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Regioselective synthesis of 3-heteroarylpiperidin-2-ones and diazacyclopenta[*a*]phenalenone via carbenoid reactions

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ABSTRACT

Rhodium(II) catalyzed carbenoid reactions of 3-diazopiperidin-2-ones were carried out with indoles and pyrroles to afford the respective (3-indol-3-yl)- and (3-pyrrol-2-yl)piperidones with regioselectivity. Interestingly, the reaction of bis-diazoimide in the presence of $Rh_2(OAc)_4$ catalyst furnished diazacyclopenta[*a*]phenalenone in a tandem manner.

1. Introduction

Diazocarbonyl compounds have been used for important structural and functional group transformations in various reports. The synthetic utilization of rhodium(II) acetate dimer catalyzed reactions of α-diazocarbonyl compounds to synthesize a variety of molecular architectures and biologically interesting molecules is well documented.[1] Besides, the ever-growing synthetic applications of this protocol to synthesize biologically important molecules make the immense involvement into this methodology. Transition metal catalyzed carbenoid insertion reactions of α-diazocarbonyl compounds are one of the most important tools in synthetic organic chemistry.[2] Generally, these metallo-carbenoid methodologies are known to provide various functionalized molecules via C–C bond formation with selectivity.

3-Aryl/heteroaryl substituted *N*-containing heterocycles and their derivatives have been thoroughly investigated in the last two decades in view of their important biological properties,[3] for example, bis-indole alkaloid **1**,[3a,b] 3-arylpiperidine derivatives **2**[3c,d] and preclamol **3**[3e] (Fig. 1). In continuation of our ongoing research work[4] on α-diazocarbonyl compounds, we herein report the synthesis of (3-indol-3-yl-) or (3-pyrrol-2-yl)piperidones and diazacyclopenta[*a*]phenalenone via $Rh_2(OAc)_4$ catalyzed intermolecular carbenoid reactions of various *N*-alkylated 3-diazopiperidin-2-ones.

2. Results and discussion

The starting material diazo amide **4a** was synthesized[5] from L-ornithine monohydrochloride by alumina catalyzed cyclization and then diazotization. N-Alkylation reactions of 3-diazopiperidin-2-ones were performed to yield various substituted 3-heteroarylpiperidin-2-one systems. Towards this, 3-diazopiperidin-2-one was treated with sodium hydride in DMF at 0 °C and then various alkyl halides such as methyl iodide, allyl bromide or benzyl

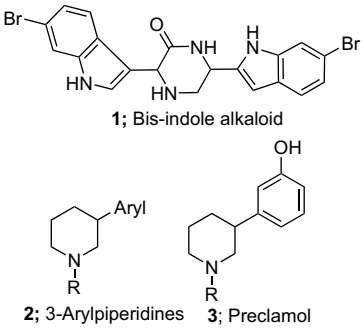

Figure 1.

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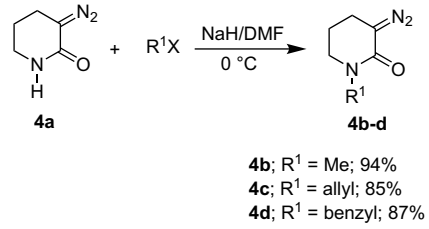
bromide to give the corresponding *N*-alkylated diazo derivatives **4b–d** (Scheme 1).



Scheme 1. Synthesis of *N*-alkylated 3-diazopiperidin-2-ones.

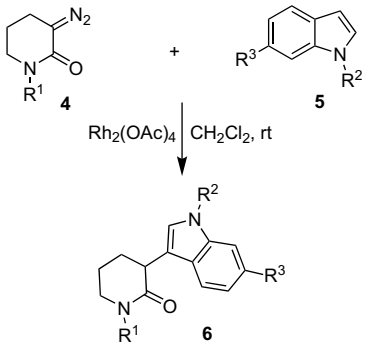
Initially, we investigated the carbenoid reaction of 3-diazopiperidin-2-one **4a** with *N*-methylindole **5a** using $Rh_2(OAc)_4$ catalyst in dichloromethane at room temperature furnishing **6a** in 80% yield (Table 1, entry a) via C-alkylation at 3-position of indole.

Table 1
Synthesis of 3-indolylpiperidin-2-ones **6**

Entry	R^1	R^2	R^3	Product	Time (min)	Yield[a] (%)
a	H	Me	H	**6a**	20	80
b	H	Allyl	H	**6b**	15	81
c	Me	Me	H	**6c**	15	78
d	Allyl	Me	H	**6d**	15	85
e	Allyl	Allyl	H	**6e**	15	89
f	Me	Benzyl	H	**6f**	25	72
g	Me	Allyl	H	**6g**	30	75
h	Me	COMe	H	—	240	—
i	Allyl	Ts	H	—	240	—
j	H	Allyl	Br	—	240	—

[a] Yields (unoptimized) refer to isolated pure compounds **6**.

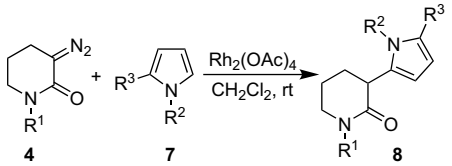
Further, we elaborated this carbenoid reaction with different N-substituted indoles **5** and α-diazoamides **4** to afford the corresponding 3-indolylpiperidin-2-ones **6b–h** (Scheme 2, Table 1) in good yields with regioselectivity. All these rhodium carbenoid reactions proceeded readily at room temperature only with 0.5 mol % of the rhodium(II) acetate catalyst.



Scheme 2. Reaction of 3-diazopiperidin-2-ones with *N*-alkylated indoles.

The reaction of diazoamides **4a**/**4c** with 2-methylindole or 1,2-dimethyl- or 1-allyl-2-methylindoles did not furnish any expected alkylation products. In our previous report,[6] we have described the N–H insertion reactions of 3-diazopiperidin-2-ones with various aromatic amines and indoles with chemoselectivity and observed the exceptional reactivity of the diazo amide **4** towards the N–H bonds. Whereas the Rh(II)-catalyzed reactions of diazoamides **4** with *N*-protected indoles gave the C-alkylation products at 3-position.

These regioselective C-alkylation reactions of diazoamides **4** were further demonstrated by performing the reactions with substituted or unsubstituted pyrroles. Towards this, reaction of diazo amide **4a** and unsubstituted pyrrole **7a** with a catalytic amount of rhodium(II) acetate was resulted the C-alkylation at the electron rich 2-position of pyrrole to afford product **8a** (Scheme 3, Table 2, entry a) with complete regio- and chemoselectivity. Similar C-alkylation reaction was further extended with various substituted pyrroles and 3-diazopiperidin-2-ones to furnish several 3-pyrrolylpiperidin-2-ones **8b–g**. We did not observe the corresponding N–H insertion product even in the absence of substitution on pyrrole N-atom. This is in contrary to our previous report,[6] where the rhodium catalyzed reaction of diazo amide **4** is known to furnish N–H insertion product with indoles.



Scheme 3. Reaction of 3-diazopiperidin-2-ones with pyrroles.

Diazo amide **4a** was treated under similar reaction condition with 2-allylpyrrole where the 2-position of pyrrole is blocked. Here, the carbenoid has underwent C-alkylation to 5-position of pyrrole (but not to the 3-position) when 2-position is blocked by the allyl group (entry **8d**).

Table 2
Synthesis of 3-pyrrolylpiperidin-2-ones **8**

Entry	R^1	R^2	R^3	Product	Time (min)	Yield[a] (%)
a	H	H	H	**8a**	20	85
b	H	Benzyl	H	**8b**	15	79
c	Allyl	H	H	**8c**	15	88
d	H	H	Allyl	**8d**	15	75
e	Benzyl	H	H	**8e**	25	75
f	Allyl	Benzyl	H	**8f**	15	85
g	H	COPh	H	**8g**	240	—
h	Me	COMe	H	**8h**	240	—

[a] Yields (unoptimized) refer to isolated pure compounds **8**.

Rh(II)-catalyzed carbenoid reactions of diazoamides were performed at room temperature and no significant improvement in yield observed by elevating the temperature of the reaction medium. When the reaction was conducted at 0 °C, diazo amide **4** remained unaffected and the decomposition of diazo group was observed with evolution of nitrogen bubbles only at the temperature of the reaction reaches 13 °C. Diazoamides **4** remained unaffected or unreacted when the above experiments were carried out in the presence of copper(II) acetoacetonate or copper(II) acetoacetate as the catalyst for diazo decomposition. No carbenoid reactions were observed when diazoamides **4** treated with indoles having electron withdrawing substituents such as *N*-acetylindole **5h**, *N*-tosylindole **5i**, 5-bromo-1-allyl-1*H*-indole **5j**. These observations could support the anticipated mechanism for the formation of alkylation products, which will proceed through the formation of the zwitterionic intermediate **9**. The intermediate **9** carries positive charge on the indole ring, which could likely be stabilized by the electron rich substituent on N-atom of indole or pyrrole (Fig. 2).[4a] The zwitterion can be anticipated to be formed from the direct nucleophilic substitution or the cleavage of the initially formed cyclopropane products derived from diazo amide **4** and indole or

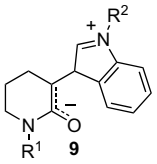
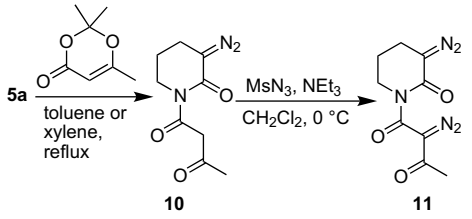


Figure 2. The possible formation of the zwitterionic intermediates.

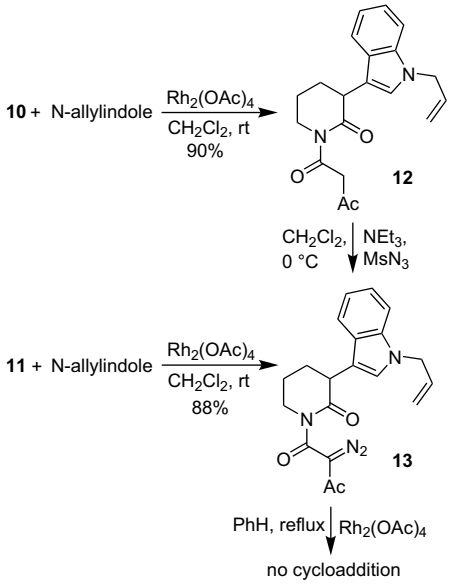
pyrrole in the presence of Rh(II) catalyst. Finally, the proton transfer of the zwitterion intermediate forms the C-alkylation product.

Next, we planned to utilize this rhodium carbenoid reaction to synthesize some interesting fused heterocyclic system. Thus, we aimed to employ the combination of carbenoid reaction and ylide formation methodologies in a tandem manner. For this purpose, the substitution on diazo amide **4a** was extended to derive another diazo functional group using diketene acetone adduct and methanesulfonyl azide to afford the bis-diazoimide **11** (Scheme 4).

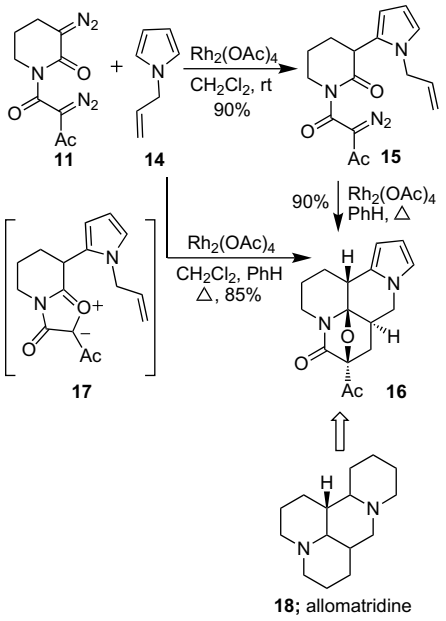


Scheme 4. Synthesis of bis-diazoimide.

The IR spectrum of diazoimide **11** showed two diazo functional groups at 2114 and 2099 cm^{-1}. We have planned Rh-catalyzed reaction of the bis-diazoimide **11** to perform the alkylation as well as cycloaddition reactions to get rather interesting polycyclic compound. Thus, $Rh_2(OAc)_4$ catalyzed reaction of bis-diazoimide **11** and *N*-allylindole gave the carbenoid C-alkylation product to yield the interesting diazoimide **13** in 88% yield. Similarly, diazoimide **10** was treated with *N*-allylindole to furnish the alkylated product **12**, which can, in turn, be converted into the corresponding diazoimide **13** upon carrying out diazotization of the active methylene group using standard literature procedure. This diazoimide **13** was allowed to react with rhodium(II) acetate using benzene as the solvent under reflux. This gives no cycloaddition product; the diazo



Scheme 5. Reactions of diazoimides with *N*-allylindole.



Scheme 6. Rh(II)-catalyzed C-alkylation and cycloaddition reactions.

group has got decomposed to give undetected junk products (Scheme 5). When bis-diazoimide **11** was treated with *N*-allylpyrrole **14** in dichloromethane at room temperature, the cyclic diazo group got selectively decomposed in the presence of $Rh_2(OAc)_4$ at room temperature to furnish the corresponding C-alkylation product **15** at 2-position of pyrrole as described in Scheme 6. The IR spectrum of compound **13** showed a strong peak at 2102 cm^{-1}, which is characteristic of the presence of diazo functional group. Even though the starting material has two diazo groups, successful selective decomposition of the cyclic diazo group was performed. The acyclic diazo functional group remain unaffected despite the presence of rhodium(II) acetate catalyst. No cyclopropanation products were obtained via the diazo group and olefin present on allyl group. Diazoimide **15** was further treated with Rh(II)-catalyst in benzene under reflux to afford the corresponding interesting polycyclic system **16** with 90% yield in a diastereoselective manner (Scheme 6). ^1H and ^{13}C NMR spectral analyses confirmed the formation of a single isomer. The energy minimization calculations were performed at MM2 level and the stereochemistry was tentatively assigned based on these calculations. The skeletal structure of the cycloadduct **16** is closely related to an alkaloid, allomatridine.[7]

Mechanistically, the rhodium(II)-carbenoid derived from diazoimide **11** furnished isomünchnone **17** as an intermediate, which subsequently underwent the intramolecular 1,3-dipolar cycloaddition to the olefin functionality. These reaction steps could also be performed in a one pot manner. Thus, diazoimide **11** was allowed to react with *N*-allylpyrrole in the presence of rhodium(II) acetate catalyst in dichloromethane and then evaporated the solvent yielding the crude reaction mixture under nitrogen atmosphere. To the above crude reaction mixture, benzene was added and refluxed for 30 min to afford product **16** in a single step via tandem insertion–cyclization–cycloaddition methodology. These reactions represent an important methodology to generate complex polycyclic systems from simple starting materials.

3. Conclusion

In conclusion, we have described a mild and convenient regioselective method to synthesize indol-3-yl- or pyrrol-3-ylpiperidones in good yield in the presence of $Rh_2(OAc)_4$ catalyst.

This protocol is a versatile method for various heteroarylpiperidines. The carbenoid reaction with pyrrole afforded 2-pyrrolylpiperidones with chemoselectivity. The $Rh_2(OAc)_4$ catalyzed reaction of bis-diazoimide furnished the diazacyclopenta[*a*]phenalenone ring system in a tandem manner with diastereoselectivity.

4. Experimental section

4.1. General

All reactions were carried out in oven-dried glassware under an atmosphere of argon. All solvents were freshly purified by distillation. All the starting materials used are purchased from Aldrich. IR spectra were recorded using KBr or CH_2Cl_2 on a Perkin–Elmer Spectrum GX FT-IR spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded (200 and 50.3 MHz, respectively) on a Bruker Avance DPX 200 spectrometer using $CDCl_3$. Chemical shifts for proton and carbon resonances are reported in parts per million (δ) relative to tetramethylsilane (δ 0.00) and chloroform (δ 77), respectively. Multiplicities are indicated by singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and br s (broad singlet). Coupling constants (*J*) were reported in hertz (Hz). Carbon types were determined from ^{13}C NMR and DEPT-135 experiments. High resolution mass analyses were performed using electrospray ionization (ESI) technique on a Waters QTof-micro mass spectrometer. Microanalysis (C, H, N) was performed using a Perkin–Elmer 4100 elemental analyzer. Analytical thin layer chromatography (TLC) was performed on silica and components were visualized by observation under iodine, UV-light or sulfuric acid charring. Column chromatography was performed on a silica gel (100–200 mesh) column.

4.2. General experimental procedure for the synthesis of 3-diazomethylpiperidin-2-one (4b)

Sodium hydride, 60% in wax (770 mg, 19.2 mmol), was taken in positive nitrogen flow and washed with 20 mL of dry hexane for three times. To this 50 mL of dry DMF was added. 3-Diazopiperidin-2-one (**4a**) (2 g, 16 mmol) dissolved in 10 mL of DMF was added to the stirred suspension of sodium hydride at 0 °C. After 15 min iodomethane (1.2 mL, 19.2 mmol) was added in drops. The temperature was maintained for 20 min at 0 °C. The progress of the reaction mixture was monitored using TLC. Then the reaction mixture was poured into 200 mL of ice-cold water and extracted with dichloromethane (3×25 mL). The combined organic layers were washed thoroughly with water and stored over dry sodium sulfate. The DCM layer was evaporated and the flash column chromatography of the reaction mixture over alumina furnished the title compound **4b** (2.1 g, 94%) as a yellow liquid. R_f (70% EtOAc/hexane) 0.58; ν_{max} (Neat) 3311, 3258, 2898, 2089, 1640, 1482, 1411, 1348, 794, 638 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 3.12 (2H, t, *J*=5.2 Hz), 2.84–2.57 (5H, m), 1.78–1.75 (2H, m); ^{13}C (50.3 MHz, $CDCl_3$) 162.2 (C=O), 48.8 (CH_2), 34.7 (CH_3), 21.8 (CH_2), 21.3 (CH_2). HRMS (ESI): MNa^+, found 162.0651; $C_6H_9N_3O$ requires 162.0643.

4.2.1. 1-Allyl-3-diazopiperidin-2-one (*4c*)

Sodium hydride, 60% in wax (770 mg, 19.2 mmol), was taken in positive nitrogen flow and washed with 20 mL of dry hexane for three times. To this 50 mL of dry DMF was added. Diazo amide **4a** (2 g, 16 mmol) dissolved in 10 mL of DMF was added to the stirred suspension of sodium hydride at 0 °C. After 15 min allyl bromide (1.7 mL, 19.2 mmol) was added. Further workup as described in the previous steps gave the title compound **4c** (2.2 g, 85%) as a yellow liquid. R_f (60% EtOAc/hexane) 0.6; ν_{max} (Neat) 3005, 2962, 2863, 2086, 1609, 1483, 1461, 1438, 1356, 1216, 927, 755 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 5.86–5.66 (1H, m), 5.17 (2H, d, *J*=11.5 Hz), 4.06–3.88 (2H, m), 3.54–3.20 (2H, m), 2.96–2.76 (2H, m), 1.78–1.64 (2H, m); ^{13}C (50.3 MHz, $CDCl_3$) 163.1 (C=O), 133.8 (CH), 117.9 (CH_2), 50.1 (CH_2), 46.9 (CH_2), 22.6 (CH_2), 22.2 (CH_2). HRMS (ESI): MNa^+, found 188.0793; $C_8H_{11}N_3O$ requires 188.0800.

4.2.2. 1-Benzyl-3-diazopiperidin-2-one (*4d*)

Sodium hydride, 60% in wax (770 mg, 19.2 mmol), was taken in positive nitrogen flow and washed with 20 mL of dry hexane for three times. To this 50 mL of dry DMF was added. Diazo amide **4a** (2 g, 16 mmol) dissolved in 10 mL of DMF was added to the stirred suspension of sodium hydride at 0 °C. After 15 min benzyl bromide (2.3 mL, 19.2 mmol) was added. Further workup as described in the previous steps gave the title compound **4d** (2.9 g, 87%) as a yellow liquid. R_f (55% EtOAc/hexane) 0.55; ν_{max} (Neat) 3323, 3261, 2890, 2092, 1617, 1479, 1400, 1339, 792, 639 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 7.27 (5H, s), 4.60 (2H, s), 3.15 (2H, t, *J*=5.2 Hz), 2.74–2.68 (2H, m), 1.87–1.78 (2H, m); ^{13}C (50.3 MHz, $CDCl_3$) 164.9 (C=O), 137.7 (*quat*-C), 128.9 (CH), 128.3 (CH), 127.7 (CH), 50.7 (CH_2), 46.7 (CH_2), 22.3 (CH_2), 21.8 (CH_2). HRMS (ESI): MNa^+, found 238.0962; $C_{12}H_{13}N_3O$ requires 238.0956.

4.3. General experimental procedure for the synthesis of compounds (6 and 8)

3-(1-Alkyl-1*H*-indol-3-yl)piperidin-2-one (**6**): a 50 mL two-necked round bottomed flask was charged with diazo amide **4** (2 mmol) and *N*-alkylindole or pyrrole (2.2 mmol) and the flask fluxed with argon using vacuum. Under argon positive flow, 50 mL of freshly distilled dichloromethane and stirred well. Rhodium(II) acetate dimer (0.5 mol %) was added and shortly after, rapid evolution of N_2 was observed. Argon atmosphere has been maintained throughout the course of the reaction. The progress of the reaction mixture was monitored by using TLC. The solvent was removed under reduced pressure. The crude reaction mixture was subjected to column chromatography using silica gel to furnish the *C*-alkylated products.

4.3.1. 3-(1-Methyl-1H-indol-3-yl)piperidin-2-one (*6a*)

Diazo amide **4a** (250 mg, 2 mmol) was allowed to react with *N*-methylindole (290 mg, 2.2 mmol) in 50 mL of freshly distilled dichloromethane in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the general procedure to afford the title compound **6a** (80%) as a brownish solid. [Found: C, 73.51; H, 7.23; N, 12.38. $C_{14}H_{16}N_2O$ requires: C, 73.66; H, 7.06; N, 12.27.] R_f (50% EtOAc/hexane) 0.6; mp 75–76 °C; ν_{max} (KBr) 3313, 3211, 2940, 1656, 1495, 1428, 1319, 1097, 824, 651 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 7.55 (1H, d, *J*=7.8 Hz, arom-*H*), 7.29–7.04 (4H, m), 6.96 (1H, s, arom-*H*), 4.08–3.92 (1H, m), 3.73 (3H, s, C*H*$_3$), 3.46–3.24 (2H, m), 2.29–2.01 (1H, m), 1.99–1.67 (3H, m); ^{13}C (50.3 MHz, $CDCl_3$) 175.4 (C=O), 136.8 (*quat*-C), 127.7 (CH), 127.2 (*quat*-C), 122.1 (CH), 119.6 (CH), 119.4 (CH), 109.6 (CH), 43.1 (CH_2), 40.2 (CH), 33.2 (CH_3), 29.7 (CH_2), 21.4 (CH_2); MS (EI) *m*/*z* 228 (M^+, 20%), 1205 (8), 119 (20), 115 (33), 87 (48), 70 (14), 59 (62), 44 (100).

4.3.2. 3-(1-Allyl-1H-indol-3-yl)piperidin-2-one (*6b*)

Diazo amide **4a** (250 mg, 2 mmol) was allowed to react with *N*-allylindole (345 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **6b** (81%) as a yellow solid. [Found: C, 75.80; H, 7.10; N, 11.07. $C_{16}H_{18}N_2O$ requires: C, 75.56; H, 7.13; N, 11.01%.] R_f (50% EtOAc/hexane) 0.58; mp 74–75 °C; ν_{max} (KBr) 3413, 3061, 1637, 1496, 1451, 1265, 1169, 1121, 734 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 7.56 (1H, d, *J*=7.3 Hz, arom-*H*), 7.26–7.08 (3H, m, arom-*H*), 6.99 (1H, s, arom-*H*), 6.8 (1H, br s,

N*H*), 5.98–5.92 (1H, m, C*H*), 5.22–5.16 (2H, m, CH_2), 4.69–4.65 (2H, m, CH_2), 3.98 (1H, t, *J*=3.2 Hz, CH_2), 3.46–3.32 (2H, m, NCH_2), 2.27–2.20 (1H, m), 1.94–1.78 (3H, m); ^{13}C (50.3 MHz, $CDCl_3$) 171.6 (C=O), 136.5 (*quat*-C), 134.2 (CH), 127.8 (*quat*-C), 126.7 (CH), 120.3 (CH), 119.9 (CH), 119.8 (CH), 118.1 (CH_2), 115.4 (*quat*-C), 110.4 (CH), 49.5 (CH_2), 43.4 (CH_2), 40.4 (CH), 29.6 (CH_2), 21.4 (CH_2). MS (EI) *m*/*z* 255 $(M+1)^+$.

*4.3.3. 1-Methyl-3-(1-methyl-1H-indol-3-yl)piperidin-2-one (**6c**)*

Diazo amide **4b** (280 mg, 2 mmol) was allowed to react with *N*-methylindole (290 mg, 2.2 mmol) in 50 mL of freshly distilled dichloromethane in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the general procedure to furnish the title compound **6c** (78%) as a brownish solid. [Found: C, 74.44; H, 7.52; N, 11.54. $C_{15}H_{18}N_2O$ requires: C, 74.35; H, 7.49; N, 11.56%.] R_f (50% EtOAc/hexane) 0.6; mp 88–89 °C; ν_{max} (KBr) 3052, 2932, 1636, 1500, 1469, 1325, 735 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.52 (1H, d, *J*=7.6 Hz, arom-*H*), 7.44–7.03 (3H, m, arom-*H*), 6.85 (1H, s, arom-*H*), 3.97 (1H, t, *J*=5.9 Hz, CH), 3.68 (3H, s, CH_3), 3.48–3.20 (2H, m, NCH_2), 3.03 (3H, s, CH_3), 2.13–2.08 (1H, m), 1.928–1.73 (3H, m); ^{13}C (50.3 MHz, $CDCl_3$) 171.8 (C=O), 137.6 (*quat*-C), 127.4 (CH), 122.0 (CH), 119.6 (CH), 119.3 (CH), 115.1 (*quat*-C), 109.8 (CH), 50.8 (CH_2), 40.5 (CH), 35.6 (CH_3), 33.1 (CH_3), 29.6 (CH_2), 21.4 (CH_2). MS (EI) *m*/*z* 242.

*4.3.4. 1-Allyl-3-(1-methyl-1H-indol-3-yl)piperidin-2-one (**6d**)*

Diazo amide **4c** (330 mg, 2 mmol) was allowed to react with *N*-methylindole (290 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **6d** (85%) as a brownish thick oil. [Found: C, 75.89; H, 7.47; N, 10.34. $C_{17}H_{20}N_2O$ requires: C, 76.09; H, 7.51; N, 10.44%.] R_f (45% EtOAc/hexane) 0.6; ν_{max} (film) 3394, 3055, 1641, 1486, 1264, 1172, 1120, 739 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.51 (1H, t, *J*=7.4 Hz, arom-*H*), 7.48–7.02 (3H, m, arom-*H*), 6.83 (1H, d, *J*=5.7 Hz, arom-*H*), 5.81–5.74 (1H, m), 5.23–5.08 (2H, m), 4.1–3.91 (3H, m), 3.64 (3H, s, CH_3), 3.36–3.23 (2H, m), 2.11–2.06 (1H, m), 1.92–1.62 (3H, m); ^{13}C (50.3 MHz, $CDCl_3$) 170.3 (C=O), 136.7 (*quat*-C), 132.7 (CH), 127.2 (*quat*-C), 126.5 (CH), 121.1 (CH), 118.7 (CH), 118.4 (CH), 117.0 (CH_2), 114.9 (*quat*-C), 109.6 (CH), 48.9 (CH_2), 46.6 (CH_2), 39.7 (CH), 32.1 (CH_3), 28.6 (CH_2), 20.6 (CH_2). MS (EI) *m*/*z* 268 (M, 100), 183 (50), 170 (85), 151 (75), 144 (60), 109 (70), 77 (28), 41 (88).

*4.3.5. 1-Allyl-3-(1-allyl-1H-indol-3-yl)piperidin-2-one (**6e**)*

Diazo amide **4c** (330 mg, 2 mmol) was allowed to react with *N*-allylindole (345 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **6e** (89%) yield as a brownish solid. [Found: C, 77.63; H, 7.59; N, 9.40. $C_{19}H_{22}N_2O$ requires: C, 77.52; H, 7.53; N, 9.52%.] R_f (45% EtOAc/hexane) 0.55; mp 65–66 °C; ν_{max} (KBr) 3341, 3291, 2944, 1662, 1495, 1429, 1212, 739 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.55 (1H, d, *J*=1.3 Hz, arom-*H*), 7.29–7.04 (3H, m, arom-*H*), 6.91 (1H, s, arom-*H*), 5.95–5.90 (2H, m), 5.26–5.14 (4H, m), 4.67–4.63 (2H, m), 4.12–3.95 (3H, m), 3.40–3.31 (2H, m), 2.18–1.81 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 170.5 (C=O), 136.4 (*quat*-C), 133.4 (CH), 132.9 (CH), 127.1 (*quat*-C), 125.6 (CH), 121.3 (CH), 119.1 (CH), 118.8 (CH), 117.2 (CH_2), 117.1 (CH_2), 114.8 (*quat*-C), 109.5 (CH), 49.6 (CH_2), 48.6 (CH_2), 47.4 (CH_2), 40.1 (CH), 28.8 (CH_2), 20.9 (CH_2); MS (EI) *m*/*z* 294 (M^+, 80), 196 (20), 168 (40), 154 (35), 109 (45), 55 (28), 44 (100), 42 (80).

*4.3.6. 1-Methyl-3-(1-benzyl-1H-indol-3-yl)piperidin-2-one (**6f**)*

Diazo amide **4b** (280 mg, 2 mmol) was allowed to react with *N*-benzylindole (290 mg, 2.2 mmol) in 50 mL of freshly distilled dichloromethane in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the general procedure to furnish the title compound **6f** (72%) as a brownish solid. [Found: C, 78.99; H, 7.00; N, 8.84. $C_{21}H_{22}N_2O$ requires: C, 79.21; H, 6.96; N, 8.80%.] R_f (50% EtOAc/hexane) 0.55; mp 95–96 °C; ν_{max} (KBr) 3334, 3269, 2893, 2718, 1625, 1480, 1407, 1344, 790, 639 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.51 (1H, d, *J*=8.4 Hz, arom-*H*), 7.31–7.04 (8H, m, arom-*H*), 6.95 (1H, s, arom-*H*), 5.25 (2H, s), 4.01 (1H, t, *J*=6.4 Hz), 3.44–3.27 (2H, m, CH_2), 3.04 (3H, s), 2.21–1.72 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 171.7 (C=O), 137.7 (*quat*-C), 137.5 (*quat*-C), 128.8 (CH), 128.5 (CH), 127.3 (CH), 127.6 (CH), 122.3 (CH), 119.4 (CH), 119.2 (CH), 115.0 (*quat*-C), 109.9 (CH), 50.4 (CH_2), 40.7 (CH), 34.4 (CH_3), 29.8 (CH_2), 21.5 (CH_2). MS (EI) *m*/*z* 318.

*4.3.7. 1-Methyl-3-(1-allyl-1H-indol-3-yl)piperidin-2-one (**6g**)*

Diazo amide **4b** (280 mg, 2 mmol) was allowed to react with *N*-allylindole (345 mg, 2.2 mmol) in 50 mL of freshly distilled dichloromethane in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the general procedure to furnish the title compound **6g** (75%) as a thick brownish oil. [Found: C, 75.95; H, 7.51; N, 10.38. $C_{17}H_{20}N_2O$ requires: C, 76.09; H, 7.51; N, 10.44%.] R_f (50% EtOAc/hexane) 0.57; ν_{max} (film) 3388, 3054, 1639, 1496, 1244, 1131, 1116, 738 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.53 (1H, d, *J*=3.5 Hz, arom-*H*), 7.29–7.04 (3H, m, arom-*H*), 6.90 (1H, s, arom-*H*), 5.98–5.91 (1H, m, CH), 5.19–5.15 (2H, m, CH_2), 4.66 (2H, d, *J*=5.4 Hz, CH_2), 3.98 (2H, d, *J*=3.1 Hz, CH_2), 3.44–3.28 (2H, m, NCH_2), 2.98 (3H, s, CH_3), 2.19–1.55 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 171.0 (C=O), 136.5 (*quat*-C), 133.5 (CH), 127.2 (*quat*-C), 125.8 (CH), 121.4 (CH), 119.2 (CH), 118.9 (CH), 117.1 (CH_2), 114.9 (*quat*-C), 109.6 (CH), 50.2 (CH_2), 48.7 (CH_2), 39.9 (CH), 35.0 (CH_3), 28.9 (CH_2), 20.8 (CH_2). MS (EI) *m*/*z* 268.

*4.3.8. 3-(1H-Pyrrol-2-yl)piperidin-2-one (**8a**)*

Diazo amide **4a** (250 mg, 2 mmol) was allowed to react with pyrrole (150 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **8a** (85%) as a thick brownish liquid. [Found: C, 65.95; H, 7.30; N, 17.27. $C_9H_{12}N_2O$ requires: C, 65.83; H, 7.37; N, 17.06%.] R_f (85% EtOAc/hexane) 0.62; ν_{max} (film) 3394, 3302, 1654, 1491, 1355, 1325, 1267, 1100, 734 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 9.60 (1H, br s, N*H*), 6.78 (1H, br s, N*H*), 6.72 (1H, s, arom-*H*), 6.13 (1H, d, *J*=2.5 Hz, arom-*H*), 5.99 (1H, s, C*H*), 3.61 (1H, t, *J*=7.0 Hz), 3.30–3.24 (2H, m), 2.32–1.64 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 173.7 (C=O), 129.9 (*quat*-C), 117.9 (CH), 108.2 (CH), 104.9 (CH), 43.1 (CH_2), 39.9 (CH), 26.3 (CH_2), 19.8 (CH_2). MS (EI) *m*/*z* 164 (M^+, 43), 149 (12), 133 (25), 119 (15), 106 (8), 99 (100), 91 (14), 70 (28), 55 (38), 43 (42).

*4.3.9. 3-(1-Benzyl-1H-pyrrol-2-yl)piperidin-2-one (**8b**)*

Diazo amide **4a** (250 mg, 2 mmol) was allowed to react with *N*-benzylpyrrole (475 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % $Rh_2(OAc)_4$ as described in the general procedure to afford the title compound **8b** (79%) as a thick brownish liquid. [Found: C, 75.70; H, 7.02; N, 11.21. $C_{16}H_{18}N_2O$ requires: C, 75.56; H, 7.13; N, 11.01%.] R_f (50% EtOAc/hexane) 0.60; ν_{max} (film) 3339, 3298, 3055, 2931, 1642, 1495, 1453, 1265, 737 cm^{-1}; ^{1}H (200 MHz, $CDCl_3$) 7.34–7.30 (3H, m), 7.03–6.99 (2H, m), 6.62 (1H, d, *J*=1.5 Hz), 6.30 (1H, br s), 6.15 (1H, t, *J*=1 Hz), 6.06 (1H, s), 5.36 (1H, d, *J*=16.4 Hz, benzylic *H*), 5.11 (1H, d, *J*=16.4 Hz, benzylic *H*), 3.47 (1H, t, *J*=8.3 Hz, C*H*), 3.42–3.31 (2H, m), 1.95–1.27 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 172.8 (C=O), 139.4 (*quat*-C), 132.0 (*quat*-C), 129.3 (CH), 127.9 (CH), 127.2 (CH), 122.6 (CH), 107.9 (CH), 107.3 (CH), 51.4 (CH_2), 43.2 (CH_2), 40.3 (CH), 28.3 (CH_2), 22.2 (CH_2). MS (EI) *m*/*z* 254 (M^+, 45), 170 (20), 156 (45), 135 (12), 115 (30), 91 (90), 87 (28), 59 (88), 44 (100).

*4.3.10. 1-Allyl-3-(1H-pyrrol-2-yl)piperidin-2-one (**8c**)*

Diazo amide **4c** (330 mg, 2 mmol) was allowed to react with pyrrole (150 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described

in the above procedure to afford the title compound **8c** (88%) as a thick brownish liquid. [Found: C, 70.49; H, 7.92; N, 13.80. $C_{12}H_{16}N_2O$ requires: C, 70.56; H, 7.90; N, 13.71%.] R_f (55% EtOAc/hexane) 0.62; ν_{max} (film) 3076, 3055, 2939, 2867, 1634, 1489, 1349, 1275, 1194, 926, 741 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 9.45 (1H, br s, *pyrrole*-NH), 6.73 (1H, s, arom-*H*), 6.13 (1H, d, *J*=2.8 Hz, arom-*H*), 5.98 (1H, s, CH), 5.77–5.68 (1H, m, allylic), 5.18–5.08 (2H, m, CH_2), 4.06–3.94 (2H, m, NCH_2), 3.67 (1H, t, *J*=6.7 Hz, CH_2), 3.31–3.25 (2H, m, NCH_2), 2.31–1.55 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 170.9 (C=O), 133.1 (CH), 130.2 (*quat*-C), 118.1 (CH_2), 117.9 (CH), 108.2 (CH), 104.6 (CH), 50.5 (CH_2), 48.4 (CH_2), 40.4 (CH), 26.5 (CH_2), 22.1 (CH_2). MS (EI) *m*/*z* 204.

4.3.11. 3-(5-Allyl-1H-Pyrrol-2-yl)piperidin-2-one (*8d*)

Diazo amide **4a** (250 mg, 2 mmol) was allowed to react with 3-allylpyrrole (150 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **8d** (75%) as a thick brownish liquid. [Found: C, 70.61; H, 7.85; N, 13.47. $C_{12}H_{16}N_2O$ requires C, 70.56; H, 7.90; N, 13.71%.] R_f (50% EtOAc/hexane) 0.55; ν_{max} (film) 3339, 3292, 2951, 1656, 1490, 1419, 1323, 1266, 737 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 9.20 (1H, br s, pyrrole–NH), 6.55 (1H, s), 5.92–5.72 (3H, m, allylic, arom-*H*), 5.15–4.92 (2H, m, CH_2), 3.57–3.14 (5H, m), 2.20–1.74 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 173.6 (C=O), 139.3 (*quat*-C), 136.6 (CH), 116.7 (CH_2), 114.6 (*quat*-C), 105.6 (CH), 104.9 (CH), 43.2 (CH_2), 40.0 (CH), 33.1 (CH_2), 26.1 (CH_2), 21.6 (CH_2). MS (EI) *m*/*z* 204 (M^+, 48).

4.3.12. 1-Benzyl-3-(1H-pyrrol-2-yl)piperidin-2-one (*8e*)

Diazo amide **4d** (430 mg, 2 mmol) was allowed to react with pyrrole (150 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **8e** (75%) yield as a thick brownish liquid. [Found: C, 75.46; H, 7.19; N, 11.08. $C_{16}H_{18}N_2O$ requires: C, 75.56; H, 7.13; N, 11.01%.] R_f (55% EtOAc/hexane) 0.58; ν_{max} (film) 3391, 2942, 2915, 2856, 1623, 1552, 1485, 1450, 1346, 1247, 1095, 775 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 9.69 (1H, br s, N*H*), 7.30–7.19 (5H, m), 6.73 (1H, s), 6.14 (1H, d, *J*=2.7 Hz), 5.99 (1H, s), 4.69 (1H, d, *J*=14.6 Hz), 4.47 (1H, d, *J*=14.6 Hz), 3.72 (1H, t, *J*=6.7 Hz), 3.22–3.16 (2H, m), 2.29–1.69 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 171.1 (C=O), 137.5 (*quat*-C), 130.2 (*quat*-C), 129.2 (CH), 128.5 (CH), 128.0 (CH), 117.9 (CH), 108.2 (CH), 104.6 (CH), 51.1 (CH_2), 48.4 (CH_2), 40.5 (CH), 26.5 (CH_2), 22.0 (CH_2); MS (EI) *m*/*z* 254 (M^+, 40), 92 (20), 84 (100), 54 (15), 49 (94).

4.3.13. 1-Allyl-3-(1-benzyl-1H-pyrrol-2-yl)piperidin-2-one (*8f*)

Diazo amide **4c** (330 mg, 2 mmol) was allowed to react with *N*-benzylpyrrole (475 mg, 2.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **8f** (85%) as a thick brownish liquid. [Found: C, 77.58; H, 7.55; N, 9.61. $C_{19}H_{22}N_2O$ requires: C, 77.52; H, 7.53; N, 9.52%.] R_f (50% EtOAc/hexane) 0.55; ν_{max} (film) 3342, 3290, 2888, 1637, 1490, 1352, 1421, 1322, 1260, 739 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 7.32–7.22 (3H, m), 7.00 (2H, d, *J*=6.7 Hz), 6.62 (1H, t, *J*=2.2 Hz), 6.15–5.73 (3H, m), 5.48–5.08 (4H, m), 4.02–3.84 (3H, m), 3.51–3.21 (2H, m), 2.02–1.66 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 169.5 (C=O), 138.9 (*quat*-C), 132.8 (CH), 131.8 (*quat*-C), 128.6 (CH), 127.2 (CH), 126.3 (CH), 121.2 (CH_2), 117.3 (CH), 107.1 (CH), 106.3 (CH), 50.7 (CH_2), 49.7 (CH_2), 47.3 (CH_2), 39.9 (CH), 21.9 (CH_2), 19.3 (CH_2). MS (EI) *m*/*z* 294 (M^+, 52).

4.3.14. 1-(3-Diazo-2-oxopiperidin-1-yl)butane-1,3-dione (*10*)

Diazo amide **4a** (1 g, 8 mmol) and 2,2,6-trimethyl-[1,3]dioxin-4-one (1.3 mL, 9 mmol) were taken in a round bottom flask fitted with a condenser circulating with water at 10 °C under nitrogen atmosphere. To this 50 mL of toluene was added and the reaction mixture refluxed at 130 °C for 2 h. The progress of the reaction was monitored using TLC and after the completion of the reaction the solvent evaporated using vacuum. The resulting solid was subjected to flash column chromatography over silica using N_2 to give the title compound **10** (125 mg, 80%) as a yellow liquid. [Found: C, 51.75; H, 5.28; N, 20.04. $C_9H_{11}N_3O_3$ requires: C, 51.67; H, 5.30; N, 20.09%.] R_f (65% EtOAc/hexane) 0.61; ν_{max} (Neat) 3339, 2940, 2100, 1653, 1648, 1460, 1172, 739 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 4.02 (s, 2H), 3.8–3.77 (2H, m, N*CH*$_2$), 2.78 (2H, t, *J*=6.2 Hz, N*CH*$_2$), 2.25 (3H, s, *CH*$_3$), 1.95–1.87 (2H, m); ^{13}C (50.3 MHz, $CDCl_3$) 201.1 (C=O), 167.2 (C=O), 166.2 (C=O), 58.1 (*quat*-C), 53.9 (CH_2), 44.9 (CH_2), 29.7 (CH_3), 21.0 (CH_2), 20.9 (CH_2); MS (EI) *m*/*z* 209 (M^+, 209).

4.3.15. 2-Diazo-1-(3-diazo-2-oxopiperidin-1-yl)butane-1,3-dione (*11*)

1-(3-Diazo-2-oxopiperidin-1-yl)butane-1,3-dione (10 mmol) obtained in the previous step was allowed to react with triethylamine (12 mmol) and methanesulfonyl azide (11 mmol) at ice-cold condition for 10 min. The reaction mixture was allowed to stir at room temperature for 4 h. After the completion of the reaction by TLC, the reaction mixture was washed with water, evaporated using vacuum and the resulting solid was subjected to flash column chromatography over silica to give the title compound **11** (75%) as a yellow solid. [Found: C, 45.77; H, 3.99; N, 29.70. $C_9H_9N_5O_3$ requires: C, 45.96; H, 3.86; N, 29.78%.] R_f (65% EtOAc/hexane) 0.52; mp 52–53 °C; ν_{max} (KBr) 3339, 2940, 2357, 2114, 2099, 1654, 1647, 1458, 1404, 1257, 1171, 738 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 3.54 (2H, t, *J*=5.4 Hz, N*CH*$_2$), 2.68 (2H, t, *J*=6.4 Hz, N*CH*$_2$), 2.32 (3H, s, *CH*$_3$), 1.99–1.86 (2H, m); ^{13}C (50.3 MHz, $CDCl_3$) 189.6 (C=O), 165.0 (C=O), 162.2 (C=O), 65.6 (*quat*-C), 44.3 (CH_2), 28.1 (CH_3), 21.3 (CH_2), 20.5 (CH_2); MS (EI) *m*/*z* 235 (M^+, 235).

4.3.16. 1-[3-(1-Allyl-1H-indol-2-yl)-2-oxopiperidin-1-yl]-butane-1,3-dione (*12*)

Diazo amide **10** (210 mg, 1 mmol) was allowed to react with *N*-allylindole (190 mg, 1.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **12** (90%) as a yellow solid. R_f (65% EtOAc/hexane) 0.60; mp 104–105 °C; ν_{max} (KBr) 3424, 2935, 1736, 1651, 1450, 1269, 1075, 738 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 7.46 (1H, d, *J*=7.6 Hz), 7.31–7.06 (3H, m), 6.96 (1H, s), 5.99–5.91 (1H, m), 5.21–5.06 (2H, m), 4.66 (2H, d, *J*=4.2 Hz), 4.10–3.81 (5H, m), 2.26–1.84 (7H, m); ^{13}C (50.3 MHz, $CDCl_3$) 201.5 (C=O), 174.6 (C=O), 169.4 (C=O), 136.3 (*quat*-C), 133.2 (CH), 126.9 (*quat*-C), 125.7 (CH), 121.7 (CH), 119.2 (CH), 119.0 (CH), 117.3 (CH_2), 112.8 (*quat*-C), 109.7 (CH), 54.4 (CH_2), 48.6 (CH_2), 43.5 (CH_2), 42.1 (CH), 29.9 (CH_3), 27.6 (CH_2), 20.9 (CH_2). HRMS (ESI): MNa^+, found 361.1511; $C_{20}H_{22}N_2O_3$ requires 361.1528.

4.3.17. 1-[3-(1-Allyl-1H-indol-2-yl)-2-oxopiperidin-1-yl]-2-diazobutane-1,3-dione (*13*)

Diazo amide **11** (235 mg, 1 mmol) was allowed to react with *N*-allylpyrrole (130 mg, 1.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **13** (88%) as a yellow solid. R_f (60% EtOAc/hexane) 0.62; mp 107–108 °C; ν_{max} (KBr) 3433, 2938, 2101, 1738, 1652, 1460, 1401, 1271, 1079, 740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 7.53 (1H, d, *J*=7.4 Hz), 7.32–7.08 (3H, m), 6.99 (1H, s), 6.01–5.90 (1H, m), 5.22–5.06 (2H, m), 4.67 (2H, d, *J*=5.4 Hz), 4.10 (2H, t, *J*=6.6 Hz), 3.85 (1H, t, *J*=6.0 Hz), 2.45 (3H, s), 2.42–1.79 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 189.5 (C=O), 173.5 (C=O), 164.89 (C=O), 136.4 (*quat*-C), 133.2 (CH), 127.06 (*quat*-C), 125.5 (CH), 121.9 (CH), 119.4 (CH), 119.1 (CH_2), 117.4 (CH), 112.4 (*quat*-C), 109.8 (CH), 48.7 (CH_2), 46.3 (CH_2), 41.2 (CH), 28.5 (CH_3), 28.3 (CH_2), 21.7 (CH_2). HRMS (ESI): MNa^+, found 387.1451; $C_{20}H_{20}N_4O_3$ requires 387.1433.

*4.3.18. 1-[3-(1-Allyl-1H-pyrrol-2-yl)-2-oxopiperidin-1-yl]-2-diazobutane-1,3-dione (**15**)*

Diazo amide **11** (235 mg, 1 mmol) was allowed to react with *N*-allylpyrrole (130 mg, 1.2 mmol) in 50 mL of dichloromethane at room temperature in the presence of 0.5 mol % of $Rh_2(OAc)_4$ as described in the above procedure to afford the title compound **15** (90%) as a yellow solid. R_f (55% EtOAc/hexane) 0.60; mp 72–73 °C; ν_{max} (KBr) 3434, 2939, 2102, 1734, 1649, 1458, 1404, 1270, 1081, 737 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 6.56 (1H, d, *J*=5.8 Hz, arom-*H*), 6.06–5.86 (3H, m), 5.13–4.86 (2H, m), 4.53–4.36 (2H, m), 3.78–3.73 (3H, m), 2.37 (3H, s), 2.20–1.83 (4H, m); ^{13}C (50.3 MHz, $CDCl_3$) 188.8 (C=O), 172.4 (C=O), 164.2 (C=O), 134.5 (CH), 128.6 (*quat*-C), 121.3 (CH), 116.0 (CH), 106.8 (CH), 106.5 (CH), 48.9 (CH_2), 46.0 (CH_2), 41.2 (CH), 28.0 (CH_3), 26.9 (CH_2), 21.4 (CH_2). HRMS (ESI): MNa^+, found 337.1303; $C_{16}H_{18}N_4O_3$ requires 337.1277.

*4.3.19. Compound **16***

1-(3-Allyl-(1*H*-pyrrol-2-yl)-2-oxopiperidin-1-yl)-2-diazobutane-1,3-dione (100 mg, 3.2 mmol) was refluxed with argon using vacuum. Under argon positive flow, 40 mL of freshly distilled benzene was added and stirred well. $Rh_2(OAc)_4$ (0.5 mol%) was added and the mixture refluxed for 1 h to afford the title compound **16** as a colourless solid (90%). R_f (50% EtOAc/hexane) 0.58; mp 85–86 °C; ν_{max} (KBr) 3427, 3057, 2953, 2864, 1731, 1709, 1455, 1404, 1362, 1270, 1080, 736 cm^{-1}; ^1H (200 MHz, $CDCl_3$) 6.49 (1H, d, *J*=1.6 Hz, arom-*H*), 6.14 (1H, t, *J*=3.2 Hz, arom-*H*), 6.01 (1H, s, arom-*H*), 4.28–4.19 (1H, m), 3.91–3.85 (1H, m), 3.62–3.47 (2H, m), 2.85–2.71 (2H, m), 2.37 (3H, s), 2.31–2.21 (3H, m), 1.81–1.26 (3H, m); ^{13}C (50.3 MHz, $CDCl_3$) 200.1 (C=O), 169.7 (C=O), 129.3 (*quat*-C), 118.5 (CH), 109.1 (CH), 105.1 (CH), 93.0 (*quat*-C), 89.8 (*quat*-C), 48.9 (CH_2), 38.9 (CH_2), 37.3 (CH), 34.2 (CH), 33.6 (CH_2), 32.0 (CH_2), 27.2 (CH_3), 21.9 (CH_2). HRMS (ESI): MNa^+, found 309.1128; $C_{16}H_{18}N_2O_3$ requires 309.1215.

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