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Microwave induced one-pot synthesis of fluorenespiro[9.3′]-(4′-aryl)pyrrolidine/pyrrolizidine/tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione derivatives

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Abstract—A versatile one-pot method for the synthesis of new dispiro heterocycles is described using an intermolecular [3+2] cycloaddition reaction. The reaction gives excellent yields when carried out under solvent-free microwave irradiation.

1. Introduction

Concerted cycloaddition processes represent a powerful and often highly controlled entry into a wide variety of heterocyclic systems. Additional features associated with these processes include mild conditions, versatility and in particular, the ability to gain rapid access to complex, polycyclic ring frameworks.[1]

The 1,3-dipolar cycloaddition reaction of azomethine ylides with olefinic and acetylenic dipolarophiles offers an excellent route for the construction of pyrrolidines, pyrrolines, and pyrroles.[2–4] The chemistry of azomethine ylides has gained significance in recent years as it serves as an important route for the construction of nitrogen containing five-membered heterocycles, which are often central ring systems of numerous natural products.[5]

In addition, there has been considerable interest in the microwave irradiation protocol for rapid synthesis of a variety of organic compounds due to the selective absorption of microwave energy by polar molecules.[6]

2. Results and discussion

In our previous work,[7] we reported the facile syntheses of novel dispiropyrrolidines and pyrrolizidines in fairly good yields under microwave irradiation and classical heating method.

Our research group has been largely involved in the synthesis of pyrrolidine, pyrrolizidine, and thiazolidine derivatives through [3+2] cycloaddition reactions,[8–10] which are found in many naturally occurring alkaloids and known to possess several significant biological activity.[11]

Herein, we wish to report full details and studies related to the scope and limitations of our [3+2] reaction. In order to investigate the scope and the limitations of the new 1,3-dipolar cycloaddition reaction for the preparation of pyrrolidine, pyrrolizidine, and thiazolidine derivatives, the 1,2-diketone necessary for the generation of azomethine ylide was varied.

The reaction of non-stabilized azomethine ylide (generated in situ from the decarboxylative condensation of ninhydrin and sarcosine) with the dipolarophiles **3a–e** in refluxing methanol furnished dispiro heterocycles **4a–e** in moderate yields (50–56%) (Scheme 1).

The structures of these products were assigned on the basis of their IR, NMR (^{1}H and ^{13}C) as well as elemental analyses. In particular, the regiochemistry proposed for the product **4b** was established on the basis of its ^{1}H NMR spectrum exhibiting a doublet of doublet at δ 4.88 (J=8.3, 9.6 Hz) for the benzylic proton. If the other isomer **5b** was formed, one would expect a singlet instead of a doublet for the benzylic proton. The ^{13}C NMR spectrum of **4b** showed two peaks at δ 68.8 and 83.0 ppm due to the two spiro carbons. The indane-1,3-dione carbonyl carbons resonated at δ 197.3 and 203.6 ppm. The mass spectrum of **4b** showed a molecular ion peak at m/z 455 (M^+), which further confirms the

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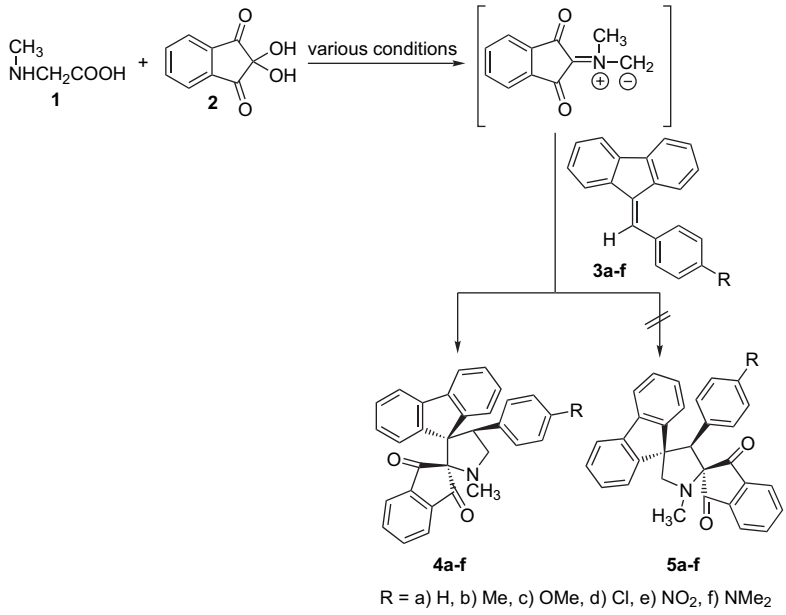


Scheme 1.

formation of the cycloadduct. Identical results were furnished by other compounds **4b–f** with identical stereochemistry. The structure of **4c** could unequivocally be established by X-ray single crystal analysis,[12] which proves the regiochemistry (Fig. 1).

In the case of **3f** as dipolarophile, the reaction was extremely sluggish affording only starting material. To gain insight into this unsuccessful cycloaddition, the reaction was subjected to microwave irradiation (600 W) in methanol. Low yield was still encountered as summarized in Table 1.

Finally, we submitted the reactants **3f**, **1**, and **2** to solvent-free microwave irradiation (600 W) ground with and without K-10 Montmorillonite clay (Methods C and D). We found that the yields of all products increased from modest to excellent (50–56% to 84–94%). In particular, to our surprise, the yield of **4f** increased drastically from 5% (Method A) to 88% (Method D) in short reaction time.

Having the best conditions in hand, we examined next the reaction of the same dipolarophile with non-stabilized azomethine ylides generated from cyclic secondary amino acids, proline or thiazolidine-4-carboxylic acid with ninhydrin (Scheme 2).

As observed in the earlier case, the yields of [3+2] cycloaddition reaction of **3a–f** with ninhydrin and proline or thiazolidine-4-carboxylic acid did not improve by the Methods A and B. However, when the above reaction was carried out under solvent-free conditions, by irradiating the reactants under microwave (600 W) with and without K-10 Montmorillonite clay, the products were obtained in excellent yields with high regioselectivity and in a short duration of time (Table 2).

The cycloadducts were characterized by spectral and elemental analyses. The ^{1}H NMR spectrum of **7d** showed a doublet for the benzylic proton at δ 4.37. The methylene protons of the pyrrolizidine ring system showed a multiplet in the region δ 1.25–3.08. The ^{13}C NMR spectrum of **7d** exhibits two peaks at δ 198.7 and 200.1 ppm for the carbonyl carbons of indane-1,3-dione ring system. Finally the structure of the product **7d** was confirmed by a peak at *m*/*z* 501.5 (M^{+}) in mass spectrum and it showed satisfactory elemental analysis.

In conclusion, we have developed a simple, one-pot and new method for the synthesis of dispiropyrrolidine/pyrrolizidine/

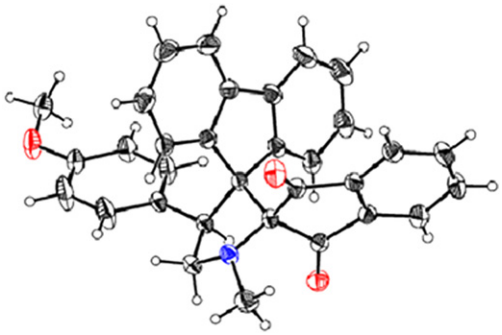
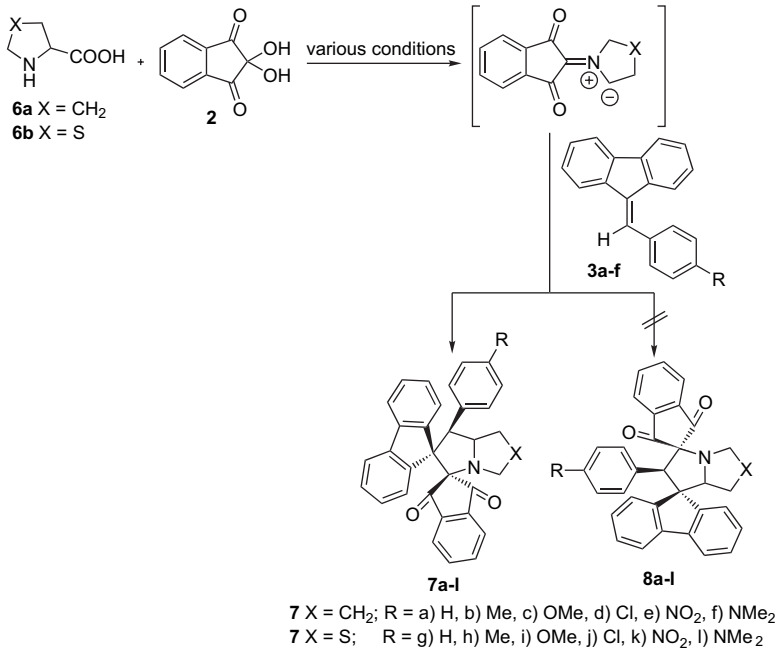


Figure 1. ORTEP diagram of **4c**.

Table 1. Influence of conventional heating and microwave irradiation on 1,3-dipolar cycloaddition reaction of **3a–f** with **1** and **2**

4	*Method A*		*Method B*		*Method C*		*Method D*	
	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
a	2.0	52	6.0	55	3.0	84	2.5	88
b	1.0	55	5.0	57	2.0	78	2.0	84
c	1.5	52	8.0	54	2.5	85	3.0	87
d	2.0	50	5.5	53	3.0	89	3.5	90
e	1.0	56	5.0	60	2.0	91	2.5	94
f	2.0	5	9.0	15	4.0	80	3.0	88

Method A: conventional methanol reflux; *Method B*: methanol/MW; *Method C*: K-10 Montmorillonite clay/MW; *Method D*: neat/MW.



Scheme 2.

Table 2. Influence of conventional heating and microwave irradiation on 1,3-dipolar cycloaddition reaction of **3a–f** with **6** and **2**

7	*Method A*		*Method B*		*Method C*		*Method D*	
	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
a	1.5	55	5.0	58	3.0	78	2.5	83
b	1.0	57	4.5	60	3.0	82	3.0	85
c	1.5	60	4.8	62	2.5	80	3.0	84
d	2.0	59	5.2	65	3.5	85	2.5	89
e	1.0	62	4.0	64	3.0	87	3.5	90
f	2.5	7	6.0	20	3.5	77	3.0	81
g	3.0	50	5.5	58	4.0	80	3.5	85
h	2.5	57	6.0	60	3.5	83	4.0	87
i	3.5	56	6.0	64	4.5	86	3.7	90
j	4.0	52	5.5	64	4.5	81	4.0	89
k	3.0	63	5.0	66	4.0	88	4.5	93
l	5.0	5	8.0	18	6.0	80	5.5	87

Method A: conventional methanol reflux; *Method B*: methanol/MW; *Method C*: K-10 Montmorillonite clay/MW; *Method D*: neat/MW.

pyrrolo[1,2-*c*]thiazole derivatives by [3+2] cycloaddition methodology. Of the various conditions employed, the solvent-free and solid-support approach accelerated by microwave irradiation was found to be synthetically useful in achieving high yields with substantial reduction in time when compared to conventional heating.

3. Experimental

3.1. General

All melting points are uncorrected. IR spectra were recorded on a SHIMADZU FT-IR 8300 instrument. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on JEOL 400 MHz and 100 MHz, respectively. MS spectra were recorded on a Finnigan MAT-8230 GC-Mass spectrometer.

3.2. General procedure for the synthesis of dispiro heterocycles

Method A: A solution of ninhydrin **2** (1 mmol), sarcosine **1**/proline **6a**/thiazolidine-4-carboxylic acid **6b** (1 mmol), and 9-arylidene fluorenes **3a–f** (1 mmol) was refluxed in methanol. Completion of the reaction was evidenced by TLC analysis. The solvent was removed in vacuo. The crude product was subjected to column chromatography using petroleum ether–ethyl acetate as an eluent.

Method B: A solution of ninhydrin **2** (1 mmol), sarcosine **1**/proline **6a**/thiazolidine-4-carboxylic acid **6b** (1 mmol), and 9-arylidene fluorenes **3a–f** (1 mmol) in methanol was irradiated under microwave conditions (600 W). After completion of the reaction, the solvent was evaporated and the crude product was subjected to column chromatography using petroleum ether–ethyl acetate as an eluent.

Method C: A mixture of ninhydrin **2** (1 mmol), sarcosine **1**/proline **6a**/thiazolidine-4-carboxylic acid **6b** (1 mmol), and 9-arylidene fluorenes **3a–f** (1 mmol) was ground with K-10 Montmorillonite clay and irradiated under microwave conditions (600 W). After completion of the reaction, the product was extracted with dichloromethane, the organic layer dried over $MgSO_4$, the solvent removed in vacuo and the residue crystallized from methanol.

Method D: A mixture of ninhydrin **2** (1 mmol), sarcosine **1**/proline **6a**/thiazolidine-4-carboxylic acid **6b** (1 mmol), and 9-arylidene fluorenes **3a–f** (1 mmol) was ground and irradiated under microwave conditions (600 W). After completion of the reaction, the mixture was allowed to stand at room temperature until it solidified and the product was recrystallized from methanol.

3.2.1. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-phenyl)pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4a). Pale yellow solid,

mp 177–179 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.69–8.12 (17H, m, Ph), 4.91 (1H, dd, J=8.3, 9.6 Hz, C*H*Ph), 4.24 (1H, dd, J=7.2, 8.3 Hz, NCH_2), 3.90 (1H, dd, J=7.2, 9.6 Hz, NCH_2), 2.58 (3H, s, NCH_3); δ_C (100 MHz, $CDCl_3$) 203.6, 197.2, 142.8, 141.8, 141.7, 141.3, 140.8, 139.9, 136.3, 135.5, 129.5, 128.4, 128.1, 128.0, 127.2, 126.6, 126.4, 124.8, 122.6, 122.1, 119.6, 119.1, 82.9, 68.8, 57.5, 51.3, 36.3; m/z 441 (M^+). Anal. Calcd for $C_{31}H_{23}NO_2$: C, 84.35; H, 5.21; N, 3.17%. Found: C, 84.55; H, 5.35; N, 2.98%.

3.2.2. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-*p*-methylphenyl)pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4b). Yellow solid, mp 176–178 °C; ν_{max} (KBr): 1739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.58–8.12 (16H, m, Ph), 4.88 (1H, dd, J=8.3, 9.6 Hz, C*H*Ph), 4.21 (1H, dd, J=7.0, 8.3 Hz, NCH_2), 3.88 (1H, dd, J=7.0, 9.6 Hz, NCH_2), 2.57 (3H, s, NCH_3), 2.04 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 203.6, 197.3, 143.0, 141.8, 141.7, 141.3, 140.8, 139.9, 135.9, 135.5, 133.1, 129.6, 128.3, 128.1, 127.9, 126.6, 126.4, 124.8, 122.6, 122.2, 119.6, 119.1, 83.00, 68.8, 57.7, 50.9, 36.3, 20.8; m/z 455 (M^+). Anal. Calcd for $C_{32}H_{25}NO_2$: C, 84.39; H, 5.49; N, 3.08%. Found: C, 84.58; H, 5.60; N, 3.18%.

3.2.3. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-*p*-methoxyphenyl)pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4c). Yellow solid, mp 185–186 °C; ν_{max} (KBr): 1739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.53–7.62 (16H, m, Ph), 4.71 (1H, dd, J=8.2, 9.8 Hz, C*H*Ph), 4.02 (1H, dd, J=7.4, 8.2 Hz, NCH_2), 3.86 (1H, dd, J=7.4, 9.8 Hz, NCH_2), 3.64 (3H, s, OCH_3), 2.41 (3H, s, NCH_3); δ_C (100 MHz, $CDCl_3$) 200.7, 199.9, 143.2, 142.1, 135.8, 134.2, 133.6, 130.9, 130.3, 130.1, 129.9, 128.7, 128.0, 127.8, 127.7, 127.3, 126.0, 122.6, 122.0, 120.9, 119.0, 116.6, 113.4, 113.3, 112.5, 71.0, 73.9, 52.0, 54.8, 48.5, 31.7; m/z 471 (M^+). Anal. Calcd for $C_{32}H_{25}NO_3$: C, 81.53; H, 5.31; N, 2.97%. Found: C, 81.75; H, 5.47; N, 3.08%.

3.2.4. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-*p*-chlorophenyl)pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4d). Pale yellow solid, mp 182–184 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.64–7.84 (16H, m, Ph), 4.80 (1H, dd, J=8.4, 9.4 Hz, C*H*Ph), 4.30 (1H, dd, J=7.1, 8.4 Hz, NCH_2), 3.92 (1H, dd, J=7.1, 9.4 Hz, NCH_2), 2.53 (3H, s, NCH_3); δ_C (100 MHz, $CDCl_3$) 199.3, 198.0, 141.3, 140.2, 140.1, 139.5, 138.7, 136.7, 130.8, 128.4, 128.2, 128.1, 127.8, 127.6, 127.1, 126.9, 126.2, 124.2, 123.0, 120.5, 120.2, 119.4, 118.1, 117.8, 110.2, 80.8, 69.4, 57.2, 52.2, 34.2; m/z 475.5 (M^+). Anal. Calcd for $C_{31}H_{22}NO_2Cl$: C, 78.23; H, 4.63; N, 2.94%. Found: C, 78.48; H, 4.79; N, 3.09%.

3.2.5. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-*p*-nitrophenyl)-pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4e). Yellow solid, mp 190 °C; ν_{max} (KBr): 1741 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.45–7.56 (16H, m, Ph), 4.84 (1H, dd, J=8.4, 10.0 Hz, C*H*Ph), 4.36 (1H, dd, J=7.3, 8.4 Hz, NCH_2), 3.81 (1H, dd, J=7.3, 10.0 Hz, NCH_2), 2.35 (3H, s, NCH_3); δ_C (100 MHz, $CDCl_3$) 203.5, 198.9, 141.2, 133.8, 130.9, 130.5, 130.0, 128.8, 128.4, 128.1, 127.8, 127.4, 125.0, 124.6, 124.0, 123.7, 122.4, 121.6, 121.5, 120.8, 119.8, 116.9, 115.2, 114.8, 113.1, 111.2, 79.7, 68.2, 56.3, 51.1, 36.1; m/z 486 (M^+). Anal. Calcd for $C_{31}H_{22}N_2O_4$: C, 76.54; H, 4.53; N, 5.76%. Found: C, 76.70; H, 4.68; N, 5.92%.

3.2.6. Fluorenespiro[9.3′]-1-*N*-methyl-(4′-*p*-*N*,*N*-dimethylphenyl)pyrrolidinespiro[2′.2″]indan-1″,3″-dione (4f). Yellow solid, mp 175–177 °C; ν_{max} (KBr): 1738 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.50–7.44 (16H, m, Ph), 4.80 (1H, dd, J=8.7, 9.6 Hz, C*H*Ph), 4.39 (1H, dd, J=7.4, 8.7 Hz, NCH_2), 3.84 (1H, dd, J=7.4, 9.6 Hz, NCH_2), 2.80 (6H, s, NCH_3), 2.43 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 202.6, 197.2, 141.8, 141.5, 138.3, 137.6, 136.6, 133.2, 132.0, 131.1, 130.2, 129.4, 128.8, 128.2, 127.9, 127.3, 126.1, 125.6, 124.1, 123.6, 122.6, 121.7, 120.1, 119.2, 116.7, 110.3, 70.5, 67.9, 55.5, 52.4, 34.7, 34.4, 33.2; m/z 484 (M^+). Anal. Calcd for $C_{33}H_{28}N_2O_2$: C, 81.82; H, 5.78; N, 5.78%. Found: C, 82.06; H, 5.97; N, 5.63%.

3.2.7. Fluorenespiro[9.3′]-(4′-phenyl)pyrrolizidinespiro [2′.2″]indan-1″,3″-dione (7a). Pale yellow solid, mp 158–160 °C; ν_{max} (KBr): 1745 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.45–7.17 (17H, m, Ph), 4.53–4.55 (1H, m, H_b), 4.33 (1H, d, J=9.6 Hz, C*H*Ph), 1.30–2.94 (6H, m, pyrrolizidine); δ_C (100 MHz, $CDCl_3$) 202.0, 200.1, 141.2, 132.8, 132.0, 130.0, 128.4, 128.1, 127.8, 125.7, 125.3, 125.1, 124.4, 124.0, 123.7, 122.4, 121.6, 121.5, 120.8, 119.8, 116.9, 116.1, 115.2, 114.8, 113.1, 73.1, 70.8, 57.1, 46.5, 34.1, 31.8, 30.4; m/z 467 (M^+). Anal. Calcd for $C_{33}H_{25}NO_2$: C, 84.79; H, 5.35; N, 2.99%. Found: C, 85.03; H, 5.49; N, 2.84%.

3.2.8. Fluorenespiro[9.3′]-(4′-*p*-methylphenyl)pyrrolizidinespiro[2′.2″]indan-1″,3″-dione (7b). Yellow solid, mp 156–157 °C; ν_{max} (KBr): 1738 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.62–7.81 (16H, m, Ph), 4.58–4.60 (1H, m, H_b), 4.52 (1H, d, J=9.4 Hz, C*H*Ph), 2.37 (3H, s, CH_3), 1.26–2.17 (6H, m, pyrrolizidine); δ_C (100 MHz, $CDCl_3$) 199.9, 198.8, 142.5, 140.5, 139.3, 136.7, 132.7, 130.5, 130.3, 129.1, 129.0, 128.5, 128.3, 127.7, 127.4, 127.2, 126.5, 125.9, 125.6, 125.2, 124.8, 124.4, 121.0, 120.4, 119.2, 118.9, 110.6, 80.6, 76.3, 56.3, 47.3, 34.6, 34.1, 33.0; m/z 481 (M^+). Anal. Calcd for $C_{34}H_{27}NO_2$: C, 84.82; H, 5.61; N, 2.91%. Found: C, 85.08; H, 5.48; N, 3.06%.

3.2.9. Fluorenespiro[9.3′]-(4′-*p*-methoxyphenyl)pyrrolizidinespiro[2′.2″]indan-1″,3″-dione (7c). Pale yellow solid, mp 163–165 °C; ν_{max} (KBr): 1739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.34–8.34 (16H, m, Ph), 4.63–4.69 (1H, m, H_b), 4.35 (1H, d, J=9.5 Hz, C*H*Ph), 3.55 (3H, s, OCH_3), 2.13–3.08 (6H, m, pyrrolizidine); δ_C (100 MHz, $CDCl_3$) 204.0, 198.4, 158.2, 142.3, 141.4, 141.0, 140.8, 140.3, 139.9, 135.4, 135.2, 131.7, 130.8, 129.5, 129.4, 128.1, 126.6, 126.4, 125.0, 124.2, 125.6, 122.1, 119.4, 119.1, 114.0, 112.7, 73.8, 69.9, 56.5, 54.8, 47.3, 33.7, 31.8, 30.0; m/z 497 (M^+). Anal. Calcd for $C_{34}H_{27}NO_3$: C, 82.09; H, 5.43; N, 2.82%. Found: C, 82.33; H, 5.63; N, 2.70%.

3.2.10. Fluorenespiro[9.3′]-(4′-*p*-chlorophenyl)pyrrolizidinespiro[2′.2″]indan-1″,3″-dione (7d). Pale yellow solid, mp 140 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.59–8.33 (16H, m, Ph), 4.62–4.67 (1H, m, H_b), 4.37 (1H, d, J=9.5 Hz, C*H*Ph), 1.25–3.08 (6H, m, pyrrolizidine); δ_C

(100 MHz, $CDCl_3$) 200.1, 198.7, 141.4, 139.3, 137.2, 136.3, 135.4, 133.9, 130.7, 129.7, 129.5, 128.8, 128.4, 127.4, 127.1, 126.7, 126.5, 125.6, 124.9, 124.3, 123.7, 122.2, 120.3, 119.8, 119.6, 119.2, 73.6, 69.6, 56.6, 47.2, 34.0, 31.7, 30.1; *m/z* 501.5 (M^+). Anal. Calcd for $C_{33}H_{24}NO_2Cl$: C, 78.96; H, 4.78; N, 2.79%. Found: C, 79.18; H, 4.95; N, 2.64%.

3.2.11. Fluorenespiro[9.3′]-(4′-*p*-nitrophenyl)pyrrolizidinespiro[2′.2″]indan-1″,3″-dione (7e). Yellow solid, mp 160–162 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.44–7.25 (16H, m, Ph), 4.49–4.51 (1H, m, H_b), 4.33 (1H, d, *J*=9.6 Hz, C*H*Ph), 1.34–2.90 (6H, m, pyrrolizidine); δ_C (100 MHz, $CDCl_3$) 202.1, 199.7, 142.3, 141.4, 139.3, 136.8, 135.9, 130.7, 129.4, 128.3, 128.0, 127.8, 127.3, 126.0, 125.1, 124.5, 124.1, 123.9, 122.0, 121.7, 121.5, 119.7, 117.8, 116.4, 114.4, 110.5, 54.9, 46.0, 31.3, 31.1, 30.5; *m/z* 512 (M^+). Anal. Calcd for $C_{33}H_{24}N_2O_4$: C, 77.34; H, 4.68; N, 5.47%. Found: C, 77.56; H, 4.86; N, 5.34%.

3.2.12. Fluorenespiro[9.3′]-(4′-*p*-*N*,*N*-dimethylphenyl)-pyrrolizidinespiro[2′.2″]indan-1″,3″-dione (7f). Pale yellow solid, mp 152–154 °C; ν_{max} (KBr): 1738 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.60–7.59 (16H, m, Ph), 4.55–4.58 (1H, m, H_b), 4.30 (1H, d, *J*=9.4 Hz, C*H*Ph), 2.53 (6H, s, CH_3), 1.30–2.94 (6H, m, pyrrolizidine); δ_C (100 MHz, $CDCl_3$) 198.0, 194.6, 141.6, 140.4, 137.0, 136.6, 136.3, 136.0, 135.8, 134.7, 133.7, 133.0, 131.5, 128.0, 126.5, 126.1, 125.8, 125.7, 121.9, 120.1, 119.1, 118.2, 117.4, 115.9, 110.1, 107.6, 56.5, 45.5, 35.6, 35.0, 34.5, 33.0, 32.6; *m/z* 510 (M^+). Anal. Calcd for $C_{35}H_{30}N_2O_2$: C, 82.35; H, 5.88; N, 5.49%. Found: C, 82.54; H, 6.08; N, 5.34%.

3.2.13. Fluorenespiro[9.3′]-(4′-phenyl)tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7g). Pale yellow solid, mp 169–170 °C; ν_{max} (KBr): 1739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.70–7.91 (17H, m, Ph), 4.72–4.74 (1H, m, H_b), 4.51 (1H, d, *J*=8.7 Hz, C*H*Ph), 4.19 (1H, d, *J*=7.4 Hz, NCH_2), 3.70 (1H, d, *J*=7.4 Hz, NCH_2), 3.45 (1H, dd, *J*=4.0, 10.0 Hz, SCH_2), 3.20 (1H, dd, *J*=5.4, 10.0 Hz, SCH_2); δ_C (100 MHz, $CDCl_3$) 203.5, 195.0, 143.0, 142.4, 137.0, 136.1, 135.5, 134.1, 132.3, 131.8, 129.6, 129.5, 129.2, 129.0, 128.5, 128.0, 127.2, 126.5, 126.1, 124.9, 123.3, 122.0, 121.9, 121.0, 120.0, 115.8, 67.9, 65.3, 61.8, 54.3, 52.2, 35.5; *m/z* 485 (M^+). Anal. Calcd for $C_{32}H_{23}NO_2S$: C, 79.17; H, 4.74; N, 2.88%. Found: C, 79.43; H, 4.90; N, 2.74%.

3.2.14. Fluorenespiro[9.3′]-(4′-*p*-methylphenyl)tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7h). Yellow solid, mp 174–175 °C; ν_{max} (KBr): 1742 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.59–8.36 (16H, m, Ph), 4.95–4.97 (1H, m, H_b), 4.46 (1H, d, *J*=8.6 Hz, C*H*Ph), 4.28 (1H, d, *J*=7.6 Hz, NCH_2), 3.79 (1H, d, *J*=7.6 Hz, NCH_2), 3.49 (1H, dd, *J*=3.3, 10.2 Hz, SCH_2), 3.19 (1H, dd, *J*=5.5, 10.2 Hz, SCH_2), 2.05 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 203.4, 196.3, 142.1, 141.3, 141.0, 139.8, 136.4, 135.7, 135.5, 131.5, 129.3, 128.3, 128.1, 126.6, 126.5, 124.7, 122.8, 122.3, 119.6, 119.2, 81.9, 73.9, 73.1, 55.8, 51.3, 37.0, 20.7; *m/z* 499 (M^+). Anal. Calcd for $C_{33}H_{25}NO_2S$: C, 79.35; H, 5.01; N, 2.80%. Found: C, 79.56; H, 5.20; N, 2.68%.

3.2.15. Fluorenespiro[9.3′]-(4′-*p*-methoxyphenyl)tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7i). Yellow solid, mp 181–183 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.52–7.83 (16H, m, Ph), 4.81–4.83 (1H, m, H_b), 4.55 (1H, d, *J*=8.6 Hz, C*H*Ph), 4.35 (1H, d, *J*=7.6 Hz, NCH_2), 3.63 (3H, s, OCH_3), 3.53 (1H, d, *J*=7.6 Hz, NCH_2), 3.40 (1H, dd, *J*=3.4, 9.8 Hz, SCH_2), 3.23 (1H, dd, *J*=5.5, 9.8 Hz, SCH_2); δ_C (100 MHz, $CDCl_3$) 199.5, 193.9, 139.7, 137.9, 135.0, 134.2, 132.7, 132.5, 131.8, 129.3, 128.8, 128.4, 127.3, 126.1, 124.8, 124.2, 123.8, 123.2, 122.1, 121.5, 121.1, 120.9, 119.0, 115.8, 113.1, 112.5, 79.9, 72.1, 69.0, 58.2, 54.7, 52.1, 35.6; *m/z* 515 (M^+). Anal. Calcd for $C_{33}H_{25}NO_3S$: C, 76.89; H, 4.85; N, 2.72%. Found: C, 77.11; H, 4.66; N, 2.85%.

3.2.16. Fluorenespiro[9.3′]-(4′-*p*-chlorophenyl)tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7j). Pale Yellow solid, mp 172–174 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.71–7.94 (16H, m, Ph), 4.53–4.55 (1H, m, H_b), 4.45 (1H, d, *J*=8.5 Hz, C*H*Ph), 4.21 (1H, d, *J*=8.0 Hz, NCH_2), 3.80 (1H, d, *J*=8.0 Hz, NCH_2), 3.40 (1H, dd, *J*=4.0, 9.8 Hz, SCH_2), 3.17 (1H, dd, *J*=5.6, 9.8 Hz, SCH_2); δ_C (100 MHz, $CDCl_3$) 203.9, 201.6, 144.1, 141.9, 140.0, 136.5, 135.0, 134.4, 132.5, 131.2, 129.6, 129.1, 128.4, 127.9, 127.0, 126.5, 126.3, 125.6, 124.3, 123.7, 123.0, 122.4, 121.6, 119.0, 115.8, 113.9, 69.3, 68.0, 63.6, 57.2, 52.4, 34.4; *m/z* 519.5 (M^+). Anal. Calcd for $C_{32}H_{22}NO_2SCl$: C, 73.92; H, 4.23; N, 2.69%. Found: C, 74.18; H, 4.42; N, 2.53%.

3.2.17. Fluorenespiro[9.3′]-(4′-*p*-nitrophenyl)tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7k). Yellow solid, mp 185–187 °C; ν_{max} (KBr): 1739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.64–7.81 (16H, m, Ph), 4.55–4.58 (1H, m, H_b), 4.50 (1H, d, *J*=8.6 Hz, C*H*Ph), 4.10 (1H, d, *J*=7.8 Hz, NCH_2), 3.85 (1H, d, *J*=7.8 Hz, NCH_2), 3.41 (1H, dd, *J*=3.8, 10.0 Hz, SCH_2), 3.23 (1H, dd, *J*=5.5, 10.0 Hz, SCH_2); δ_C (100 MHz, $CDCl_3$) 204.7, 197.1, 142.0, 141.5, 140.6, 139.0, 137.9, 137.1, 136.0, 133.6, 133.2, 131.3, 129.0, 128.8, 127.7, 127.0, 126.6, 125.3, 124.7, 124.6, 123.3, 123.0, 120.2, 117.9, 116.2, 71.8, 66.4, 62.3, 58.9, 55.2, 37.1; *m/z* 530 (M^+). Anal. Calcd for $C_{32}H_{22}N_2O_4S$: C, 72.45; H, 4.15; N, 5.28%. Found: C, 72.70; H, 4.28; N, 5.10%.

3.2.18. Fluorenespiro[9.3′]-(4′-*p*-*N*,*N*-dimethylphenyl)-tetrahydropyrrolo[1,2-*c*]thiazolespiro[2′.2″]indan-1″,3″-dione (7l). Yellow solid, mp 166–168 °C; ν_{max} (KBr): 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.53–7.28 (16H, m, Ph), 4.50–4.52 (1H, m, H_b), 4.47 (1H, d, *J*=8.6 Hz, C*H*Ph), 4.25 (1H, d, *J*=7.7 Hz, NCH_2), 3.90 (1H, d, *J*=7.7 Hz, NCH_2), 3.39 (1H, dd, *J*=3.6, 10.0 Hz, SCH_2), 3.18 (1H, dd, *J*=5.6, 10.0 Hz, SCH_2), 2.70 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 198.0, 196.6, 1432.5, 139.6, 138.7, 136.5, 134.4, 134.1, 133.2, 133.1, 132.2, 128.0, 127.6, 127.1, 126.6, 125.0, 121.3, 120.7, 119.8, 119.2, 118.9, 117.2, 115.9, 110.8, 108.2, 106.6, 67.0, 65.7, 61.5, 56.7, 54.0, 37.1, 36.7, 36.6, 35.8, 35.5; *m/z* 528 (M^+). Anal. Calcd for $C_{34}H_{28}N_2O_2S$: C, 77.27; H, 5.30; N, 5.30%. Found: C, 77.48; H, 5.50; N, 5.42%.

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References and notes

1. Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, *105*, 2765.
2. Tsuge, O.; Kanemasa, S. *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Academic: San Diego, 1989; Vol. 45, p 231.
3. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, NY, 1984; Vols. 1 and 2.
4. Grigg, R.; Sridharan, V. *Advances in Cycloaddition*; Curran, D. P., Ed.; Jai: London, 1993; Vol. 3, p 161.
5. (a) Daly, J. W.; Spande, T. W.; Whittaker, N.; Highet, R. J.; Feigl, D.; Noshimori, N.; Tokuyama, T.; Meyers, C. W. *J. Nat. Prod.* **1986**, *46*, 210; (b) Waldmann, H. *Synlett* **1995**, 133.
6. (a) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. *Chem. Soc. Rev.* **1998**, *27*, 213; (b) Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717; (c) Varma, R. S. Organic Synthesis Using Microwaves and Supported Reagents. In *Microwaves in Organic Synthesis*; Loupy, A., Ed.; Wiley-VCH: Weinheim, 2002; p 181.
7. Jayashankaran, J.; Rathna Durga, R.; Raghunathan, R. *Tetrahedron Lett.* **2004**, *49*, 7303.
8. (a) Shanmugasundaram, M.; Arulananda Babu, A.; Raghunathan, R.; Padmamalar, E. J. *Heteroat. Chem.* **1999**, *10*, 3316; (b) Shanmugasundaram, M.; Raghunathan, R.; Bhanumathi, S.; Padmamalar, E. J. *Heteroat. Chem.* **1998**, *9*, 327; (c) Shanmugasundaram, M.; Raghunathan, R. *Tetrahedron* **2000**, *56*, 5241.
9. (a) Manikandan, S.; Shanmugasundaram, M.; Raghunathan, R.; Malar, E. J. P. *Heterocycles* **2000**, *53*, 579; (b) Manikandan, S.; Ashraf, M. M.; Raghunathan, R. *Synth. Commun.* **2001**, *31*, 3593; (c) Manikandan, S.; Raghunathan, R. *J. Chem. Res., Synop.* **2001**, 424; (d) Manikandan, S.; Jayashankaran, J.; Raghunathan, R. *Synth. Commun.* **2003**, *33*, 4059.
10. (a) Jayashankaran, J.; Manikandan, S.; Raghunathan, R. *Synth. Commun.* **2003**, *33*, 499; (b) Subramaniyan, G.; Raghunathan, R. *Tetrahedron* **2001**, *57*, 2909; (c) Amalraj, A.; Raghunathan, R. *Tetrahedron* **2001**, *57*, 10293; (d) Subramaniyan, G.; Raghunathan, R.; Martin Castro, A. M. *Synthesis* **2002**, 2440.
11. (a) Yoda, H.; Shimojo, T.; Takabe, K. *Tetrahedron Lett.* **1999**, *40*, 1335; (b) Kato, A.; Adachi, I.; Miyauchi, M.; Ikeda, K.; Komae, T.; Kizu, H.; Kameda, Y.; Watson, A. A.; Nash, R. J.; Wormald, M. R.; Fleet, G. W. J.; Asano, N. *Carbohydr. Res.* **1999**, *316*, 95; (c) Yoda, H.; Egawa, T.; Takabe, K. *Tetrahedron Lett.* **2003**, *44*, 1643; (d) Chikkanna, D.; Singh, O. V.; Kong, S. B.; Han, H. *Tetrahedron Lett.* **2005**, *46*, 8865.
12. Subbiahpandi, A.; Selvanayagam, S.; Velmurugan, D.; Ravikumar, K.; Jayashankaran, J.; Raghunathan, R. *Acta Crystallogr.* **2005**, *E61*, 3059.