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The Rhodium(II) Carbenoid Cyclization-Cycloaddition Cascade of α-Diazo Dihydroindolinones for the Synthesis of Novel Azapolymeric Ring Systems†

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Abstract

Tandem carbonyl ylide formation-1,3-dipolar cycloaddition of α-diazo N-acetyl-tetrahydro-β-carbolin-1-one derivatives occur efficiently in the presence of a dirhodium catalyst to afford bimolecular cycloadducts in high yield. The Rh(II)-catalyzed reaction also takes place intramolecularly to give products derived from trapping of the carbonyl ylide dipole with a tethered alkene. The power of the intramolecular cascade sequence is that it rapidly assembles a pentacyclic ring system containing three new stereocenters and two adjacent quaternary centers stereospecifically in a single step and in high yield.

Keywords

α-diazo dihydroindolinones; rhodium(II); synthesis; carbenoid; intramolecular; dipolar cycloaddition; azapentacycles

1. Introduction

Novel strategies for the stereoselective synthesis of oxy-polycyclic ring systems continue to receive considerable attention in the field of synthetic organic chemistry.1–7 Construction of complex oxygen heterocycles through tandem cascade chemistry8–10 has been a particularly fruitful area of investigation, and the synthesis of various natural products by the use of domino reactions has been carried out by numerous investigators.11–14 One of the more interesting examples of this approach is the cyclization of a metallocarbenoid intermediate generated from the diazo precursor 1 onto a neighboring carbonyl group to furnish a carbonyl ylide dipole 2.15,16 The cycloaddition chemistry of the resulting 1,3-dipole with various dipolarophiles has been extensively studied and also applied to the synthesis of numerous natural products.17 Highly substituted tetrahydrofuran structural units of such natural compounds as the ionophores, brevetoxins, and other marine products can be obtained by this route.18 The synthesis of illudins,19 phorbol ester derivatives,20 and different sesquiterpenes21 has also been achieved using the carbenoid cyclization-carbonyl ylide cycloaddition process.22 In most cases, 1,3-dipolar cycloaddition reactions of carbonyl ylides proceed with varying exolendo,
regio-, and facial selectivity depending on the properties of the substrates and reaction conditions. With limited exceptions, alkyl and aryl ketones were usually the source of the interacting carbonyl group and the resulting dipole was generated by the transition metal-catalyzed decomposition of the diazo alkanedione in benzene at 80 °C. Our group has also been interested in the formation of push-pull dipoles from the Rh(II)-catalyzed reaction of α-diazoamides and noted that a smooth intramolecular 1,3-dipolar cycloaddition occurred across both alkenyl and heteroaromatic π-bonds to provide novel azapentacyclic compounds in good yield and in a stereocontrolled fashion. The recent synthesis of (±)-aspidophytine nicely demonstrated the utility of this cascade methodology for the construction of complex aspidosperma alkaloids. Thus, the Rh(II)-catalyzed reaction of indole produced cycloadduct in 97% yield via the intermediacy of the carbonyl ylide dipole. The acid lability of cycloadduct was exploited to provide the complete skeleton of aspidophytine in several additional steps (Scheme 2).

In more recent studies directed toward the total synthesis of vinca alkaloids, our retrosynthetic analysis envisaged the azapentacyclic framework of H-epivincamine to arise from a metal carbene cyclization-cycloaddition cascade (Scheme 3). Using this metal-catalyzed domino reaction as the key step, the core skeleton of H-epivincamine retroanalyzes most straightforwardly to diazo amidoester.

2. Results and Discussion

For the initial investigation into establishing the feasibility of this particular approach towards the synthesis of various members of the vinca alkaloid family, we chose to examine the Rh(II)-catalyzed behavior of the simpler α-diazo indolo-amide as a test substrate. Compound was easily prepared by treating carboline with acetic anhydride under refluxing conditions followed by reaction of the resulting N-acetyl carboline with sodium hydride and ethyl 2-diazomalonyl chloride (Scheme 4). Heating compound at 80 °C in the presence of catalytic Rh_{2}(OAc)_{4} generates a rhodium carbenoid intermediate which undergoes cyclization with the neighboring amido group to form a transient carbonyl ylide dipole. Subsequent bimolecular trapping of the dipole with various common dipolarophiles led to the expected [3+2]-cycloadducts (i.e. 15). Table 1 illustrates the scope of the cycloaddition by showcasing the reaction with a variety of commercially available dipolarophiles. In a typical experiment, refluxing a solution of with Rh_{2}(OAc)_{4} in benzene at 80 °C in the presence of an equivalent of a trapping agent affords cycloadducts in ca 75% yield with complete regio- and diastereoselectivity. In general, the cascade reaction sequence produced only the exo-cycloaddition product isolated as a single diastereomer. When benzaldehyde was used as the trapping agent, the cycloaddition also proceeded with high selectivity and afforded cycloadduct in 85% yield as the only isolable product. The exclusive formation of cycloadducts is consistent with the regiochemistry predicted by FMO theory. The most favorable interaction is between the HOMO of the carbonyl ylide dipole and the LUMO of the dipolarophile. The preferred exo-selectivity is associated with fewer non-bonded interactions in the transition state for the cycloaddition process.

Push-pull carbonyl ylide dipoles represent useful intermediates for the synthesis of complex azapolycyclic frameworks as found in different classes of alkaloids. Since only limited reports are available describing the bimolecular cycloaddition behavior of these dipoles, we thought it would be worthwhile to further probe the facility of their reactivity with various trapping agents. With this in mind, the Rh(II)-induced carbenoid cyclization-cycloaddition sequence was extended to the α-diazo oxindole system. Our initial studies centered on the bimolecular cycloaddition chemistry of α-diazo dihydroindolinone (R_{1} = Me; R_{2} = OMe). Our intention...
was to examine the regio and stereoselective aspects of the reaction (Scheme 5) using α-diazo oxindolo-amide 20a as a model system.

Toward this goal, α-diazo dihydroindolinone 20a was treated with dimethylacetylene dicarboxylate (DMAD) in the presence of catalytic Rh$_2$(OAc)$_4$ at 80 °C in benzene and this resulted in the formation of cycloadduct 23 in 98% yield. A similar cycloaddition cascade occurred when the reaction was carried out using methyl propiolate. In this case, a 1:1-mixture of both regioisomeric adducts 24a and 25a were obtained in 80% overall yield. The observed regioselectivity of the cycloaddition is significantly lower with this particular α-diazo amide than that previously encountered with the related diazo indolo amide 13. The exact reason for this difference in product distribution is unclear but is speculated to be related to steric interactions in the transition state leading to the type I cycloadduct 24a (HOMO dipole controlled). These steric interactions are more severe in the transition state when the carbomethoxy group of the dipolarophile and the substituent groups on the oxindole are adjacent to each other (i.e., 24a). Consequently, the electronically less preferred FMO product 25a becomes more significant with this system and stands in contrast with the results encountered with the related diazo indolo amide 13. In support of this suggestion we have also studied the Rh(II)-catalyzed reaction of α-diazo dihydroindolinone 20b which contains the much larger TBS group attached to the oxindole ring.

Reaction of this system with methyl propiolate afforded a 1:3-mixture of regioisomeric cycloadducts in 70% overall yield. The major adduct formed (25b) corresponds to the sterically less crowded product and not the one expected on the basis of FMO considerations.

The Rh(II)-catalyzed reaction was also carried out using 20a with N-phenylmaleimide as the added dipolarophile. The $^1$H-NMR of the crude reaction mixture showed a 3:2-mixture of exoendo-diastereomers in 95% yield. We did not observe any product resulting from the cycloaddition of the transient carbonyl ylide across the C=O group of N-phenylmaleimide. Another experiment that was performed involved the use of 20a with methyl acrylate in the presence of Rh$_2$(OAc)$_4$ as described above. The $^1$H-NMR of the crude reaction showed a mixture of four diastereomers in the ratio of 4.5:2:1.5:1. Chromatographic purification of the reaction mixture did not lead to the complete separation of the various isomers and thus the determination of the stereochemistry of each cycloadduct remains undefined. Nevertheless, on the basis of similarity in spectral data, it is clear that the cycloaddition produced a mixture of regioisomers in both the exo and endo orientations and without any significant selectivity differences.

After performing the cycloaddition of 20a with various C=C bonds, we decided to extend the cascade reaction using benzaldehyde as the trapping agent. A survey of the literature revealed that only a few reports are available dealing with the reactions of carbonyl ylides with carbonyl groups as hetero-dipolarophiles. The Rh(II)-catalyzed reaction of diazo amide 20a was carried out in the presence of a slight excess of benzaldehyde in benzene at 80 °C. The reaction was monitored by TLC and column chromatographic purification of the crude reaction mixture afforded cycloadduct 28 as the exclusive cycloadduct in 98% yield (see Figure 2). The assignment of the exo orientation of the phenyl group on the dioxa bicyclic framework is based on extensive precedent for related transformations. The regiochemistry observed is readily rationalized in terms of maximum overlap of the dipole HOMO-dipolarophile LUMO and the high selectivity observed may be due to the much larger coefficient on the oxygen atom of the carbonyl group.

The cascade reactions discussed above are of interest due to the potential for rapid generation of molecular complexity from a readily available diazo substrate. Earlier studies from our group established that the Rh(II)-catalyzed tandem carbonyl ylide formation-1,3-dipolar
cycloaddition also occurred intramolecularly when non-activated C=C bonds were used to trap the dipole.\(^{32}\) At this point, we decided to study the intramolecular cycloaddition behavior of several related \(\alpha\)-diazo dihydroindolinones. In this spirit we first prepared \(\alpha\)-diazo dihydroindolitone \(^{31}\) starting from isatin and the Grignard reagent derived from 4-bromo-1-butene (Scheme \(^6\)). The resulting alcohol \(^{29}\) was converted to the corresponding TBS ether \(^{30}\) using TBSCI and the required diazo functionality was then introduced using 2-diazo malonyl chloride.\(^{29}\) Exposure of \(^{31}\) to the standard Rh(II) reaction conditions afforded the intramolecular cycloadduct \(^{32}\) as the only product in 70% isolated yield. We also carried out a similar cyclization-cycloaddition cascade with the homologous \(\alpha\)-diazo dihydroindolione \(^{35}\) which contains a five-carbon tether, \(n=2\) (to form a six-membered ring). The resulting cycloadduct \(^{36}\) was isolated in comparable yield (\(i.e., \) 69%). Even in the presence of DMAD, the same two cycloadducts (\(^{32}\) and \(^{36}\)) were obtained as the only products of the cycloaddition reaction. Thus, the rapidity of the intramolecular cycloaddition of both \(\alpha\)-diazo dihydroindoliones \(^{31}\) and \(^{35}\) significantly overshadows any bimolecular processes. The power of this intramolecular cascade sequence is that it rapidly assembles a pentacyclic ring system containing three new stereocenters and two adjacent quaternary centers stereospecifically in a single step and in high yield. What is also noteworthy about the intramolecular cycloaddition is that it creates a ring fused to the cycloadduct, the size of which is dictated by the length of the tether connected to the dipolarophile.

Bolstered by this positive result, we next examined the Rh(II)-catalyzed chemistry of several related alkanyl ethers (\(i.e., \) \(^{37}\)–\(^{39}\)). Exposure of \(^{37}\) to \(\text{Rh}_2\text{(OAc)}_4\) in benzene produced cycloadduct \(^{40}\) in 72% yield (Scheme \(^7\)). A related set of results was encountered with \(\alpha\)-diazo dihydroindolinones \(^{38}\) and \(^{39}\). The intramolecular cycloaddition reaction occurred smoothly giving rise to cycloadducts \(^{41}\) and \(^{42}\) in 82% and 80%, respectively.

Of the many questions concerning the factors that govern the outcome of intramolecular carbonyl ylide trapping reactions, one that is easily formulated focuses upon the course of the reaction as a function of the length of the tether connecting the reacting groups. The primary spatial requirement for intramolecular cycloaddition is that the distance between the dipole and alkene should be sufficiently close so that effective overlap of the \(\pi\)-orbitals can occur. Our earlier studies showed that the ring size of the resulting dipole also played a significant role in the efficiency of the tandem cyclization-cycloaddition process.\(^{33}\) After studying the successful intramolecular cycloaddition reactions of the \(\alpha\)-diazo 3-alkoxy substituted dihydroindolinones \(^{37}\)–\(^{39}\), we embarked on a study whose primary focus was concerned with exploration of the chemoselectivity of the cycloaddition across different \(\pi\)-bonds contained within the same substrate. To perform the Rh(II)-catalyzed tandem ylide generation and competitive cycloaddition reactions, \(\alpha\)-diazo dihydroindolinones \(^{43}\)–\(^{45}\) were selected as prototypical substrates. Treatment of the \(\alpha\)-diazo substrate \(^{43}\) with catalytic \(\text{Rh}_2\text{(OAc)}_4\) afforded a 5:1-mixture of two cycloadducts. The major product isolated (\(46\), 55%) corresponded to internal trapping of the carbonyl ylide intermediate across the ether substituted \(\pi\)-bond (Scheme \(^8\)). The minor product (\(47\), 11%) was that derived from cycloaddition across the alkanyl \(\pi\)-bond contained within the all-carbon tether. Thus, there is a clear preference for cycloaddition across the ether tethered alkene even though the distance connecting the two reacting centers is essentially the same. The effect of changing the tether length was then probed by studying the Rh(II)-metal catalyzed reaction of \(\alpha\)-diazo dihydroindolinones \(^{44}\) and \(^{45}\). The Rh(II)-catalyzed reaction of \(^{44}\), which contains two unequal tether units, proceeded smoothly and afforded cycloadduct \(^{48}\) in 79% yield as the exclusive product. Reaction of the isomeric \(\alpha\)-diazo hydroindolinion \(^{45}\) also occurred readily in the presence of a catalytic amount of \(\text{Rh}_2\text{(OAc)}_4\) to give a single intramolecular cycloadduct \(^{49}\) in 75% yield. As was the case with the homologous system \(^{44}\), cycloaddition of the carbonyl ylide dipole took place exclusively across the ether substituted \(\pi\)-bond.
One explanation that could account for the preferred selectivity observed is that the intramolecular cycloaddition reactions of α-diazo hydroindolinones 43–45 are governed by FMO factors. Regiochemical control in [3+2] dipolar cycloadditions has generally been rationalized on the basis of FMO considerations.34 For carbonyl ylides, the HOMO of the dipole is dominant for reactions with electron deficient dipolarophiles, while the LUMO becomes important for cycloaddition to more electron-rich species.35 The presence of an electron withdrawing oxygen atom (inductive effect) might be expected to lower the LUMO level of the proximal π-bond and thereby promote the HOMO-controlled cycloaddition. Although this suggestion is not unreasonable, it seems to us as though the oxygen atom is simply too far removed from the π-bond to significantly influence its LUMO energy level. Rather, we suspect that the origin of the rate differences resides in either ground state conformational effects or in relative strain within the transition states. With the all carbon tether, the two methylene carbons adjacent to the quaternary center probably adopt an anti-conformation so as to minimize non-bonded interactions, and the olefinic π-bond is thus projected away from the carbonyl ylide dipole. A gauche-conformation about these two methylene carbons is required for the cycloaddition reaction to proceed. Placement of an oxygen atom within the tether will change the preferred conformation and this effectively places the olefinic π-bond in closer proximity to the dipole. Consequently, the minimum energy conformers within the ether linkage are closer to the reactive conformers necessary for the cycloaddition, thereby facilitating the reaction.

3. Conclusion

In conclusion, several trends have surfaced from our investigations in this area. First and foremost, these studies have demonstrated that the intramolecular tandem cyclization-cycloaddition reaction of α-diazo dihydroindolinones is a viable method for quickly assembling complex azapoly cyclic ring systems from easily prepared precursors. Both alkenes and tethered alkenyl ethers readily undergo the intramolecular cycloaddition giving rise to five, six and seven-membered rings fused to a dihydroindolinone backbone. The distribution of regioisomeric products from the internal cycloaddition appears to correlate well with conformational effects in the transition state for the reaction. We are continuing to explore the scope, generality and synthetic applications of the Rh(II)-catalyzed tandem cyclization-cycloaddition reaction of α-diazo dihydroindolinones and will report additional findings at a later date.

4. Experimental

4.1 General

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70eV. Unless otherwise noted, all reactions were performed in flame dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexane mixture as the eluent unless specified otherwise.

4.1.1 2-Acetyl-2,3,4,9-tetrahydro-β-carbolin-1-one (12)—To a stirred solution of 2.4 g (12.9 mmol) of carboline 1136 in 100 mL of refluxing toluene was added 3.6 mL (26 mmol) of triethylamine and 6.1 mL (65 mmol) of acetic anhydride. The resulting mixture was heated at reflux for 8 h and the solvent was removed under reduced pressure. The residue was partitioned between EtOAc and water and the layers were separated. The aqueous layer was washed twice with EtOAc and the combined organic extracts were washed with a saturated sodium bicarbonate solution, brine, and dried over Na2SO4. The organic extracts were filtered and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 1.9 g (65%) of carboline 12 as a white solid; mp 229–230 °C; IR (neat)
3301, 2934, 1687, 1663, and 1287 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 9.10 (brs, 1H), 7.64 (d, 1H, $J = 8.3$ Hz), 7.45 (d, 1H, $J = 8.7$ Hz), 7.39 (t, 1H, $J = 8.3$ Hz), 7.19 (t, 1H, $J = 8.7$ Hz), 4.35 (t, 2H, $J = 6.4$ Hz), 3.07 (t, 2H, $J = 6.4$ Hz), and 2.67 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 20.8, 27.3, 43.9, 112.5, 120.8, 121.1, 124.1, 124.8, 126.4, 126.7, 138.6, 161.8, and 173.1

4.1.2 3-(2-Acetyl-1-oxo-1,2,3,4-tetrahydro-β-carbolin-9-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (13)—To a suspension of 0.47 g (12 mmol) of NaH in 20 mL of THF cooled to 0 °C was added 1.8 g (8 mmol) of carboline dissolved in 30 mL of THF via cannula. The solution was allowed to stir at 0 °C for 30 min, after which time 2.1 g (12 mmol) of ethyl 2-diazomalonyl chloride dissolved in 20 mL of THF was added. The resulting mixture was stirred at 0 °C for 2 h, quenched with water, and extracted with EtOAc. The combined organic layers were washed with brine and dried over Na$_2$SO$_4$. The organic extracts were filtered and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 2.0 g (70%) of α-diazo indole as a yellow oil: IR (neat) 2133, 1720, 1683, 1650, and 1307 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.87 (d, 1H, $J = 8.6$ Hz), 7.60 (d, 1H, $J = 7.9$ Hz), 7.46 (t, 1H, $J = 8.6$ Hz), 7.30 (t, 1H, $J = 7.9$ Hz), 4.36-4.29 (m, 2H), 4.17 (q, 2H, $J = 7.0$ Hz), 3.00 (t, 2H, $J = 6.4$ Hz), 2.59 (s, 3H), and 1.22 (t, 3H, $J = 7.0$ Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.2, 21.0, 27.4, 42.0, 61.6, 114.1, 120.9, 123.5, 125.3, 128.5, 128.6, 129.3, 139.1, 159.9, 160.3, 161.7, and 172.8.

4.1.3 Rh(II)-Catalyzed Dipolar Cycloadduct 16—The general procedure described above was followed using 0.1 g (0.27 mmol) of α-diazo indolo amide, 0.4 g (0.4 mmol) of maleic anhydride, and 2 mg of rhodium(II) acetate in 5 mL of benzene. The resulting mixture was heated at reflux for 1 h and the solvent was removed under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.09 g (75%) of cycloadduct as a white solid: mp 246–247 °C; IR (neat) 2975, 1788, 1755, 1731, and 1662 cm$^{-1}$; $^1$H-NMR (400 MHz, CD$_3$CN) $\delta$ 8.17 (d, 1H, $J = 7.0$ Hz), 7.65 (d, 1H, $J = 7.9$ Hz), 7.43-7.34 (m, 2H), 5.30-5.20 (m, 1H), 4.45-4.39 (m, 2H), 3.75 (s, 4H), 3.45-3.40 (m, 2H), 2.90-2.72 (m, 3H), 2.26 (s, 3H), and 1.37 (t, 3H, $J = 7.0$ Hz); $^{13}$C-NMR (100 MHz, CD$_3$CN) $\delta$ 14.0, 20.4, 25.1, 33.7, 40.9, 49.8, 53.0, 62.9, 85.0, 116.1, 119.6, 125.1, 125.3, 125.5, 128.5, 128.6, 129.3, 139.1, 159.9, 160.3, 161.7, and 172.8.

4.1.5 Rh(II)-Catalyzed Dipolar Cycloadduct 18—The general method described above was followed using 0.1 g (0.27 mmol) of α-diazo indole, 0.04 mL (0.4 mmol) of methyl acrylate, and 2 mg of rhodium(II) acetate in 5 mL of benzene. The resulting mixture was heated at reflux for 1 h and the solvent was removed under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.09 g (77%) of cycloadduct as a white solid: mp 176–177 °C; IR (neat) 2987, 2953, 1755, 1736, 1655, 1455, and 1385 cm$^{-1}$; $^1$H-NMR (400 MHz, CD$_3$CN) $\delta$ 8.20 (d, 1H, $J = 7.9$ Hz), 7.51 (d, 1H, $J = 7.6$ Hz), 7.47-7.37 (m, 2H), 4.45-4.37 (m, 3H), 4.06-3.86 (m, 3H), 3.50-3.26 (m, 2H), 2.22 (s, 3H), and 1.38 (t, 3H, $J = 7.0$ Hz); HRMS Calcd. for [C$_{22}$H$_{18}$N$_2$O$_8$ + H$^+$]: 439.1136. Found 439.1137.

4.1.6 Rh(II)-Catalyzed Dipolar Cycloadduct 19—The general method described above was followed using 0.1 g (0.27 mmol) of α-diazo indole, 0.04 mL (0.4 mmol) of methyl acrylate, and 2 mg of rhodium(II) acetate in 5 mL of benzene. The resulting mixture was heated at reflux for 1 h and the solvent was removed under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.09 g (77%) of cycloadduct as a white solid: mp 176–177 °C; IR (neat) 2987, 2953, 1755, 1736, 1655, 1455, and 1385 cm$^{-1}$; $^1$H-NMR (400 MHz, CD$_3$CN) $\delta$ 8.20 (d, 1H, $J = 7.9$ Hz), 7.51 (d, 1H, $J = 7.6$ Hz), 7.47-7.37 (m, 2H), 4.45-4.37 (m, 3H), 4.06-3.86 (m, 3H), 3.50-3.26 (m, 2H), 2.22 (s, 3H), and 1.38 (t, 3H, $J = 7.0$ Hz); HRMS Calcd. for [C$_{22}$H$_{18}$N$_2$O$_8$ + H$^+$]: 439.1136. Found 439.1137.
propiolate, and 2 mg of rhodium(II) acetate in 5 mL of benzene. The resulting mixture was heated at reflux for 1 h and the solvent was removed under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.09 g (78%) of cycloadduct 18 as a white solid; mp 211–212 °C; IR (neat) 2950, 1753, 1716, 1675, and 1655 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CD\(_3\)CN) \(\delta\) 8.04 (d, 1H, \(J = 7.9\) Hz), 7.60 (d, 1H, \(J = 7.0\) Hz), 7.42-7.33 (m, 2H), 7.15 (s, 1H), 4.40-4.35 (m, 2H), 4.27-4.24 (m, 1H), 3.66 (s, 3H), 3.55-3.48 (m, 1H), 2.93-2.91 (m, 2H), 2.24 (s, 3H), and 1.33 (t, 3H, \(J = 7.3\) Hz).

4.1.6 Rh(II)-Catalyzed Dipolar Cycloadduct 19—The general method described above was followed using 0.1 g (0.27 mmol) of \(\alpha\)-diazo indole 13, 0.04 mL (0.4 mmol) of benzaldehyde, and 2 mg of rhodium(II) acetate in 5 mL of benzene. The resulting mixture was heated at reflux for 1 h and the solvent was removed under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.1 g (85%) of cycloadduct 19 as a white foamy solid; IR (neat) 2984, 1754, 1729, 1686, 1664, and 1373 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97-7.95 (m, 1H), 7.60-7.57 (m, 1H), 7.45-7.34 (m, 2H), 7.27-7.18 (m, 5H), 5.86 (s, 1H), 4.70 (ddd, 1H, \(J = 13.3, 9.2,\) and 4.4 Hz), 4.52-4.39 (m, 2H), 3.80 (ddd, 1H, \(J = 13.3, 9.2,\) and 4.4 Hz), 3.03-2.87 (m, 2H), 2.54 (s, 3H), and 1.40 (t, 3H, \(J = 7.3\) Hz); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 13.9, 20.2, 24.9, 43.1, 63.4, 79.3, 88.7, 106.9, 116.0, 117.2, 120.0, 125.2, 126.2, 126.6, 127.6, 128.0, 128.5, 129.1, 130.7, 133.0, 133.9, 160.3, 163.7, and 172.5; HRMS Calcd. for \([C_{25}H_{22}N_2O_6]^+\): 447.1551. Found 447.1557.

4.1.7 2-Diazo-3-(3-methoxy-3-methyl-2-oxo-2,3-dihydro-indol-1-yl)-3-oxo-propionic Acid Ethyl Ester (20a)—To a solution of 0.07 g (0.4 mmol) of 3-methoxy-3-methyl-1,3-dihydro-indol-2-one37 in 10 mL of THF at 0 °C was added to 0.03 g (0.8 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.12 g (0.8 mmol) sample of ethyl 2-diazomalonyl chloride29 was added and the solution was stirred 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na\(_2\)SO\(_4\). After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.1 g (85%) of 20a as a pale yellow oil; IR (neat) 2986, 2144, 1770, 1729, 1666, 1608, and 1466 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.31 (t, 3H, \(J = 7.3\) Hz), 1.63 (s, 3H), 3.09 (s, 3H), 4.26–4.32 (m, 2H), 7.25 (t, 1H, \(J = 7.3\) Hz), 7.36–7.40 (m, 2H), and 7.66 (d, 1H, \(J = 7.6\) Hz); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.3, 24.8, 53.5, 62.0, 80.0, 114.4, 123.8, 125.3, 126.8, 127.2, 127.6, 128.9, 130.0, 139.2, 160.0, 160.2, and 175.8.

4.1.8 Rh(II)-Catalyzed Dipolar Cycloadduct 23—To a solution containing 0.1 g (0.32 mmol) of diazo hydroindolinone 20a in 15 mL of benzene was added 0.2 mL (1.6 mmol) of dimethylacetylene dicarboxylate and a catalytic amount of Rh\(_2\)(OAc)\(_4\). The mixture was heated at reflux for 2 h. The reaction mixture was then concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.14 g (98%) of cycloadduct 23 as a colorless oil; IR (neat) 2991, 2954, 2832, 2279, 1732, 1600, and 1442 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.38 (t, 3H, \(J = 7.1\) Hz), 2.05 (s, 3H), 3.22 (s, 3H), 3.45 (s, 3H), 3.92 (s, 3H), 4.39 (q, 2H, \(J = 7.0\) Hz), 7.00–7.03 (m, 1H), 7.23–7.25 (m, 2H), and 7.71–7.73 (m, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.3, 24.8, 53.5, 62.0, 80.0, 114.4, 123.8, 125.3, 128.0, 130.0, 139.2, 160.0, 160.2, and 175.8; HRMS Calcd. for \([C_{21}H_{21}NO_9]^+\): 432.1294. Found 432.1292.

4.1.9 Rh(II)-Catalyzed Dipolar Cycloadducts 24a and 25a—To a solution of 0.1 g (0.32 mmol) of \(\alpha\)-diazo hydroindolinone 20a in 10 mL of benzene was added 0.2 mL (1.6 mmol) of dimethylacetylene dicarboxylate and a catalytic amount of Rh\(_2\)(OAc)\(_4\). The mixture was heated at reflux for 1 h, concentrated under reduced pressure and subjected to flash silica gel
of MHz, CDCl$_3$ (400 MHz, CDCl$_3$). To a solution of 0.07 g (0.2 mmol) of diazo hydroindolinone 20a in 15 mL of benzene was added 0.11 g (0.66 mmol) of N-phenylmaleimide and a catalytic amount of Rh$_2$(OAc)$_4$. The mixture was heated at reflux for 2 h, concentrated under reduced pressure and subjected to flash silica gel chromatography to give a mixture of diastereoisomeric cycloadducts 26a (0.06 g, 57%) and 26b (0.04 g, 38%); isomer 26a: IR (neat) 2986, 2940, 2835, 1756, 1722, 1607, 1484, and 1378 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.41 (t, 3H, $J = 7.1$ Hz), 2.11 (s, 3H), 3.20 (s, 3H), 4.18 (d, 1H, $J = 8.6$ Hz), 4.28 (d, 1H, $J = 8.6$ Hz), 4.47 (q, 2H, $J = 7.3$ Hz), 7.10 (d, 2H, $J = 7.0$ Hz), and 7.24–7.49 (m, 7H); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.3, 23.4, 48.7, 52.3, 54.0, 63.6, 79.6, 91.2, 105.8, 114.0, 125.7, 126.2, 126.7, 129.0, 129.5, 131.3, 133.2, 136.3, 163.4, 163.5, 169.3, and 169.7. Isomer 26b: IR (neat) 2985, 2941, 1762, 1722, 1598, 1484, and 1214 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.41 (t, 3H, $J = 7.1$ Hz), 2.06 (s, 3H), 3.45 (s, 3H), 3.90 (d, 1H, $J = 6.7$ Hz), 4.03 (d, 1H, $J = 6.7$ Hz), 4.45 (q, 2H, $J = 7.0$ Hz), and 7.25–7.52 (m, 9H); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.3, 27.4, 47.9, 51.9, 55.5, 63.2, 82.1, 88.0, 106.5, 114.6, 124.5, 125.8, 126.7, 129.5, 130.2, 131.5, 134.2, 137.7, 161.4, 169.0, 170.8, and 171.0.

4.1.11 Rh(II)-Catalyzed Dipolar Cycloadduct 28—to a solution of 0.1 g (0.3 mmol) of diazo hydroindolinone 20a in 15 mL of benzene was added 0.06 g (57%) and 0.04 g (38%) of benzaldehyde and a catalytic amount of Rh$_2$(OAc)$_4$. The mixture was heated at reflux for 1 h, concentrated under reduced pressure and subjected to flash silica gel chromatography to give a clear oil; IR (neat) 2985, 2677, 2565, 2142, 1770, 1726, 1689, and 1454 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.32 (t, 3H, $J = 7.0$ Hz), 1.63 (s, 3H), 3.09 (s, 3H), 4.26–4.32 (m, 2H), 7.37 (d, 1H, $J = 7.6$ Hz), 7.47–7.51 (m, 3H), 7.61–7.67 (m, 2H), and 8.13 (d, 4H, $J = 7.3$ Hz); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.2, 24.7, 53.4, 62.0, 79.9, 114.3, 123.8, 125.3, 127.9, 128.4, 129.3, 129.9, 130.1, 133.7, 139.1, 160.0, 160.1, 172.1, and 175.7; HRMS Calcd. for [C$_{22}$H$_{21}$NO$_6$ + H$^+$]: 396.1447. Found 396.1445.

4.1.12 3-(tert-Butyl-dimethyl-silyloxy)-3-methyl-1,2-dihydro-indol-2-one—to a solution of 0.2 g (1.2 mmol) of 3-hydroxy-3-methyl-1,3-dihydro-indol-2-one$^{38}$ in 10 mL of CH$_2$Cl$_2$ at 0 °C was added 1.0 mL (7.0 mmol) of triethylamine and 0.7 mL (3.0 mmol) of tert-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf). After stirring for 15 min at 0 °C, the reaction mixture was allowed to warm to rt and was stirred for an additional 2 h. The mixture was extracted with CH$_2$Cl$_2$ and the combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The crude residue was then taken up in 2 mL of THF, followed by 2 mL of acetic acid and 2 mL of water. After heating at reflux for 3 h, the mixture was warmed to rt and was extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.25 g (74%) of the titled compound as an off-white solid; mp 144–146 °C; IR (neat) 3168, 2927, 2856, 1733, 1691, 1622, and 1472 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 0.21 (s, 3H), –0.03 (s, 3H), 0.88 (s, 9H), 1.57 (s, 3H), 6.88 (d, 1H, $J = 7.9$ Hz), 7.06 (dt, 1H, $J = 7.6$ and 1.0 Hz), 7.25 (dt, 1H, $J = 7.9$ and 1.0 Hz), 7.32 (d, 1H, $J = 7.6$ Hz), and 8.32 (brs, 1H); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ –3.8, –3.4, 18.3, 25.9, 26.8, 75.8, 110.3, 123.0, 124.2, 129.4, 133.4, 139.6, and 180.1.

4.1.13 3-[3-(tert-Butyl-dimethyl-silyloxy)-3-methyl-2-oxo-2,3-dihydroindol-1-yl]-2-diazo-3-oxo-propionic Acid Ethyl Ester (20b)—To a solution of 0.24 g (0.87 mmol) of the above compound in 10 mL of THF at 0 °C was added to 0.07 g (1.7 mmol) of

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NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.3 g (1.7 mmol) of ethyl 2-
 diazomalonyl chloride\(^2^9\) was added and the solution was stirred for 3 h. The mixture was then
quenched with water and extracted with EtOAc. The combined organic layers were washed
with water, brine, and dried over Na\(_2\)SO\(_4\). After removal of the solvent under reduced pressure,
the residue was subjected to flash silica gel chromatography to give 0.31 g (86%) of \(20b\) as a
yellow oil; IR (neat) 2956, 2929, 2857, 2140, 1773, 1732, 1667, 1609, and 1467 cm\(^{-1}\); \(^1\)H-
NMR (400 MHz, CDCl\(_3\)) \(\delta = 0.17\) (s, 3H), \(-0.06\) (s, 3H), 0.88 (s, 9H), 1.31 (t, 3H, \(J = 7.1\) Hz),
1.63 (s, 3H), 4.26–4.31 (m, 2H), 7.20 (dt, 1H, \(J = 7.6\) and 1.0 Hz), 7.32–7.39 (m, 2H), and 7.62
(d, 1H, \(J = 7.9\) Hz); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta = -3.6, -3.2, 14.5, 18.3, 25.8, 27.7, 62.1,\)
76.0, 114.5, 129.9, 125.2, 124.7, 132.4, 138.1, 140.3, 160.5, 160.6, and 177.3.

\subsection{4.1.14 Rh(II)-Catalyzed Dipolar Cycloaducts 24b and 25b—} To a solution containing
0.085 g (0.2 mmol) of \(20b\) in 10 mL of benzene was added 0.06 mL (0.6 mmol) of methyl
propiolate and a catalytic amount of Rh\(_2\)(OAc)_4. The mixture was heated at reflux for 1 h,
concentrated under reduced pressure and subjected to flash silica gel chromatography to give
0.29 g (86%) of \(25b\) as a yellow solid; mp 71–73 °C; IR (neat) 3263, 2955, 2932, 2897, 2858,
2271, 1730, 1618, 1609, and 1467 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.6\) and \(0.9\) Hz), 7.20 (dt, 1H,
\(J = 7.6\) and 1.0 Hz), 7.32–7.39 (m, 2H), and 7.62 (d, 1H, \(J = 7.9\) Hz); \(^{13}\)C-NMR (100 MHz,
CDCl\(_3\)) \(\delta = -3.9, -3.1, -2.8, 14.0, 14.2, 18.3, 25.7, 25.8, 27.6, 28.2, 51.2,
52.3, 61.2, 61.5, 73.1, 74.1, 110.0, 115.9, 120.2, 124.0, 124.5, 125.3, 125.8, 126.9, 127.0,
127.4, 128.1, 128.8, 129.9, 138.8, 140.3, 141.5, 142.6, 157.7, 158.1, 160.5, 161.8, 162.7,
and 164.6.

\subsection{4.1.15 3-But-3-enyl-3-hydroxy-1,3-dihydro-indol-2-one (29)—} Magnesium turnings
(30)—3-But-3-enyl-3-(tert-butyldimethylsilyloxy)-1,3-dihydro-indol-2-one (30)—To a solution of 0.15 g (0.7 mmol) of the above alcohol \(29\) in 10 mL of CH\(_2\)Cl\(_2\) at 0°C
C was added 0.6 mL (4.2 mmol) of triethylamine and 0.4 mL (1.8 mmol) of tert-
butyldimethylsilyl trifluoromethanesulfonate (TBSOTf). After stirring for 15 min at 0 °C, the
reaction mixture was allowed to warm to rt and was stirred for an additional 2 h. The mixture
was extracted with CH\(_2\)Cl\(_2\) and the combined organic layers were washed with brine, dried
over Na\(_2\)SO\(_4\), and concentrated under reduced pressure. The crude residue was then taken up
in 1 mL of THF, followed by 1 mL of acetic acid and 1 mL of water. After heating at reflux
for 3 h, the mixture was warmed to rt and was extracted with EtOAc. The combined organic

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layers were washed with water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.2 g (89%) of **30** as a pale yellow oil; IR (neat) 3250, 2955, 2929, 2857, 1725, 1621, 1472 and 1189 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ = 0.24 (s, 3H), $\delta$ = 0.12 (s, 3H), 0.89 (s, 9H), 1.32 (t, 3H, $J$ = 7.2 Hz), 1.97–2.04 (m, 2H), 3.49–4.98 (m, 2H), 5.52–5.79 (m, 1H), 6.86 (d, 1H, $J$ = 7.9 Hz), 7.06 (dt, 1H, $J$ = 7.6 and 1.0 Hz), 7.24–7.31 (m, 2H), and 8.00 (brs, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ = –3.9, –3.4, 18.4, 25.9, 27.3, 39.4, 78.0, 110.1, 114.9, 122.9, 124.9, 129.5, 131.9, 138.0, 140.0, and 179.9.

4.1.17 3-[3-But-3-enyl-3-(tert-butyl-dimethylsilyloxy)-2-oxo-2,3-dihydroindol-1-yl]-2-diazoo-3-oxo-propionic Acid Ethyl Ester (**31**)—To a solution of 0.36 g (1.1 mmol) of the above oxindole **30** in 10 mL of THF at 0 °C was added 0.99 g (2.2 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.4 g (2.2 mmol) of ethyl 2-diazomalonyl chloride$^{29}$ was added and the solution was stirred 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.3 g (57%) of **31** as a pale yellow oil; IR (neat) 3079, 2930, 2857, 2140, 1771, 1666, 1466 and 1350 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ = 0.22 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 1.32 (t, 3H, $J$ = 7.2 Hz), 1.97–2.04 (m, 2H), 2.12–2.28 (m, 2H), 4.25–4.34 (m, 2H), 4.92–5.02 (m, 2H), 5.72–5.84 (m, 1H), 7.21 (t, 3H, $J$ = 7.5 Hz), 7.33–7.38 (m, 2H), and 7.63 (d, 1H, $J$ = 7.6 Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ = 3.8, –3.2, 14.5, 18.4, 25.9, 27.9, 40.2, 62.1, 78.2, 114.7, 115.1, 124.5, 125.1, 129.8, 131.2, 138.0, 138.7, 160.2, and 177.1.

4.1.18 Rh(II)-Catalyzed Dipolar Cycloadduct **32**—To a solution of 0.26 g (0.6 mmol) of diazo hydroindolinone **31** in 15 mL of benzene was added a catalytic amount of Rh$_2$(OAc)$_4$ and the mixture was heated at reflux for 2 h. The reaction mixture was concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.18 g (70%) of **32** as a clear oil; IR (neat) 3254, 2955, 2939, 2857, 1716, 1623, 1472, and 1207 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ = 7.3 and 1.3 Hz), 7.36–7.41 (m, 2H), 3.65 (s, 1H), 4.88–4.96 (m, 2H), 5.62–5.72 (m, 1H), 6.89 (d, 1H, $J$ = 7.6 Hz), 7.07 (dt, 1H, $J$ = 7.6 and 0.9 Hz), 7.24 (dt, 1H, $J$ = 7.6 and 1.3 Hz), 7.35 (d, 1H, $J$ = 7.3 Hz), and 8.81 (brs, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ = 3.8, 13.4, 38.0, 77.3, 110.7, 115.3, 123.3, 124.4, 129.8, 130.8, 138.1, 140.7, and 181.3.
4.1.20 3-(tert-Butyl-dimethylsilyloxy)-3-pent-4-enyl-1,3-dihydro-indol-2-one (34)—To a solution containing 0.6 g (2.8 mmol) of the above alcohol 33 in 10 mL of 
CH$_2$Cl$_2$ at 0 °C was added 2.3 mL (16.6 mmol) of triethylamine and 1.6 mL (6.9 mmol) of tert-butyldimethylsilyl trifluoromethanesulphonate (TBSOTf). After stirring for 15 min, the reaction mixture was warmed to rt and was stirred for an additional 2 h. The mixture was then 
extracted with CH$_2$Cl$_2$ and the combined organic layers were washed with brine, dried over 
Na$_2$SO$_4$, and concentrated under reduced pressure. The crude residue was then taken up in 2 
ml of THF, followed by 2 mL of acetic acid and 2 mL of water. After heating at reflux for 3 
h, the reaction mixture was cooled to rt and extracted with EtOAc. The combined organic layers 
were washed with water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under 
reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.85 g 
(92%) of 34 as a yellow oil; IR (neat) 2955, 2930, 2139, 1771, 1732, 1664 and 1465 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 0.25 (s, 3H, $-CH_3$), 0.75 (s, 3H, $-CH_3$), 0.88 (s, 9H, $-CH_2-CH_3$), 1.25–1.48 (m, 
2H), 1.87–1.93 (m, 2H), 1.99–2.04 (m, 2H), 4.90–4.97 (m, 2H), 5.67–5.78 (m, 1H), 6.86 (d, 
1H, $J = 7.9$ Hz), 7.05 (dt, 1H, $J = 7.6$ and 0.6 Hz), 7.22–7.30 (m, 2H), and 8.31 (brs, 
1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 3.9, −3.4, 18.4, 22.2, 25.9, 33.9, 39.8, 78.3, 110.2, 115.0, 
122.8, 124.9, 129.4, 131.3, 138.6, 140.1, and 180.2.

4.1.21 3-[3-(tert-Butyl-dimethylsilyloxy)-2-oxo-3-pent-4-enyl-2,3-dihydro-
indol-1-yl]-2-diazo-3-oxo-propionic Acid Ethyl Ester (35)—To a solution containing 0.6 g (2.8 mmol) of the above oxindole 34 in 10 mL of THF at 0 °C was added to 0.03 g (0.8 mmol) 
of NaH (60% dispersion in mineral oil). After stirring for 30 min, 1.7 g (10 mmol) of ethyl 2-
diazomalonyl chloride$^{29}$ was added and the solution was stirred 3 h. The mixture was then 
quenched with water and extracted with EtOAc. The combined organic layers were washed with 
water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, 
the residue was subjected to flash silica gel chromatography to give 0.19 g (60%) of 
cycloadduct as a pale yellow oil; IR (neat) 3249, 2953, 2929, 1725, 1621, 1471, 1250 and 1121 
$cm^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 0.25 (s, 3H, $-CH_3$), 0.81 (s, 9H, $-CH_2-CH_3$), 1.24 (t, 3H, $J = 7.2$ Hz), 1.35–1.53 
(m, 2H), 1.82–1.86 (m, 2H), 1.94–2.00 (m, 2H), 4.19–4.25 (m, 2H), 4.84–4.93 (m, 2H), 5.62– 
5.71 (m, 1H), 7.12 (t, 1H, $J = 7.6$ Hz), 7.25–7.29 (m, 2H), and 7.54 (d, 1H, $J = 7.6$ Hz); $^{13}$C-
NMR (100 MHz, CDCl$_3$) $\delta$ 3.8, −3.2, 14.5, 18.4, 21.7, 21.7, 25.9, 29.9, 33.8, 40.5, 60.6, 62.1, 
78.4, 114.7, 115.0, 124.5, 125.0, 129.7, 131.3, 138.5, 160.2, and 177.0.

4.1.22 Rh(II)-Catalyzed Dipolar Cycloadduct 36—To a solution containing 0.19 g (0.4 
mmol) of diazo hydroindolinone 35 in 15 mL of benzene was added a catalytic amount of 
Rh$_2$(OAc)$_4$ and the mixture was heated at reflux. After heating for 2 h, the reaction mixture 
was concentrated under reduced pressure and subjected to flash silica gel chromatography to 
give 0.13 g (69%) of cycloadduct 36 as a pale yellow oil; IR (neat) 2935, 2857, 1758, 1733, 
1607, 1480, and 1252 $cm^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ −0.35 (s, 3H, $-CH_3$), −0.24 (s, 3H, $-CH_3$), 
0.80 (s, 9H), 1.22–1.28 (m, 2H), 1.34 (t, 3H, $J = 7.2$ Hz), 1.79–1.87 (m, 2H), 1.97–2.55 (m, 3H), 
2.38 (dt, 1H, $J = 14.0$ and 9.5 Hz), 2.56 (dd, 1H, $J = 14.0$ and 9.5 Hz), 3.40–4.40 (m, 2H), 7.14 
(t, 1H, $J = 7.3$ Hz), and 7.34–7.41 (m, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ −3.6, −3.5, 14.2, 
18.5, 21.8, 25.9, 28.0, 33.6, 36.0, 43.8, 62.3, 75.3, 91.2, 102.4, 114.5, 124.8, 131.0, 135.3, 136.4, 
164.0, and 165.1; HRMS Calcd. for [C$_2$H$_3$NO$_3$Si + H$^+$]: 444.2201. Found 444.2196.

4.1.23 3-Allyloxy-3-methyl-1,3-dihydro-indol-2-one—To a solution of 0.15 g (0.9 
mmol) of 3-hydroxy-3-methyl-1,3-dihydro-indol-2-one$^{38}$ in 10 mL of toluene was added 0.3 
ml (4.6 mmol) of allyl alcohol and 0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction 
mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. 
The combined organic extracts were washed with a sodium bicarbonate solution, H$_2$O, brine, 
and dried over Na$_2$SO$_4$. Concentration under reduced pressure followed by flash silica gel 
chromatography gave 0.12 g (65%) of the titled compound as a clear oil; IR (neat) 3251, 2981,
2928, 2862, 1725, 1621, and 1472 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.63 (s, 3H), 3.61–3.66 (m, 1H), 3.75–3.80 (m, 1H), 5.11 (dd, 1H, $J = 10.5$ and 1.6 Hz), 5.20 (dd, 1H, $J = 17.2$ and 1.6 Hz), 5.82–5.92 (m, 1H), 6.98 (d, 1H, $J = 7.6$ Hz), 7.10 (dt, 1H, $J = 7.6$ and 1.0 Hz), 7.29 (dt, 1H, $J = 7.6$ and 1.3 Hz), 7.34 (d, 1H, $J = 7.6$ Hz), and 9.45 (brs, 1H); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 24.4, 67.2, 79.8, 110.9, 117.7, 123.3, 124.3, 129.5, 130.0, 134.2, 140.8, and 179.9.

4.1.24 3-(3-Allyloxy-3-methyl-2-oxo-2,3-dihydro-indol-1-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (37)—To a solution of 0.12 g (0.6 mmol) of the above lactam in 10 mL of THF at 0 °C was added to 0.05 g (1.2 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.2 g (1.2 mmol) of ethyl 2-diazomalonyl chloride$^{29}$ was added and the solution was stirred for 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.15 g (75%) of 37 as a yellow oil; IR (neat) 2984, 2928, 2856, 2145, 1771, 1732, 1667, 1608, and 1466 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.31 (t, 3H, $J = 7.3$ Hz), 1.65 (s, 3H), 3.62–3.67 (m, 1H), 3.72–3.77 (m, 1H), 4.24–4.32 (m, 2H), 5.11 (d, 1H, $J = 10.5$ Hz), 5.18 (d, 1H, $J = 17.2$ Hz), 5.78–5.87 (m, 1H), 7.24 (t, 1H, $J = 7.5$ Hz), 7.36–7.40 (m, 2H), and 7.65 (d, 1H, $J = 7.8$ Hz); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.5, 25.3, 62.2, 67.5, 79.6, 114.6, 117.9, 124.0, 125.5, 128.6, 130.2, 134.0, 139.2, 160.3, 160.4, and 176.1.

4.1.25 Rh(II)-Catalyzed Dipolar Cycloadduct 40—To a solution containing 0.15 g (0.44 mmol) of 37 in 10 mL of benzene was added a catalytic amount of Rh$_2$(OAc)$_4$ and the mixture was heated at reflux for 2 h. The reaction mixture was then concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.1 g (72%) of cycloadduct 40 as a clear oil; IR (neat) 2980, 2870, 1754, 1608 and 1471 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.39 (t, 3H, $J = 7.3$ Hz), 1.65 (s, 3H), 2.29 (dd, 1H, $J = 12.7$ and 6.0 Hz), 2.53 (dd, 1H, $J = 12.7$ and 8.3 Hz), 2.66–2.74 (m, 1H), 3.66 (dd, 1H, $J = 11.4$ and 8.6 Hz), 4.12 (dd, 1H, $J = 8.3$ and 7.0 Hz), 4.39–4.45 (m, 2H), 7.19 (dt, 1H, $J = 7.3$ and 1.6 Hz), 7.35–7.41 (m, 2H), and 7.46 (d, 1H, $J = 7.6$ Hz); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 14.1, 18.9, 32.0, 50.7, 62.6, 70.1, 80.2, 96.7, 111.3, 114.3, 125.6, 130.3, 133.6, 137.0, 161.9, and 164.3; HRMS Calcd. for [C$_{17}$H$_{17}$NO$_5$ + H$^+$]: 316.1185. Found 316.1183.

4.1.26 3-But-3-enyloxy-3-methyl-1,3-dihydro-indol-2-one—To a solution containing 0.15 g (0.9 mmol) of 3-hydroxy-3-methyl-1,3-dihydro-indol-2-one$^{38}$ in 10 mL of toluene was added 0.4 mL (4.5 mmol) of 3-buten-1-ol and 0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. The combined organic layers were washed with a sodium bicarbonate solution, water, brine, and dried over Na$_2$SO$_4$. Concentration under reduced pressure followed by flash silica gel chromatography gave 0.13 g (67%) of the titled compound as a red oil; IR (neat) 3250, 3081, 2980, 2928, 2870, 1725, 1621, and 1472 cm$^{-1}$; 1H-NMR (400 MHz, CDCl$_3$) $\delta$ 1.60 (s, 3H), 2.28–2.34 (m, 2H), 3.10 (dt, 1H, $J = 8.3$ and 7.0 Hz), 3.28 (dt, 1H, $J = 8.3$ and 7.0 Hz), 4.98–5.06 (m, 2H), 5.68–5.79 (m, 1H), 6.97 (d, 1H, $J = 7.6$ Hz), 7.10 (t, 1H, $J = 7.3$ Hz), 7.28–7.32 (m, 2H), and 9.22 (brs, 1H); 13C-NMR (100 MHz, CDCl$_3$) $\delta$ 24.4, 34.4, 65.1, 79.8, 110.8, 116.7, 123.3, 124.3, 129.7, 129.8, 134.9, 140.7, and 179.9.

4.1.27 3-(3-But-3-enyloxy-3-methyl-2-oxo-2,3-dihydro-indol-1-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (38)—To a solution of 0.13 g (0.6 mmol) of the above lactam in 10 mL THF at 0 °C was added to 0.05 g (1.2 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.2 g (1.2 mmol) sample of ethyl 2-diazomalonyl chloride$^{29}$ was added and the solution was stirred for 3 h. The mixture was then quenched with water and
extracted with EtOAc. The combined organic layers were washed with water, brine, and dried
over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was subjected
to flash silica gel chromatography to give 0.18 g (85%) of 41 as an orange oil; IR (neat) 3250, 3079, 2979, 2145, 1725, 1105, 1030, 1005, 968, 802, 756, 692, 676, 630, 593, 554, 510, 470, 430, and 350 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.38 (t, 3H, J = 7.6 Hz), 7.28 (t, 1H, J = 7.6 Hz), 7.10 (t, 1H, J = 7.6 Hz), 7.06–7.08 (m, 1H), 7.02–7.04 (m, 1H), 6.94 (dd, 2H, J = 8.3 and 7.0 Hz), 3.65 (dd, 1H, J = 11.1 and 4.4 Hz), 3.95–4.00 (m, 1H), 4.37–4.43 (m, 2H), 7.15 (dt, 1H, J = 7.3 and 1.3 Hz), and 7.30–7.39 (m, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 14.2, 22.1, 27.9, 34.7, 39.4, 61.9, 62.4, 78.4, 90.7, 100.5, 113.9, 124.3, 125.2, 130.1, 134.6, 136.8, 163.6, and 164.8; HRMS Calcd. for [C₁₈H₁₉NO₅ + H⁺]: 330.1341. Found 330.1340.

4.1.29 3-Methyl-3-pent-4-enyloxy-1,3-dihydro-indol-2-one—To a solution of 0.2 g (1.2 mmol) of 3-hydroxy-3-methyl-1,3-dihydro-indol-2-one38 in 10 mL of THF at 0 °C was added to a solution of 0.06 g (1.4 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.2 g (1.4 mmol) of ethyl 2-diazo-3-methyl-3-hydroxypropanoate was added to the mixture and the solution was stirred at rt for 3 h. The mixture was then quenched in a sodium bicarbonate solution, and 1.3 mL (12.0 mmol) of 4-penten-1-ol and 0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na₂SO₄. Concentration under reduced pressure followed by flash silica gel chromatography gave 0.16 g (57%) of the titled compound as a pale yellow oil; IR (neat) 3250, 3079, 2979, 2145, 1725, 1105, 1030, 1005, 968, 802, 756, 692, 676, 630, 593, 554, 510, 470, 430, and 350 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.31 (t, 3H, J = 7.6 Hz), 7.26–7.32 (m, 2H), and 8.46 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 14.6, 25.4, 29.3, 30.3, 62.2, 65.6, 79.7, 114.6, 115.0, 123.9, 125.5, 129.0, 130.0, 138.3, 139.2, 160.1, 160.2, and 178.2.

4.1.30 2-Diazo-3-(3-methyl-2-oxo-3-pent-4-enyloxy-2,3-dihydro-indol-1-yl)-3-oxo-propionic Acid Ethyl Ester (39)—To a solution of 0.16 g (0.7 mmol) of the above compound in 10 mL of THF at 0 °C was added to 0.06 g (1.4 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.2 g (1.4 mmol) of ethyl 2-diazomalonyl chloride29 was added and the solution was stirred at rt for 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.19 g (72%) of 39 as a pale yellow oil; IR (neat) 2983, 2935, 2876, 1756, 1607, and 1477 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.31 (t, 3H, J = 7.3 Hz), 1.63 (s, 3H), 2.26–2.31 (m, 2H), 3.11 (dt, 1H, J = 8.3 and 7.0 Hz), 3.24 (dt, 1H, J = 8.3 and 7.0 Hz), 4.25–4.31 (m, 2H), 4.95–5.06 (m, 2H), 5.68–5.79 (m, 1H), 7.24 (t, 1H, J = 7.5 Hz), 7.35–7.39 (m, 2H), and 7.65 (d, 1H, J = 7.9 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 14.5, 25.3, 29.3, 30.3, 62.2, 65.5, 79.8, 114.6, 116.8, 124.0, 125.5, 128.9, 130.1, 134.8, 139.2, 160.3, 160.4, and 176.2.

4.1.31 Rh(II)-Catalyzed Dipolar Cycloadduct 42—To a solution containing 0.12 g (0.34 mmol) of 38 in 10 mL of benzene was added a catalytic amount of Rh₂(OAc)₄ and the mixture was heated at reflux for 2 h. The reaction mixture was then concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.09 g (82%) of cycloadduct 42 as a clear oil; IR (neat) 2928, 2935, 2876, 1756, 1607, and 1477 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.38 (t, 3H, J = 7.1 Hz), 1.62 (s, 3H), 1.62–1.71 (m, 1H), 1.88–1.95 (m, 1H), 2.00 (dd, 1H, J = 12.7 and 4.8 Hz), 2.32–2.39 (m, 1H), 2.59 (dd, 1H, J = 12.7 and 8.3 Hz), 3.65 (dt, 1H, J = 11.1 and 4.4 Hz), 3.95–4.00 (m, 1H), 4.37–4.43 (m, 2H), 7.15 (dt, 1H, J = 7.3 and 1.3 Hz), and 7.30–7.39 (m, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 12.7, 22.1, 27.9, 34.7, 39.4, 61.9, 62.4, 78.4, 90.7, 100.5, 113.9, 124.3, 125.2, 130.1, 134.6, 136.8, 163.6, and 164.8; HRMS Calcd. for [C₁₈H₁₉NO₅ + H⁺]: 330.1341. Found 330.1340.
Rh₂(OAc)₄ and the mixture was heated at reflux for 2 h. The reaction mixture was then concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.13 g (80%) of cycloadduct 42 as a clear oil; IR (neat) 3482, 2986, 2946, 1758, 1607, 1486, and 1374 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.36 (t, 3H, J = 7.1 Hz), 1.79 (s, 3H), 1.76–1.87 (m, 5H), 2.70–2.78 (m, 2H), 3.97–3.99 (m, 2H), 4.33–4.41 (m, 2H), 7.16 (t, 1H, J = 7.5 Hz), 7.31–7.35 (m, 2H), and 7.42 (d, 1H, J = 7.6 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 14.4, 20.4, 31.0, 33.6, 36.7, 46.2, 62.5, 66.4, 83.5, 88.4, 109.3, 114.0, 123.4, 125.4, 136.3, 137.8, 165.2, and 168.1; HRMS Calcd. for [C₁₉H₂₁NO₅ + H⁺]: 344.1493. Found 344.1489.

4.1.32 3-But-3-enyloxy-3-pent-4-enyl-1,3-dihydro-indol-2-one—To a solution of 0.16 g (0.7 mmol) of alcohol 33 in 10 mL of toluene was added 0.3 mL (3.5 mmol) of 3-butene-1-ol and 0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. The combined organic extracts were washed with a sodium bicarbonate solution, water, brine, and dried over Na₂SO₄. Concentration under reduced pressure followed by flash silica gel chromatography gave 0.11 g (55%) of the titled compound as a yellow solid; mp 78–79 °C; IR (neat) 3250, 2925, 2869, 1722, 1621, and 1471 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.21–1.40 (m, 2H), 1.95–2.03 (m, 4H), 2.27–2.32 (m, 2H), 3.10 (dt, 1H, J = 8.6 and 7.0 Hz), 3.27 (dt, 1H, J = 8.6 and 7.0 Hz), 4.89–5.06 (m, 4H), 5.66–5.77 (m, 2H), 6.92 (d, 1H, J = 8.1 Hz), 7.10 (t, 1H, J = 6.8 Hz), 7.26–7.30 (m, 2H), and 8.68 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.2, 33.9, 34.4, 37.6, 64.9, 82.9, 110.5, 115.2, 116.7, 123.2, 124.8, 128.5, 129.8, 135.0, 138.3, 141.2, and 179.2.

4.1.33 3-(3-But-3-enyloxy-2-oxo-3-pent-4-enyl-2,3-dihydro-indol-1-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (43)—To a solution of 0.11 g (0.4 mmol) of the above compound in 10 mL of THF at 0 °C was added to 0.03 g (0.8 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, 0.14 g (0.8 mmol) of ethyl 2-diazomalonyl oxo-propionic Acid Ethyl Ester (43) in 10 mL of benzene was added to a catalytic amount of Rh(II)-Catalyzed Dipolar Cycloadducts 46 and 47—To a solution containing 0.1 g (0.24 mmol) of 43 in 10 mL of benzene was added a catalytic amount of Rh₂(OAc)₄ and the mixture was heated at reflux for 2 h. The reaction mixture was then concentrated under reduced pressure and subjected to flash silica gel chromatography to give a mixture of cycloadducts. The major isomer 46 (55%) was obtained as a clear oil; IR (neat) 3076, 2951, 2862, 1732, 1640, 1607, and 1480 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.39 (t, 3H, J = 7.3 Hz), 1.47–1.67 (m, 3H), 1.83–1.92 (m, 2H), 1.96–2.04 (m, 4H), 2.22–2.29 (m, 1H), 2.55 (dd, 1H, J = 12.4 and 8.3 Hz), 3.55 (dt, 1H, J = 11.4 and 2.9 Hz), 3.93–3.97 (m, 1H), 4.37–4.43 (m, 2H), 4.92 (d, 1H, J = 10.2 Hz), 4.97 (dd, 1H, J = 17.2 and 1.9 Hz), 5.72–5.78 (m, 1H), 7.15 (dt, 1H, J = 7.6 and 1.3 Hz), and 7.31–7.40 (m, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 14.4, 22.1, 28.8, 34.0, 35.1, 35.8, 40.9, 62.6, 62.8, 80.6, 91.3, 100.0, 114.2, 114.9, 125.0, 125.6, 130.2, 134.4, 135.5, 138.7, 163.0, and 165.1; HRMS Calcd. for [C₂₂H₂₅NO₅ + H⁺]: 384.1806. Found 384.1803.
The minor isomer (11%) 47 was obtained as a clear oil; IR (neat) 3075, 2939, 2868, 1756, 1732, 1606, and 1480 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.25–1.28 (m, 2H), 1.37 (t, 3H, \(J = 7.0\) Hz), 1.82–1.92 (m, 2H), 1.95–2.05 (m, 3H), 2.16–2.21 (m, 2H), 2.42–2.47 (m, 1H), 2.54–2.59 (m, 1H), 3.01 (dt, 1H, \(J = 8.6\) and 7.0 Hz), 3.55 (dt, 1H, \(J = 8.6\) and 7.0 Hz), 4.35–4.43 (m, 2H), 4.92–5.00 (m, 2H), 5.63–5.73 (m, 1H), 7.20 (dt, 1H, \(J = 7.3\) and 1.0 Hz), and 7.37–7.48 (m, 3H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.4, 22.0, 28.1, 31.4, 34.7, 35.6, 44.8, 62.5, 63.7, 91.4, 101.8, 114.3, 116.3, 125.0, 125.3, 131.2, 133.3, 135.4, 135.8, and 165.0.

4.1.35 3-But-3-enyl-3-but-3-enyloxy-1,3-dihydro-indol-2-one—To a solution of 0.16 g (0.8 mmol) of alcohol 29 in 10 mL of toluene was added 0.3 mL (4.0 mmol) of 3-buten-1-ol and 0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. The combined organic extracts were washed with a sodium bicarbonate solution, water, brine, and dried over Na\(_2\)SO\(_4\). Concentration under reduced pressure followed by flash silica chromatography gave 0.12 g (57%) of the titled compound as a clear oil; IR (neat) 3256, 3079, 2923, 1721, 1621, and 1471 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.95–2.08 (m, 4H), 2.28–2.33 (m, 2H), 3.11 (dt, 1H, \(J = 8.3\) and 7.0 Hz), 3.29 (dt, 1H, \(J = 8.3\) and 7.0 Hz), 4.88 (d, 1H, \(J = 10.2\) Hz), 4.94 (d, 1H, \(J = 17.2\) Hz), 4.99 (d, 1H, \(J = 10.2\) Hz), 5.03 (dd, 1H, \(J = 17.2\) and 1.6 Hz), 5.69–5.78 (m, 2H), 6.95 (d, 1H, \(J = 7.8\) Hz), 7.10 (t, 1H, \(J = 7.5\) Hz), 7.28–7.31 (m, 2H), and 9.10 (brs, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 27.2, 34.4, 37.1, 65.0, 82.7, 110.7, 115.0, 116.7, 123.2, 124.8, 128.3, 129.9, 135.0, 137.6, 141.3, and 179.3.

4.1.36 3-(3-But-3-enyl-3-but-3-enyloxy-2-oxo-2,3-dihydro-indol-1-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (44)—To a solution of 0.09 g (0.35 mmol) of the above compound in 10 mL of THF at 0 °C was added to 0.03 g (0.7 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.12 g (0.7 mmol) sample of ethyl 2-diazomalonyl compound in 10 mL of THF at 0 °C was added to 0.03 g (0.7 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.12 g (0.7 mmol) sample of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.12 g (0.7 mmol) sample of ethyl 2-diazomalonyl chloride was added and the solution was stirred for 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na\(_2\)SO\(_4\). After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.13 g (92%) of 44 as a yellow oil; IR (neat) 3078, 2925, 2855, 2141, 1770, 1731, 1664, and 1607 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.24–1.28 (m, 2H), 1.32 (t, 3H, \(J = 7.1\) Hz), 2.00–2.14 (m, 2H), 2.26–2.31 (m, 2H), 3.12 (dt, 1H, \(J = 8.6\) and 6.7 Hz), 3.25 (dt, 1H, \(J = 8.6\) and 6.7 Hz), 4.26–4.33 (m, 2H), 4.90 (d, 1H, \(J = 10.2\) Hz), 4.95 (d, 1H, \(J = 17.2\) Hz), 5.01 (d, 1H, \(J = 10.5\) Hz), 5.05 (d, 1H, \(J = 17.2\) Hz), 5.70–5.79 (m, 2H), 7.24 (dt, 1H, \(J = 7.6\) and 1.0), 7.34–7.41 (m, 2H), and 7.67 (d, 1H, \(J = 8.3\) Hz); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.5, 27.0, 34.4, 38.0, 62.2, 65.4, 82.4, 114.8, 115.2, 116.8, 124.5, 125.4, 127.6, 130.1, 134.9, 137.6, 139.6, 160.2, and 175.8.

4.1.37 Rh(II)-Catalyzed Dipolar Cycloadduct 48—To a solution containing 0.1 g (0.25 mmol) of 44 in 10 mL of benzene was added a catalytic amount of Rh(2)(OAc)\(_4\) and the mixture was heated at reflux for 2 h. The reaction mixture was concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.07 g (79%) of cycloadduct 48 as a clear oil; IR (neat) 3076, 2978, 2949, 2859, 1756, 1734, 1607, and 1478 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.38 (t, 3H, \(J = 7.0\) Hz), 1.59–1.66 (m, 1H), 1.82–2.29 (m, 7H), 2.55 (dd, 1H, \(J = 12.4\) and 8.3 Hz), 3.55 (dt, 1H, \(J = 11.4\) and 2.9 Hz), 3.93–3.98 (m, 1H), 4.36–4.43 (m, 2H), 4.90 (d, 1H, \(J = 10.2\) Hz), 4.98 (dd, 1H, \(J = 17.2\) and 1.6 Hz), 5.70–5.80 (m, 1H), 7.15 (t, 1H, \(J = 6.7\) Hz), and 7.32–7.40 (m, 3H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.1, 27.0, 28.6, 34.8, 35.3, 40.7, 62.3, 62.6, 80.2, 91.1, 99.7, 114.0, 114.7, 124.8, 125.4, 130.1, 134.2, 135.1, 138.0, 162.7, and 164.8.

4.1.38 3-Allyloxy-3-pent-4-yl-1,3-dihydro-indol-2-one—To a solution of 0.32 g (1.5 mmol) of alcohol 33 in 10 mL of toluene was added 0.5 mL (7.5 mmol) of allyl alcohol and

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0.03 g (0.1 mmol) of p-toluenesulfonic acid. The reaction mixture was heated at reflux for 12 h. After cooling to rt, the mixture was extracted with EtOAc. The combined organic extracts were washed with a sodium bicarbonate solution, water, brine, and dried over Na₂SO₄. Concentration under reduced pressure followed by flash silica gel chromatography gave 0.11 g (30%) of the titled compound as a yellow oil; IR (neat) 3253, 3079, 2926, 2863, 1723, 1621, and 1471 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.22–1.29 (m, 1H), 1.34–1.44 (m, 1H), 1.96–2.06 (m, 4H), 3.61–3.66 (m, 1H), 3.74–3.80 (m, 1H), 4.88–4.96 (m, 2H), 5.09 (dd, 1H, J = 10.5 and 1.3 Hz), 5.19 (dd, 1H, J = 17.2 and 1.3 Hz), 5.65–5.72 (m, 1H), 5.81–5.90 (m, 1H), 6.97 (d, 1H, J = 7.6 Hz), 7.10 (t, 1H, J = 7.9 Hz), 7.27–7.32 (m, 2H), and 9.37 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.2, 33.9, 37.6, 66.9, 83.0, 110.8, 115.2, 117.4, 123.2, 124.8, 128.2, 130.0, 134.3, 138.2, 141.4, and 179.6.

4.1.39 3-(3-Allyloxy-2-oxo-3-pent-4-enyl-2,3-dihydro-indol-1-yl)-2-diazo-3-oxo-propionic Acid Ethyl Ester (45)—To a solution of 0.07 g (0.3 mmol) of the above compound in 10 mL of THF at 0 °C was added to 0.02 g (0.6 mmol) of NaH (60% dispersion in mineral oil). After stirring for 30 min, a 0.1 g (0.6 mmol) sample of ethyl 2-diazomalonyl chloride was added and the solution was stirred for 3 h. The mixture was then quenched with water and extracted with EtOAc. The combined organic layers were washed with water, brine, and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.09 g (78%) of 45 as a yellow oil; IR (neat) 3079, 2982, 2930, 2871, 2148, 1774, 1730, 1705, 1662, and 1465 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.32 (t, 3H, J = 7.1 Hz), 1.30–1.38 (m, 1H), 1.40–1.50 (m, 1H), 1.97–2.05 (m, 4H), 3.63–3.67 (m, 1H), 3.73–3.77 (m, 1H), 4.26–4.36 (m, 2H), 4.90–4.98 (m, 2H), 5.11 (dd, 1H, J = 10.5 and 1.6 Hz), 5.19 (dd, 1H, J = 17.5 and 1.6 Hz), 5.66–5.88 (m, 2H), 7.24 (dt, 1H, J = 7.6 and 1.0 Hz), 7.36–7.41 (m, 2H), and 7.66 (d, 1H, J = 7.9 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 14.5, 21.9, 33.8, 38.4, 63.0, 67.3, 82.6, 114.8, 115.3, 117.6, 124.5, 125.4, 127.5, 130.2, 134.1, 138.2, 139.6, 158.8, 160.2, and 175.9.

4.1.40 Rh(II)-Catalyzed Dipolar Cycloadduct 49—To a solution containing 0.09 g (0.22 mmol) of 45 in 10 mL of benzene was added a catalytic amount of Rh₂(OAc)₄ and the mixture was heated at reflux for 2 h. The reaction mixture was concentrated under reduced pressure and subjected to flash silica gel chromatography to give 0.06 g (75%) of 49 as a clear oil; IR (neat) 3075, 2980, 2944, 2869, 1757, 1608, and 1471 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.29–1.40 (m, 1H), 1.38 (t, 3H, J = 7.1 Hz), 1.61–1.69 (m, 1H), 1.95–2.06 (m, 4H), 2.25 (dd, 1H, J = 12.7 and 6.0 Hz), 2.48 (dd, 1H, J = 12.7 and 8.3 Hz), 2.63–2.71 (m, 1H), 3.65 (dd, 1H, J = 11.8 and 8.6 Hz), 4.12 (dd, 1H, J = 8.3 and 7.0 Hz), 4.38–4.43 (m, 2H), 4.93 (d, 1H, J = 10.2 Hz), 4.98 (dd, 1H, J = 17.2 and 1.9 Hz), 5.70–5.78 (m, 1H), 7.17 (dt, 1H, J = 7.6 and 1.6 Hz), and 7.33–7.42 (m, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 14.4, 22.8, 32.0, 33.3, 34.0, 51.0, 62.8, 70.9, 82.7, 97.0, 111.5, 114.5, 115.2, 125.7, 126.4, 130.5, 134.2, 136.4, 138.3, 162.3, and 164.5; HRMS Calcd. for [C₂₁H₂₃NO₅ + H⁺]: 370.1649. Found 370.1644.

Acknowledgements

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References


37. Hinman RL, Bauman CP. J Org Chem 1964;2431

Figure 2.
Scheme 1.
Scheme 2.
Scheme 3.
Scheme 4.
Scheme 5.

20a; \( R_1 = \text{Me}; R_2 = \text{OMe} \)

20b; \( R_1 = \text{Me}; R_2 = \text{OTBS} \)

21

22

\[ \text{Rh(II)} \rightarrow \]
Scheme 6.
Scheme 7.
Scheme 8.
Table 1
Bimolecular Cycloadditions of α-Diazo Amide 13 Using Various Dipolarophiles

<table>
<thead>
<tr>
<th>entry</th>
<th>dipolarophile</th>
<th>product (yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Dipolarophile 1" /></td>
<td><img src="image2" alt="Product 1" /> 16 (75%)</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Dipolarophile 2" /></td>
<td><img src="image4" alt="Product 2" /> 17 (77%)</td>
</tr>
<tr>
<td>3</td>
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</tr>
<tr>
<td>4</td>
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<td><img src="image8" alt="Product 4" /> 19 (85%)</td>
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</tbody>
</table>

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