI) m/z = 370 (M^+). Anal. Calcd for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found: C, 80.9; H, 5.63.
12. Crystallographic data for the compound **6e** in this Letter have been deposited with the Cambridge Crystallographic Data centre as Supplemental Publication No. CCDC 702995. Copies of the data can be obtained, free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ,UK (fax: +44 01223 336033 or email: deposit@ccdc.cam.ac.uk).
13. *General procedure for* **8d**: Following the general procedure as described above, **8d** was obtained from 1-(4-chlorophenyl)-2-(9*H*-fluoren-9-ylidene)ethanone (**7b**) (1 mmol, 0.316 g), dimedone (**2b**) (1 mmol, 0.14 g, 1 equiv), and $NaHCO_3$ (3 mmol, 0.252 g, 3 equiv) in the presence of ceric ammonium nitrate (2.5 mmol, 1.37 g, 2.5 equiv) in 82% (0.373 g) yield as a light yellow solid.
Spectral data for compound **8d** (Table 3): mp = 186 °C. IR: ν_{max} = 1369, 1447, 1631, 1585, 1660, 2937, 3087 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, 1H, J = 8.45 Hz), 7.57–7.63 (m, 2H), 7.48 (t, 1H, J = 7.65 Hz), 7.32–7.43 (m, 3H), 7.14–7.19 (m, 3H), 6.99–7.05 (m, 2H), 5.26 (s, 1H), 2.38–2.61 (m, 4H), 1.36 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.9, 193.8, 177.9, 146.4, 140.7, 140.1, 139.8, 139.3, 134.9, 130.7, 130.4, 129.4, 129.2, 128.4, 128.1, 126.7, 123.1, 120.3, 120.0, 112.7, 95.9, 55.3, 51.1, 38.3, 34.8, 28.9, 28.5. MS (EI) m/z = 454 (M^+), 456 ((M^++2). Anal. Calcd for $C_{29}H_{23}ClO_3$: C, 76.56; H, 5.10. Found: C, 76.00; H, 4.89.