Pergamon

Tetrahedron 56 (2000) 8063–8069

TETRAHEDRON

Intramolecular Carbenoid Insertions: the Reactions of α-Diazoketones Derived from Pyrrolyl and Indolyl Carboxylic Acids with Rhodium(II) Acetate

Mohamed Salim and Alfredo Capretta*

Institute of Molecular Catalysis, Department of Chemistry, Brock University, St. Catharines, Ontario, Canada L2S 3A1.

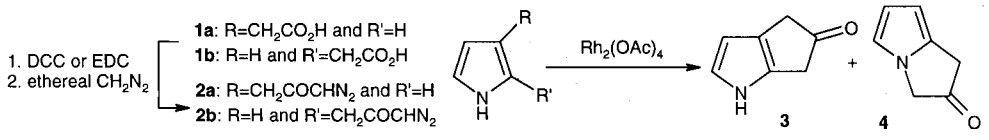
Received 14 July 2000; accepted 15 August 2000

Abstract—α-Diazoketones derived from pyrrolyl- and indolyl-carboxylic acids were prepared and their $Rh_2(OAc)_4$ catalyzed decomposition chemistry was studied. These reactions generally resulted in the alkylation of the heteroaromatic system by the ketocarbenoid and in some instances the systems underwent CH or NH insertions. Evidence that some of these reactions proceed via a cyclopropane intermediate is presented. The methodology described provides facile access to fused pyrrolyl– or indolyl–cycloalkanone systems wherein the carbonyl is beta to the heteroaromatic system. © 2000 Elsevier Science Ltd. All rights reserved.

Insertions of α-ketocarbenoids into pyrrolyl and indolyl systems have been reported previously by a number of groups.[1] The chemical outcome of these reactions is dependant on several factors but especially the nature of the substituent on the nitrogen and the catalyst employed. For example, reactions of pyrroles and *N*-alkyl pyrroles with metal-stabilized carbenoids derived from α-diazocarbonyl compounds generally result in alkylation products.[2] However, the introduction of an electron withdrawing group (an acyl moiety, for example) onto the nitrogen of the heterocycle allows for the isolation of cyclopropane containing products.[3] The nature of the carbenoid structure can also have a dramatic effect.[4] Davies, for example, has used the metal-catalyzed decomposition of vinyldiazomethanes in the presence of pyrroles for a tandem cyclopropanation/Cope rearrangement and entry to the tropane system.[5] Intramolecular reactions of α-ketocarbenoids tethered at the nitrogen of a pyrrole or indole fragment have also been reported previously by Galeazzi,[6] Jefford[7] and Müller.[8]

Our work involving the intramolecular insertion of carbenoids into furanyl, benzofuranyl, thienyl and benzothienyl moieties has shown that atypical chemistry can be induced if the carbenoid and the aromatic system are separated by a single methylene tether.[9] A natural extension of this work involves the investigation of the analogous nitrogenous heterocyclic systems and we have prepared and studied the chemistry of α-diazoketones derived from pyrrolyl- and indolyl-carboxylic acids. The systems prepared herein differ from those studied by others in that the catalyst used is rhodium(II) acetate exclusively and in that the tethered α-diazoketone is linked at either the C2 or C3 position of the heteroaromatic rather than at the nitrogen.

Preparation of the desired α-diazoketones containing pyrrole moieties, 1-diazo-3-(3-pyrrolyl)-2-propanone (**2a**, Scheme 1) and 1-diazo-3-(2-pyrrolyl)-2-propanone (**2b**), could not be achieved using the standard protocol wherein the precursor carboxylic acid, 2-(3-pyrrolyl)acetic acid (**1a**) or 2-(2-pyrrolyl)acetic acid (**1b**), is treated with either sulphonyl chloride or oxalyl chloride to generate the acid chloride and then reacted with diazomethane. Under these conditions, derivitization takes place at the pyrrole. However, use of a carbodiimide coupling agent,[10] such as DDC (1,3-dicyclohexylcarbodiimide) or

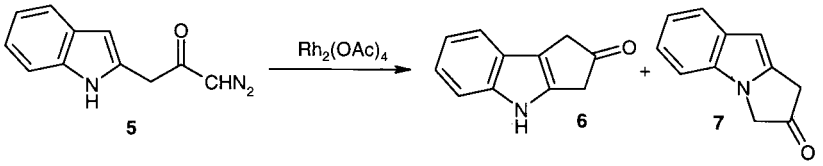


Scheme 1.

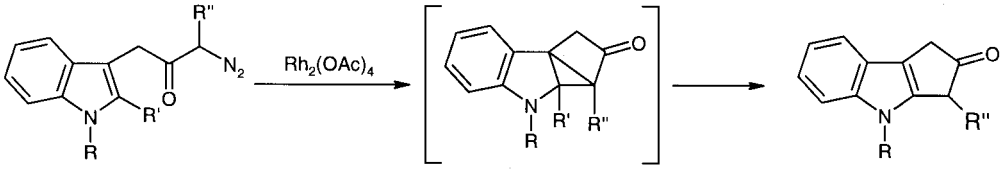
Keywords: carbenoids; pyrrole; indole; cyclopropanation.

* Corresponding author. Tel.: +1-905-688-5550 ext. 3848; fax:+1-905-688-2789; e-mail: fcaprett@chemiris.labs.brocku.ca

PII: S0040-4020(00)00725-0



Scheme 2.



8: R = H; R' = H; R'' = H
10: R = CH_3; R' = H; R'' = H
13: R = H; R' = CH_3; R'' = H
15: R = H; R' = H; R'' = CH_3

9: R = H; R' = H; R'' = H
11: R = CH_3; R' = H; R'' = H
14: R = H; R' = CH_3; R'' = H
16: R = H; R' = H; R'' = CH_3

6: R = H; R'' = H
12: R = CH_3; R'' = H
17: R = H; R'' = CH_3

Scheme 3.

EDC (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide), prevented any undesired side reactions and allowed for the preparation of the required α-diazoketones in good yield. Decomposition of **2a** in dichloromethane using rhodium(II) acetate gave 4,6-dihydrocyclopenta[*b*]pyrrol-5(1*H*)-one (**3**, in 85% yield) while decomposition of the isomeric diazoketone **2b** under the same conditions gave the bicyclic **3** (in 24% yield) and 1*H*-pyrrolizin-2(3*H*)-one (**4**, in 65% yield).

Mechanistically, one can rationalize the alkylation products, **3** for example, as having arisen from either a zwitterionic or cyclopropane intermediate. A zwitterionic route would have the electrophilic carbenoid attacking the pyrrole to give a dipolar intermediate which could rearomatize to give the alkylation product **3**. The second possibility involves the addition of the carbenoid across a π-bond of the pyrrole to give a cyclopropane intermediate which then unravels and rearomatizes to give **3**. The matter may be further complicated, however. If the cyclopropane is formed in a stepwise fashion, the cyclopropane pathway merges into the dipolar mechanism. An extension of the arguments used to explain intermolecular reactions of carbenoids and pyrroles would seem to favor the mechanism involving the zwitterionic intermediates.[1] In addition, the production of **4** marks the first example of an apparent insertion into a pyrrole N–H bond and is likely the result of nitrogen ylide formation followed by 1,2-H migration rather than a concerted, single step.

1-Diazo-3-(2-indolyl)-2-propanone (**5**, Scheme 2) behaved much like its pyrrole analog (**2b**) with $Rh_2(OAc)_4$ catalyzed decomposition leading to an alkylation product (3,4-dihydrocyclopenta[*b*]indol-2(3*H*)-one, **6**) and an NH insertion product (1*H*-pyrrolo[1,2-*a*]indol-2(3*H*)-one, **7**). In a similar fashion, decomposition of 1-diazo-3-(3-indolyl)-2-propanone **8** (Scheme 3) allowed for the production of **6**. However, when the transformation of **8**→**6** was followed via NMR spectroscopy, an intermediate cyclopropane **9** could be clearly seen. Proton assignments were made by preparing a series of indolyl diazoketones (**10**, **13** and **15**) and carrying out their $Rh_2(OAc)_4$ induced decomposition. Spectra of cyclopropanes **11**, **14**, and **16** were collected and compared with those of **9** thereby securing its structure. It is worth pointing out that this outcome is in marked contrast to the previously reported work on the α-diazoketone derived from 3-indoleacetic acid which, upon treatment with $BF_3{\cdot}Et_2O$, allowed for the preparation of 1,2,3,4-tetrahydro-cyclopent[*b*]indol-2-one via a proposed spirocyclic intermediate.[11]

The existence of a cyclopropane intermediate in the indole series came, initially, as very much of a surprise since a zwitterionic intermediate in this series should be stabilized

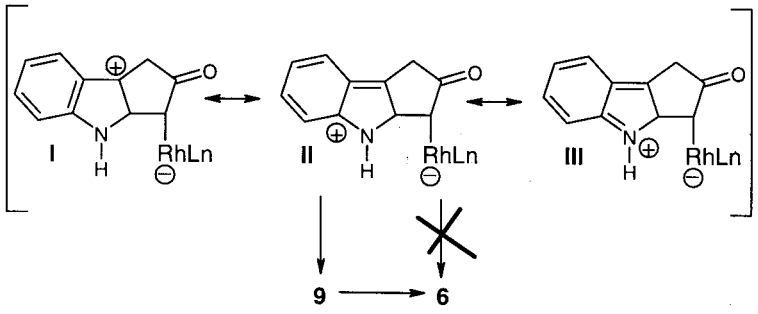
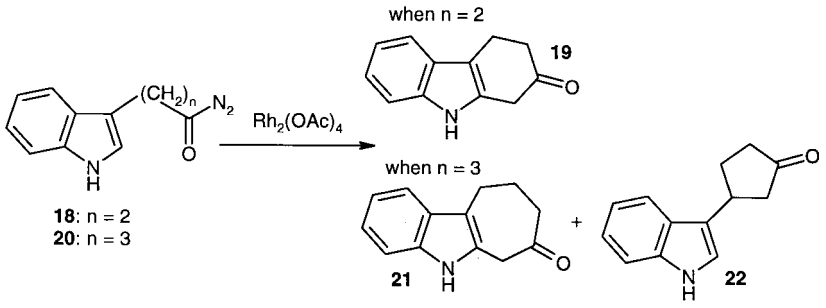


Figure 1.



Scheme 4.

to a greater extent over that of the analogous pyrrole system due to delocalization of charge through the fused benzo moiety and onto the nitrogen (Fig. 1). In light of the formation **9** in the transformation of **8→6**, this is, clearly, not the case. It may be argued that the resonance contributor with the intact aromatic system (**I**) is favored over those wherein the aromaticity is disrupted (**II** and **III**). With the positive charged more localized on the benzylic carbon shown in **I**, the reaction pathway is diverted to the more energetically stable cyclopropane and then onto the alkylation product isolated.

The effect of a longer methylene tether between the indole and the diazoketone was also investigated in order to determine the scope of the chemistry (Scheme 4). Reaction of the commercially available indole-3-propionic acid with thionyl chloride followed by addition to an ethereal solution of diazomethane resulted in the formation of 1-diazo-4(-3-indole)-2-butanone **18** in 70% yield. When this diazoketone was treated with rhodium(II) acetate, 1,3,4,9-tetrahydro-2*H*-carbazol-2-one (**19**) was the sole product isolated in 75% yield. Interestingly, no ^{1}H NMR evidence for an intermediate cyclopropane was obtained.

Diazoketone **20**[12] was prepared from the commercially available indole-3-butyric acid and treatment with $Rh_2(OAc)_4$ in dichloromethane resulted in the formation of two products inseparable via column chromatography: 6,8,9,10-tetrahydrocyclohepta[*b*]indol-7(5*H*)-one (**21**) and the CH insertion product 3-(1*H*-indol-3-yl)cyclopentanone (**22**). Structural assignments were achieved through careful study of the mixture via ^{13}C NMR. It should be noted that the production of **22** was not unexpected as there is a great deal of precedence for the formation of five membered rings via intramolecular C–H insertions.[13]

The chemistry described above has not only provided an increased understanding of the mechanism involved in the intramolecular insertion of carbenoids into pyrroles and indoles but has also allowed for the development of a facile synthetic route to an interesting class of heterocycle. The methodology provides access to fused pyrrolyl- or indolyl–cycloalkanone systems wherein the carbonyl is *beta* to the heteroaromatic system (in contrast to a Friedel–Crafts acylation which would place the carbonyl in the *alpha* position). Work is currently being directed towards the preparation of a series of analogous α-diazoketones containing various substituents on the pyrrole or indole nitrogen in an effort to examine the effect of electron withdrawing or electron donating substituents on the resultant $Rh_2(OAc)_4$ catalyzed decomposition chemistry.

Experimental

Starting materials were purchased from Aldrich Chemical Co. and used without further purification. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-300 Digital FT spectrometer (at 300.13 and 75.03 MHz, respectively) with chloroform-d as the solvent and internal reference unless otherwise noted. Low resolution mass spectra (MS) and high resolution mass spectra (HRMS) were obtained on Concept 1S double focusing mass spectrometer interfaced to a Kratos DART acquisition system and a SUN Spectrostation 10 workstation using XMACH3 software. Ions were generated using electron impact (EI). Silica gel used for column chromatography (5.0% of 100 mesh up; 47.6% of 100–200 mesh and 47.4% of 200 mesh down) was purchased from Aldrich Chemical Co. Silica gel 60 F_{254} (E. Merck Co.) plates of 0.2 mm thickness were used for analytical thin layer chromatography (TLC).

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-(3-pyrroyl)-2-propanone (2a). Pyrrole-3-acetic acid[14] (**1a**) (0.50 g, 4.0 mmol) was dissolved in dry dichloromethane (30 mL) and treated with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.84 g, 4.4 mmol). Stirring under argon was continued for two hours at which time the reaction mixture was added to a cooled (ice bath), ethereal solution of diazomethane (14 mmol). The solution was stirred for two hours during which time a black precipitate formed. The solution was filtered and the filtrate was concentrated under reduced pressure. The product was purified by column chromatography using silica gel and ethyl acetate/hexane (1:3) as the eluent to afford 1-diazo-(3-pyrroyl)-2-propanone (**2a**) (0.27 g, 1.8 mmol, 45% yield). The product showed: R_f=0.44 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.53 (2H, s, CH_2), 5.26 (1H, s, CHN_2), 6.14 (1H, m, ArH), 6.71 (1H, s, ArH), 6.78 (1H, m, ArH), 8.20 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 39.7 (CH_2), 54.1 (CHN_2), 109.1, 115.8, 116.9, 118.5, 195.1 (CO).

To a solution of 1-diazo-(3-pyorryl)-2-propanone (**2a**) (0.10 g, 0.67 mmol) in dichloromethane (35 mL) was added a catalytic amount of rhodium(II) acetate (~10 mg). The solution was stirred under argon at room temperature for four hours. The solvent was removed by

evaporation under reduced pressure and the residue was purified by column chromatography using silica gel and ethyl acetate/hexane (1:1) as the eluent. The product 4,6-dihydrocyclopenta[*b*]pyrrol-5(1*H*)-one (**3**) (0.068 g, 0.57 mmol, 85% yield) showed: R_f=0.26 (ethyl acetate/hexane, 1:4); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.34 (2H, s, CH_2), 3.38 (2H, s, CH_2), 6.26 (1H, s, ArH), 6.77 (1H, s, ArH), 8.32 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 39.5 (CH_2), 40.7 (CH_2), 104.8, 119.7, 129.4, 216.5 (CO); MS (*m*/*z* [RI%]): 121 $[M]^+$ (50), 93 $[M-CO]^+$ (100); HRMS: For C_7H_7NO calculated 121.0528, observed 121.0533.

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo(2-pyrrolyl)-2-propanone (2b). Pyrrole-2-acetic acid[2] (**2a**) (0.50 g, 4.0 mmol) and 1,3-dicyclohexylcarbodiimide (DCC) (0.89 g, 4.3 mmol) were dissolved in dichloromethane (60 mL) and the reaction mixture was stirred under argon at room temperature for one hour. The solution was slowly added to stirred, cooled (ice bath) solution of ethereal diazomethane (12 mmol) and, after 3 h, the solvent was removed by evaporation under reduced pressure. The dicyclohexylurea (DCU) was removed from the residue by crystallization several times from ether. The reaction mixture was then purified by column chromatography using silica gel and ethyl acetate/hexane (1:2) as the eluent. The product (**2b**) was isolated as yellow crystals (0.48 g, 3.2 mmol, 80% yield) and showed: R_f=0.27 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.59 (2H, s, CH_2), 5.25 (1H, s, CHN_2), 5.99 (1H, s, ArH), 6.12 (1H, m, ArH), 6.72 (1H, m, ArH), 8.71 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 40.0 (CH_2), 55.2 (CHN_2), 108.1, 108.9, 118.6, 124.5, 193.1 (CO); MS (*m*/*z* [RI%]): 149 $[M]^+$ (40), 121 $[M-N_2]^+$ (12), 93 $[M-N_2-CO]^+$ (34), 80 $[M-COCHN_2]^+$ (100); HRMS: For $C_7H_7N_3O$ calculated 149.0589, observed 149.0593.

To a stirred solution of 1-diazo(2-pyrrolyl)-2-propanone (**2b**) (0.26 g, 1.7 mmol) in dry dichloromethane (40 mL), a catalytic amount of rhodium(II) acetate (~10 mg) was added. The reaction mixture was stirred under argon at room temperature for 2 h. The solvent was removed by evaporation under a reduced pressure and the products were purified by column chromatography using silica gel and ethyl acetate/hexane (1:4) as the eluent. Two products were collected: 4,6-dihydrocyclopenta[*b*]pyrrol-5(1*H*)-one (**3**) (0.05 g, 0.41 mmol, 24% yield) and 1*H*-pyrrolizin-2(3*H*)-one (**4**) (0.13 g, 1.1 mmol, 65% yield). Product **4** showed: R_f=0.57 (ethyl acetate/hexane, 1:4); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.55 (2H, s, CH_2), 4.41 (2H, s, CH_2), 6.03 (1H, d, ArH), 6.29 (1H, m, ArH), 6.78 (1H, d, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 37.9 (CH_2), 54.8 (CH_2), 102.2, 111.6, 115.9, 130.5, 210.1 (CO); MS (*m*/*z* [RI%]): 121 $[M]^+$ (50), 93 $[M-CO]^+$ (100); HRMS: For C_7H_7NO calculated 121.0528, observed 121.0534.

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-3-(2-indolyl)-2-propanone (5). To a solution of indole-2-acetic acid[15] (0.1 g, 0.57 mmol) dissolved in dry dichloromethane (35 mL) was added dicyclohexylcarbodiimide (DCC) (0.13 g, 0.63 mmol). The reaction mixture was stirred under an argon atmosphere for one hour. The resulting solution was added slowly to a cooled (ice bath) solution of ethereal diazomethane (20 mL). The reaction mixture was stirred for another hour and the solvent removed under a reduced pressure to give a solid residue. The dicyclohexylurea (DCU) was removed by crystallization from ether, and the supernatant purified by column chromatography using silica gel and ethyl acetate/hexane (1:2) as eluent. The product 1-diazo-3-(2-indolyl)-2-propanone (**5**) (0.056 g, 0.28 mmol, 50% yield) showed: R_f=0.23 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.37 (2H, s, CH_2), 5.28 (1H, br, CHN_2), 6.32 (1H, s, ArH), 7.11 (2H, m, ArH), 7.31 (1H, d, J=8 Hz, ArH), 7.54 (1H, d, J=8 Hz, ArH), 8.72 (1H, br, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 40.5 (CH_2), 55.6 (CHN_2), 102.5, 111.3, 120.3, 120.5, 122.3, 128.7, 131.8, 136.9, 192.1 (CO); MS [EI]$^+$ (*m*/*z* [RI%]): 199 $[M]^+$ (7), 171 $[M-N_2]^+$ (31), 143 $[M-N_2-CO]^+$ (52), 130 $[M-COCHN_2]^+$ (27); HRMS: For $C_{11}H_9N_3O$ calculated 199.0746, observed 199.0753.

To a stirred solution of 1-diazo-3-(2-indolyl)-2-propanone (**5**) (50 mg, 0.25 mmol) in dry dichloromethane (20 mL), a catalytic amount of rhodium(II) acetate (~5 mg) was added. The reaction mixture was stirred under argon at room temperature for 2 h. The solvent was evaporated, and the residue was purified by column chromatography using silica gel and ethyl acetate: hexane (1:2) as eluent to give 3,4-dihydrocyclopenta[*b*]indol-2(3*H*)-one (**6**) and 1*H*-pyrrolo[1,2-*a*]indol-2(3*H*)-one (**7**) (NH insertion product), in 25 and 70% yield, respectively. The product **6** showed: R_f=0.42 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.54 (2H, s, CH_2), 3.57 (2H, s, CH_2), 7.20 (2H, m, ArH), 7.42 (1H, d, ArH), 7.51 (1H, d, ArH), 8.12 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 39.8 (CH_2), 39.8 (CH_2), 112.0, 114.2, 119.4, 120.8, 122.5, 124.8, 136.4, 138.8, 214.6 (CO); MS [EI]$^+$ (*m*/*z* [RI%]): 171$[M]^+$ (48), 143 $[M-CO]^+$ (100), 115 $[M-C_2H_4CO]$ (15); HRMS: For $C_{11}H_9NO$ calculated 171.0684, observed 171.0695. The product **7** showed: R_f=0.68 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.75 (2H, s, CH_2), 4.51 (2H, s, NCH_2), 6.40 (1H, s, ArH), 7.20 (2H, m, ArH), 7.28 (1H, d, ArH), 7.64 (1H, d, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 38.0 (CH_2), 52.7 (CH_2), 96.2, 110.1, 120.8, 121.3, 122.0, 130.9, 134.0, 136.9, 209.0 (CO); MS [EI]$^+$ (*m*/*z* [RI%]): 171$[M]^+$ (70), 143 $[M-CO]^+$ (100), 115 $[M-C_2H_4CO]^+$ (31); HRMS: For $C_{11}H_9NO$ calculated 171.0684, observed 171.0689.

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-3-(3-indoly)-3-propanone (8). A solution of indole-3-acetic acid (0.40 g, 2.3 mmol) in a dry tetrahydrofuran (30 mL) was cooled to 0°C (ice bath) and stirred under argon. Two drops of dry dimethylformamide were added to the flask. Thionyl chloride (0.3 g, 2.5 mmol) was slowly added and the reaction mixture stirred for another two hours. The solvent was removed under reduced pressure, and redissolved in dry dichloromethane. The acid chloride was slowly added to a cooled, ethereal solution of diazomethane and the reaction mixture was stirred for two hours. The product was purified by chromatography on silica gel using ethyl acetate/hexane (1:2) as the eluent to give 1-diazo-3-(3-indoly)-3-propanone (**8**) (0.40 g, 1.9 mmol, 83% yield). The compound showed: R_f=0.44 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.79 (2H, s, CH_2), 5.21 (1H, s, CHN_2), 7.11 (1H, s, ArH), 7.22 (2H, m, ArH), 7.30(1H, d,, ArH), 7.90 (1H, d, ArH), 8.36

(1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 38.4 (CH_2), 54.7 (CHN_2), 109.4, 111.8, 119.1, 120.4, 122.9, 123.9, 127.5, 136.7, 194.7 (CO); MS [EI]$^+$ (*m/z* [RI%]): 199 $[M]^+$ (14), 171 $[M-N_2]^+$ (83), 143 $[M-N_2-CO]^+$ (83), 130 $[M-COCHN_2]^+$ (100), 115 $[M-CH_2COCHN_2]^+$ (28); HRMS: For $C_{11}H_9N_3O$ calculated 199.0746, observed 199.0754.

To a stirred solution of 1-diazo-3-(3-indoly)-3-propanone (**8**) (0.15 g, 0.75 mmol) in dry dichloromethane (40 mL), a catalytic amount of rhodium(II) acetate (~10 mg) was added. The reaction mixture was stirred under argon at room temperature for 2 h. The solvent was evaporated, and the residue was purified by column chromatography using silica gel and ethyl acetate/hexane (1:2) as the eluent to give 3,4-dihydrocyclopenta[*b*]indol-2(3*H*)-one (**6**) (126 mg, 0.74 mmol, 95% yield). Intermediate cyclopropane (**9**) was observed when a solution of 1-diazo-3-(3-indolyl)-3-propanone (**8**) (~5 mg) in $CDCl_3$ was treated with a catalytic amount of rhodium(II) acetate and the reaction monitored by ^{1}H NMR. Intermediate **9** (which appeared after approximately 5 min and was completely converted to **6** over the next 60 min) showed: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.55 (1H, dd, J=16, 3 Hz), 2.85 (1H, dd, J=16, 3 Hz), 4.41 (1H, br t), 5.23 (1H, br) and 6.70–7.60 (Ar-H).

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-3-(3-[1-methyl indolyl])-2-propanone (10). 1-Methyl indole-3-acetic acid[16] (0.30 g, 1.6 mmol) was dissolved in dry dichloromethane (25 mL) and the solution was stirred under argon. Oxalyl chloride (0.24 g, 1.9 mmol) was added slowly followed by two drops of DMF and the reaction mixture stirred at room temperature for one hour. The solvent was evaporated under a reduced pressure. Dry benzene (10 mL) was added and subsequently evaporated under a reduced pressure. The residue was redissolved in dry dichloromethane (15 mL) and added dropwise to an ethereal solution of diazomethane (35 mL) at 0°C. The reaction mixture was stirred for another two hours at which time the solution was filtered and the solvent evaporated under a reduced pressure. The residue was purified by column chromatography using silica gel and ethylacetate/hexane (1:2) as the eluent to give the desired product (**10**) (0.29 g, 1.36 mmol, 85% yield) which showed: R_f=0.48 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.77 (2H, s, CH_2), 3.80 (3H, s, CH_3), (1H, s, CHN_2), 7.01 (1H, s, NCH), 7.20 (1H, t, ArH), 7.27 (1H, d, ArH), 7.34 (1H, t, ArH), 7.58 (1H, d, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 33.2 (CH_3), 38.3 (CH_2), 54.5 (CHN_2), 107.9, 109.9, 119.2, 119.9, 122.5, 128.0, 128.5, 137.5, 194.6 (CO); MS [EI]$^+$ (*m/z* [RI%]): 213 $[M]^+$ (34%),185 $[M-N_2]^+$ (25%), 157 $[M-CON_2]^+$ (22%), 144 $[M-COCHN_2]^+$ (100%); HRMS: For $C_{12}H_{11}N_3O$ calculated 213.0902, observed 213.0911.

To a solution of rhodium(II) acetate (~20 mg) in dichloromethane (40 mL) was added a solution of 1-diazo-3-(1-methyl-3-indole)-2-propanone (0.2 g, 0.94 mmol) in dichloromethane via a syringe pump. The reaction was allowed to stir under an argon atmosphere at room temperature for an additional 30 min at which time the solvent was evaporated under a reduced pressure. The residue was purified by filtration through a short pad of silica gel using dichloromethane as the eluent. Compound **12** (0.16 g, 0.89 mmol, 95% yield) showed: R_f=0.73 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.51 (2H, s, CH_2), 3.56 (2H, s, CH_2), 3.73 (3H, s, CH_3), 7.18 (1H, t, ArH), 7.27(1H, t, ArH), 7.34 (1H, d, ArH), 7.50 (1H,d, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.7 (CH_2), 38.7 (CH_2), 40.4 (CH_3), 110.0, 111.9, 119.3, 120.2, 121.8, 124.8, 139.4, 139.5, 214.3 (CO); MS [EI]$^+$ (*m/z* [RI%]): 185 $[M]^+$ (75%), 157 $[M-CO]^+$ (100%), 142 $[M-COCH_3]^+$ (13%), 128 $[M-CH_2CO-CH_3]^+$ (4%); HRMS: For $C_{12}H_{11}NO$ calculated 185.0841, observed 185.0843.

Intermediate cyclopropane (**11**) was observed when a solution of 1-diazo-3-(1-methyl-3-indolyl)-2-propanone (~5 mg) in $CDCl_3$ was treated with a catalytic amount of rhodium(II) acetate and the reaction monitored by ^{1}H NMR (a spectrum taken every 5 min). Intermediate **11** (which appeared after approximately 5 min and was completely converted to **12** over the next 60 min) showed: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.64 (1H, dd, J=16, 4 Hz), 2.99 (1H, dd, J=16, 4 Hz), 3.32 (3H, CH_3), 4.41 (1H, br t), 7.02–7.49 (Ar).

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-3-(2-methyl indolyl)-2-propanone (13). 2-Methyl indole-3-acetic acid (0.2 g, 1.0 mmol) was dissolved in dry tetrahydrofuran (25 mL), cooled to 0°C and stirred under an atmosphere of argon. Oxalyl chloride (0.15 g, 1.2 mmol) was added slowly followed by two drops of DMF. The reaction mixture was stirred at room temperature for one hour. The solvent was evaporated under a reduced pressure, dry benzene (10 mL) was added and subsequently evaporated under a reduced pressure. The residue was redissolved in dry tetrahydrofuran (15 mL) and was added dropwise to a cooled (ice bath) solution of diazomethane in ether (25 mL). The reaction mixture was stirred for another hour, filtered, and the solvent evaporated under a reduced pressure. The residue was purified by column chromatography using silica gel and ethyl acetate/hexane (1:2) as the eluent, to give **13** (0.16 g, 0.75 mmol, 75% yield). The compound showed: R_f=0.27 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.36 (3H, s, CH_3), 3.73 (2H, s, CH_2), 5.13 (1H, s, CHN_2), 7.18 (2H, m, ArH), 7.28 (1H, d, ArH), 7.48 (1H, d, ArH), 8.51 (1H, s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.1 (CH_3), 37.4 (CH_2), 54.3 (CHN_2), 105.3, 110.9, 118.2, 120.3, 122.0, 128.8, 133.5, 135.7, 194.9 (CO); MS [EI]$^+$ (*m/z* [RI%]): 213 $[M]^+$ (20),185 $[M-N_2]^+$ (59), 144 $[M-COCHN_2]^+$ (100); HRMS: For $C_{12}H_{11}N_3O$ calculated 213.0902, observed 213.0909.

1-Diazo-3(3-[2-methyl indolyl])-2-propanone (**13**) (0.12 g, 0.56 mmol) was dissolved in dry dichloromethane (40 mL) and treated with a catalytic amount of rhodium(II) acetate (~10 mg). The reaction mixture was stirred for three hours under argon at room temperature. The solvent was evaporated under a reduced pressure and the residue purified using silica gel column chromatography with ethyl acetate/hexane (1:3) as the eluent. Cyclopropane **14** (0.067 g, 0.36 mmol, 65% yield) showed: R_f=0.29 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.52 (3H, s, CH_3), 2.65 (1H, d, J=15 Hz, one of CH_2), 2.78 (1H, d, J=15 Hz, one of CH_2), 4.38 (1H, br, N–H), 6.04 (1H, s, CH), 6.85 (1H, d, J=8 Hz,

ArH), 6.91 (1H, t, J=7 Hz, ArH), 7.35 (1H, t, J=8 Hz, ArH), 7.53 (1H, d, J=7 Hz, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.7 (CH_3), 52.4 (CH_2), 71.7 (CH), 112.7, 116.9, 120.2, 120.4, 125.8, 133.9, 154.9, 182.4, 206.7 (CO); MS $[EI]^+$ (m/z [RI%]): 185 $[M]^+$ (79), 170 $[M-CH_3]^+$ (100), 157 $[M-CO]^+$ (31), 144 $[M-CO-CH]^+$ (10), 115 $[M-CH_3-CH_2COCH]^+$ (20); HRMS: For $C_{12}H_{11}NO$ calculated 185.0841, observed 185.0841.

$Rh_2(OAc)_4$ catalyzed decomposition of 2-diazo-4-(3-indolyl)-3-butanone (15). To a solution of indole-3-acetic acid (0.30 g, 1.7 mmol) dissolved in dry tetrahydrofuran (35 mL) and stirred under argon at 0°C, was added thionyl chloride (0.22 g, 1.8 mmol) and two drops of dry dimethylformamide. Twenty minutes following the addition, the color of the reaction mixture changed to brown. Stirring was continued for another two hours. The solvent was removed by evaporation under a reduced pressure and the residue redissolved in a dry tetrahydrofuran (20 mL). The solution was added dropwise to a stirred solution of ethereal diazoethane (roughly three equivalents) at 0°C. The reaction mixture was stirred for another two hours at which time a few drops of acetic acid were added to destroy the excess of the diazoethane. The reaction mixture was filtered and evaporated to dryness under a reduced pressure. The product was purified by chromatography on silica gel using ethyl acetate/hexane (1:2) as the eluent. The product (**15**) was isolated in 65% yield (0.24 g, 1.1 mmol) and showed: R_f=0.28 (ethyl acetate/hexane, 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.9 (3H, s, CH_3CN_2), 3.91 (2H, s, CH_2), 6.99 (1H, s, ArH), 7.15 (2H, m, ArH), 7.31 (1H, d, ArH), 7.61 (1H, d, ArH), 8.28 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4 (CH_3), 35.6 (CH_2), 62.4 (CN_2), 108.3, 111.2, 118.4, 118.8, 119.7, 122.2, 123.2, 127.0, 136.1, 192.4 (CO); MS (m/z [(RI%)]: 213 $[M]^+$ (3), 185 $[M-N_2]^+$ (56), 170 $[M-N_2-CH_3]^+$ (6), 157 $[M-CH_2CN_2]^+$ (27), 130 $[M-COCN_2(CH_3)]^+$ (100); HRMS: For $C_{12}H_{11}N_3O$ calculated 213.0902, observed 213.0903.

2-Diazo-4-(3-indolyl)-3-butanone (**15**) (0.10 g, 0.47 mmol) was dissolved in dry dichloromethane (20 mL) and treated with a catalytic amount of rhodium(II) acetate (~10 mg). The reaction mixture was stirred for three hours under argon at room temperature. The solvent was evaporated under a reduced pressure and the residue purified using silica gel column chromatography with dichloromethane as the eluent. The yield of the isolated product (**17**) was 90% (78 mg, 0.42 mmol) which showed: R_f=0.54 (dichloromethane); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.46 (3H, d, J=7 Hz, CH_3), 3.54–3.62 (3H, m, CH+CH_2), 7.20 (2H, m, ArH), 7.42 (1H, d, J=8 Hz, ArH), 7.53 (1H, d, J=8 Hz, ArH), 8.14 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.9 (CH_3), 38.9 (CH_2), 44.3 (CH_2), 112.1, 112.3, 119.5, 120.8, 122.5, 124.8, 138.8, 142.1, 217.6 (CO); MS (m/z [RI%]): 185 $[M]^+$ (56), 157 $[M-CO]^+$ (100), 130 $[M-C_3H_3O]^+$ (47), 115 $[M-C_4H_6O]^+$ (5); HRMS: For $C_{12}H_{11}NO$ calculated 185.0841, observed 185.0850.

Intermediate cyclopropane (**16**) was observed when a solution of 2-diazo-4-(3-indolyl)-3-butanone (**15**) (~5 mg) in $CDCl_3$ was treated with a catalytic amount of rhodium(II) acetate and the reaction monitored by ^{1}H NMR (a spectrum taken every 10 min). Intermediate **16** (which appeared after approximately 5 min and was completely converted to **17** over the next 60 min) showed: ^{1}H NMR ($CDCl_3$, 300 MHz): δ1.80 (3H, CH_3), 2.59 (1H, dd, J=16, 3 Hz), 3.00 (1H, dd, J=16, 3 Hz), 4.45 (1H, br t), 6.95–7.60 (Ar).

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-4(3-indolyl)-2-butanone (18). Indole-3-propionic acid (0.30 g, 1.5 mmol) was dissolved in dry tetrahydrofuran (30 mL) and stirred under an argon atmosphere at 0°C. Dimethylformamide (two drops) were added to the reaction flask followed by thionyl chloride (0.22 g, 1.9 mmol). The reaction mixture was stirred for two hours at 0°C at which time the solvent was removed by evaporation under a reduced pressure. The residue was redissolved in dry tetrahydrofuran and immediately added slowly to a stirred ethereal solution of diazomethane (50 mL, ~5 mmol) at 0°C. The reaction mixture was stirred for two hours, filtered and the solvent evaporated to dryness under a reduced pressure. The product was purified by column chromatography on silica gel using ethyl acetate/hexane (1:2) as the eluent to give 1-diazo-4(-3-indolyl)-2 butanone (**18**) (0.23 g, 1.1 mmol, 70% yield). The product showed: R_f=0.48 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.69 (2H, t, J=7 Hz, CH_2), 3.10 (2H, t, J=7 Hz, CH_2), 5.12 (1H, s, CHN_2), 6.91 (1H, s, ArH), 7.17 (2H, m, ArH), 7.32 (1H, d, ArH), 7.58 (1H, d, ArH), 8.36 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.5(CH_2), 41.1 (CH_2), 54.5 (CHN_2), 111.2, 114.3, 118.4, 119.0, 121.7, 121.7, 126.9, 136.2, 195.1 (CO); MS (m/z [RI%]): 213 $[M]^+$ (5), 185 $[M-N_2]^+$ (37), 156 $[M-N_2-CO]^+$ (29), 143 $[M-COCHN_2]^+$ (27), 130 $[M-CH_2COCHN_2]^+$ (100), 115 $[M-CH_2CH_2COCHN_2]^+$ (9); HRMS: For $C_{12}H_{11}N_3O$ calculated 213.0902, observed 213.0898.

1-Diazo-4(-3-indolyl)-2-butanone (**18**) (0.10 g, 0.47 mmol) was dissolved in dry dichloromethane (30 mL) under an argon atmosphere and treated with rhodium(II) acetate (~10 mg). The reaction mixture was stirred at room temperature for three hours at which time the solvent was removed by evaporation under a reduced pressure. The product was purified by chromatography on silica gel using ethyl acetate/hexane (1:2) as the eluent. 1,3,4,9-Tetrahydro-2*H*-carbazol-2-one (**19**) was isolated in 75% yield (65 mg, 0.35 mmol). The product showed: R_f=0.48 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.76 (2H, t, J=7 Hz, CH_2), 3.08 (2H, t, J=7 Hz, CH_2), 3.61 (2H, s, CH_2), 7.15 (2H, m, ArH), 7.30 (1H, d, ArH), 7.49 (1H, d, ArH), 7.86 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.2 (CH_2), 38.8 (CH_2), 39.9 (CH_2), 109.9, 111.3, 118.5, 120.2, 122.4, 127.0, 130.5, 137.0, 208.8 (CO); MS $[EI]^+$ (m/z [RI%]): 185 $[M]^+$ (93), 156 $[M-CO]^+$ (38), 143 $[M-CH_2CO]^+$ (100), 130 $[M-C_2H_4CO]^+$ (14), 115 $[M-C_3H_6CO]^+$ (11); HRMS: For $C_{12}H_{11}NO$ calculated 185.0841, observed 185.0842.

$Rh_2(OAc)_4$ catalyzed decomposition of 1-diazo-5-(3-indolyl)-2-pentanone (18). A solution of indole-3-butyric acid (0.4 g, 1.96 mmol) and two drops of dry dimethylformamide in dry tetrahydrofuran (50 mL) were cooled (ice bath) and stirred under an argon atmosphere. Thionyl chloride (280 mg, 2.36 mmol) was added and the reaction

mixture was stirred for one hour. The solution was slowly transferred to a cooled, ethereal solution of diazomethane (50 mL, 6 mmol) and allowed to react for two hours. The solvent was removed by evaporation under a reduced pressure and the resultant residue was purified by column chromatography on silica gel using ethyl acetate/hexane (1:2) as the eluent. The product, 1-diazo-5-(3-indolyl)-2-pentanone (**18**) (0.29 g, 1.3 mmol, 65% yield) was a isolated as a yellow solid and showed: R_f=0.51 (ethyl acetate/hexane, 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.96 (2H, m, CH_2), 2.32 (2H, br t, CH_2), 2.73 (2H, t, CH_2), 6.92 (1H, s, ArH), 7.08 (2H, m, ArH), 7.30 (1H, d, ArH), 7.52 (1H, d, ArH), 8.71 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.9 (CH_2), 26.0 (CH_2), 40.9 (CH_2), 54.8 (CHN_2), 111.8, 115.5, 119.1, 119.3, 122.1, 122.3, 127.8, 136.8, 195.8 (CO); MS [*m/z* (RI%)]: 227 $[M]^+$ (6), 199 $[M-N_2]^+$ (19), 170 $[M-N_2HCO]^+$ (25), 156 $[M-COCH_2N_2]^+$ (8), 143 $[M-C_3H_4N_2O]^+$ (100), 130 $[M-C_2H_4COCHN_2]^+$ (74), 115 $[M-C_5H_7N_2O]^+$ (13); HRMS: For $C_{13}H_{13}N_3O$ calculated 227.1059, observed 227.1073.

1-Diazo-5-(3-indolyl)-2-pentanone (**18**) (0.10 g, 0.44 mmol) was dissolved in dry dichloromethane (20 mL) under an argon atmosphere and treated with rhodium(II) acetate (~10 mg). The reaction was stirred at room temperature for three hours at which time the solvent was removed by evaporation under a reduced pressure. Chromatography of the reaction products on silica gel (using ethyl acetate/hexane 1:1) yield **21** and **22** as an inseparable mixture in 78% yield. The products showed an R_f=0.34 (ethyl acetate/hexane, 1:1). Compound (**21**) showed ^{13}C NMR ($CDCl_3$, 75 MHz): 22.5, 25.0, 43.2, 44.1, 111.0, 112.1, 119.5, 119.9, 122.4, 122.8, 127.0, 137.1, 207.4. Compound (**22**) showed ^{13}C NMR ($CDCl_3$, 75 MHz): 30.3, 34.2, 38.6, 45.7, 111.8, 118.4, 119.0, 120.0, 120.4, 125.4, 129.3, 135.8, 220.0. Tentative assignments were made based on the intensities of the signals and by a comparison of the observed chemical shifts with those of similar compounds.

Acknowledgements

The authors wish to thank Brock University and the Natural Sciences and Engineering Research Council of Canada for their financial support, Mr Tim Jones (Brock University) for mass spectral analysis and Dr Christopher S. Frampton (Roche Products, UK) for X-ray crystallography.

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12. Preparation of the diazoketone was achieved using the standard conditions wherein carboxylic acid is first converted to the acid chloride which is then treated with ethereal diazomethane. Curiously, if the acid chloride was concentrated prior to addition to diazomethane, 2,3,4,9-tetrahydrocarbazol-1-one was formed in 95% yield. Its structure was unambiguously determined by NMR (^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.24 (2H, m, CH_2), 2.68 (2H, t, J=6 Hz, CH_2), 2.98 (2H, t, J=6 Hz, CH_2), 7.13 (1H, m, ArH), 7.36 (1H, m, ArH), 7.49 (1H, d, J=8 Hz, ArH), 7.64 (1H, d, J=8 Hz, ArH), 9.96 (1H, br, N–H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.29, (CH_2), 24.89 (CH_2), 38.17 (CH_2), 112.75, 120.13, 121.15, 125.64, 126.86, 129.62, 131.12, 138.16, 191.70 (CO)); MS (*m/z* (RI%) 185 $[M]^+$ (100), 156 $[M-CO]^+$ (25), 143 $[M-CH_2CO]^+$ (24), 129 $[M-C_2H_4CO]^+$ (72), 115 $[M-C_4H_6O]^+$ (5); HRMS: For $C_{12}H_{11}NO$ calculated 185.08406, observed 185.08385) and X-ray crystallography (see Fig. 2). Crystals were monoclinic having a space group of $P2(1)/n$, a=10.247(3) Å, b=5.8100(18) Å, c=15.877(3) Å, β=97.49(3)°, V=937.2(4) Å^3, and Z=4; the final R factor was 0.0546 for 8897 measured reflections). This Friedel–Crafts chemistry can be avoided if the acid chloride in added directly to the diazomethane without prior concentration. Using this procedure, purification by using column chromatography on silica gel gave the desired 1-diazo-5(-3-indole)-2-pentanone in 65% yield along with small amounts of the methyl ester of the starting acid and 2,3,4,9-tetrahydrocarbazol-1-one.

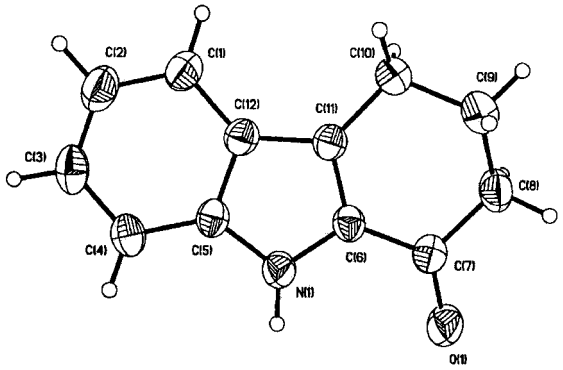

Figure 2. ORTEP of 2,3,4,9-tetrahydrocarbazol-1-one.

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