DIASTEREOSELECTIVE SYNTHESIS AND STRUCTURE OF SPIROISOXAZOLINE DERIVATIVES

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ABSTRACT: Synthesis of a series of novel spiroisoxazolines has been accomplished in good yields by regio- and diastereoselective 1,3-dipolar cycloaddition of (E)-2-arylidene-(2H)-indanones 1a-d and (E)-2-arylidene-(2H)-3-methylindanones 2a-d to arylnitrile oxides 3e-g. The structure of the spiroadducts was elucidated by 1H and 13C NMR. The proposed regio- and stereochemistry of spiranic compounds 4ae-dg and 5ae-dg has been corroborated by two single crystal X-Ray diffraction studies.

Keywords: 1,3-dipolar cycloaddition, regiochemistry, stereochemistry, spiroisoxazolines.

RESUME : La cycloaddition 1,3-dipolaire des (E)-2-arylidène-(2H)-indanones 1a-d et des (E)-2-arylidène-(2H)-3-méthylindanones 2a-d sur les arynitriloxydes 3e-g a permis de synthétiser respectivement les spiroisoxazolines 4ae-dg et 5ae-dg avec des bons rendements chimiques. La structure des cycloadduits obtenus a été déterminée suite à une étude spectroscopique en RMN1H et RMN13C. La régio- et la stéréochimie ont été confirmées par une étude radiocristallographique des composés spiranniques 4cf et 5ag.

Mots clés: Cycloaddition 1,3-dipolaire, régiochimie, stéréochimie, spiroisoxazolines.

INTRODUCTION

Spiro-isoxazoline derivatives have attracted a great deal of attention in recent years because of their biological properties such as herbicidal, plant growth regulatory activities [1-3], anti-tumor agent [3] and anti-HIV activity against the Haitian RF strain of HIV-1 [4-6]. They have also proven to be a good precursor for many synthetic intermediates including β-amino alcohols and β-hydroxy ketones [7-9]. Although a plethora of reports are available for the synthesis of isoxazoline derivatives, they appears to be few for spiro-isoxazoline derivatives. Furthermore, many indanone derivatives have been utilized as versatile intermediates for many natural and pharmaceutical products [10-12]. The high synthetic utility and pharmacological importance have prompted us to synthesize some biologically interesting spiroisoxazoline derivatives.

As part of our research on bicyclic spiroicompounds, we have showed that the reaction of arynitrile oxides with some 2-arylmethylene-1,3-indanediones [13] or (Z)-3-arylidene-2(3H)-benzofuranones [14] leads to a single spirocompound. The reaction was regioselective (100%). The structures of the spiroadducts were elucidated by 1H, 13C NMR and MS spectral studies. To the best of our knowledge the reaction of (E)-2-arylidene-(2H)-indanones 1a-d and (E)-2-arylidene-(2H)-3-methylindanones 2a-d with arynitrile oxides 3e-g has not been previously reported.

RESULTS AND DISCUSSION

We have subjected dipolarophiles 1a-d and 2a-d to cycloaddition reactions (48 h at reflux in toluene) with the arynitrile oxides 3e-g according to Scheme 1. The [3+2] cycloaddition reaction led to single adducts in each case, as evidenced by TLC and 1H NMR examination of the crude reaction mixture. The reaction yielded regioselectively (100%) respectively a series of the

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spiro[3,4-diaryl-2-isoxazoline-5:2’-indanones] 4ae-dg and the spiro[3,4-diaryl-2-isoxazoline-5:2’-3’-methylindanones] 5ae-dg. The regiochemistry of the reaction was similar to that observed for an olefin activated by an electron-withdrawing group, which was always situated at the 5-position of the resulting spiroisoxazoline derivatives [13-17]. The structure of each product 4ae-dg and 5ae-dg has been confirmed by spectroscopic data. The $^1$H NMR spectra exhibited a singlet around $\delta = 4.81$-4.97 ppm attributed for the benzylic proton 4-H. Since, in the case of the reverse regioisomers 4’ae-dg and 5’ae-dg, one should have observed a chemical shift value higher than 6 ppm for the 5-H proton [18]. The $^{13}$C NMR data also confirmed this result: the chemical shifts of the spiro carbon atoms (C-5,2’) were found between 92.83 ppm and 97.82 ppm because of the deshielding effect of the oxygen atom. In the case of the structures 4’ae-dg and 5’ae-dg, the chemical shift values of spiro carbon atoms (C-4,2’) should be below 60 ppm [18-20].

The cycloaddition of (E)-2-arylidene-(2H)-indanones (1a-e) with arynitrile oxides (3e-g) led to cycloadducts 4ae-dg with two new chiral centers, i.e. the quaternary spiroatom C-5,2’ and the C-4 of isoxazole ring (Scheme 1). The relative stereochemistry of these carbon [rel-(4R, 5,2’R)] results from preservation of the (E) configuration of the initial olefin. This stereochemistry was encountered in all categories of cycloadducts and conformed to the favoured approach of the two reagents. The product stereochemistry is revealed by study of Aromatic Solvent Induced Shift (A.S.I.S) data of the cycloadducts in two solvents CDCl$_3$ and C$_6$D$_6$. Indeed, the displacement of the signal of proton 4-H of the cycloadduct 4af in CDCl$_3$ ($\delta$ (4-H) = 4.95 ppm) towards downfield in C$_6$D$_6$ ($\delta$ (4-H) = 4.97 ppm) show that 4-H atom is close to the carbonyl group and that, therefore, arynitrile oxides cycloaddition proceeds with retention of configuration at the starting double bond of dipolarophiles (1a-g).

The structure and the regiochemistry of cycloadduct were corroborated by X-Ray crystal analysis of the product 4cf (Figure 1) [21].

Scheme 1
For the cycloaddition of dipolarophiles 2a-d with arylnitrile oxides 3e-g, the attack of the 1,3-dipole proceeds from the sterically less hindered side, i.e. opposite of the methyl group (methyl present in the arylidene moiety). The reaction proceeds with 100% regio- and diastereoselectively and give exclusively the anti-diastereoisomer (Scheme 2). The corresponding syn-diastereoisomer have not been detected in the crude reaction mixture by NMR spectroscopy.

The cycloadducts 5ae-dg present three new chiral centers, i.e. the quaternary spiroatom C-5,2’, C-4 of ring isoxazole and C-3’. The relative stereochemistry of these carbon [rel-(4R, 5,2’R, 3’R)] results from preservation of the (E) configuration of the initial olefin and anti approach of the 1,3-dipole 3e-g to the dipolarophile 2a-d. The structure and stereochemistry of the cycloadducts were corroborated by X-Ray crystal analysis of the product 5ag (Figure 2)\textsuperscript{[21]}.

**Scheme 2**
CONCLUSION

In conclusion, efficient syntheses of novel spiro-isoxazolines have been demonstrated by the (100%) regio- and stereoselective of (E)-2-arylidene-(2H)-indanones 2a-d and (E)-2-arylidene-(2H)-3'-methylindanones 3a-d with nitrile oxides 3e-g. The regiochemistry of the cycloaddition reaction studied is independent of the electronic nature of the substituent on the arylidene ring of the dipolarophile. A part from the regioselectively aspect, the spiroisoxazolines prepared should be of interest as precursors for the synthesis of a variety of amino alcohols derivatives that could be readily converted to $\beta$-lactams$^{[22]}$.

EXPERIMENTAL

Reactions were carried out under an atmosphere of dry N₂. Solvents were purified by standard methods and freshly distilled under nitrogen and dried before use.

Melting points were determined on a Kofler bank. IR spectra were recorded from KBr on a Perkin-Elmer 197 spectrometer; only structurally significant bands are reported. NMR spectra were recorded on a Bruker-Spectrospin AC 300 spectrometer operating at 300 MHz for $^1$H and 75.5 MHz for $^{13}$C. Chemical shifts were measured relative to TMS in CDCl₃ as solvent. Materials: thin-layer chromatography (TLC): TLC plates (Merck, silica gel 60 F254 0.2 mm 200 × 200 nm); substances were detected using UV light at 254 nm.

(E)-2-arylidene-(2H)-indanones 1a-d and (E)-2-arylidene-(2H)-3-methylindanones 2a-d were obtained by condensation of aldehydes $Ar'_1$CHO with respectively indanone and 3-methylindanone according to reported methods$^{[23,24]}$. The arylnitrile oxides were prepared in situ by deshydrohalogenation of the corresponding benzohydroxyaminoyl chlorides 3e-g according to ref$^{[25-29]}$.

General procedure for the preparation of the cycloadducts 4ae-dg and 5ae-dg

To a magnetically stirred solution of dipolarophiles 1a-d or 2a-d (3.33 mmol) and the appropriate precursor (3.33 mmol) of arylnitrile oxides 3e-g in dry toluene, was refluxed under nitrogen for 15 min. Et₃N (2 mL) was then added and the mixture was stirred and refluxed for 48 h. After filtration of triethylamine hydrochloride, the solvent was evaporated under reduced pressure and the residue recrystallised from ethanol to give the product 4 and 5 respectively.

Spiro [3,4-diphenyl-2-isoxazoline-5:2'-indanone] (4ae)

Yield (37%); yellow needles; Mp 207°C; IR (KBr): ν 1753, 1605 cm⁻¹; $^1$H NMR (CDCl₃): δ 2.88 (dd, J=18, 3'-H); 4.89 (s, 4-H); 7.08-7.77 (m, aromatic H) ppm; $^{13}$C NMR (CDCl₃): δ 35.71 (C-3'); 57.94 (C-4); 93.52 (C-5,2'); 125.64-151.41 (aromatic C); 159.41 (C-3); 201.55 (C-1') ppm.

Spiro [3-(p-tolyl)-4-phenyl-2-isoxazoline-5:2'-indanone] (4af)

Yield (56%); yellow needles; Mp 186 C; IR (KBr): ν 1737, 1608 cm⁻¹; $^1$H NMR (CDCl₃): δ 2.30 (s, CH₃); 2.95 (dd, J=18, 3'-H); 4.95 (s, 4-H); 7.07-7.84 (m, aromatic H) ppm; $^{13}$C NMR (CDCl₃):
δ 21.85 (CH₃); 35.72 (C-3’); 58.05 (C-4); 93.15 (C-5,2’); 125.62-151.56 (aromatic C); 159.38 (C-3); 201.68 (C-1’) ppm.

**Spiro [3-(p-anisyl)-4-phenyl-2-isoxazoline-5:2’-indanone] (4ag)**

Yield (76%); yellow needles; Mp 185°C; IR (KBr): ν 1739, 1606 cm⁻¹; ¹H NMR (CDCl₃): δ 2.68 (dd, J=18 Hz, 3’-H); 3.66 (s, OCH₃); 4.84 (s, 4-H); 6.68-7.73 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 35.77 (C-3’); 55.60 (OCH₃); 58.13 (C-4); 93.15 (C-5,2’); 114.85-161.28 (aromatic C); 159.00 (C-3); 201.70 (C-1’) ppm.

**Spiro [3-phenyl-4-(p-tolyl)-2-isoxazoline-5:2’-indanone] (4be)**

Yield (54%); yellow needles; Mp 190°C; IR (KBr) 1755, 1608 cm⁻¹; ¹H NMR (CDCl₃): δ 2.24 (s, CH₃); 2.87 (dd, J=18 Hz, 3’-H); 4.85 (s, 4-H); 7.16-7.82 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 21.59 (CH₃); 35.67 (C-3’); 57.69 (C-4); 93.20 (C-5,2’); 125.58, 126.59, 128.02, 128.56, 128.70, 128.93, 129.10, 129.46, 130.37, 134.02, 134.93, 136.32, 151.60 (aromatic C); 156.66 (C-3); 200.20 (C-1’) ppm.

**Spiro [3,4-di(p-tolyl)-2-isoxazoline-5:2’-indanone] (4bf)**

Yield (72%); white needles; Mp 200°C; IR (KBr): ν 1759, 1608 cm⁻¹; ¹H NMR (CDCl₃): δ 2.21 (s, CH₃); 2.22 (s, CH₃); 2.87 (dd, J=18 Hz, 3’-H); 4.85 (s, 4-H); 6.93-7.75 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 21.58 (CH₃); 21.84 (CH₃); 35.71 (C-3’); 57.79 (C-4); 93.01 (C-5,2’); 124.77, 125.57-151.62 (aromatic C); 159.46 (C-3); 201.81 (C-1’) ppm.

**Spiro [3-(p-anisyl)-4-(p-tolyl)-2-isoxazoline-5:2’-indanone] (4bg)**

Yield (68%); yellow needles; Mp 180°C; IR (KBr): ν 1754, 1608 cm⁻¹; ¹H NMR (CDCl₃): δ 2.21 (s, CH₃), 2.89 (dd, J=18 Hz, 3’-H); 3.67 (s, OCH₃), 4.81 (s, 4-H), 6.67-7.73 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 21.58 (CH₃); 35.70 (C-3’); 55.65 (OCH₃); 57.89 (C-4); 92.91 (C-5,2’); 114.36-161.24 (aromatic C); 159.12 (C-3); 201.89 (C-1’) ppm.

**Spiro [3-phenyl-4-(p-anisyl)-2-isoxazoline-5:2’-indanone] (4ce)**

Yield (64%); yellow crystals; Mp 182°C; IR (KBr): ν 1711, 1605 cm⁻¹; ¹H NMR (CDCl₃): δ 2.89 (dd, J=18 Hz, 3’-H); 3.77 (s, OCH₃); 4.92 (s, 4-H); 6.84-7.91 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 35.28 (C-3’); 55.48 (OCH₃); 57.06 (C-4); 92.87 (C-5,2’); 114.51-160.89 (aromatic C); 159.47 (C-3); 194.51 (C-1’) ppm.

**Spiro [4-(p-anisyl)-3-(p-tolyl)-2-isoxazoline-5:2’-indanone] (4cf)**

Yield (51%); yellow needles; Mp 190°C; IR (KBr): ν 1735, 1610 cm⁻¹; ¹H NMR (CDCl₃): δ 2.22 (s, CH₃), 2.89 (dd, J=18 Hz, 3’-H); 3.79 (s, OCH₃); 4.82 (s, 4-H); 6.76-7.92 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 21.83 (CH₃); 35.70 (C-3’); 55.64 (OCH₃); 57.52 (C-4); 93.04 (C-5,2’); 114.86-161.24 (aromatic C); 159.76 (C-3); 201.89 (C-1’) ppm.

**Spiro [3,4-di(p-tolyl)-2-isoxazoline-5:2’-indanone] (4cg)**

Yield (75%); yellow needles; Mp 174°C; IR (KBr): ν 1754, 1608 cm⁻¹; ¹H NMR (CDCl₃): δ 2.88 (dd, J=18 Hz, 3’-H); 3.77 (s, OCH₃); 3.68 (s, OCH₃); 4.85 (s, 4-H); 6.65-8.09 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 35.37 (C-3’); 55.60 (OCH₃); 57.32 (OCH₃); 92.84 (C-5,2’); 113.94-161.24 (aromatic C); 159.55 (C-3); 201.00 (C-1’) ppm.

**Spiro [3-(p-anisyl)-4-(p-nitrophenyl)-2-isoxazoline-5:2’-indanone] (4df)**

Yield (41%); yellow needles; Mp 195°C; IR (KBr): ν 1752, 1600 cm⁻¹; ¹H NMR (CDCl₃): δ 2.87 (dd, J=18 Hz, 3’-H); 4.97 (s, 4-H); 6.98-8.30 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 37.52 (C-3’); 56.80 (C-4); 92.30 (C-5,2’); 125.64-151.41 (aromatic C); 159.51 (C-3); 198.52 (C-1’) ppm.

**Spiro [4-(p-nitrophenyl)-3-(p-tolyl)-2-isoxazoline-5:2’-indanone] (4dfb)**

Yield (31%); yellow needles; Mp 195°C; IR (KBr): ν 1754, 1600 cm⁻¹; ¹H NMR (CDCl₃): δ 2.21 (s, CH₃); 2.90 (dd, J=18 Hz, 3’-H); 4.87 (s, 4-H); 6.88-8.12 (m, aromatic H) ppm; ¹³C NMR (CDCl₃): δ 21.91 (CH₃); 35.62 (C-3’); 57.66 (C-4); 93.40 (C-5, 2’); 123.45-151.56 (aromatic C); 159.63 (C-3); 199.10 (C-1’) ppm.
Spiro [3-(p-anisyl)-4-(p-nitrophenyl)-2-isoxazoline-5:2’-indanone] (4dg)
Yield (54%); yellow needles; Mp 210°C; IR (KBr): ν 1755, 1608 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 2.89 (dd, J=18 Hz, 3’-H); 3.65 (s, OCH\(_3\)); 4.88 (s, 4-H); 6.78-8.12 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 35.75 (C-3’); 55.82 (OCH\(_3\)); 57.85 (C-4); 93.44 (C-5,2’); 114.41-161.52 (aromatic C); 159.43 (C-3); 199.20 (C-1’) ppm.

Spiro [3,4-diphenyl-2-isoxazoline-5:2’-3’-methylindanone] (5ae)
Yield (32%); white needles; Mp 210°C; IR (KBr): ν 1753, 1605 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.58 (d, J=7.2 Hz, CH\(_3\)); 3.36 (q, 3’-H); 4.90 (s, 4-H); 7.19-7.73 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 19.70 (Me); 39.45 (C-3’); 51.90 (C-4); 95.53 (C-5, 2’); 124.20-161.02 (aromatic C); 157.31 (C-3); 197.94 (C-1’) ppm.

Spiro [3-(p-tolyl)-4-phenyl-2-isoxazoline-5:2’-3’-methylindanone] (5af)
Yield (45%); white needles; Mp 221°C; IR (KBr): ν 1752, 1600 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.67 (d, J=7.2 Hz, CH\(_3\)); 2.30 (s, CH\(_3\)); 3.45 (q, 3’-H); 4.96 (s, 4-H); 7.09-7.83 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 21.41 (Me); 21.85 (Me); 40.50 (C-3’); 53.03 (C-4); 95.53 (C-5, 2’); 124.20-161.02 (aromatic C); 158.43 (C-3); 199.00 (C-1’) ppm.

Spiro [3-(p-anisyl)-4-phenyl-2-isoxazoline-5:2’-3’-methylindanone] (5ag)
Yield (45%); white crystals; Mp 206°C; IR (KBr): ν 1754, 1600 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.67 (d, J=7.2 Hz, CH\(_3\)); 3.43 (q, 3’-H); 3.76 (s, OCH\(_3\)); 4.94 (s, 4-H); 6.97-7.82 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 20.85 (Me); 40.50 (C-3’); 53.21 (C-4); 95.45 (C-5, 2’); 114.05-161.74 (aromatic C); 158.45 (C-3); 199.12 (C-1’) ppm.

Spiro [3-phenyl-4-(p-tolyl)-2-isoxazoline-5:2’-3’-methylindanone] (5be)
Yield (45%); white needles; Mp 221°C; IR (KBr): ν 1752, 1600 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.61 (d, J=7.2 Hz, CH\(_3\)); 2.24 (s, CH\(_3\)); 3.36 (q, 3’-H); 4.86 (s, 4-H); 7.06-7.74 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 21.21 (Me); 21.55 (Me); 40.91 (C-3’); 53.01 (C-4); 96.05 (C-5, 2’); 124.20-162.53 (aromatic C); 158.84 (C-3); 199.45 (C-1’) ppm.

Spiro [3,4-di(p-tolyl)-2-isoxazoline-5:2’-3’-methylindanone] (5bf)
Yield (51%); yellow needles; Mp 144°C; IR (KBr): ν 1769, 1608 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.63 (d, J=7.2 Hz, CH\(_3\)); 2.30 (s, CH\(_3\)); 3.44 (q, 3’-H); 4.94 (s, 4-H); 7.09-7.82 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 21.21 (Me); 21.55 (Me); 40.51 (C-3’); 52.72 (C-4); 95.55 (C-5, 2’); 124.20-162.17 (aromatic C); 158.47 (C-3); 199.25 (C-1’) ppm.

Spiro [3-(p-anisyl)-4-(p-tolyl)-2-isoxazoline-5:2’-3’-methylindanone] (5bg)
Yield (58%); white needles; Mp 208°C; IR (KBr): ν 1756, 1600 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.70 (d, J=7.2 Hz, CH\(_3\)); 2.33 (s, CH\(_3\)); 3.43 (q, 3’-H); 4.91 (s, 4-H); 6.80-7.82 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 20.85 (Me); 40.51 (C-3’); 53.21 (C-4); 95.45 (C-5, 2’); 124.20-161.74 (aromatic C); 158.42 (C-3); 199.22 (C-1’) ppm.

Spiro [3-phenyl-4-(p-anisyl)-2-isoxazoline-5:2’-3’-methylindanone] (5ce)
Yield (51%); yellow needles; Mp 144°C; IR (KBr): ν 1769, 1608 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.70 (d, J=7.2 Hz, CH\(_3\)); 2.29 (s, CH\(_3\)); 3.44 (q, 3’-H); 4.94 (s, 4-H); 7.06-7.74 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 21.21 (Me); 21.55 (Me); 40.91 (C-3’); 53.01 (C-4); 96.05 (C-5, 2’); 124.20-161.52 (aromatic C); 158.84 (C-3); 199.45 (C-1’) ppm.

Spiro [3,4-di(p-anisyl)-2-isoxazoline-5:2’-3’-methylindanone] (5cg)
Yield (40%); white needles; Mp 217°C; IR (KBr): ν 1754, 1605 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.71 (d, J=7.2 Hz, CH\(_3\)); 3.41 (q, 3’-H); 3.76 (s, OCH\(_3\)); 3.78 (s, OCH\(_3\)); 4.90 (s, 4-H); 6.80-7.81 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 21.10 (Me); 21.85 (Me); 40.25 (C-3’); 52.52 (C-4); 55.32 (OCH\(_3\)); 95.41 (C-5, 2’); 114.04-161.82 (aromatic C); 158.45 (C-3); 199.22 (C-1’) ppm.

Spiro [4-(p-anisyl)-3-(p-tolyl)-2-isoxazoline-5:2’-3’-methylindanone] (5cf)
Yield (52%); white needles; Mp 210°C; IR (KBr): ν 1750, 1605 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): δ 0.62 (d, J=7.2 Hz, CH\(_3\)); 3.45 (q, 3’-H); 3.70 (s, OCH\(_3\)); 4.85 (s, 4-H); 6.82-7.80 (m, aromatic H) ppm; \(^13\)C NMR (CDCl\(_3\)): δ 20.51 (Me); 40.51 (C-3’); 52.81 (C-4); 55.32 (OCH\(_3\)); 95.41 (C-5, 2’); 114.05-161.02; 162.53(aromatic C); 158.45 (C-3); 199.22 (C-1’) ppm.
aromatic H); $^{13}$C NMR (CDCl$_3$): $\delta$ 20.80 (Me); 40.51 (C-3'); 52.44 (C-4); 55.21 (OCH$_3$); 55.32 (OCH$_3$); 95.22 (C-5, 2'); 114.04-161.83 (aromatic C); 159.42 (C-3); 199.30 (C-1') ppm.

**Spiro [3-phenyl-4-(p-nitrophenyl)-2-isoxazoline-5:2'-3'-methylindanone] (5de)**

Yield (50%); yellow needles; Mp 200°C; IR (KBr): v 1753, 1605 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 0.62 (d, J=7.2 Hz, CH$_3$); 3.70 (q, 3'-H), 4.90 (s, 4-H), 6.98-8.30 (m, aromatic H) ppm; $^{13}$C NMR (CDCl$_3$): $\delta$ 20.41 (Me); 42.68 (C-3'); 56.04 (C-4); 97.01 (C-5, 2'); 122.72-161.02 (aromatic C); 158.91 (C-3); 197.44 (C-1') ppm.

**Spiro [4-(p-nitrophenyl)-3-(p-tolyl)-2-isoxazoline-5:2'-3'-methylindanone] (5df)**

Yield (40%); yellow needles; Mp 185°C; IR (KBr): v 1754, 1605 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 0.61 (d, J=7.2 Hz, CH$_3$); 2.24 (s, CH$_3$); 3.72 (q, 3'-H); 4.91 (s, 4-H); 6.98-7.97 (m, aromatic H); $^{13}$C NMR (CDCl$_3$): $\delta$ 20.40 (Me); 21.25 (Me); 42.62 (C-3'); 56.62 (C-4); 97.82 (C-5,2'); 122.72-158.78; (aromatic C); 155.52 (C-3); 199.15 (C-1') ppm.

**Spiro [3-(p-anisyl)-4-(p-nitrophenyl)-2-isoxazoline-5:2'-3'-methylindanone] (5dg)**

Yield (51%); white needles; Mp 216°C; IR (KBr): v 1754, 1605 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 0.69 (d, J=7.2 Hz, CH$_3$); 3.42 (q, 3'-H); 3.78 (s, OCH$_3$); 4.91 (s, 4-H); 6.75-7.85 (m, aromatic H); $^{13}$C NMR (CDCl$_3$): $\delta$ 20.80 (Me); 42.68 (C-3'); 52.15 (C-4); 55.31 (OCH$_3$), 95.22 (C-5,2'); 114.62-161.02 (aromatic C); 159.01 (C-3); 199.35 (C-1') ppm.

**REFERENCES**

[21] Crystallographic data of 4cf and 5ag have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number mk1m_1 and mk581. Copie of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK, fax: 144-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk