One-pot synthesis of some new spiro 6H-indolo[b-1,2]quinazoline-12-one-[1,2,4]triazolines

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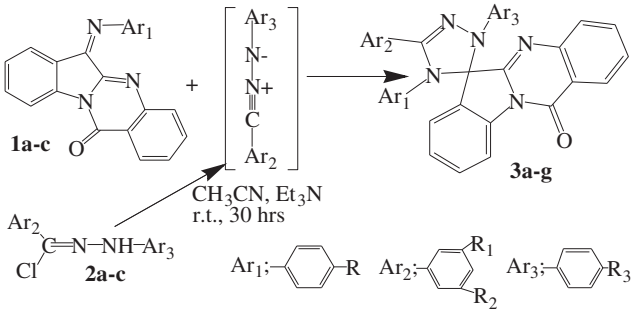
The title compounds **3a–g** were prepared by the cycloaddition reaction of nitrilimines and tryptanthrinimines using conventional methods and in good yields.

Keywords: 1,3-dipolar cycloaddition, nitrilimines, tryptanthrinimines, isatinimines, triazolines

1,3-Dipolar cycloaddition is an important versatile standard methods for construction of many five membered heterocycles. Among the known 1,3-dipoles, nitrilimines are one of the extensively used classes.[1,2] Compounds which are 1,2,4-triazoles such as triazolam, etizolam and alprazolam, are known as antiseptic and analgesic drugs.[3] On the other hand compounds with the tryptanthrin backbone have a broad-spectrum of biological activity[4–6] and we believe that spirotriazoles based on tryptanthrin could have enhanced biological activity.

In continuation of our earlier work on the synthesis of spirotriazolines[7] we now report the synthesis of a series of novel spirotriazolines **3a–g** with a new skeleton by reaction of the corresponding tryptanthrinimines **1a–c** and nitrilimines, under ambient conditions and in high yields. The reagents and reaction conditions are shown in Scheme 1 and the product structures and yields are summarised in Table 1. Nitrilimines were generated *in situ* to form the corresponding hydrazonylchlorides **2a–c** and triethylamine as base.[8] In most cases, products were obtained in asufficiently pure form, however, more purification of products may be achieved by column chromatography with a suitable solvent. It is noticeable that tryptanthrin is not suitable for imination with amines and we synthesised the tryptanthrinimines we required, based on our new simple method,[9] via the reaction of isatinimines and isatoic anhydride.

The structures of products (**3a–g**) were assigned on the basis of their elemental analysis, ^{1}H NMR, ^{13}C NMR and mass spectral data, as well as the IR spectra. In the IR spectra signals at 1670–1690 cm^{-1} and 1589–1637 cm^{-1} are due to carbonyl absorption of the tryptanthrin skeleton and the C=N group respectively. In the ^{13}C NMR spectra, the carbonyl absorptions appeared at about 159 ppm, imine carbons (C=N) show absorption at 144–154 ppm and a signal at 87–90 ppm is attributed to the spiro carbon atom.



Scheme 1

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Table 1 Synthesis of spiro 6H-indolo[b-1,2]quinazoline-12-one-[1,2,4]triazolines **3a–g**

Product **4**	R	R_1	R_2	R_3	Yield/%*
A	H	H	H	H	93
B	H	H	H	NO_2	92
C	CH_3	H	H	H	70
D	CH_3	H	H	NO_2	72
E	CH_3	NO_2	NO_2	H	70
F	Cl	H	H	H	75
G	Cl	H	H	NO_2	73

*Pure isolated products.

Experimental

Melting points were measured on the Electrothermal 9100 apparatus and are uncorrected. Elemental analysis for C, H and N were performed using a heraus CHN rapid analyzer. IR spectra were measured on a Bomen FT-IR-MB 100 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-300 advance spectrometer. Mass spectra were recorded on a Shimadzu QP 1100 EX mass spectrometer. Benzoyl chloride, 3,5-dinitrobenzoyl chloride, phenylhydrazine and p-nitrophenylhydrazine were obtained from Merck and used without further purification.

Preparation of 6H-indolo[b-1,2]quinazoline-12-one-[1,2,4] triazoline **4a;** *typical procedure***:** To a magnetically stirred solution of hydrazonylchloride **2a** (0.050 g, 0.22 mmol) and tryptanthrinimines **1a** (0.048 g, 0.22 mmol) in CH_3CN (10 ml), a mixture of triethylamine (25µl, 0.25mmol) in CH_3CN (5 ml) at room temperature was added dropwise over 15 min. The reaction mixture was then stirred for 30 h. The reaction mixture was filtered to remove triethylammonium chloride, the solvent evaporated under reduced pressure and the crude product was purified by column chromatography (petroleum ether/ ethyl acetate: 10/2 as eluent) to obtain pure product **4a** (0.10 g, 93% yield) (Table 1).

Compound **3a**: yellow crystals, m.p. 105–106°C. IR (KBr): ν/cm^{-1}: 1678 (C=0), 1642 and 1595 (2C=N). ^{1}H NMR ($CDCl_3$), δ 6.43–7.96 (23H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 90.66 (spiro carbon), 114.93, 120.66, 122.22, 126.59, 126.70, 127.21, 127.40, 127.66, 127.92, 127.95, 128.08, 128.36, 128.43, 128.61, 128.93, 129.24, 129.37, 129.46, 129.77, 130.22, 132.42, 138.07, 139.55, 143.26 (aromatic carbons), 148.36, 154.82 (2C=N), 159.90 (C=0). MS *m/z*, (%): 517 (M$^+$, 22), 412 (27), 322 (90), 194 (37). Anal. calc. for $C_{34}H_{23}N_5O$, C, 78.93; H, 4.45; N, 13.53. Found C, 78.89; H, 4.41; N, 13.49.

Compound **3b**: yellow crystals, m.p. 124–125 °C. IR (KBr) ν/ cm^{-1}: 1687 (C=0), 1640, 1592 (2C=N). ^{1}H NMR ($CDCl_3$), δ 6.54–7.98 (22H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 89.544 (spiro carbon), 112.56, 118.16, 122.23, 126.16, 126.17, 126.27, 126.87, 127.45, 127.64, 128.26, 128.39, 128.72, 128.81, 128.92, 128.93, 129.56, 130.65, 133.24, 135.27, 136.99, 139.55, 139.99, 146.97, 147.00 (aromatic carbons), 150.56, 153.62 (2C=N), 159.58 (C=0). MS *m/z*, (%): 562 (M$^+$, 60), 412 (98), 322(100), 239 (52). Anal. calc. for $C_{34}H_{22}N_6O_3$, C, 72.59; H, 3.94; N, 14.94. Found C, 72.55; H, 3.91; N, 14.90.

Compound **3c**: orange-brown crystals, m.p. 117°C. IR (KBr) ν/cm^{-1}: 1685 (C=0), 1640 and 1594 (2C=N). ^{1}H NMR ($CDCl_3$), δ 2.20 (s, CH_3), 6.67–7.79 (22H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 21.41 (CH_3), 88.56 (spiro carbon), 111.38, 114.77, 120.63, 124.31, 127.09, 127.77, 128.02, 128.22, 128.40, 128.50, 128.93, 129.38, 129.60, 129.68, 129.97, 131.65, 135.63, 137.25, 141.00, 143.91 (aromatic carbons), 148.83, 154.73 (2C=N), 159.37 (C=0). MS *m/z*, (%): 531 (M$^+$, 36), 402 (100), 337 (5), 194 (26). Anal. calc. for $C_{35}H_{25}N_5O$, C, 79.08; H, 4.74; N, 13.17. Found C, 78.05; H, 4.71; N, 13.14.

Compound **3d**: orange crystals, m.p. 130°C. IR (KBr) ν/cm^{-1}: 1682 (C=0), 1637 and 1593 (2C=N). ^{1}H NMR ($CDCl_3$), δ 2.24 (s, CH_3), 6.89–8.03 (21H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 21.468 (CH_3), 87.184 (spiro carbon), 111.71, 112.31, 124.90, 126.23, 126.83, 126.95, 128.32, 128.69, 128.72, 130.29, 130.52, 132.55, 134.42, 138.30, 139.82, 140.73, 147.24 (aromatic carbons), 151.10, 154.63 (2C=N), 159.042 (C=0). MS *m*/*z*, (%): 576 (M^+, 29), 447 (100), 336 (29), 239 (12). Anal. Calc. for $C_{35}H_{24}N_6O_3$, C, 72.90; H, 4.20; N, 14.58. Found C, 72.85; H, 4.16; N, 14.56 %.

Compound **3e**: orange crystals, m.p. 140°C. IR (KBr) ν/cm^{-1}: 1680 (C=0), 1637 and 1598 (2C=N). ^{1}H NMR ($CDCl_3$), δ 2.26 (s, CH_3), 6.80–9.32 (18H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 21.40 (CH_3), 89.29 (spiro carbon), 111.72, 115.01, 115.12, 118.02, 118.52, 121.204, 121.88, 124.61, 125.05, 126.56, 127.14, 127.38, 128.23, 128.46, 128.82, 129.64, 130.18, 130.76, 131.73, 132.30, 134.08, 139.01, 141.10, 142.75 (aromatic carbons), 144.71, 148.61 (2C=N), 159.65 (C=0). MS *m*/*z*, (%): 621 (M^+, 21), 492 (62). Anal. calc. for $C_{35}H_{23}N_7O_5$, C, 67.63; H, 3.73; N, 15.77. Found C, 67.60; H, 3.69; N, 15.72.

Compound **3f**: orange crystals, m.p. 125 °C. IR (KBr) ν/cm-1: 1682 (C=O), 1641 and 1585 (2C=N). ^{1}H NMR ($CDCl_3$), δ 6.53–9.21 (22H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 89.44 (spiro carbon), 118.29, 119.91, 122.24, 126.16, 126.5, 127.56, 127.70, 128.42, 128.67, 128.96, 129.10, 129.55, 129.84, 129.88, 130.23, 130.82, 133.48, 135.14, 135.63, 139.53, 140.17, 146.84, 146.93 (aromatic carbons), 149.21 and 150.14 (2C=N), 159.51 (C=O). MS *m*/*z*, (%): 553 (M^+, 20), 518(15), 376(30). Anal. calc. for $C_{34}H_{22}ClN_5O$, C, 73.98; H, 4.02; N, 12.69. Found: C, 73.95; H, 4.00; N, 12.63 .

Compound **3g**: orange crystals, m.p. 142 °C. IR (KBr) ν/cm^{-1}: 1682 (C=0), 1641 and 1589 (2C=N). ^{1}H NMR ($CDCl_3$), δ 6.83–9.45 (21H, m, aromatic protons). ^{13}C NMR ($CDCl_3$), δ 88.65 (spiro carbon), 112.15, 113.02, 117.96, 119.93, 122.23, 127.32, 128.07, 128.34, 128.38, 128.54, 128.71, 128.77, 128.87, 129.17, 129.23, 129.27, 129.40, 129.44, 129.50, 129.54, 129.95, 139.55, 141.06, 143.15 (aromatic carbons), 149.21, 150.14 (2C=N), 159.51 (C=0). MS *m*/*z*, (%): 597 (M^+, 16), 356 (37), 239 (45). Anal. calc. for $C_{34}H_{21}ClN_6O_3$ (597.038), C, 68.40; H, 3.54; N, 14.08. Found C, 68.36; H, 3.52; N, 14.05.

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