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A novel entry into a new class of spiroheterocyclic framework: regioselective synthesis of dispiro[oxindole-cyclohexanone]-pyrrolidines and dispiro[oxindole-hexahydroindazole]pyrrolidines

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Abstract—2,6-Bis(arylmethylidene)cyclohexanones undergo a regioselective 1,3-dipolar cycloaddition reaction with the azomethine ylide derived from isatin and sarcosine by a decarboxylative route affording a series of 1-*N*-methyl-spiro[2.3^{1}]oxindole-spiro[3.2^{11}]6^{11}-arylmethylidenecyclohexanone-4-aryl-pyrrolidines which were further annulated to give a series of novel 1-*N*-methyl-spiro[2.3^{1}]oxindole-spiro[3.7^{11}](3^{11}-aryl)$\Delta^{11,7^{11}}$a-hexahydro-2*H*-indazole-4-aryl-pyrrolidines. The structures of which were established by spectroscopic techniques as well as single crystal X-ray analysis. © 2001 Published by Elsevier Science Ltd.

1. Introduction

Intermolecular 1,3-dipolar reactions are considered one of the most useful processes for the construction of five-membered ring containing the pyrrolidine structural unit.[1,2] This method is widely used in the synthesis of natural products such as alkaloids and pharmaceuticals.[3] Spiro compounds represent an important class of naturally occurring substances characterised by highly pronounced biological properties.[4–6] Pyrrolidine and oxindole alkaloids[7] constitute another class of compounds with significant biological activity which are normally found in rhyncophylline, corynoxeine, nitraphylline, vincatine, horsifiline, etc.[8] Bis(arylmethylidene)cyclohexanones have also drawn much attention due to their important pharmacological properties.[9]

As a part of our ongoing research program in the area of cycloaddition reactions,[10–12] we herein report the facile synthesis of the dispiro[oxindole-hexahydroindazole]pyrrolidine ring systems through regioselective cycloaddition of bis-dipolarophile 2,6-bis(arylmethylidene)cyclohexanones (**1a**–**f**) with the ylide generated from isatin **2** and sarcosine **3** by a decarboxylative route.

2. Results and discussion

Refluxing a solution of 2,6-bis(arylmethylidene)cyclohexanones (**1a**–**f**) in methanol with isatin **2** and sarcosine **3** afforded 1-*N*-methyl-spiro[2.3^{1}]oxindole-spiro[3.2^{11}]6^{11}-arylmethylidenecyclohexanone-4-aryl-pyrrolidines (**4a**–**f**) (Scheme 1 and Table 1). The reaction gave a single product in all cases, as evidenced by thin layer chromatography (TLC). The reaction afforded a series of novel spiro derivatives (**4a**–**f**) through regioselective cycloaddition of azomethine ylide to one of the exocyclic double bonds of the bis(arylmethylidene)cyclohexanones in all cases. No trace of the other regioisomer (**5a**–**f**) was detected.

The cycloaddition proceeded to afford the *syn–endo* cycloadduct. The regio- and stereochemical outcome of the cycloaddition was determined by spectroscopic data and X-ray analysis of **4a** (Fig. 1). After the formation of the mono-adduct the reaction failed to proceed to give bis-adduct even with excess of 1,3-dipole and prolonged reaction times. Thus, addition occurs at only one of the exocyclic double bonds. The other one remains unaffected. This may be due to the steric hindrance of the spiropyrrolidine ring which prevents attack of the 1,3-dipole on the other exocyclic double bond.

However bis-adducts are formed if simple 1,3-dipoles generated from paraformaldehyde and sarcosine are used in the above reaction.[13] The IR spectra of **4a** reveals the presence of a carbonyl peak at 1668.3 cm^{-1} showing an increase of 10 cm^{-1} from the normal value observed for bis(benzylidene)cyclohexanone indicating the loss of

Keywords: 1,3-dipolar cycloaddition; 2,6-bis(arylmethylidene)cyclohexanones; decarboxylative route; isatin; sarcosine; dispiropyrrolidines.

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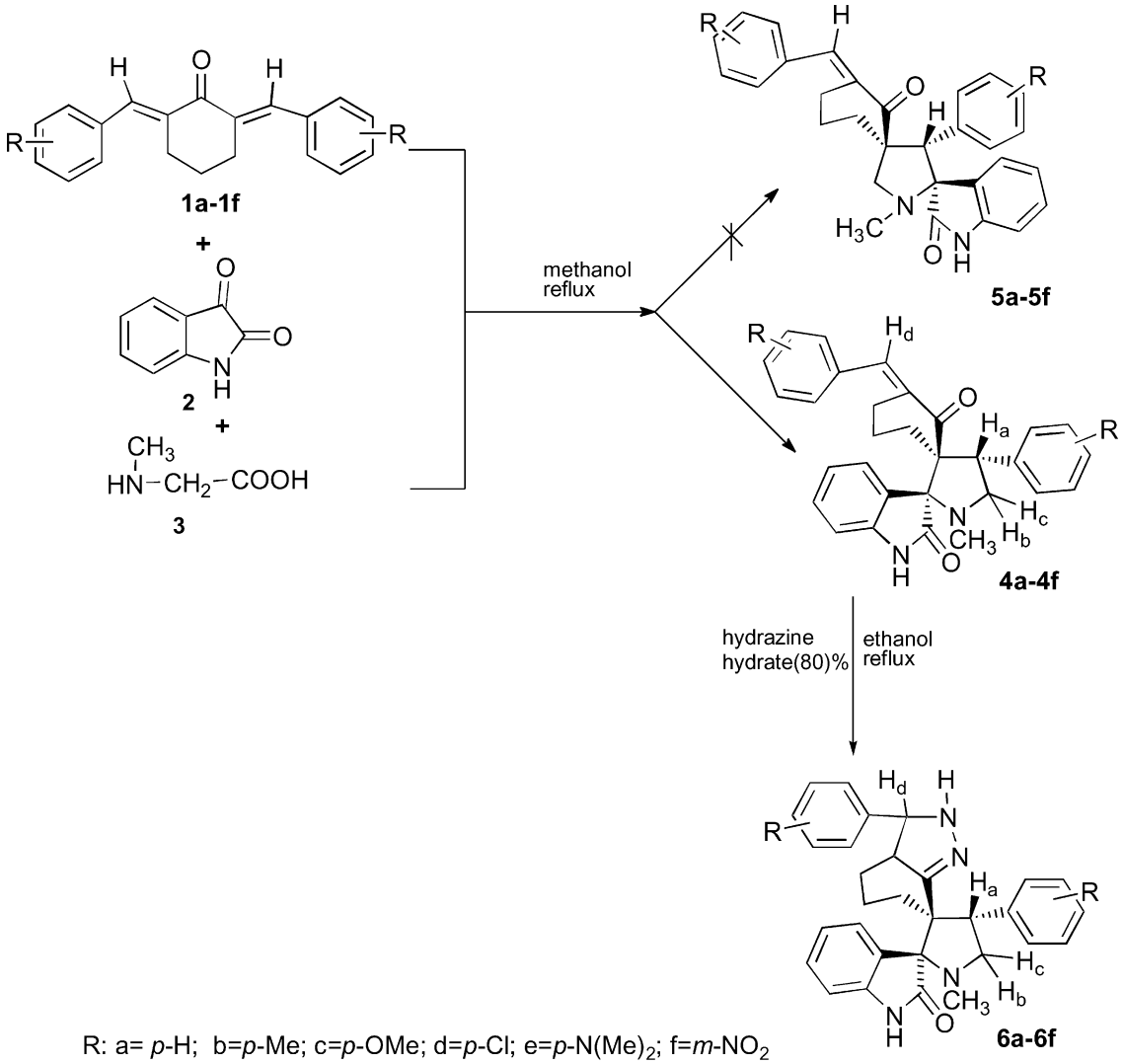

Scheme 1.

conjugation. It also exhibited a peak at 1708.8 cm^{-1} due to the carbonyl group of the oxindole and at 3253.7 cm^{-1} due to the –NH of the oxindole.

The ^1H NMR spectrum of **4a** exhibits peaks at δ values 1.44–2.41 (m, 6H, cyclohexyl), 2.14 (s, 3H, $-NCH_3$), 3.44 (dd, J=9.0, 7.5 Hz, 1H, H_c), 3.94 (dd, J=10.8, 9.0 Hz, 1H, H_b), 4.87 (dd, J=10.8, 7.5 Hz, 1H, H_a), 6.77–7.48 (m, 14H, ArH), 7.23 (s, 1H, H_d), 8.55 (bs, 1H, –NH). ^{13}C NMR spectra of (**4a**–**f**) add conclusive support for the proposed structures. ^{13}C NMR spectra of **4a** exhibits the presence of benzylic carbon at δ 57.62, spiro carbons at δ 63.86 and 76.68, *N*-methyl carbon at δ 34.70, $N-CH_2$ at δ 49.25, cyclohexanone carbonyl carbon at δ 202.61, oxindole carbonyl carbon at δ 177.99 and benzylidene carbon at δ 135.74. These observed chemical shift values confirmed the proposed structure. The mass spectrum of **4a** showed a peak at m/z 448 (M^+). Identical results were obtained with other derivatives of bis(arylmethylidene)cyclohexanones and it has been observed that cycloaddition takes place regioselectively across only one of the exocyclic double bond as evidenced by the presence of the benzylidene proton in the NMR spectrum, a singlet peak at δ 7.23.

Table 1. 1,3-Dipolar cycloaddition reaction of bis(arylmethylidene) cyclohexanones (**1a**–**f**) and azomethine ylide generated from isatin **2** and sarcosine **3** followed by annulation with hydrazine hydrate

Entry	Product	R	Time (h)	Yield (%)
1	**4a**	*p*-H	4	90
2	**4b**	*p*-Me	3	95
3	**4c**	*p*-OMe	3	80
4	**4d**	*p*-Cl	3	95
5	**4e**	*p*-$N(Me)_2$	7	55
6	**4f**	*m*-NO_2	2.5	80
7	**6a**	*p*-H	0.5	95
8	**6b**	*p*-Me	0.5	80
9	**6c**	*p*-OMe	0.5	80
10	**6d**	*p*-Cl	0.5	90
11	6e	*p*-$N(Me)_2$	0.5	70
12	**6f**	*m*-NO_2	0.5	80

The dispiro[oxindole/cyclohexanonone]pyrrolidines (**4a**–**f**) were further annulated by using hydrazine hydrate in ethanol at reflux to give a series of novel 1-*N*-methyl-spiro-[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-aryl)Δ^{11},7^{11}a-hexahydro-2*H*-indazole-4-aryl-pyrrolidines (**6a**–**f**). The structure of each product was confirmed by spectroscopic data. The

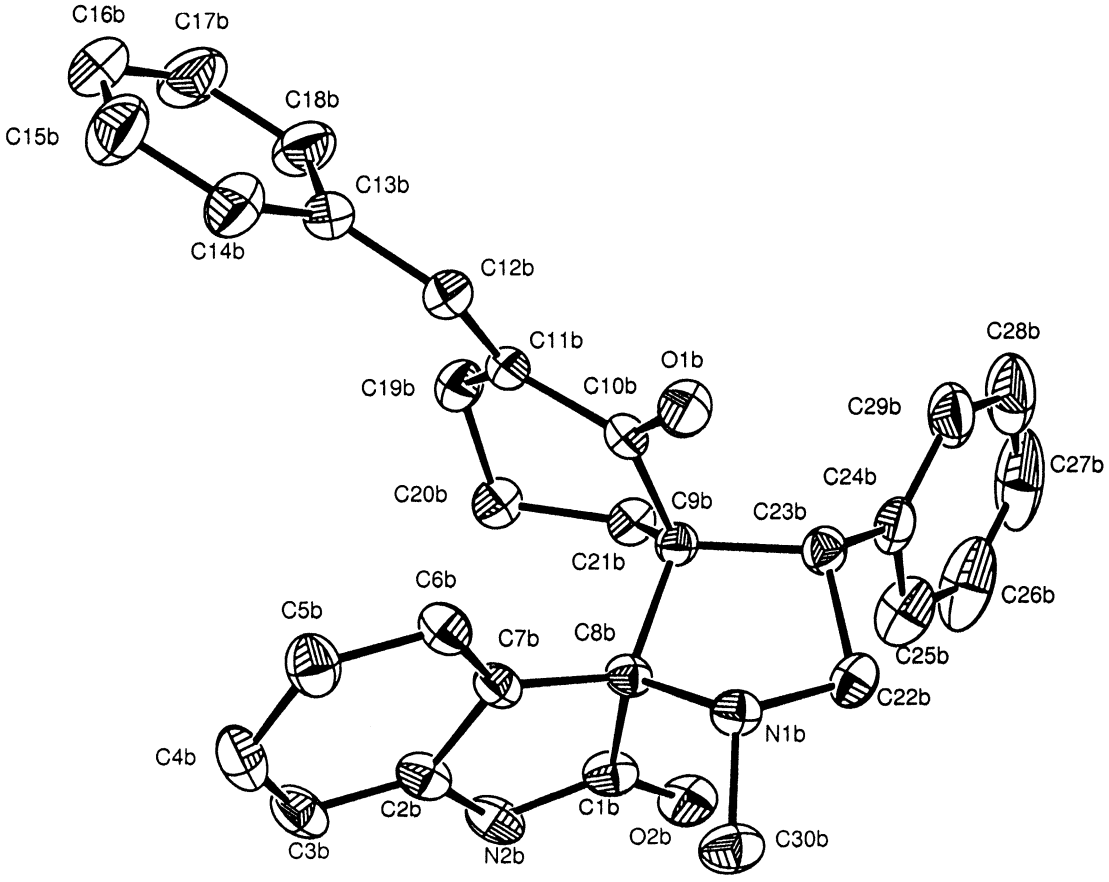

Figure 1. ORTEP diagram of **4a**.

IR spectrum of **6a** revealed the complete disappearance of the carbonyl group of the cyclohexanone and exhibited a peak at 1699.0 cm^{-1} due to the carbonyl group of the oxindole and 3281 cm^{-1} due to the NH. The ^1H NMR spectrum of **6a** showed peaks at δ values 0.59–2.33 (m, 7H, cyclohexyl), 2.20 (s, 3H, $-NCH_3$), 3.37 (dd, J=9.0, 7.5 Hz, 1H, H_c), 3.91 (dd, J=10.8, 9.0 Hz, 1H, H_b), 4.19 (d, J=13.2 Hz, 1H, H_d), 4.94 (dd, J=10.8, 7.5 Hz, 1H, H_a), 6.01 (bs, 1H, NH–indazole), 6.77–7.58 (m, 14H, ArH), 8.77 (bs, 1H, NH–oxindole). The ^{13}C NMR spectrum of **6a** revealed the absence of the carbonyl carbon of the cyclohexanone and exhibited a peak at δ 177.12 due to the carbonyl group of the oxindole. ^{13}C NMR showed signals for other carbons in accordance with expectations. The mass spectrum of **6a** also showed a molecular ion peak at m/z 462 (M^+) confirming the aforementioned structure. Identical results were obtained with other derivatives (**4a**–**f**).

To the best of our knowledge to date there has been no report of the cycloaddition reaction of the 1,3-dipole azomethine ylide derived from isatin and sarcosine with bis(arylmethylidene)cyclohexanones dipolarophiles.

3. Conclusion

A facile and efficient synthesis of a new class of dispiro-[oxindole/cyclohexanone]pyrrolidine ring systems from azomethine ylide generated from isatin and sarcosine with bis(arylmethylidine)cyclohexanones has been described. Annulation of dispiro[oxindole/cyclohexanone]pyrrolidines ring systems with hydrazine hydrate yielded novel dispiro[oxindole/hexahydroindazole]pyrrolidines. The cycloaddition studied is of interest since it paves the way for the synthesis of a variety of biologically important spiroxindole derivatives using easily available starting materials.

4. Experimental

4.1. General

All melting points are uncorrected. IR spectra were recorded on a SHIMADZU FT-IR 8300 instrument. Mass spectra were recorded on a JEOL DX 303 HF spectrometer with a MASPEC system (msw/9629). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a JEOL spectrometer at 400 and 100 MHz, respectively. Elemental analyses were carried out on a CEST 1106 instrument. The starting materials (**1a**–**f**) were prepared as per the literature procedure.[14–19] The X-ray structure of **4a** was solved by direct methods using the program SHELXS86.[20] The structure was refined by the full matrix least squares method using SHELXL93.[21]

4.2. General procedure for the cycloaddition reaction of 2,6-bis (arylmethylidene)cyclohexanones (1a–f) and the ylide generated from isatin and sarcosine

A mixture of 2,6-bis(arylmethylidene)cyclohexanones

(**1a**–**f**) (0.5 mmol), isatin 2 (0.5 mmol) and sarcosine **3** (0.5 mmol) were refluxed in methanol (20 mL) until the disappearance of the starting materials as evidenced by the TLC. The reaction conditions are listed in Table 1. After the reaction was over the solvent was removed in vacuo and the residue was chromatographed on silica gel using hexane–ethyl acetate (5:1) as eluent to give (**4a**–**f**).

4.3. General procedure for the annulation of 4a–f with hydrazine hydrate to give 6a–f

A mixture of **4a**–**f** (0.5 mmol) and 80% hydrazine hydrate (2 mL) was refluxed in ethanol (15 mL). The reaction conditions are listed in Table 1. The reaction mixture was cooled, filtered and then the product was recrystallised from ethanol to give (**6a**–**f**).

4.3.1. Crystallographic data for compound 4a.[22] Molecular formula: $C_{30}H_{28}N_2O_2$. Molecular weight 448.54, triclinic, PT, a=12.36424(1) Å, b=13.0640(2) Å, c=17.1439(3) Å, D_c=1.249 mg/m^3, V=2386.16(6) Å^3, α=110.066(1), β=93.200(1), γ=110.53(1). Mo Kα radiation, λ=0.71073 Å, absorption coefficient=0.078 mm^{-1}, F(000)=952. The crystal is pale yellow and slap shaped. Number of atoms=62. A crystal with dimensions of 0.36×0.24×0.16 mm^3 was used for X-ray data collection at 293 K on a Siemens SMART CCD area detector using molybdenum radiation and a graphite mono chromator. θ range for data collection was 1.29–29.45°. A total of 17 070 reflections were measured. R indices on all data was R_1=0.1405, wR_2= 0.1536. Goodness of fit on F^2 was 0.798.

4.3.2. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-benzylidenecyclohexanone-4-phenyl-pyrrolidine 4a. 0.20 g, 90%. Pale yellow crystal, mp: 215–216°C; IR (KBr): 1668.3, 1708.8, 3253.7 cm^{-1}, ^{1}H NMR: δ 1.44–2.41 (m, 6H), 2.14 (s, 3H), 3.44 (dd, J=9.0, 7.5 Hz, 1H), 3.94 (dd, J=10.8, 9.0 Hz, 1H), 4.87 (dd, J=10.8, 7.5 Hz, 1H), 6.77–7.48 (m, 14H), 7.23 (s, 1H), 8.55 (bs, 1H); ^{13}C NMR: 19.37, 28.43, 30.95, 34.70, 49.25, 57.62, 63.86, 76.68, 109.45, 122.63, 126.73, 128.03, 128.11, 128.18, 128.32, 129.25, 129.76, 130.31, 135.74, 137.37, 138.38, 139.22, 141.44, 177.99, 202.61; MS m/z: 448 (M$^+$); Anal. calcd for $C_{30}H_{28}N_2O_2$: C, 80.33; H, 6.29; N, 6.25. Found: C, 80.24; H, 6.32; N, 6.24.

4.3.3. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-(*p*-methyl)benzylidenecyclohexanone-4-(*p*-methyl)phenyl-pyrrolidine 4b. 0.23 g, 95%. Yellow solid, mp: 218–219°C; IR (KBr): 1681.8, 1703.2, 3251.8 cm^{-1}, ^{1}H NMR: δ 1.26–1.87 (m, 6H), 2.12 (s, 3H), 2.29 (s, 3H), 2.33 (s, 3H), 3.40 (dd, J=9.0, 7.5 Hz, 1H), 3.89 (dd, J=10.8, 9.0 Hz, 1H), 4.82 (dd, J=10.8, 7.5 Hz, 1H), 6.60–7.40 (m, 12H), 7.28 (s, 1H), 8.26 (bs, 1H); ^{13}C NMR: 19.39, 21.04, 21.26, 28.56, 30.92, 34.73, 49.01, 57.78, 63.72, 76.68, 109.35, 122.61, 126.82, 128.38, 128.79, 128.84, 129.17, 129.93, 130.23, 130.76, 133.00, 136.17, 136.27, 136.64, 138.41, 138.48, 141.36, 177.88, 202.65; MS m/z: 476 (M$^+$); Anal. calcd for $C_{32}H_{32}N_2O_2$: C, 80.64; H, 6.77; N, 5.88. Found: C, 80.61; H, 6.75; N, 5.89.

4.3.4. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-(*p*-methoxy)benzylidenecyclohexanone-4-(*p*-methoxy)phenyl-pyrrolidine 4c. 0.20 g, 80%. Yellow solid, mp: 230–231°C; IR (KBr): 1668.0, 1710.0, 3265.3 cm^{-1}, ^{1}H NMR: δ 0.94–2.35 (m, 6H), 2.14 (s, 3H), 3.76 (s, 3H), 3.78 (s, 3H), 3.40 (dd, J=9.0, 7.5 Hz, 1H), 4.10 (dd, J=10.8, 9.0 Hz, 1H), 4.78 (dd, J=10.8, 7.5 Hz, 1H), 6.79–7.42 (m, 12H), 7.23 (s, 1H), 9.13 (bs, 1H); ^{13}C NMR: 19.14, 28.46, 30.73, 34.64, 48.77, 55.04, 58.01, 63.28, 76.68, 109.38, 113.34, 113.48, 122.40, 122.61, 128.20, 128.32, 129.09, 131.25, 131.68, 135.21, 138.37, 141.51, 158.22, 159.54, 178.07, 202.67; MS m/z: 508 (M$^+$); Anal. calcd for $C_{32}H_{32}N_2O_4$: C, 75.57; H, 6.34; N, 5.51. Found: C, 75.60; H, 6.32; N, 5.54.

4.3.5. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-(*p*-chloro)benzylidenecyclohexanone-4-(*p*-chloro)phenyl-pyrrolidine 4d. 0.25 g, 95%. Yellow solid, mp: 205–206°C; IR (KBr): 1679.9, 1703.5, 3255.6 cm^{-1}, ^{1}H NMR: δ 1.1–2.23 (m, 6H), 2.08 (s, 3H), 3.44 (dd, J=9.0, 7.5 Hz, 1H), 3.91 (dd, J=10.8, 9.0 Hz, 1H), 4.83 (dd, J=10.8, 7.5 Hz, 1H), 6.60–7.40 (m, 12H), 7.30 (s, 1H), 8.26 (bs, 1H); ^{13}C NMR: 19.29, 28.41, 30.96, 34.65, 48.60, 57.71, 63.72, 76.68, 109.48, 122.64, 126.53, 128.29, 128.34, 128.37, 128.67, 129.37, 130.61, 131.02, 131.48, 131.65, 132.62, 134.07, 134.23, 137.17, 137.72, 141.33, 177.62, 202.18; MS m/z: 517 (M$^+$); Anal. calcd for $C_{30}H_{26}Cl_2N_2O_2$: C, 69.63; H, 5.06; N, 5.41. Found: C, 69.91; H, 5.03; N, 5.44.

4.3.6. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-(*p*-*N*,*N*-dimethyl)benzylidenecyclohexanone-4-(*p*-*N*,*N*-dimethyl)phenyl-pyrrolidine 4e. 0.15 g, 55%. Pale yellow solid, mp: 220–221°C; IR (KBr): 1679.5, 1716.5, 3254.0 cm^{-1}, ^{1}H NMR: δ 1.20–2.44 (m, 6H), 2.11 (s, 3H), 2.88 (s, 6H), 2.95 (s, 6H), 3.40 (dd, J=9.0, 7.5 Hz, 1H), 3.95 (dd, J=10.8, 9.0 Hz, 1H), 4.75 (dd, J=10.8, 7.5 Hz, 1H), 6.60–7.40 (m, 12H), 7.30 (s, 1H), 8.60 (bs, 1H); ^{13}C NMR: 19.29, 28.82, 30.77, 34.86, 40.36, 40.72, 49.15, 58.21, 63.20, 76.68, 109.08, 111.18, 112.46, 122.58, 123.96, 128.56, 129.02, 131.14, 132.19, 132.48, 132.86, 139.54, 147.93, 150.22, 150.62, 177.43, 202.47; MS m/z: 534 (M$^+$); Anal. calcd for $C_{34}H_{38}N_4O_2$: C, 76.38; H, 7.16; N, 10.48. Found: C, 76.32; H, 7.14; N, 10.51.

4.3.7. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.2^{11}]6^{11}-(*m*-nitro)benzylidenecyclohexanone-4-(*m*-nitro)phenyl-pyrrolidine 4f. 0.22 g, 80%. Yellow solid, mp: 190–191°C; IR (KBr): 1671.0, 1710.7, 3245.0 cm^{-1}, ^{1}H NMR: δ 1.30–2.35 (m, 6H), 2.16 (s, 3H), 3.56 (dd, J=9.0, 7.5 Hz, 1H), 4.12 (dd, J=10.8, 9.0 Hz, 1H), 4.90 (dd, J=10.8, 7.5 Hz, 1H), 6.80–8.18 (m, 12H), 7.30 (s, 1H), 8.46 (bs, 1H); ^{13}C NMR: 19.09, 28.18, 31.22, 34.59, 48.72, 57.91, 63.60, 76.68, 110.00, 122.08, 122.73, 122.90, 124.06, 125.13, 126.04, 128.21, 129.08, 129.22, 129.82, 135.36, 135.82, 136.79, 137.17, 139.34, 141.51, 141.54, 147.99, 148.30, 177.56, 201.47; MS m/z: 538 (M$^+$); Anal. calcd for $C_{30}H_{26}N_4O_6$: C, 66.91; H, 4.87; N, 10.40. Found: C, 66.95; H, 4.84; N, 10.43.

4.3.8. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-phenyl-pyrrolidine 6a. 0.1 g, 95%. White solid, mp: 198–199°C; IR (KBr): 1699.0, 3281.0 cm^{-1}, ^{1}H NMR: δ 0.59–2.33 (m, 7H), 2.20 (s, 3H), 3.37 (dd, J=9.0, 7.5 Hz, 1H), 3.91 (dd, J=10.8, 9.0 Hz, 1H), 4.19 (d, J=13.2 Hz, 1H), 4.94 (dd,

J=10.8, 7.5 Hz, 1H), 6.01 (bs, 1H), 6.71–7.58 (m, 14H), 8.77 (bs, 1H); ^{13}C NMR: 21.68, 29.91, 33.32, 35.07, 49.12, 53.85, 56.18, 57.44, 73.06, 76.57, 109.26, 122.90, 126.51, 127.25, 127.48, 128.01, 128.27, 128.68, 128.93, 129.08, 130.31, 139.73, 140.94, 140.97, 158.76, 178.31; MS *m/z*: 462 (M^+); Anal. calcd for $C_{30}H_{30}N_4O$: C, 77.89; H, 6.54; N, 12.11. Found: C, 77.89; H, 6.52; N, 12.09.

4.3.9. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-(*p*-methyl)phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-(*p*-methyl)phenyl-pyrrolidine 6b. 0.10 g, 82%. White solid, mp: 245–246°C; IR (KBr): 1701.1, 3290.0 cm^{-1}, ^{1}H NMR: δ 0.55–1.68 (m, 7H), 2.17 (s, 3H), 2.29 (s, 3H), 2.32 (s, 3H), 3.30 (dd, J=9.0, 7.5 Hz, 1H), 3.86 (dd, J=10.8, 9.0 Hz, 1H), 4.12 (d, J=13.2 Hz, 1H), 4.85 (dd, J=10.8, 7.5 Hz, 1H), 6.25 (bs, 1H), 6.74–7.72 (m, 12H), 10.07 (bs, 1H); ^{13}C NMR: 19.96, 20.46, 28.88, 32.10, 33.92, 34.09, 47.20, 52.47, 54.54, 56.14, 71.46, 76.30, 108.48, 120.87, 126.14, 126.95, 127.53, 127.62, 127.70, 127.84, 128.87, 134.56, 135.62, 137.11, 141.33, 157.36, 177.12; MS *m/z*: 490 (M^+); Anal. calcd for $C_{32}H_{34}N_4O$: C, 78.34; H, 6.98; N, 11.42. Found: C, 78.36; H, 6.95; N, 11.47.

4.3.10. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-(*p*-methoxy)phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-(*p*-methoxy)phenyl-pyrrolidine 6c. 0.10 g, 80%. White solid, mp: 258–259°C; IR (KBr): 1701.1, 3273.0 cm^{-1}, ^{1}H NMR: δ 0.63–2.30 (m, 7H), 2.16 (s, 3H), 3.35 (dd, J=9.0, 7.5 Hz, 1H), 3.77 (s, 3H), 3.80 (s, 3H), 3.84 (dd, J=10.8, 9.0 Hz, 1H), 4.13 (d, J=13.2 Hz, 1H), 4.88 (dd, J=10.8, 7.5 Hz, 1H), 5.85 (bs, 1H), 6.70–7.45 (m, 12H), 8.60 (bs, 1H); ^{13}C NMR: 21.70, 29.91, 33.32, 35.08, 48.42, 53.65, 55.21, 56.10, 57.70, 72.60, 76.58, 109.22, 113.41, 113.70, 122.85, 128.32, 128.72, 128.90, 129.19, 131.22, 131.75, 132.84, 140.96, 158.30, 159.02, 159.07, 178.31; MS *m/z*: 522 (M^+); Anal. calcd for $C_{32}H_{34}N_4O_3$: C, 73.54; H, 6.56; N, 10.72. Found: C, 73.54; H, 6.52; N, 10.76.

4.3.11. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-(*p*-chloro)phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-(*p*-chloro)phenyl-pyrrolidine 6d. 0.12 g, 90%. White solid, mp: 253–254°C; IR (KBr): 1699.2, 3278.8 cm^{-1}, ^{1}H NMR: δ 0.51–2.54 (m, 7H), 2.11 (s, 3H), 3.27 (dd, J=9.0, 7.5 Hz, 1H), 3.83 (dd, J=10.8, 9.0 Hz, 1H), 4.16 (d, J=13.2 Hz, 1H), 4.87 (dd, J=10.8, 7.5 Hz, 1H), 6.20 (bs, 1H), 6.75–7.76 (m, 12H), 10.10 (bs, 1H); ^{13}C NMR: 20.41, 28.94, 32.15, 33.85, 46.96, 52.73, 54.49, 56.05, 70.66, 76.07, 108.63, 120.76, 126.79, 126.85, 127.05, 127.58, 127.73, 130.42, 130.72, 131.37, 137.47, 139.14, 141.34, 156.83, 176.97; MS *m/z*: 531 (M^+); Anal. calcd for $C_{30}H_{28}Cl_2N_4O$: C, 67.80; H, 5.31; N, 10.54. Found: C, 67.81; H, 5.33; N, 10.51.

4.3.12. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-(*p*-*N*,*N*-dimethyl)phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-(*p*-*N*,*N*-dimethyl)phenyl-pyrrolidine 6e. 0.09 g, 70%. White solid, mp: 205–206°C; IR (KBr): 1706.9, 3280.2 cm^{-1}, ^{1}H NMR: δ 1.20–2.30 (m, 7H), 2.12 (s, 3H), 2.89 (s, 6H), 2.92 (s, 6H), 3.30 (dd, J=9.0, 7.5 Hz, 1H), 3.80 (dd, J=10.8, 9.0 Hz, 1H), 4.12 (d, J=13.2 Hz, 1H), 4.85 (dd, J=10.8, 7.5 Hz, 1H), 6.01 (bs, 1H), 6.66–7.50 (m, 12H), 8.30 (bs, 1H); ^{13}C NMR: 19.97, 21.45, 28.86, 33.51, 34.08, 40.35, 40.72, 47.21, 52.48, 54.56, 56.51, 71.48, 76.25, 108.49, 120.86, 126.14, 126.95, 127.58, 127.67, 127.75, 127.86, 128.95, 134.59, 135.64, 137.12, 141.35, 158.35, 177.28; MS *m/z*: 548 (M^+); Anal. calcd for $C_{34}H_{40}N_6O$: C, 74.42; H, 7.35; N, 15.32. Found: C, 74.45; H, 7.35; N, 15.30.

4.3.13. 1-*N*-Methyl-spiro[2.3^1]oxindole-spiro[3.7^{11}](3^{11}-(*m*-nitro)phenyl)$\Delta^{1^{11}}$,7^{11}a-hexahydro-2*H*-indazole-4-(*m*-nitro)phenyl-pyrrolidine 6f. 0.11 g, 80%. Pale yellow solid, mp: 179–180°C; IR (KBr): 1708.8, 3342.0 cm^{-1}, ^{1}H NMR: δ 0.56–2.35 (m, 7H), 2.19 (s, 3H), 3.45 (dd, J=9.0, 7.5 Hz, 1H), 3.89 (dd, J=10.8, 9.0 Hz, 1H), 4.36 (d, J=13.2 Hz, 1H), 5.02 (dd, J=10.8, 7.5 Hz, 1H), 6.10 (bs, 1H), 6.83–8.37 (m, 12H), 8.65 (bs, 1H); ^{13}C NMR: 21.51, 29.92, 33.56, 34.95, 48.86, 54.35, 55.89, 57.47, 71.79, 76.68, 109.91, 121.81, 122.04, 122.60, 123.04, 125.04, 128.28, 128.91, 129.23, 129.47, 133.47, 136.49, 141.06, 141.92, 143.30, 148.11, 148.25, 158.16, 178.58; MS *m/z*: 552 (M^+); Anal. calcd for $C_{30}H_{28}N_6O_5$: C, 65.21; H, 5.10; N, 15.21. Found: C, 65.21; H, 5.08; N, 15.24.

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