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 ^{1}H and ^{13}C 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 arylnitriloxydes **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 RMN^{1}H et RMN^{13}C. 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 arylnitrile 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 ^{1}H, ^{13}C 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 arylnitrile 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 arylnitrile oxides **3e-g** according to **Scheme 1**. The [3+2] cycloaddition reaction led to single adducts in each case, as evidenced by TLC and ^{1}H NMR examination of the crude reaction mixture. The reaction yielded regioselectively (100%) respectively a series of the

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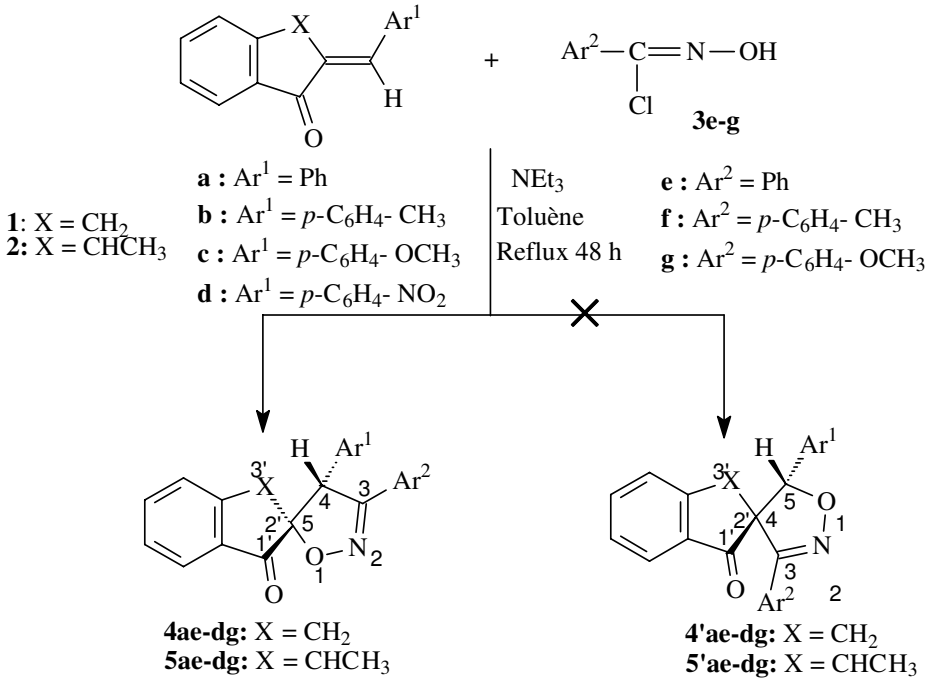
spiro[3,4-diaryl-2-isoxazoline-5:2'-indanones] **4ae-dg** and the spiro[3,4-diaryl-2-isoxazoline-5:2'-3'-methylindanones] **5ae-dg**. The regiochemistry of the reaction was similar to that observed for an olefin activated by an electron-withdrawing group, which was always situated at the 5-position of 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 δ= 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].



Scheme 1

The cycloaddition of (E)-2-arylidene-(2H)-indanones (**1a-e**) with arylnitrile 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_6D_6. Indeed, the displacement of the signal of proton 4-H of the cycloadduct **4af** in $CDCl_3$ (δ (4-H) = 4.95 ppm) towards downfield in C_6D_6 (δ (4-H) = 4.97 ppm) show that 4-H atom is close to the carbonyl group and that, therefore, arylnitrile 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].

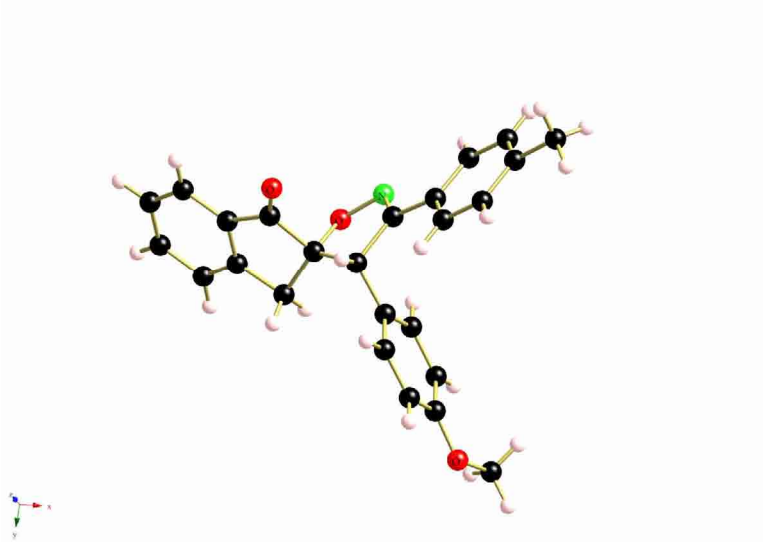
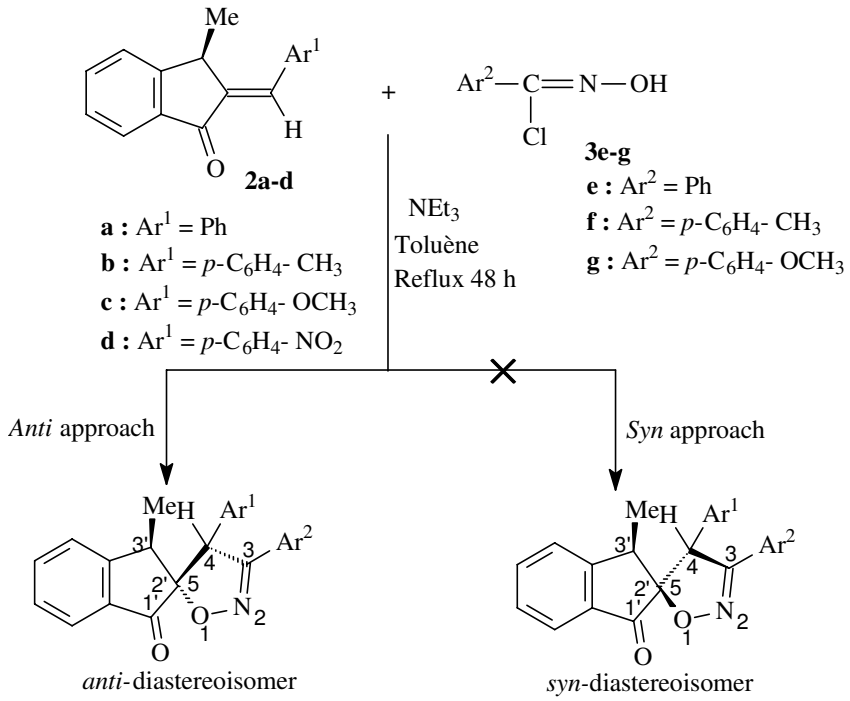


Figure 1

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**)[21].



Scheme 2

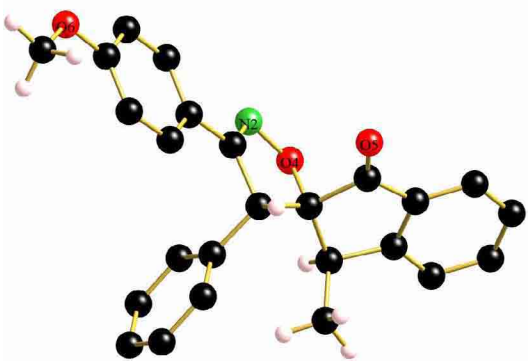


Figure 2

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 β-lactams[22].

EXPERIMENTAL

Reactions were carried out under an atmosphere of dry N_2. 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 $CDCl_3$ as solvent. Materials: thin-layer chromatography (TLC): TLC plates (Merck, silica gel 60 F_{254} 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^1CHO 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. Et_3N (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** ($CDCl_3$): δ 2.88 (dd, J=18, 3'-H); 4.89 (s, 4-H); 7.08-7.77 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): 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** ($CDCl_3$): δ 2.30 (s, CH_3); 2.95 (dd, J=18, 3'-H); 4.95 (s, 4-H); 7.07-7.84 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$):

δ 21.85 (CH_3); 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} ; **^{1}H NMR** ($CDCl_3$): δ 2.68 (dd, J=18 Hz, 3'-H); 3.66 (s, OCH_3); 4.84 (s, 4-H); 6.68-7.73 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 35.77 (C-3'); 55.60 (OCH_3); 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}; **^{1}H NMR** ($CDCl_3$): δ 2.24 (s, CH_3); 2.87 (dd, J=18 Hz, 3'-H), 4.85 (s, 4-H); 7.16-7.82 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 21.59 (CH_3); 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}; **^{1}H NMR** ($CDCl_3$): δ 2.21 (s, CH_3); 2.22 (s, CH_3); 2.87 (dd, J=18 Hz, 3'-H); 4.85 (s, 4-H); 6.93-7.75 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 21.58 (CH_3); 21.84 (CH_3); 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}; **^{1}H NMR** ($CDCl_3$): δ 2.21 (s, CH_3), 2.89 (dd, J=18 Hz, 3'-H); 3.67 (s, OCH_3), 4.81 (s, 4-H), 6.67-7.73 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 21.58 (CH_3); 35.70 (C-3'); 55.65 (OCH_3); 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} ; **^{1}H NMR** ($CDCl_3$): δ 2.89 (dd, J=18 Hz, 3'-H); 3.77 (s, OCH_3); 4.92 (s, 4-H); 6,84-7,91 (m, aromatic H) ppm;**^{13}C NMR** ($CDCl_3$): δ 35.28 (C-3'); 55.48 (OCH_3); 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} ; **^{1}H NMR** ($CDCl_3$): δ 2.22 (s, CH_3), 2.89 (dd, J=18 Hz, 3'-H); 3.79 (s, OCH_3); 4.82 (s, 4-H); 6,76-7,92 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 21.83 (CH_3); 35.67 (C-3'); 55.64 (OCH_3); 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-anisyl)-2-isoxazoline-5:2'-indanone] (4cg)

Yield (75%); yellow needles; Mp 174 C; **IR** (KBr): ν 1754, 1608 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 2.88 (dd, J=18 Hz, 3'-H); 3.66 (s, OCH_3); 3.68 (s, OCH_3); 4.85 (s, 4-H); 6.65-8.09 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 35.37 (C-3'); 55,71 (OCH_3); 55.80 (OCH_3); 57.32 (C-4); 92.84 (C-5,2'); 113.94-161.24 (aromatic C); 159.55 (C-3); 201.00 (C-1') ppm.

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

Yield (41%); yellow needles; Mp 190 C; **IR** (KBr): ν 1752, 1600 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 2.87 (dd, J=18 Hz, 3'-H); 4.97 (s, 4-H); 6.98-8.30 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): 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] (4df)

Yield (31%); yellow needles; Mp 195°C; **IR** (KBr): ν 1754, 1600 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 2.21 (s, CH_3); 2.90 (dd, J=18 Hz, 3'-H); 4.87 (s, 4-H); 6.88-8.12 (m, aromatic H) ppm; **^{13}C NMR** ($CDCl_3$): δ 21.91 (CH_3); 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); 94.52 (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); **^{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'); 125.29-162.09 (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); **^{13}C NMR** ($CDCl_3$): δ 20.85 (Me); 40.50 (C-3'); 53.21 (C-4); 55.32 (OMe), 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 195°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); **^{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'); 125.63-162.53 (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** (300 MHz, $CDCl_3$): δ 0.70 (d, J=7.2 Hz, CH_3); 2.29 (s, CH_3); 2.32 (s, CH_3); 3.44 (q, 3'-H); 4.94 (s, 4-H), 7.09-7.82 (m, aromatic H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 21.21 (Me); 20,9 (Me); 21.51 (Me); 40.51 (C-3'); 52.72 (C-4); 95.55 (C-5, 2'); 125.30-162.17 (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); 3.76 (s, OCH_3); 4.91 (s, 4-H), 6.80-7.82 (m, aromatic H); **^{13}C NMR** ($CDCl_3$): δ 20.85 (Me); 21.24 (Me), 40.51 (C-3'); 52.81 (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 [3-phenyl-4-(p-anisyl)-2-isoxazoline-5:2'-3'-methylindanone] (5ce)
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); **^{13}C NMR** ($CDCl_3$): δ 20.51 (Me); 40.25 (C-3'); 52.52 (C-4); 55.32 (OCH_3); 95.31 (C-5,2'); 114.05-161.02; 162.53(aromatic C); 158.42(C-3); 199.21 (C-1') ppm.

Spiro [4-(p-anisyl)-3-(p-tolyl)-2-isoxazoline-5:2'-3'-methylindanone] (5cf)
Yield (30%); white needles; Mp 176°C; **IR** (KBr): ν 1754, 1600 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 0.63 (d, J=7.2 Hz, CH_3); 222 (s, CH_3); 3.45 (q, 3'-H); 3.71 (s, OCH_3), 4.84 (s, 4-H); 6.79-7.74 (m, aromatic H); **^{13}C NMR** ($CDCl_3$): δ 21.10 (Me); 21,85 (Me); 40.81 (C-3'); 52.71 (C-4); 55.60 (OCH_3), 95.75 (C-5, 2'), 114.99-162.51 (aromatic C);159.78 (C-3); 199.61 (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); **^{13}C NMR** ($CDCl_3$): δ 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): ν 1753, 1605 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 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** ($CDCl_3$): δ 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): ν 1754, 1605 cm^{-1}**; ^{1}H NMR** ($CDCl_3$): δ 0.61 (d, J=7.2 Hz, CH_3); 224 (s, CH_3); 3.72 (q, 3'-H); 4.91 (s, 4-H); 6.98-7.97 (m, aromatic H); **^{13}C NMR** ($CDCl_3$): δ 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): ν 1754, 1605 cm^{-1}; **^{1}H NMR** ($CDCl_3$): δ 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** ($CDCl_3$): δ 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.

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