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Dipolar cycloaddition of carbonyl ylides to 2-oxoindolinylidenes: a facile approach towards the synthesis of functionalized spiroindolenins

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This paper is dedicated to Professor Al Padwa

Abstract—Oxoindolinylidenes undergo regiospecific dipolar cycloaddition with carbonyl ylides affording highly functionalized spiroindolenin systems in high yield. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Spiroindolenins are interesting compounds with potential application in the synthesis of a variety of biologically important natural products.[1] The Diels–Alder and dipolar cycloaddition reactions of oxoindolinylidenes offer a convenient route for the construction of spiroindolenins and related compounds.[2–5] Dipolar cycloaddition reactions of azomethine ylides with the oxoindolinylidenes have been studied in some detail[3–5] and this strategy was recently exploited as the key step in the total synthesis of spirotryprostatin B, a biologically active natural product.[6] The addition of carbonyl ylides[7] to oxoindolinylidenes however, has remained unexplored. Against this literature background and in the context of our interest in constructing heterocycles using dipolar species,[8] we have investigated the cycloaddition of carbonyl ylides to oxoindolinylidenes and the results are presented here.

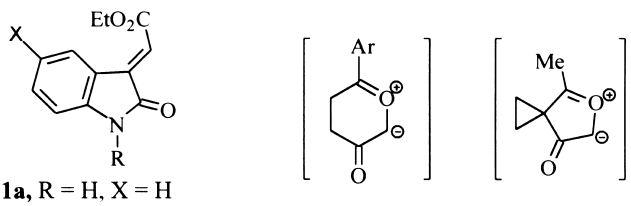
The oxoindolinylidene acetates and carbonyl ylides selected for our study are shown in Fig. 1.

2. Results and discussion

Our studies were initiated with the rhodium(II) acetate catalyzed decomposition of 1-diazo-5-phenyl-2,5-pentanedione **4a** in the presence of 3-ethoxycarbonylmethylene-2-oxoindole **1a**. The reaction proceeded smoothly to afford *endo* and *exo* adducts in a total yield of 98% (Scheme 1).

The cycloadducts were separated by column chromatography and characterized on the basis of spectroscopic data. The IR spectrum of the *endo* adduct showed the –NH absorption band at 3225 cm^{-1} and the carbonyl absorption bands were observed at 1734 and 1707 cm^{-1}. The regio- and stereochemical assignment of the structure is derived from proton NMR analysis. The bridgehead proton on C-1 appeared as a doublet at δ 4.81 (J=8.1 Hz) and the proton on C-7 resonated as a doublet at δ 4.11 (J=8.4 Hz). In the ^{13}C NMR spectrum, the three carbonyl signals were observed at δ 203.34 (C-2), 179.50 (ester) and 168.44 (lactam).

The IR spectrum of the *exo* adduct **6a** showed two strong bands at 1735 and 1700 cm^{-1}. The -NH absorption band was observed at 3219 cm^{-1}. In the ^1H NMR spectrum, the bridgehead proton on C-1 and the proton on C-7 appeared as doublets at δ 5.18 (J=3.1 Hz) and 3.82 (J=3.1 Hz),



1a, R = H, X = H
1b, R = Me, X = H
1c, R = Bn , X = H
1d, R = H, X = Br

1d

2a, Ar = phenyl
2b, Ar = 2-thienyl

3

Figure 1.

Keywords: cycloaddition; spiroindolenins; oxoindolinylidenes.

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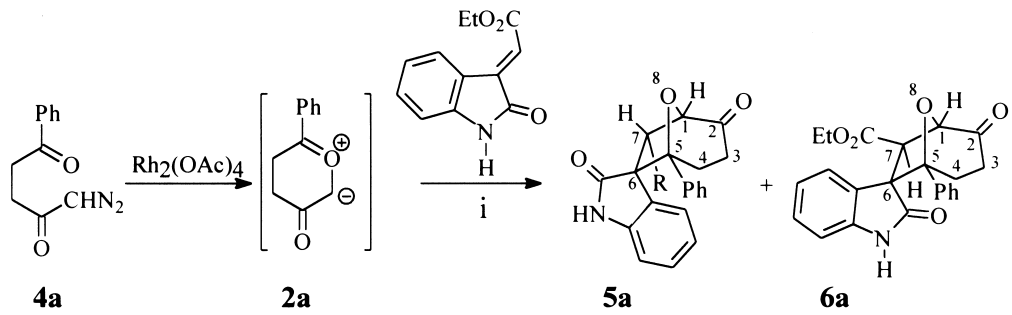


4a **2a** **5a** **6a**

Scheme 1. (i) Toluene, rt, 45 min, 98% (1.1:1).

respectively. In the ^{13}C NMR spectrum, the signals due to the three carbonyl groups were visible at δ 205.75, 176.85 and 167.91. Finally, the assigned structure was unequivocally established by single crystal X-ray analysis (Fig. 2).[†]

Under similar experimental conditions, the reaction of other oxoindolinylidene derivatives with the diazoketones furnished similar spiro-oxabicyclic compounds. The results are summarized in Table 1.

Subsequent to these investigations, we became interested in the dipolar addition of the thienyl substituted carbonyl ylide with the oxoindolinylidenes. The rhodium(II) acetate catalyzed decomposition of 1-diazo-5-(2-thienyl)-2,5-pentanedione **4b** in toluene solution of oxoindolinylidenes **1a**–**d** afforded the cycloadducts in good yields (Table 2).

After having studied the reactivity of oxoindolinylidenes towards six-membered carbonyl ylides, we turned our attention to the reaction of oxoindolinylidene acetates towards a five-membered carbonyl ylide. When a solution of 1-acetyl-1-diazoacetyl cyclopropane **7** and oxoindolinylidene **1a** was treated with catalytic amount of rhodium(II) acetate at room temperature, the reaction afforded all the four possible isomeric products as shown in Scheme 2.

The products were separated by column chromatography followed by fractional crystallization and the structure of the products was ascertained on the basis of spectroscopic analysis. In the ^{1}H NMR spectrum of the *endo* adduct **8a**, the bridgehead protons H_4 and H_5 displayed a doublet at δ 4.89 (J=5.6 Hz, 1H) and 3.99 (J=5.6 Hz, 1H), respectively. The other three products were characterized with NOESY and nOe difference experiments.

The *exo*-adduct **9a** showed characteristic coupling of 0.8 Hz for the bridge-head proton in the 500 MHz NMR spectrum which indicated that the protons involved are attached to vicinal carbons in the norbornane framework, and that the proton on the adjacent carbon is on the *endo* side of the bicyclic system. NOESY spectrum showed cross peaks between H15-Me17, Me17-H13, Me17-H16 and H4-H5. The nOe intensities measured by difference nOe experiments are shown in Fig. 3. The *endo* structure of the adduct **10a** was confirmed by the nOe of H13-H15′=5% which is possible only if the aromatic ring is *endo* (Fig. 4).

The reaction of *N*-methyl and *N*-benzyl oxoindolinylidenes with the diazoketone followed a similar course. The results of these experiments are presented in Table 3.

In order to rationalize the observed mode of addition, we have carried out some theoretical calculations using semi-empirical PM3 method with the aid of TITAN software (version 1).[9] The correlation diagram for the reaction of oxoindolinylidene **1a** with the carbonyl ylide **2a** is given in Fig. 5 as an illustrative example.

From the correlation diagram in Fig. 5, it is clear that the most favorable interaction is HOMO(dipole)–LUMO(dipolarophile) interaction. Although both HOMO(dipole)–LUMO(dipolarophile) and LUMO(dipole)–HOMO(dipolarophile) interactions are symmetry allowed. However, the latter interaction is unimportant due to the large energy gap compared to the other. Thus, it is a HOMO controlled reaction according to Sustmann's classification of 1,3-dipolar cycloaddition reactions.[10]

In conclusion, we have shown that highly functionalized spiroindolenin systems can be synthesized using dipolar cycloaddition of carbonyl ylides to oxoindolinylidene derivatives. It is found that the aryl substituted six-membered carbonyl ylides (both phenyl and 2-thienyl) react with high regioselectivity whereas the one example of the alkyl substituted five-membered analogue reacts almost regiorandomly. It is conceivable that the cycloadducts may be amenable to a number of potentially useful synthetic transformations.

3. Experimental

All reactions were carried out in oven dried glassware under an atmosphere of argon, unless otherwise mentioned. Analytical thin layer chromatography was performed on silica gel tlc plates. Purification by column chromatography was carried out using silica gel (100–200 mesh). Mixtures of ethyl acetate and hexane were used as eluents. After the chromatographic separation, the solvents were removed using a Büchi-EL rotary evaporator. Melting points were recorded on Fisher Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Bomem MB series FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Brüker 300 MHz NMR

[†] The crystal data has been deposited in CCDC and details can be obtained from CCDC by citing the reference number CCDC 180240.

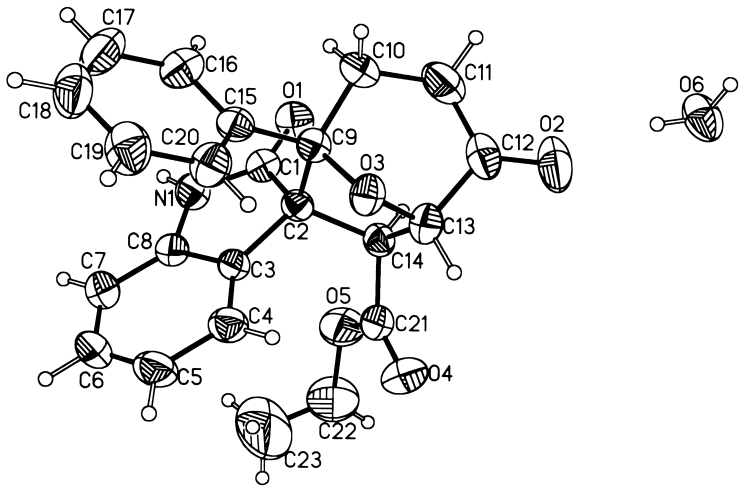


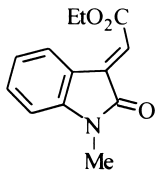
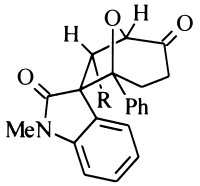
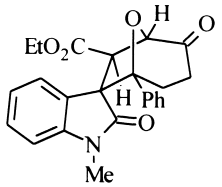
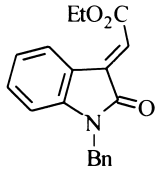
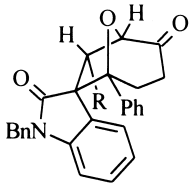
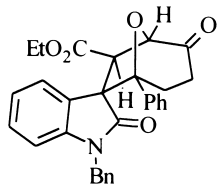
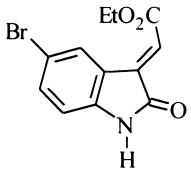
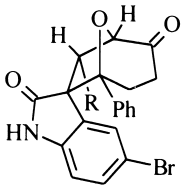
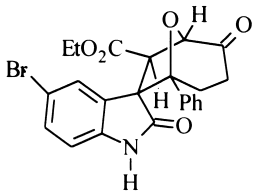
Figure 2. Single crystal X-ray structure of **6a**.

spectrometer using chloroform-d as solvent, unless otherwise mentioned. The chemical shifts are given in δ scale with tetramethylsilane as internal standard. High-resolution mass spectra were recorded on a Finnigan MAT model 8430 instrument. Elemental analyses were done using Perkin–Elmer 2400 CHNS Analyzer. All solid products were purified by recrystallization from an appropriate solvent system. Solvents used for the experiments (toluene, ether and dichloromethane) were distilled and dried by employing standard procedures. The diazoketones were prepared from the corresponding carboxylic acids following the literature procedures.[11–13]

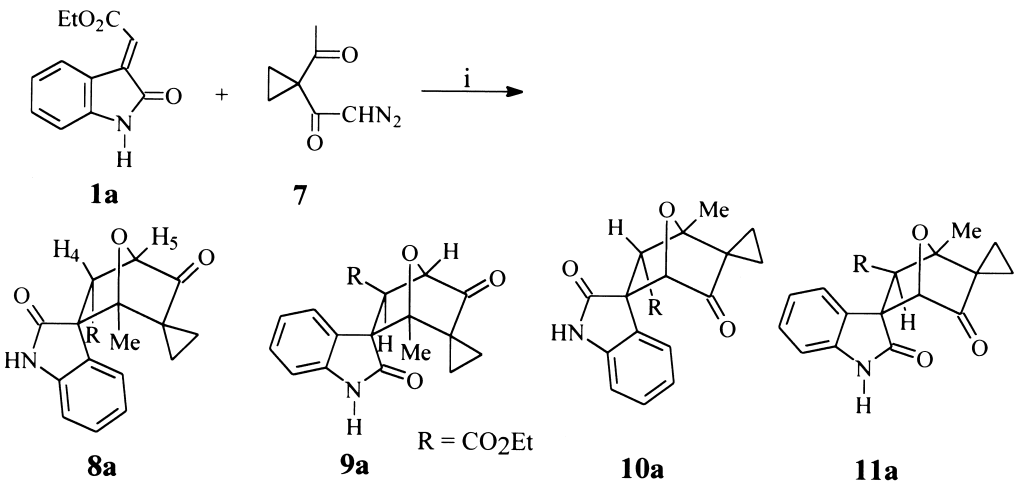
3.1. General procedure for the rhodium(II) catalyzed cycloaddition reaction of 1-diazoalkane diones with oxoindolinylidenes

A toluene solution of oxoindolinylidene acetate and 1.5 equiv. of appropriate diazoalkanedione was purged

Table 1. Cycloaddition reactions of diazoketone **4a** with oxoindolinylidenes

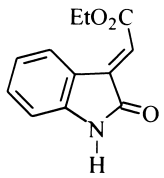
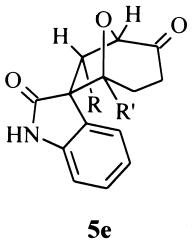
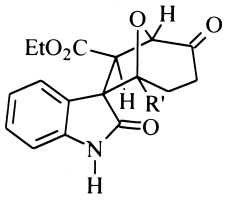
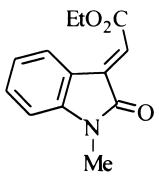
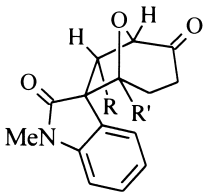
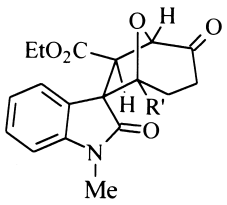
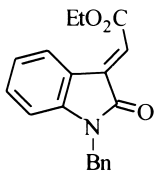
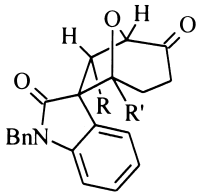
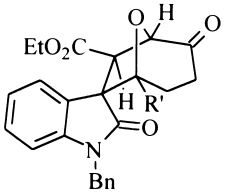
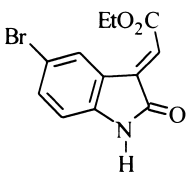
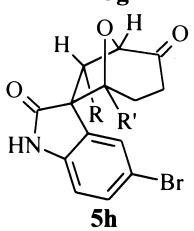
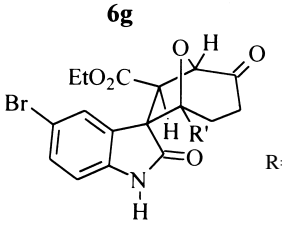
Entry	Oxoindolinylidene	Time (h)	Products	Yield (%)[a] (ratio)
1	 **1b**	2	 **5b**  **6b**	87 (98)[b] (2:1)
2	 **1c**	1	 **5c**  **6c**	89 (97)[b] (2:1)
3	 **1d**	0.5	 **5d**  **6d**	97 (2:1)

Reaction conditions: $Rh_2(OAc)_4$, rt.
[a] Isolated yield.
[b] Yield based on recovered oxoindolinylidene is given in parantheses.



Scheme 2. (i) $Rh_2(OAc)_4$, toluene, argon, rt, 30 min, 93% (1:1:1.5:1).

Table 2. Reaction of oxoindolinylidenes with the thienyldiazoketone **4b**

Entry	Oxoindolinylidene	Time (h)	Products	Yield (%)[a] (ratio)
1	 **1a**	0.5	 **5e**  **6e**	95 (2:1)
2	 **1b**	2	 **5f**  **6f**	95 (2:1)
3	 **1c**	1	 **5g**  **6g**	88 (98)[b] (1.1:1)
4	 **1d**	0.5	 **5h**  **6h**	70 (82)[b] (2:1)

R = CO_2Et, R′ = thienyl

R=CO_2Et, R′=thienyl

Reaction conditions: $Rh_2(OAc)_4$, toluene, rt.

[a] Isolated yield.

[b] Yield based on recovered oxoindolinylidene is given in parantheses.

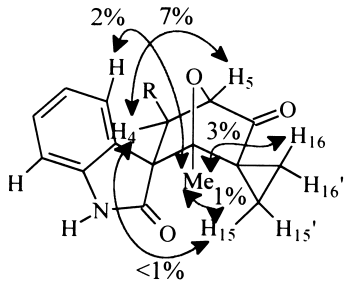


Figure 3. Selected nOe data of **9a**.

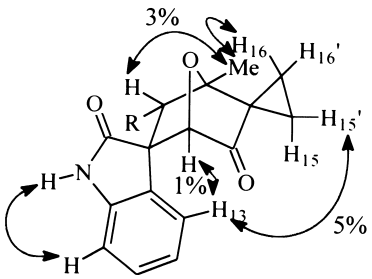


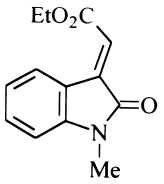
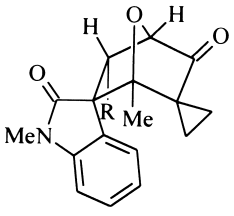
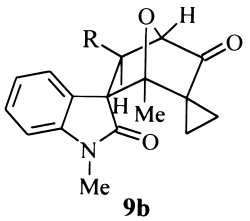
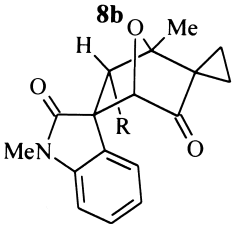
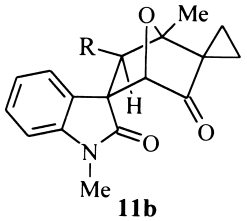
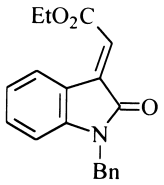
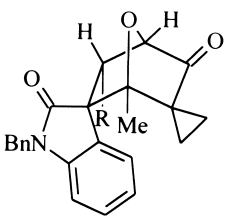
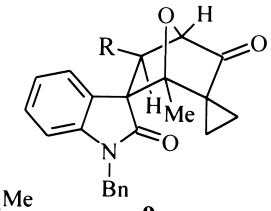
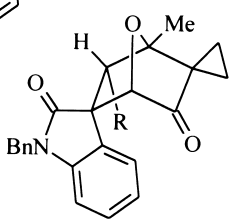
Figure 4. Selected nOe data of **10a**.

with argon. To this solution, catalytic amount of rhodium(II) acetate (2 mg) was added and stirred under argon atmosphere at room temperature. When the reaction was over (as indicated by tlc), the solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel using the appropriate hexane–ethyl acetate mixture as the eluent to give the pure cycloadducts. Wherever necessary, further separation of the isomeric products was carried out by fractional crystallization. The products were identified on the basis of spectroscopic data.

3.2. Cycloadducts 5a and 6a

A solution of oxoindolinylidene acetate **1a** (0.217 g, 1 mmol) and 1-diazo-5-phenyl-2,5-pentanedione **4a** (0.303 g, 1.5 mmol) in toluene (15 mL) was treated with catalytic amount (2 mg) of rhodium(II) acetate at room temperature under an atmosphere of argon and was stirred for 45 min. followed by chromatography on a silica gel column (100–200 mesh) using 10% ethyl acetate–hexane as eluent afforded the *endo* adduct **5a** (0.203 g, 52%) as an off-white crystalline solid and the *exo* adduct **6a** (0.180 g, 46%) as colorless crystalline solid.

Table 3. Reaction of oxoindolinylidenes with the diazocompound **7**

Entry	Oxoindolinylidene	Time (h)	Products	Yield (%)[a] (ratio)
1	 **1b**	0.5	 **8b**  **9b**  **10b**  **11b**	93 (3:2:3:2)
2	 **1c**	1	 **8c**  **9c**  R= CO_2Et **10c**	98 (1:1:1)

Reaction conditions: $Rh_2(OAc)_4$, toluene, rt.

[a] Isolated yield.

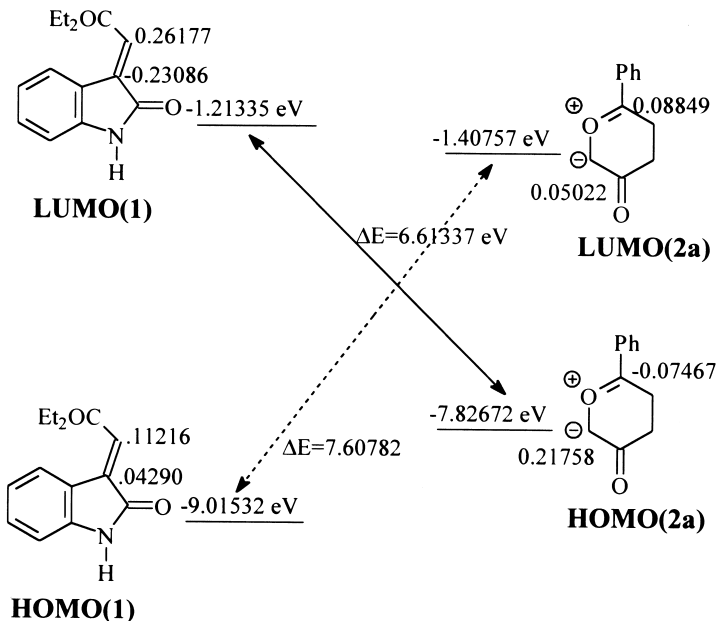


Figure 5. The correlation diagram for the reaction of **1a** with **2a**.

3.2.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-1,2-dihydro-2,2′-dioxo-5′-phenylspiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5a. Recrystallized from EtOAc–hexane, mp 164°C (decomposed). IR (KBr) $\nu_{(max)}$: 3225, 1734, 1707, 1619, 1473, 1446, 1372, 1347, 1303, 1185, 1160, 1029 cm^{-1}. ^1H NMR: δ 8.18 (s, 1H, exchangeable with D_2O), 7.45 (d, J=7.5 Hz, 1H), 7.32 (t, J=7.3 Hz, 1H), 7.12 (brs, 5H), 6.86 (d, J=7.6 Hz, 2H), 4.81 (d, J=8.1 Hz, 1H), 4.11 (d, J=8.4 Hz, 1H), 3.85–3.79 (m, 2H), 3.13–3.07 (m, 1H), 2.81–2.67 (m, 2H), 2.24–2.15 (m, 1H), 0.81 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 203.34, 179.50, 168.44, 142.63, 140.51, 129.74, 127.88, 127.64, 123.76, 122.43, 110.38, 87.75, 82.25, 63.34, 61.25, 55.32, 33.83, 33.05, 13.65. Anal. calcd for $C_{23}H_{21}NO_5$: C, 70.57; H, 5.40; N, 3.57. Found: C, 70.76; H, 5.42; N, 3.73.

3.2.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-5′-phenylspiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6a. Recrystallized from EtOAc–hexane, mp 195–197°C. IR (KBr) $\nu_{(max)}$: 3219, 1735, 1700, 1619, 1473, 1447, 1372, 1345, 1303, 1242, 1188, 1160 cm^{-1}. ^1H NMR: δ 8.35 (s, 1H), 7.10–6.90 (m, 7H), 6.70 (t, J=7.4 Hz, 1H), 6.61 (d, J=7.6 Hz, 1H), 5.18 (d, J=3.1 Hz, 1H), 3.82 (d, J=3.1 Hz, 1H), 3.65 (q, J=6.9 Hz, 2H), 3.25–3.08 (m, 2H), 2.69–2.60 (m, 1H), 2.30–2.17 (m, 1H), 0.62 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 205.75, 176.85, 167.91, 141.30, 139.82, 129.16, 128.38, 127.84, 127.19, 126.56, 123.31, 122.24, 108.70, 90.05, 81.00, 63.01, 61.27, 57.26, 33.34, 31.92, 13.34. HRMS calcd for $C_{23}H_{21}NO_5$: 391.1419. Found: 391.1427. X-ray Crystal data for **6a**: $C_{23}H_{20}NO_5.H_2O$ FW: 408.42. Crystal size: 0.40×0.36×0.12 mm^3, Monoclinic, space group: $P2(1)/n$. Unit cell dimensions a=8.8733(4) Å, α=90°; b=14.8316(7) Å, β=97.245(4)°; c=15.4797(8) Å, γ=90°. R indices (all data) $R1$=0.0873, $wR2$=0.1461. Volume, Z=2020.94(17) $Å^3$, 4. D calc.=1.342 mg/m^3. $F(000)$=860. Absorption coefficient=0.098 mm^{-1}. Reflections collected=38290. λ=0.71073 Å. (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

3.3. Cycloadducts 5b and 6b

Treatment of 1-diazo-5-phenyl-2,5-pentane dione **4a** (0.303 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1b** (0.231 g, 1 mmol) in toluene (10 mL), in the presence of a catalytic amount of rhodium(II) acetate at room temperature for 2 h followed by chromatographic purification of the product afforded the adduct **5b** (0.231 g, 57%) as a pale yellow semi-solid and the adduct **6b** (0.121 g, 30%) as colorless crystal.

3.3.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-7′-1,2-dihydro-2,2′-dioxo-1-methyl-5′-phenyl spiro [3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5b. IR (KBr) $\nu_{(max)}$: 1723 (broad band), 1611, 1493, 1470, 1375, 1331, 1194, 1160, 1028 cm^{-1}. ^1H NMR: δ 7.49–7.38 (m, 2H), 7.13–7.11 (m, 5H), 6.76 (d, J=7.7 Hz, 2H), 4.85 (d, J=8.3 Hz, 1H), 4.15 (d, J=8.4 Hz, 1H), 3.91–3.75 (m, 2H), 3.16–3.04 (m, 1H), 2.74–2.60 (m, 2H) 2.67 (s, 3H), 2.23–2.16 (m, 1H), 1.25 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 203.25, 176.92, 168.53, 145.29, 140.24, 129.65, 127.50, 125.18, 122.21, 108.60, 87.78, 82.40, 63.09, 61.05, 54.52, 33.45, 32.89, 25.79, 13.59. Anal. calcd for $C_{24}H_{23}NO_5$: C, 71.09; H, 5.71; N, 3.45. Found: C, 71.43; H, 5.71; N, 3.28.

3.3.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-1-methyl-5′-phenyl spiro [3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6b. Recrystallized from EtOAc–hexane solvent system, mp 180–182°C. IR (KBr) $\nu_{(max)}$: 1741, 1702, 1607, 1469, 1378, 1351, 1133, 1094, 1025 cm^{-1}. ^1H NMR: δ 7.03–6.96 (m, 7H), 6.72 (t, J=7.5 Hz, 1H), 6.54 (d, J=7.7 Hz, 1H), 5.17 (d, J=1.7 Hz, 1H), 3.80 (d, J=3.1 Hz, 1H), 3.60–3.53 (m, 2H), 3.30 (s, 3H), 3.26–3.09 (m, 2H), 2.68–2.59 (m, 1H), 2.26–2.17 (m, 1H), 0.57 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 205.76, 174.83, 167.89, 142.91, 141.32, 128.32, 127.73, 127.06, 123.18, 122.23, 107.10, 89.87, 62.60, 61.02, 57.00, 33.30, 31.83, 26.72, 13.32. HRMS. calcd for $C_{24}H_{23}NO_5$: 405.1576. Found: 405.1565.

3.4. Cycloadducts 5c and 6c

Treatment of 1-diazo-5-phenyl-2,5-pentane dione **4a** (0.303 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1c** (0.307 g, 1 mmol) in toluene (10 mL), in the presence of a catalytic amount of rhodium(II) acetate at room temperature for 1 h followed by chromatographic purification of the product afforded the adduct **5c** (0.274 g, 57%) as an off-white crystalline solid and the adduct **6c** (0.154 g, 32%) as a colorless solid.

3.4.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-1,2-dihydro-2,2′-dioxo-5′-phenyl-1-(phenylmethyl)spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5c. Recrystallized from CH_2Cl_2–hexane, mp 168–170°C. IR (KBr) $\nu_{(max)}$: 1737, 1719, 1610, 1492, 1467, 1368, 1179, 1029 cm^{-1}. ^1H NMR: δ 7.47 (d, J=7.5 Hz, 1H), 7.28–7.07 (m, 10H), 6.71 (m, 2H), 6.62 (d, J=7.7 Hz, 1H), 4.88 (d, J=8.3 Hz, 1H), 4.58 (d, J=15.7 Hz, 1H), 4.38 (d, J=15.7 Hz, 1H), 4.24 (d, J=8.4 Hz, 1H), 3.89–3.68 (m, 2H), 3.19–3.07 (m, 1H), 2.87–2.79 (m, 1H), 2.73–2.64 (m, 1H), 2.31–2.20 (m, 1H), 0.74 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 203.20, 177.50, 168.45, 144.66, 140.56, 135.03, 128.59, 128.01, 127.61, 127.41, 127.01, 125.26, 124.62, 124.06, 122.37, 109.55, 87.56, 82.18, 62.87, 61.09, 56.07, 44.00, 34.12, 33.15, 13.56. Anal calcd for $C_{30}H_{27}NO_5$: C, 74.82; H, 5.65; N, 2.90. Found: C, 74.87; H, 5.76; N, 2.93.

3.4.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-5′-phenyl-1-(phenylmethyl)spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6c. Recrystallized from EtOAc–hexane, mp 165–167°C. IR (KBr) $\nu_{(max)}$: 1740, 1702, 1607, 1468, 1377, 1350, 1094, 1025 cm^{-1}. ^1H NMR: δ 7.36–7.29 (m, 5H), 7.03–6.86 (m, 7H), 6.68 (t, J=7.3 Hz, 1H), 6.51 (d, J=7.7 Hz, 1H), 5.19 (d, J=2.9 Hz, 1H), 5.09 (d, J=15.3 Hz, 1H), 4.86 (d, J=15.2 Hz, 1H), 3.88 (d, J=2.9 Hz, 1H), 3.61–3.49 (m, 2H), 3.29–3.14 (m, 2H), 2.70–2.61 (m, 1H), 2.27–2.16 (m, 1H), 0.39 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 205.57, 175.02, 167.87, 142.14, 141.19, 135.67, 128.73, 128.18, 127.88, 127.68, 127.07, 126.23, 123.37, 122.17, 108.07, 90.09, 81.10, 62.50, 61.11, 57.21, 44.38, 33.33, 32.08, 13.11. Anal calcd for $C_{30}H_{27}NO_5$: C, 74.82; H, 5.65; N, 2.90. Found: C, 74.88; H, 5.67; N, 2.93.

3.5. Cycloadducts 5d and 6d

Treatment of 1-diazo-5-phenyl-2,5-pentane dione **4a** (0.303 g, 1.5 mmol) with 5-bromo-3-ethoxycarbonyl methylene-2-oxoindoline **1d** (0.296 g, 1 mmol) in toluene (20 mL), in presence of a catalytic amount of rhodium(II) acetate at room temperature for 30 min followed by chromatographic purification of the product afforded the *endo* adduct **5d** (0.310 g, 66%) a colorless crystalline solid and the *exo* adduct **6d** (0.146 g, 31%) as an off-white crystalline solid.

3.5.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-5-bromo-1,2-dihydro-2,2′-dioxo-5′-phenyl spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5d. Recrystallized from EtOAc–hexane, mp 240–242°C. IR (KBr) $\nu_{(max)}$: 3306, 1730, 1699, 1619, 1474, 1445, 1372, 1311, 1241, 1187 1034 cm^{-1}. ^1H NMR: δ 8.13 (s, 1H), 7.53–7.47 (m, 2H), 7.12 (brs, 4H), 6.94–6.85 (m, 1H), 6.75 (d, J=8.2 Hz, 1H), 4.80 (d, J=8.4 Hz, 1H), 4.06 (d, J=8.3 Hz, 1H), 3.93–3.91 (m, 2H), 3.03–2.94 (m, 1H), 2.80–2.62 (m, 2H), 2.31–2.23 (m, 1H), 0.91 (t, J=6.9 Hz, 3H). ^{13}C NMR: δ 203.15, 178.89, 168.26, 141.61, 140.13, 132.62, 128.82, 127.95, 127.85, 127.04, 123.80, 115.03, 111.69, 87.89, 82.26, 63.48, 61.67, 55.19, 33.35, 32.84, 13.80. HRMS. calcd for $C_{23}H_{20}NO_5Br$: 469.0524. Found: 469.0519.

3.5.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-5-bromo-1,2-dihydro-2,2′-dioxo-5′-phenyl spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6d. Recrystallized from EtOAc–hexane solvent system, mp 225–227°C. IR (KBr) $\nu_{(max)}$: 3170, 3107, 1737, 1704, 1617, 1471, 1447, 1305, 1268, 1184, 1029 cm^{-1}. ^1H NMR ($CDCl_3$+DMSO-d_6): δ 9.99 (s, 1H), 7.07–6.99 (m, 7H), 6.49 (d, J=8.2 Hz, 1H), 5.15 (d, J=1.2 Hz, 1H), 3.80 (d, J=2.9 Hz, 1H), 3.76–3.66 (m, 2H), 3.24–3.07 (m, 2H), 2.68–2.59 (m, 1H), 2.22–2.16 (m, 1H), 0.71 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 205.53, 176.26, 167.67, 140.90, 140.00, 131.14, 130.85, 128.99, 128.20, 127.77, 127.23, 123.12, 113.93, 110.40, 89.79, 80.86, 63.07, 61.31, 57.12, 33.15, 31.67, 13.29. HRMS. calcd for $C_{23}H_{20}NO_5Br$: 469.0524. Found: 469.0495.

3.6. Cycloadducts 5e and 6e

Treatment of 1-diazo-5-(2-thienyl)-2,5-pentane dione **4b** (0.312 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1a** (0.217 g, 1 mmol) in toluene (15 mL), in the presence of a catalytic amount of rhodium(II) acetate at room temperature for 30 min followed by chromatographic purification of the product afforded 0.460 g of the cycloadduct as a mixture of *endo* and *exo* isomers. Further separation of the isomers was effected by fractional crystallization.

3.6.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-1,2-dihydro-2,2′-dioxo-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5e. Recrystallised from CH_2Cl_2–hexane solvent system, mp 190°C (decomposed). IR (KBr) $\nu_{(max)}$: 3318, 1737, 1716, 1615, 1470, 1378, 1346, 1301, 1242, 1190 cm^{-1}. ^1H NMR: δ 8.43 (s, 1H, exchangeable with D_2O), 7.43–7.33 (m, 2H), 7.11 (t, J=7.5 Hz, 1H), 7.04 (d, J=4.4 Hz, 1H), 6.92 (d, J=7.6 Hz, 1H), 6.74 (t, J=6.7 Hz, 1H), 6.42 (d, J=2.5 Hz, 1H), 4.80 (d, J=8.3 Hz, 1H), 4.17 (d, J=8.3 Hz, 1H), 3.91–3.78 (m, 2H), 3.17–3.04 (m, 1H), 2.77–2.63 (m, 2H), 2.42–2.31 (m, 1H), 0.83 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 202.50, 179.41, 168.53, 142.87, 142.67, 129.86, 126.42, 125.69, 124.40, 124.15, 122.50, 122.44, 110.65, 87.36, 82.63, 63.74, 54.86, 35.09, 33.06, 13.69. Anal. calcd for $C_{21}H_{19}NO_5S$: C, 63.46; H, 4.81; N, 3.52; S, 8.06. Found: C, 63.48; H, 4.78; N, 3.82; S, 8.10.

3.6.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6e. Recrystallized from CH_2Cl_2–hexane, mp 180°C (decomposed). IR (KBr) $\nu_{(max)}$: 3171, 1740, 1696, 1474, 1240, 1194 cm^{-1}. ^1H NMR: δ 8.12 (s, 1H, exchangeable with D_2O), 7.11 (d, J=7.4 Hz, 1H), 7.01 (t, J=7.6 Hz, 1H), 6.92–6.91 (m, 1H), 6.79 (t, J=7.5 Hz, 1H), 6.67–6.64 (m, 3H), 5.17 (d, J=1.2 Hz, 1H), 3.82 (d, J=2.8 Hz, 1H), 3.68 (q, J=7.1 Hz, 2H), 3.21–3.10 (m, 2H), 2.70–2.62 (m, 1H), 2.41–2.39 (m, 1H), 0.63 (t, J=7.1 Hz,

3H). ^{13}C NMR: δ 204.96, 176.25, 167.73, 143.54, 140.00, 128.79, 128.63, 126.68, 126.26, 123.73, 122.28, 121.91, 108.83, 89.19, 81.46, 63.55, 61.35, 56.92, 33.31, 33.09, 13.34. Anal. calcd for $C_{21}H_{19}NO_5S.H_2O$: C, 60.71; H, 5.10; N, 3.37; S, 7.71. Found: C, 60.57; H, 5.15; N, 3.67; S, 7.96.

3.7. Cycloadducts 5f and 6f

Treatment of 1-diazo-5-(2-thienyl)-2,5-pentane dione **4b** (0.312 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1b** (0.231 g, 1 mmol) in toluene (10 mL), in the presence of a catalytic amount of rhodium(II) acetate at room temperature for 1.5 h followed by chromatographic purification of the product afforded 0.263 g (64%) of the cycloadduct **5f** as white crystalline solid and 31% of **6f** as a colorless semisolid.

3.7.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-1,2-dihydro-2,2′-dioxo-1-methyl-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5f. Recrystallized from CH_2Cl_2–hexane, mp 122–124°C. IR (KBr) $\nu_{(max)}$: 1743, 1719, 1609, 1493, 1468, 1376, 1350, 1189, 1157, 1098 cm^{-1}. ^{1}H NMR: δ 7.46–7.34 (m, 2H), 7.14–7.10 (m, 2H), 6.80 (d, J=5.9 Hz, 2H), 6.41 (d, J=3.1 Hz, 1H), 4.85 (d, J=8.2 Hz, 1H), 4.22 (d, J=8.2 Hz, 1H), 3.88–3.81 (m, 2H), 3.13–3.05 (m, 1H), 2.83 (s, 3H), 2.72–2.64 (m, 2H), 2.41–2.35 (m, 1H), 0.83 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 202.59, 176.85, 168.53, 145.53, 142.57, 129.86, 126.11, 125.40, 124.27, 123.71, 122.50, 122.34, 108.38, 87.49, 82.79, 63.49, 61.24, 54.33, 35.02, 33.04, 26.15, 13.70. Anal. calcd for $C_{22}H_{21}NO_5S$: C, 64.22; H, 5.14; N, 3.40; S, 7.79. Found: C, 64.09; H, 5.22; N, 3.81; S, 8.14.

3.7.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-1-methyl-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6f. IR (neat): 1735, 1708, 1607, 1364, 1249, 1094, 1027 cm^{-1}. ^{1}H NMR: δ 7.07–6.99 (m, 2H), 6.83 (d, J=4.8 Hz, 1H), 6.74 (d, J=7.6 Hz, 1H), 6.57–6.53 (m, 2H), 6.47 (d, J=3.2 Hz, 1H), 5.12 (d, J=2.1 Hz, 1H), 3.75 (d, J=3.0 Hz, 1H), 3.74–3.49 (m, 2H), 3.24 (s, 3H), 3.18–3.06 (m, 2H), 2.63–2.56 (m, 1H), 2.36–2.27 (m, 1H), 0.51 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 205.43, 174.92, 167.80, 151.28, 128.62, 128.59, 128.55, 126.11, 126.04, 123.94, 123.52, 122.28, 121.91, 121.81, 107.29, 89.03, 81.43, 61.19, 56.66, 33.32, 33.09, 13.22. HRMS calcd for $C_{22}H_{21}NO_5S$: 411.1140. Found: 411.1145.

3.8. Cycloadducts 5g and 6g

Treatment of 1-diazo-5-(2-thienyl)-2,5-pentane dione **4b** (0.312 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1c** (0.307 g, 1 mmol) in toluene (10 mL), in presence of a catalytic amount of rhodium(II) acetate at room temperature for 1 h followed by chromatographic purification of the product afforded the adduct **5g** (0.278 g, 57%) as an off-white crystalline solid and the adduct **6g** (0.156 g, 32%) as colorless crystals.

3.8.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-1,2-dihydro-2,2′-dioxo-1-(phenylmethyl)-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5g. Recrystallized from EtOAc–hexane, mp >300°C. IR (KBr) $\nu_{(max)}$: 1742, 1716, 1609, 1488, 1462, 1372, 1178, 1018 cm^{-1}. ^{1}H NMR: δ 7.45 (d, J=7.4 Hz, 1H), 7.24–7.08 (m, 8H), 6.84–6.78 (m, 2H), 6.65 (d, J=7.6 Hz, 1H), 6.47 (d, J=2.4 Hz, 1H), 4.86 (d, J=8.4 Hz, 1H), 4.68 (d, J=15.7 Hz, 1H), 4.50 (d, J=15.7 Hz, 1H), 4.29 (d, J=8.4 Hz, 1H), 3.87–3.72 (m, 2H), 3.19–3.07 (m, 1H), 2.81–2.65 (m, 1H), 2.45–2.34 (m, 1H), 0.75 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 202.40, 177.26, 168.37, 144.83, 142.70, 135.12, 129.78, 128.66, 127.51, 127.12, 126.43, 125.40, 124.45, 123.90, 122.97, 122.40, 109.64, 87.17, 82.49, 63.28, 61.19, 55.64, 44.16, 35.49, 33.21, 13.59. HRMS calcd for $C_{28}H_{25}NO_5S$: 487.1453. Found: 487.1437.

3.8.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-1,2-dihydro-2,2′-dioxo-1-(methylphenyl)-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6g. Recrystallized from EtOAc–hexane, mp 184–186°C. IR (KBr) $\nu_{(max)}$: 1735, 1705, 1610, 1489, 1467, 1370 cm^{-1}. ^{1}H NMR: δ 7.37–7.29 (m, 5H), 7.12 (d, J=7.3 Hz, 1H), 6.96 (t, J=7.6 Hz, 1H), 6.88–6.86 (m, 1H), 6.76 (t, J=7.5 Hz, 1H), 6.58–6.53 (m, 2H), 6.47–6.46 (m, 1H), 5.21 (d, J=15.2 Hz, 1H), 5.17 (d, J=1.2 Hz, 1H), 4.78 (d, J=15.4 Hz, 1H), 3.87 (d, J=3.0 Hz, 1H), 3.70–3.50 (m, 2H), 3.28–3.15 (m, 2H), 2.69–2.63 (m, 1H), 2.43–2.32 (m, 1H), 0.38 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 204.87, 174.43, 167.71, 143.43, 142.21, 135.62, 128.72, 128.45, 127.91, 127.75, 126.35, 126.10, 123.67, 122.23, 122.08, 108.25, 89.26, 81.55, 63.02, 61.23, 56.86, 44.40, 33.34, 30.86, 13.70. HRMS calcd for $C_{28}H_{25}NO_5S$: 487.1453. Found: 487.1451.

3.9. Cycloadducts 5h and 6h

Treatment of 1-diazo-5-(2-thienyl)-2,5-pentane dione **4b** (0.312 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1d** (0.296 g, 1 mmol) in toluene (20 mL), in presence of rhodium(II) acetate at room temperature for 30 min followed by chromatographic purification afforded the adducts **5h** and **6h** as a mixture in the ratio 2:1. The *endo* (colourless solid) and *exo* (off-white crystals) isomers were separated by crystallization and Pasteur style physical separation.

3.9.1. Ethyl(1′*R*,3*R*,5′*S*,7′*S*)-5-bromo-1,2-dihydro-2,2′-dioxo-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 5h. Recrystallized from ethyl acetate–hexane, mp 212–214°C. IR (KBr) $\nu_{(max)}$: 3298, 1741, 1708, 1616, 1475, 1434, 1303, 1276, 1182 cm^{-1}. ^{1}H NMR: δ 9.44 (s, 1H), 7.49–7.44 (m, 2H), 7.12–7.10 (m, 1H), 6.82–6.78 (m, 2H), 6.50–6.49 (m, 1H), 4.80 (d, J=8.4 Hz, 1H), 4.17 (d, J=8.4 Hz, 1H), 3.98–3.87 (m, 2H), 3.06–2.97 (m, 1H), 2.76–2.65 (m, 2H), 2.45–2.34 (m, 1H), 0.90 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 202.24, 178.45, 168.22, 142.65, 132.57, 128.58, 126.38, 126.26, 124.34, 122.62, 114.40, 111.84, 87.30, 82.55, 63.64, 61.54, 54.77, 34.96, 32.92, 13.70. Anal calcd for $C_{21}H_{18}NO_5SBr$: C, 52.95; H, 3.80; N, 2.94; S, 6.73. Found: C, 52.74; H, 3.87; N, 2.99; S, 6.65.

3.9.2. Ethyl(1′*R*,3*S*,5′*S*,7′*R*)-5-bromo-1,2-dihydro-2,2′-dioxo-5′-(2-thienyl)-spiro[3*H*-indole-3,6′-[8]oxabicyclo[3.2.1]octane]-7′-carboxylate 6h. Recrystallized from EtOAc–hexane, mp. 180°C (decomposed). IR (KBr) $\nu_{(max)}$: 3301, 1728, 1701, 1618, 1474, 1302, 1183 cm^{-1}. ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 10.36 (s, 1H), 7.15 (s, 1H), 7.15–

7.11 (m, 1H), 6.96–6.94 (m, 1H), 6.67–6.62 (m, 2H), 6.53 (m, 1H), 5.11 (d, J=1.5 Hz, 1H), 3.78 (d, J=2.9 Hz, 1H), 3.78–3.66 (m, 2H), 3.14–3.09 (m, 2H), 2.66–2.56 (m, 1H), 2.37–2.30 (m, 1H), 0.69 (t, J=7.2 Hz, 3H). ^{13}C NMR: δ 204.56, 175.43, 167.39, 142.96, 140.25, 130.92, 128.85, 126.10, 123.65, 121.69, 113.66, 110.42, 88.80, 81.16, 63.38, 61.23, 56.53, 33.03, 32.82, 13.13. Anal calcd for $C_{21}H_{18}NO_5SBr$: C, 52.95; H, 3.80; N, 2.94; S, 6.73. Found: C, 52.65; H, 4.09; N, 2.96; S, 6.68.

3.10. Cycloadducts 8a, 9a, 10a and 11a

Treatment of 1-acetyl-1-diazoacetyl cyclopropane **7** (0.228 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1a** (0.217 g, 1 mmol) in toluene (15 mL), in presence of rhodium(II) acetate at room temperature for 30 min followed by chromatographic purification afforded the adducts **8a** (0.070 g, 20%) and **10a** (0.106 g, 31%) as colorless crystalline solids. The adducts **9a** and **11a** were obtained as a mixture of regioisomers (0.141 g, 41%, 1:1) and were separated by fractional crystallization. **9a** was obtained as colourless solid **11a**, as needle shaped colourless crystals.

3.10.1. Ethyl(1′*R*,3″*R*,4′*R*,5′S)-1″,2″-dihydro-1′-methyl-2″,3′-dioxodispiro[cyclo-propane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 8a. Recrystallized from CH_2Cl_2–hexane, mp 224–226°C. IR (KBr) $\nu_{(max)}$: 3193, 3086, 1762, 1709, 1618, 1472, 1381, 1333, 1189, 1140, 1104 cm^{-1}. ^{1}H NMR: δ 8.98 (s, 1H, exchangeable with D_2O), 7.26–7.19 (m, 1H), 7.09 (d, J=7.5 Hz, 1H), 6.98–6.89 (m, 2H), 4.89 (d, J=5.6 Hz, 1H), 3.99 (d, J=5.6 Hz, 1H), 3.85–3.78 (m, 2H), 1.62–1.59 (m, 1H), 1.18 (s, 3H), 1.12–1.06 (m, 1H), 0.92–0.85 (m, 1H), 0.80 (t, J=7.1 Hz, 3H), 0.74–0.69 (m, 1H). ^{13}C NMR: δ 208.49, 179.97, 167.79, 141.86, 129.13, 128.01, 124.74, 121.35, 110.02, 90.54, 81.76, 61.11, 60.91, 54.28, 38.72, 15.45, 14.39, 13.68, 13.56. HRMS calcd for $C_{19}H_{19}NO_5$: 341.1263. Found: 341.1266.

3.10.2. Ethyl(1′*R*,3″*S*,4′*R*,5′*R*)-1″,2″-dihydro-1′-methyl-2″,3′-dioxodispiro[cyclo-propane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 9a. Recrystallized from $CHCl_3$–hexane, mp 143–145°C. IR (KBr) $\nu_{(max)}$: 3204, 3089, 1763, 1710, 1617, 1473, 1390, 1339, 1219 cm^{-1}. ^{1}H NMR: δ 9.07 (s, 1H), 7.31–7.22 (m, 2H), 7.04–6.99 (m, 1H), 6.89 (d, J=7.6 Hz, 1H), 5.10 (s, 1H), 3.71 (q, J=7.1 Hz, 2H), 3.61 (s, 1H), 1.64–1.59 (m, 1H), 1.13–0.92 (m, 3H), 0.86 (s, 3H), 0.67 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 210.25, 176.51, 168.45, 140.90, 129.31, 128.93, 125.99, 122.70, 109.53, 90.84, 81.82, 62.25, 61.07, 55.49, 35.83, 14.67, 14.35, 14.18, 13.48. Anal. calcd for $C_{19}H_{19}NO_5 \cdot H_2O$: C, 63.50; H, 5.89; N, 3.89. Found: C, 63.93; H, 5.41; N, 3.76.

3.10.3. Ethyl(1′*R*,3″*R*,4′*S*,6′*S*)-1″,2″-dihydro-1′methyl-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-5′,3″-[3*H*]-indole]-6′-carboxylate 10a. Recrystallized from $CHCl_3$–hexane solvent system, mp 95–97°C. IR (KBr) $\nu_{(max)}$: 3281, 2984, 1730, 1612, 1472, 1331, 1201, 1041 cm^{-1}. ^{1}H NMR: δ 9.18 (s, 1H), 7.22 (d, J=7.6 Hz, 1H), 6.98–6.91 (m, 2H), 6.76 (d, J=7.4 Hz, 1H), 4.53 (s, 1H), 3.76–3.65 (m, 2H), 3.66 (s, 1H), 1.87–1.80 (m, 1H), 1.58 (s, 3H), 1.42–1.35 (m, 1H), 1.12–1.05 (m, 1H), 0.90–0.83 (m, 1H), 0.63 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 207.36, 180.03, 168.15, 141.34, 129.19, 125.33, 124.63, 122.28, 110.14, 86.67, 86.56, 60.33, 60.14, 56.28, 37.07, 17.57, 14.52, 14.45, 13.39. Anal. calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.59; N, 4.10. Found: C, 66.67; H, 5.59; N, 4.07.

3.10.4. Ethyl(1′*R*,3″*S*,4′*S*,6′*R*)-1″,2″-dihydro-1′methyl-2″,3′-dioxodispiro[cyclo-propane-1,2′-[7]oxabicyclo[2.2.1]heptane-5′,3″-[3*H*]-indole]-6′-carboxylate 11a. Recrystallized from $CHCl_3$–hexane, mp 188–190°C. IR (KBr) $\nu_{(max)}$: 3187, 1747, 1707, 1619, 1470, 1340, 1183, 1032 cm^{-1}. ^{1}H NMR: δ 9.04 (s, 1H), 7.41 (d, J=7.4 Hz, 1H), 7.25–7.20 (m, 1H), 7.00 (t, J=7.5 Hz, 1H), 6.90 (d, J=7.6 Hz, 1H), 4.27 (s, 1H), 3.62 (q, J=7.0 Hz, 2H), 3.56 (s, 1H), 1.64 (s, 3H), 1.56–1.43 (m, 2H), 1.24–1.19 (m, 1H), 0.90–0.85 (m, 1H), 0.66 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 207.56, 175.98, 167.97, 141.08, 129.24, 129.08, 125.63, 122.72, 109.79, 87.21, 86.76, 60.24, 60.07, 59.17, 40.65, 14.98, 14.03, 13.79, 13.47. HRMS calcd for $C_{19}H_{19}NO_5$: 341.1263. Found: 341.1273.

3.11. Cycloadducts 8b, 9b, 10b and 11b

Treatment of 1-acetyl-1-diazoacetyl cyclopropane **7** (0.228 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1b** (0.231 g, 1 mmol) in toluene (15 mL), in presence of rhodium(II) acetate at room temperature for 30 min followed by chromatographic purification afforded the adducts **8b** (0.099 g, 28%) and **10b** (0.067 g, 19%) as colorless crystalline solids. The adducts **9b** and **11b** were obtained as a mixture of regioisomers (0.163 g, 46%) and were separated by fractional crystallization. The cycloadduct **9b** was obtained as colorless crystals and **11b** as pale yellow oil.

3.11.1. Ethyl(1′*R*,3″*R*,4′*R*,5′*S*)-1″,2″-dihydro-1′,1″-dimethyl-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 8b. Recrystallized from EtOAc–hexane, mp 169–171°C. IR (KBr) $\nu_{(max)}$: 1758, 1712, 1613, 1492, 1374,1350, 1265, 1188, 1141, 1091 cm^{-1}. ^{1}H NMR: δ 7.30–7.25 (m, 1H), 7.10 (d, J=7.4 Hz, 1H), 6.95 (t, J=7.6 Hz, 1H), 6.82 (d, J=7.7 Hz, 1H), 4.87 (d, J=5.6 Hz, 1H), 3.96 (d, J=5.6 Hz, 1H), 3.84–3.72 (m, 2H), 3.28 (s, 3H), 1.62–1.55 (m, 1H), 1.11–1.01 (m, 1H), 1.07 (s, 3H), 0.94–0.87 (m, 1H), 0.77 (t, J=7.1 Hz, 3H), 0.69–0.62 (m, 1H). ^{13}C NMR: δ 208.66, 177.31, 161.81, 144.57, 129.03, 127.64, 124.24, 121.26, 107.86, 90.40, 81.71, 60.71, 60.46, 54.28, 38.75, 26.65, 15.37, 14.36, 13.59, 13.35. Anal. calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.59; H, 5.95; N, 3.85.

3.11.2. Ethyl(1′*R*,3″*S*,4′*R*,5′*R*)-1″,2″-dihydro-1′,1″-dimethyl-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 9b. Recrystallized from CH_2Cl_2–MeOH, mp 119–121°C. IR (KBr) $\nu_{(max)}$: 1752, 1708, 1609, 1467, 1576, 1342, 1209, 1089 cm^{-1}. ^{1}H NMR: δ 7.34–7.27 (m, 2H), 7.03 (t, J=7.5 Hz, 1H), 6.81 (d, J=7.6 Hz, 1H), 5.08 (s, 1H), 3.68–3.61 (m, 2H), 3.57 (s, 1H), 3.23 (s, 3H), 1.68–1.64 (m, 1H), 1.11–0.94 (m, 3H), 0.81 (s, 3H), 0.62 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 210.05, 173.92, 168.36, 143.72, 128.75, 125.65, 122.57, 107.55, 90.53, 81.58, 61.58, 60.78, 55.60,

43.88, 29.24, 26.69, 14.66, 14.03, 13.33. Anal. calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.59; H, 5.95; N, 4.12.

3.11.3. Ethyl(1′*R*,3″*R*,4′*S*,6′*S*)-1″,2″-dihydro-1′,1″-dimethyl-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-5′,3″-[3*H*]-indole]-6′-carboxylate 10b. Recrystallized from EtOAc–hexane, mp 164–166°C. IR (KBr) $\nu_{(max)}$: 1748, 1728, 1611, 1497, 1472, 1377, 1332, 1194, 1178, 1154, 1035 cm^{-1}. ^1H NMR: δ 7.30–7.26 (m, 1H), 6.95 (t, J=7.5 Hz, 1H), 6.82 (t, J=7.7 Hz, 1H), 6.76 (d, J=7.5 Hz, 1H), 4.43 (s, 1H), 3.68–3.63 (m, 2H+s, 1H), 3.28 (s, 3H), 1.84–1.77 (m, 1H), 1.74–1.61 (m, 1H), 1.55 (s, 3H), 1.39–1.37 (m, 1H), 1.10–1.04 (m, 1H), 0.58 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 207.62, 177.34, 168.19, 144.12, 129.18, 125.09, 124.18, 122.26, 107.97, 86.66, 86.53, 60.29, 60.15, 55.66, 37.05, 26.85, 17.54, 14.54, 14.40, 13.33. HRMS. calcd for $C_{20}H_{21}NO_5$: 355.1419. Found: 355.1425.

3.11.4. Ethyl(1′*R*,3″*S*,4′*S*,6′*R*)-1″,2″-dihydro-1′,1″-dimethyl-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-5′,3″-[3*H*]-indole]-6′-carboxylate 11b. IR (KBr) $\nu_{(max)}$: 1744, 1715, 1611, 1492, 1470, 1374, 1349, 1335, 1183, 1135 cm^{-1}. ^1H NMR: δ 7.45 (d, J=7.5 Hz, 1H), 7.34–7.28 (m, 1H), 7.07–7.02 (m, 1H), 6.83 (d, J=7.3 Hz, 1H), 4.23 (s, 1H), 3.67–3.57 (m, 2H), 3.55 (s, 1H), 3.24 (s, 3H), 1.64 (s, 3H), 1.52–1.42 (m, 1H), 1.28–1.20 (m, 1H), 0.90–0.83 (m, 2H), 0.62 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 207.22, 173.60, 167.90, 143.51, 128.64, 125.34, 122.83, 107.66, 86.95, 86.67, 60.23, 60.11, 59.98, 40.50, 26.61, 14.83, 14.14, 13.95, 13.37. HRMS. calcd for $C_{20}H_{21}NO_5$: 355.1419. Found: 355.1423.

3.12. Cycloadducts 8c, 9c and 10c

Treatment of 1-acetyl-1-diazoacetyl cyclopropane **7** (0.228 g, 1.5 mmol) with 3-ethoxycarbonyl methylene-2-oxoindoline **1c** (0.307 g, 1 mmol) in toluene (10 mL), in the presence of rhodium(II) acetate at room temperature for 1 h followed by chromatographic purification afforded the adduct **8c** (0.147 g, 34%). The adducts **9c** and **10c** were obtained as a mixture of regioisomers (0.276 g, 64%). On fractional crystallization, **9c** was obtained as pale yellow oil and **10c** as colorless crystals.

3.12.1. Ethyl(1′*R*,3″*R*,4′*R*,5′*S*)-1″,2″-dihydro-1′-methyl-1″-(phenylmethyl)-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 8c. Recrystallized from EtOAc–hexane, mp 198–200°C. IR (KBr) $\nu_{(max)}$: 1766, 1742, 1612, 1492, 1462, 1381, 1354, 1184, 1140 cm^{-1}. ^1H NMR: δ 7.28 (brs, 5H), 7.17–7.07 (m, 2H), 6.89 (t, J=7.6 Hz, 1H), 6.70 (d, J=7.8 Hz, 1H), 4.97 (s, 2H), 4.89 (d, J=5.6 Hz, 1H), 4.05 (d, J=5.6 Hz, 1H), 3.81–3.73 (m, 2H), 1.61–1.55 (m, 1H), 1.26–1.24 (m, 1H), 1.11 (s, 3H), 1.10–1.05 (m, 1H), 0.91–0.87 (m, 1H), 0.69 (t, J=7.1 Hz, 3H). ^{13}C NMR: δ 208.63, 177.53, 167.79, 143.72, 135.43, 128.93, 128.78, 127.62, 127.23, 124.46, 121.28, 109.06, 90.53, 81.68, 60.70, 60.40, 54.89, 44.16, 38.90, 15.43, 14.49, 13.61, 13.53. HRMS. calcd for $C_{26}H_{25}NO_5$: 431.1732. Found: 431.1732.

3.12.2. Ethyl(1′*R*,3″*S*,4′*R*,5′*R*)-1″,2″-dihydro-1′-methyl-1″-(phenylmethyl)-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-6′,3″-[3*H*]-indole]-5′-carboxylate 9c. IR (KBr) $\nu_{(max)}$: 1758, 1715, 1611, 1487, 1467, 1368, 1210, 1179, 1035 cm^{-1}. ^1H NMR: δ 7.43 (d, J=7.4 Hz, 1H), 7.34–7.27 (m, 5H), 7.15 (t, J=7.6 Hz, 1H), 6.97 (t, J=7.5 Hz, 1H), 6.68 (t, J=6.8 Hz, 1H), 5.09 (s, 1H), 5.07 (d, J=15.7 Hz, 1H), 4.78 (d, J=15.5 Hz, 1H), 3.66 (s, 1H), 3.63–3.51 (m, 2H), 1.67–1.58 (m, 1H), 1.10–0.87 (m, 3H), 0.83 (s, 3H), 0.45 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 209.96, 174.08, 168.33, 142.66, 135.58, 128.64, 127.66, 127.13, 125.66, 122.82, 108.69, 90.68, 81.65, 60.83, 60.29, 55.63, 44.00, 35.75, 14.71, 14.20, 13.94, 13.16. HRMS. calcd for $C_{26}H_{25}NO_5$: 431.1732. Found: 431.1722.

3.12.3. Ethyl(1′*R*,3″*R*,4′*S*,6′*S*)-1″,2″-dihydro-1′-methyl-1″-(phenylmethyl)-2″,3′-dioxodispiro[cyclopropane-1,2′-[7]oxabicyclo[2.2.1]heptane-5′,3″-[3*H*]-indole]-6′-carboxylate 10c. Recrystallized from CH_2Cl_2–MeOH, mp 200–202°C. IR (KBr) $\nu_{(max)}$: 1745, 1072, 1609, 1491, 1372, 1348, 1086 cm^{-1}. ^1H NMR: δ 7.28–7.25 (m, 5H), 7.14 (t, J=7.6 Hz, 1H), 6.90 (t, J=7.5 Hz, 1H), 6.77 (d, J=7.4 Hz, 1H), 6.68 (d, J=7.7 Hz, 1H), 5.17 (d, J=15.7 Hz, 1H), 4.80 (d, J=15.7 Hz, 1H), 4.49 (s, 1H), 3.75 (s, 1H), 3.64–3.62 (m, 2H), 1.86–1.82 (m, 1H), 1.58 (s, 3H+m, 1H), 1.41–1.39 (m, 1H), 1.11–1.07 (m, 1H), 0.48 (t, J=7.0 Hz, 3H). ^{13}C NMR: δ 207.67, 177.58, 168.25, 143.15, 135.43, 129.07, 128.77, 127.75, 127.15, 124.99, 124.26, 122.30, 109.20, 86.76, 86.58, 60.60, 60.24, 55.71, 44.16, 37.13, 17.56, 14.58, 14.53, 13.27. Anal. calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 72.37; H, 6.00; N, 3.14.

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