Divergent Pathways in the Intramolecular Reactions between Rhodium-Stabilized Vinylcarbenoids and Pyrroles: Construction of Fused Tropanes and 7-Azabicyclo[4.2.0]octadienes

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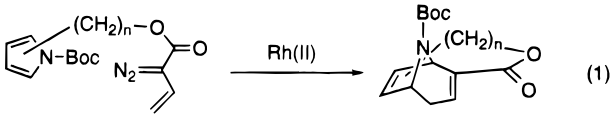
The rhodium(II)-catalyzed intramolecular reaction between vinyldiazomethanes and pyrroles leads to a novel synthesis of fused tropanes. The reaction occurs by a stepwise 3 + 4 annulation mechanism between a rhodium-stabilized vinylcarbenoid intermediate and the pyrrole rather than by the typical tandem cyclopropanation/Cope rearrangement sequence. The outcome of the reaction is very sensitive to the vinylcarbenoid structure. In particular, the presence of a 2-siloxy substituent on the vinylcarbenoid strongly favors the formation of fused tropanes. In the absence of such functionality, the formation of fused 7-azabicyclo[4.2.0]octadienes becomes the dominant reaction pathway.

The tandem cyclopropanation/Cope rearrangement between vinylcarbenoids and pyrroles[1] is the basis of a general method for the construction of the tropane skeleton.[2,3] This method has been applied to the synthesis of (±)-ferruginine[1] and (−)-anhydroecgonine methyl ester,[4] as well as a number of novel tropanes with potent CNS activity.[5] As part of a continued program to generate novel tropanes with selective neurochemical activity, we required the availability of tropanes containing conformationally constrained functionality. The intramolecular version of the reaction between vinylcarbenoids and pyrroles appeared to be a very direct method to prepare such compounds (eq 1). The development of such a process is the focus of this paper. These studies resulted in an efficient approach to the synthesis of conformationally constrained tropanes. In addition, a number of unusual transformations were observed that illustrate some of the subtle factors that govern carbenoid reactivity.[6]

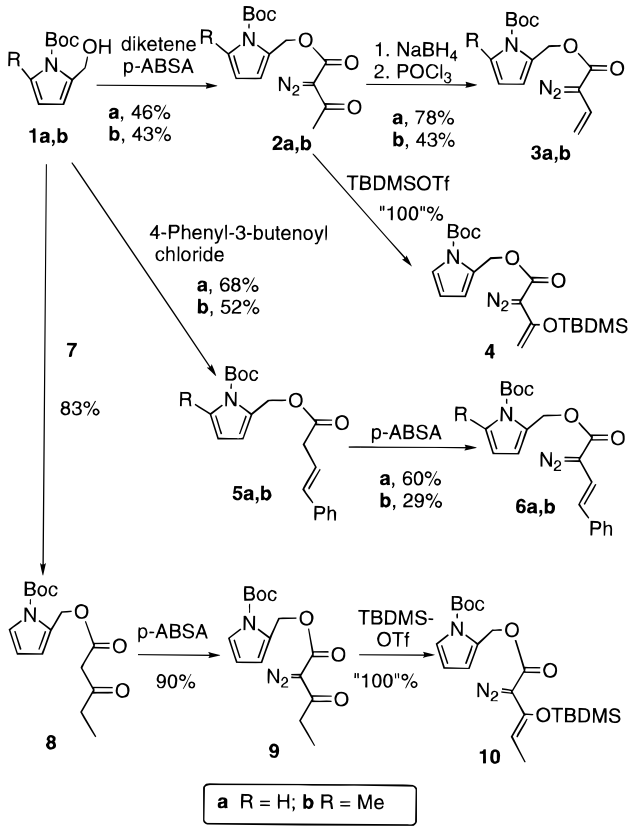


(1)

Results and Discussion

A series of vinylcarbenoid precursors were synthesized according to Schemes 1 and 2. Treatment of Boc-protected (hydroxymethyl)pyrroles **1a**,**b** with diketene and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) resulted in the formation of the diazoacetoacetates **2a**,**b**.[7] Conversion of **2a**,**b** to the vinyldiazomethanes **3a**,**b** was readily achieved by reduction of the ketone in **2a**,**b** with sodium borohydride followed by dehydration of the resulting alcohol with phosphorus oxychloride in the presence of triethylamine.[8] The silyl-substituted vinylcarbene **4** was prepared by silylation of **2a** with TBDMS triflate in the presence of triethylamine.[9] The phenyl-substituted vinyldiazomethanes **6a**,**b** were prepared in a two-step

Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* March 1, 1996.

(1) Davies, H. M. L.; Saikali, E.; Young, W. B. *J. Org. Chem.* **1991**, *56*, 5696.

(2) (a) Lounasmaa, M. *Alkaloids* **1988**, *33*, 1. (b) Fodor, G.; Dharanipragada, R. *Nat. Prod. Rep.* **1990**, *7*, 540. (c) Fodor, G.; Dharanipragada, R. *Nat. Prod. Rep.* **1986**, *3*, 181. (d) Fodor, G.; Dharanipragada, R. *Nat. Prod. Rep.* **1985**, *2*, 221. (e) Fodor, G.; Dharanipragada, R. *Nat. Prod. Rep.* **1984**, *1*, 231.

(3) For other approaches to the tropane skeleton, see (a) Willstätter, R. *Ber.* **1896**, *29*, 936. (b) Willstätter, R. *Justus Liebigs Ann. Chem.* **1903**, *326*, 23. (c) Robinson, R. *J. Chem. Soc.* **1917**, *111*, 762. (d) Hayakawa, Y.; Baba, Y.; Makino, S.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1786. (e) Tufariello, J. J.; Trybuiski, E, J. *J. Chem. Soc., Chem. Commun.* **1973**, 720. (f) Iida, H.; Watanabe, Y.; Kibayashi, C. *J. Org. Chem.* **1985**, *50*, 1818. (g) Petersen, J. S.; Toteberg-Kaulen, S.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 2948.

(4) Davies, H. M. L.; Huby, N. J. S. *Tetrahedron Lett.* **1992**, *33*, 6935.

(5) (a) Davies, H. M. L.; Saikali, E.; Huby, N. J. S.; Gilliatt, V. J.; Matasi, J. J.; Sexton, T.; Childers, S. R. *J. Med. Chem.* **1994**, *37*, 1262. (b) Bennett, B. A.; Wichems, C. H.; Hollingsworth, C. K.; Davies, H. M. L.; Thornley, C.; Sexton, T.; Childers, S. R. *J. Pharmacol. Exp. Ther.* **1995**, *272*, 1176.

(6) For a preliminary account of a portion of this work, see: Davies, H. M. L.; Matasi, J. J. *Tetrahedron Lett.* **1994**, *35*, 5209.

(7) Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D., *Synth. Commun.* **1987**, *17*, 1709.

(8) Davies, H. M. L.; Hougland, P. W.; Cantrell, W. R., Jr. *Synth. Commun.* **1992**, *22*, 971.

(9) Ueda, Y.; Roberge, G.; Vinet, V. *Can. J. Chem.* **1984**, *62*, 2936.

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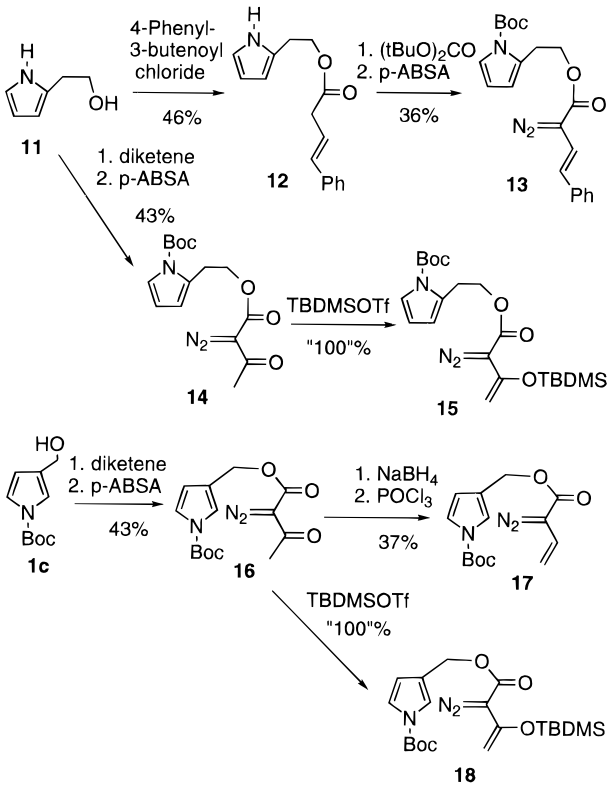
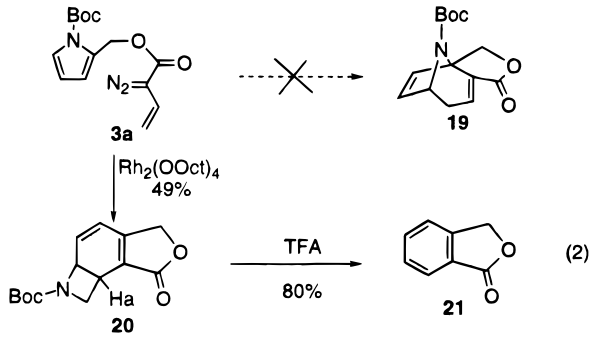
Scheme 2



sequence by reaction of **1a**,**b** with 4-phenyl-3-butenoyl chloride followed by a diazotransfer reaction on **5a**,**b** using *p*-ABSA and DBU as base.[7] The synthesis of the methyl-substituted vinyldiazomethane **10** was achieved in a related manner to the formation of **4** except that the initial reaction was carried out with the propionylated Meldrum's acid (**7**) instead of diketene.[10] The *Z* configuration of **10** was determined by NOE difference analysis which showed a distinctive enhancement of the vinyl methyl protons on irradiation of the silyl methyl protons.

The synthesis of the vinylcarbenoid precursors **13** and **15** containing a longer tether between the vinylcarbenoid and pyrrole required a slightly modified procedure because transfer of the Boc group from nitrogen to the alcohol occurred using the general procedures described in Scheme 1. The unprotected pyrrole **11** was first acylated with 4-phenyl-3-butenoyl chloride to form **12** which was then readily Boc-protected and diazotized to form **13** (Scheme 2). Similarly, **11** was acylated by diketene and converted to the diazoacetoacetate **14**. At this stage *N*-Boc protection followed by silylation proceeded uneventfully to form the vinyldiazomethane **15**. Two additional vinyldiazomethane systems, **17** and **18**, were prepared, containing a tether at the 3-position of the pyrrole ring. The synthesis of **17** and **18** required the 3-(hydroxymethyl)pyrrole **1c** as starting material and followed the procedures described in Scheme 1.

The decomposition studies began with the vinyldiazomethane **3a**. On the basis of previous studies,[1] rhodium(II) octanoate as the catalyst and either benzene or hexanes as the solvent were considered to be the optimum reaction conditions. The use of a moderately electron rich catalyst such as rhodium(II) octanoate and nonpolar solvents tends to enhance the tandem cyclopropanation/Cope rearrangement over numerous potential side reactions occurring via zwitterionic intermediates.[1] Decomposition of **3a** with rhodium(II) octanoate in refluxing benzene resulted in a very clean transformation as determined from the ^{1}H NMR of the crude reaction mixture, but the product was slightly unstable to chromatography and was isolated in only 49% yield. The spectral data of the product were inconsistent with that of the expected tropane structure **19**. Instead, the product was assigned to be the fused 7-azabicyclo[4.2.0]-octadiene **20**, based on its distinctive ^{1}H NMR spectrum at 95 °C (to avoid broadened signals due to hindered rotation), which included signals for the two vinyl protons, the diastereotopic butyrolactone protons, and the four azetidine protons. The signal for the methine proton H_a is particularly distinctive because it displays coupling to all the other azetidine protons as well as homoallylic coupling to one of the butyrolactone methylene protons. Further evidence to confirm this structural assignment was obtained by treatment of **20** with TFA which resulted in a 2 + 2 cycloreversion and the formation of the phthalide (**21**) in 80% yield.



A reasonable mechanism to explain the formation of **20** is shown in eq 3. The reaction is considered to proceed by initial intramolecular capture of the rhodium carbenoid **22** by the pyrrole, leading to a zwitterionic structure **23** rather than direct cyclopropanation.[11] Presumably, the steric constraints caused by the tether in **23** disfavor cyclopropane formation as compared to the analogous intermolecular system;[1] thus, an alternative rearrangement pathway occurs to form the unsaturated imine **24**. This type of rearrangement is known for furanocyclopropanes[12] and has been observed on flash vacuum pyrolysis of a pyrrolocyclopropane.[13] The resulting double bond geometry in **24** enables the system to undergo a thermally allowed conrotatory 8π electrocyclization to form the dihydroazocine **25**. This type of electrocyclic ring closure is well documented for the formation of cyclooctatrienes.[14] The resulting dihydroazocine **25** then undergoes a well-precedented disrotatory 6π electrocyclization[15] to form the 7-azabicyclo[4.2.0]octadiene **20**.

(10) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087.

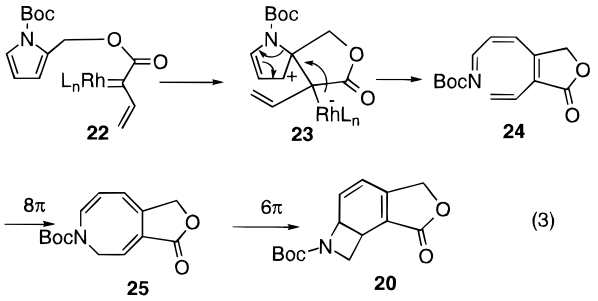
(11) Many examples are known of intramolecular reactions of carbenoids with aromatic systems proceeding through dipolar intermediates. See: (a) Doyle, M. P.; Shanklin, M. S.; Pho, H. Q.; Mahapatro, S. N. *J. Org. Chem.* **1988**, *53*, 1017. (b) Davies, H. M. L.; McAfee, M. J.; Oldenburg, C. E. M. *J. Org. Chem.* **1989**, *54*, 930.

(12) Padwa, A.; Wisnieff, T. J.; Walsh, E. J. *J. Org. Chem.* **1989**, *54*, 299 and references cited therein.

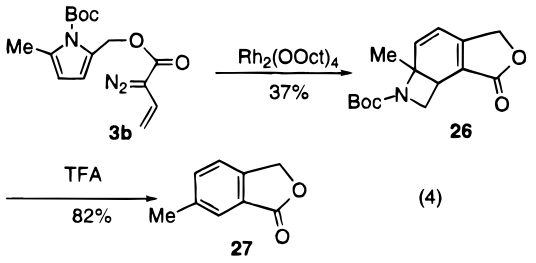
(13) Tanny, S. R.; Grossman, J.; Fowler, F. W. *J. Am. Chem. Soc.* **1972**, *94*, 6495.

(14) (a) Marvell, E. N.; Seubert, J. *J. Am. Chem. Soc.* **1967**, *89*, 3377. (b) Huisgen, R.; Dahmen, A.; Huber, H. *Tetrahedron Lett.* **1969**, 1461. (c) Huisgen, R.; Dahmen, A.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 7130. (d) Huisgen, R.; Dahmen, A.; Huber, H. *Tetrahedron Lett.* **1969**, 1465.

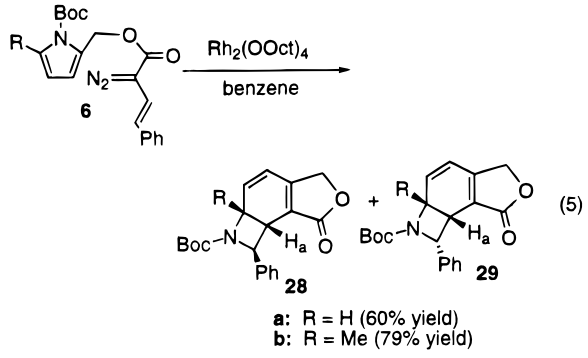
(15) Paquette, L. A.; Kakihana, T.; Kelly, J. F. *J. Org. Chem.* **1971**, *36*, 435.



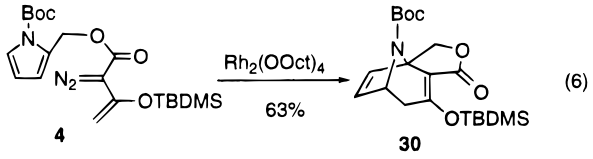
The next series of experiments explored what structural features of the vinylcarbenoid and pyrrole would be effective at altering the outcome of this chemistry so that tropane products would be formed. Rhodium(II) octanoate catalyzed decomposition of the 5-methylpyrrole derivative **3b** once again resulted in the clean formation of a fused 7-azabicyclo[4.2.0]octadiene (**26**) as determined by the ^{1}H NMR of the crude reaction mixture. This product, however, was moderately unstable to chromatographic purification and was isolated in only 37% yield. Confirmation of the structural assignment was achieved by conversion of **26** to the aromatic system **27**. The observed regiochemistry is consistent with the mechanism proposed in eq 3.



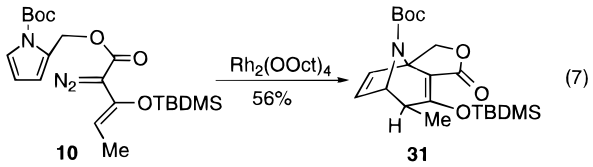
The effect of vinylcarbenoid substituents was also explored as shown in eq 5. Rhodium(II) octanoate-catalyzed decomposition of the styryldiazomethanes **6** still resulted in the exclusive formation of fused 7-azabicyclo[4.2.0]octadienes. In the case of both **6a** and **6b**, a 2:1 mixture of isomeric 7-azabicyclo[4.2.0]octadienes, **28** and **29**, were formed. These products showed greater stability to chromatography and were isolable in higher yields than was the case for **20** and **26**. The isomers were not separable by chromatography but were readily distinguished and assigned on the basis of coupling constants for the azetidine protons and the shielding effect of the phenyl ring.



As the formation of the fused 7-azabicyclo[4.2.0]-octadienes was considered to arise from zwitterionic intermediates, attempts were made to disfavor the occurrence of such intermediates so that the formation of tropanes would become the favored reaction pathway. The rhodium(II) octanoate/nonpolar solvent reaction conditions were already optimized to minimize the occurrence of zwitterionic intermediates.[1] Consequently, the emphasis was placed on introduction of functionality into the carbenoid that would limit stabilization of the negative charge in the zwitterionic intermediates. On the basis of these considerations, the decomposition of the (1-siloxyvinyl)diazomethane **4** was examined. This resulted in a major change in reaction outcome. Formation of the 7-azabicyclo[4.2.0]octadiene product was not observed, and the tropane **30** crystallized from the reaction mixture and was isolated in 63% yield.



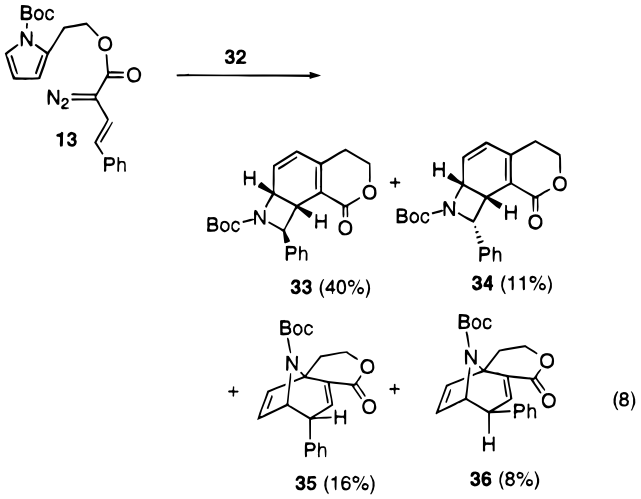
The synthesis of tropanes with control of stereochemistry at the 4-position is possible by using more elaborate siloxy-substituted vinyldiazomethanes as substrates. Rhodium(II) octanoate-catalyzed decomposition of the (*Z*)-(2-methyl-1-siloxyvinyl)diazomethane **10** resulted in the formation of the tropane **31** in 56% yield. The *exo* stereochemistry for the methyl group in **31** was assigned based on the characteristic lack of coupling in this system for the protons at the *endo* and bridgehead positions.[16,17]



Extension of this reaction to the higher homologue led to intriguing results. Decomposition of the styryldiazomethane **13** using the rhodium(II) octanoate/hexane reaction conditions resulted in inefficient capture of the carbenoid. On the assumption that a more electrophilic carbenoid would likely lead to enhanced reactivity with the pyrrole, the reaction was repeated using rhodium(II) *N*-(*p*-*tert*-butylphenylsulfonyl)prolinate (**32**)[18] as the catalyst (eq 8). Under these conditions the major products were two fused 7-azabicyclo[4.2.0]octadienes **33** and **34** (51% combined yield) along with two isomeric tropanes **35** and **36** (24% combined yield). The stereochemistry for **35** and **36** was readily assigned based on the distinctive coupling constants at the bridgehead.[16,17]

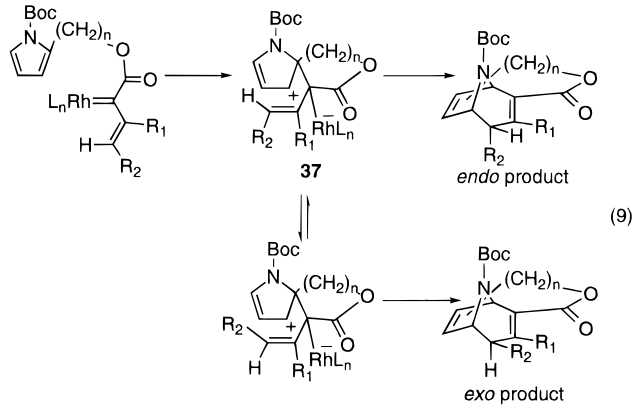
The formation of the *exo* isomer **31** and both *endo* (**35**) and *exo* (**36**) isomers of the tropanes was unexpected because the Cope rearrangement of divinylcyclopropanes proceeds through a well defined boat transition state and this would have led to the formation of only an *endo* product.[16,17] The exo product **36** was shown not to be formed by isomerization of the *endo* product **35** because **35** was stable when subjected to the reaction conditions of its formation. Therefore, it was concluded that the formation of the *exo* products **31** and **36** in these reactions must involve an intermediate capable of undergoing equilibration at the vinyl group. A possible intermediate

(16) Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817.
(17) Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203.
(18) Davies, H. M. L.; Hutcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243.



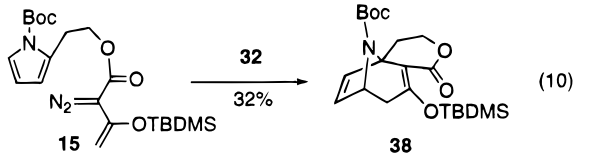
(8)

that may be capable of doing this would be the zwitterionic structure **37** (eq 9). Such a conclusion implies that in these intramolecular reactions, the formation of tropanes occurs from zwitterionic intermediates and does not involve initial formation of cyclopropanes followed by a Cope rearrangement.



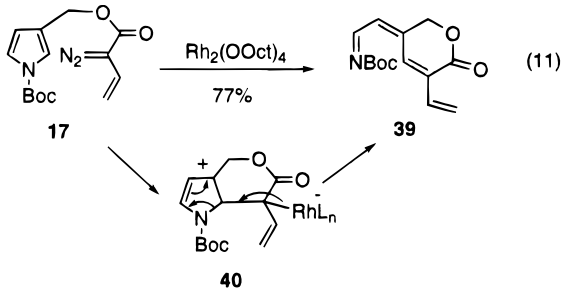
(9)

In the case of the higher homologue series, the use of the siloxy substituent once again leads to the clean formation of the tropane product. The decomposition of the (1-siloxyvinyl)diazomethane **15** was not successful when rhodium(II) octanoate was used as catalyst, but the reaction proceeded smoothly when the more electrophilic rhodium(II) *N*-(*p*-*tert*-butylphenylsulfonyl)prolinate (**32**)[18] was employed as catalyst and the tropane **38** was obtained in 32% yield after chromatography (eq 10).



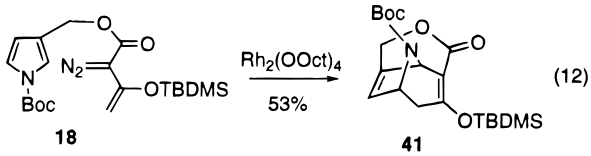
(10)

The final series of experiments explored the effect of having the vinyldiazomethane tethered to the 3-position of pyrrole. Rhodium(II) octanoate-catalyzed decomposition of the unsubstituted vinyldiazomethane **17** resulted in the formation of the trienimine **39** in moderate yield (eq 11). This would be the expected product from the zwitterionic intermediate **40**, as ring opening of **40** would form **39**, which is incapable of undergoing an 8π-electrocyclization. Related structures have been formed in intramolecular reactions of carbenoids with furans.[12]



(11)

The dramatic influence of the 1-siloxy group to enhance tropane formation was further observed in the reaction of the (1-siloxyvinyl)diazomethane **18**. Rhodium(II) octanoate-catalyzed decomposition of **18** resulted in the formation of the tropane **41** which crystallized out of the reaction mixture on cooling. The formation of this tropane, which would be expected to have significant ring strain underscores the synthetic power of the reaction between vinylcarbenoids and pyrroles to synthesize azapolycyclic compounds.



(12)

The stereochemical studies demonstrate convincingly that the tropanes are derived from zwitterionic intermediates. The presence of a siloxy group strongly favors the formation of tropanes over the 7-azabicyclo[4.2.0]-octadienes. Two possible factors can be proposed for this controlling influence. First, the siloxy group would be expected to decrease the ability of the vinyl group to delocalize the negative charge in the zwitterionic intermediate. However, it is rather surprising that the siloxy group would have such a dramatic effect, such that tropanes are the major product formed from (1-siloxyvinyl)diazomethanes while products from zwitterionic intermediates dominate from unsubstituted vinyldiazomethanes. Secondly, the presence of the siloxy group increases the nucleophilicity of the vinyl group, which may enhance attack at the allyl cation function in the zwitterion. A third factor that could play a role is that the presence of the siloxy group alters the conformation of the vinylcarbenoid such that even if the reaction proceeds through zwitterionic intermediates, the vinyl group is still ideally positioned to allow rearrangement to the tropane product to occur. In earlier studies, we have shown that the effect of bulky substituents at the central carbon of vinylcarbenoids causes a major change in product outcome that can be explained by a change in the preferred conformation of the rhodium−vinylcarbenoid complex.[19] If a similar effect is occurring here, then conformation A should be preferred for the unsubstituted vinylcarbenoid while conformer B would be favored for the (1-siloxyvinyl)cabenoid (Figure 1). The vinyl group in conformer B is appropriately positioned to enable rearrangement to the tropane to occur directly from the zwitterionic intermediate that would be formed without requiring any bond rotation. This is not the case in conformer A, and so, ring opening to the trienimine becomes the dominant pathway.

(19) Davies, H. M. L.; Hu, B.; Saikali, E.; Bruzinski, P. R. *J. Org. Chem.* **1994**, *59*, 4535.

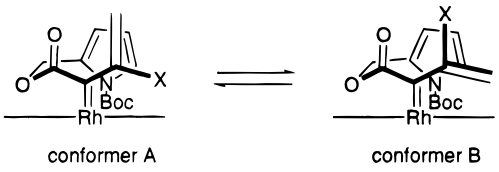


Figure 1.

In summary, we have shown that the rhodium(II)-catalyzed intramolecular reaction of vinylcarbenoids and pyrroles leads to a novel synthesis of fused tropanes. The stereochemical results of these studies are not consistent with a tandem cyclopropanation/Cope rearrangement mechanism. Instead the 3 + 4 annulation is considered to occur in a stepwise mode by means of zwitterionic intermediates that are capable of undergoing double bond isomerization prior to ring closure. Also shown is the delicate effect that a 1-siloxy substituent on the vinylcarbenoid system has on the outcome of this chemistry. Further studies to elaborate these fused tropanes to specific target molecules with selective interactions at the central nervous system will be described in due course.

Experimental Section

General Methods. Ether, hexane, and THF were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Benzene and toluene were dried over molecular sieves (4 Å). Anhydrous dimethylformamide (DMF) from Aldrich Chemical Co. was used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on 200, 300, or 400 MHz NMR spectrometers. Column chromatography was carried out on silica gel 60 (230−400 mesh). Thin layer chromatography (TLC) was performed on Whatman (TLC) plates. Pyrrole-2-carboxaldehyde, diketene, and Meldrum's acid were bought from Aldrich Chemical Co. Pyrrole-3-carboxaldehyde,[20] 5-methylpyrrole-2-carboxaldehyde,[21] 4-phenyl-3-butenoic acid,[22] 5-propionyl-Meldrum's acid (**7**),[10] and *p*-acetamidobenzenesulfonyl azide[23] were prepared by literature methods.

1-(1,1-Dimethylethoxycarbonyl)-2-(hydroxymethyl)-pyrrole (1a). DMAP (1.96 g, 16.8 mmol) and di-*tert*-butyl dicarbonate (43.75 g, 200.1 mmol) were added to a solution of pyrrole-2-carboxaldehyde (19.06 g, 200.1 mmol) in dry acetonitrile (25 mL) under an argon atmosphere. The resulting mixture was stirred at 25 °C for 24 h, and then the solvent was removed at reduced pressure and the residue was purified by column chromatography on silica gel using petroleum ether: ether (4:1) as the eluting solvent to give 1-(*tert*-butoxycarbonyl)pyrrole-2-carboxaldehyde (38.91 g, 99% yield).

To a solution of aldehyde from above (38.91 g, 199.4 mmol) in methanol (250 mL) at 0 °C was added $NaBH_4$ (7.55 g, 199.4 mmol) in portions under argon. The mixture was stirred for a further 1 h before quenching with cold water. The mixture was then extracted with ether and the ether extract was washed with saturated aqueous sodium bicarbonate and then with saturated aqueous sodium chloride. The organic phase was then dried ($MgSO_4$), and the solvent was removed under reduced pressure to give **1a** as an oil (35.53 g, 90% yield) and used without further purification: IR ($CDCl_3$) 3671, 3162, 2934, 2729, 1746, 1599 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.16 (dd, J = 3.4, 1.7 Hz, 1 H), 6.17 (dd, J = 3.4, 1.7 Hz, 1 H), 6.09 (t, J = 3.4 Hz, 1 H), 4.64 (d, J = 7.3 Hz, 2 H), 3.58 (t, J = 7.3 Hz, 1 H), 1.61 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.9, 134.7, 121.6, 113.3, 110.2, 84.3, 57.5, 27.8. Anal. Calcd for $C_9H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.79; H, 7.61; N, 7.00.

1-(1,1-Dimethylethoxycarbonyl)-2-(hydroxymethyl)-5-methylpyrrole (1b) was prepared from 5-methylpyrrole-2-carboxaldehyde (20.00 g, 183.3 mmol) in 97% overall yield by treatment with di-*tert*-butyl dicarbonate followed by $NaBH_4$ reduction according to the procedure described for the synthesis of **1a**: IR ($CDCl_3$) 3534, 3090, 2926, 1696, 1593 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.05 (d, J = 3.2 Hz, 1 H), 5.83 (d, J = 3.2 Hz, 1 H), 4.57 (d, J = 7.3 Hz, 2 H), 3.55 (t, J = 7.3 Hz, 1 H), 2.36 (s, 3 H), 1.61 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.1, 135.1, 132.3, 112.3 111.0, 84.6, 58.4, 28.0, 16.7. Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.42; H, 8.08; N, 6.52.

1-(1,1-Dimethylethoxycarbonyl)-3-(hydroxymethyl)-pyrrole (1c) was prepared from pyrrole-3-carboxaldehyde (4.25 g, 44.7 mmol) in 68% overall yield by treatment with di-*tert*-butyl dicarbonate followed by sodium borohydride reduction according to the procedure described for the synthesis of **1a**: IR ($CDCl_3$) 3671, 3162, 2934, 2729, 1746, 1599 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.18 (d, J = 2.5 Hz, 2 H), 6.22 (t, J = 2.5 Hz, 1 H), 4.50 (s, 2 H), 1.70 (br. s, 1 H), 1.56 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.7, 127.2, 120.5, 117.5, 111.5, 83.5, 58.0, 27.8; HRMS calcd for $C_{10}H_{15}NO_3$ 197.1052, found 197.1051.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-Diazo-3-oxobutanoate (2a). A 50% solution of diketene in acetone (12.79 g, 152.1 mmol) was added to a refluxing solution of **1a** (10.0 g, 50.7 mmol), *p*-acetamidobenzenesulfonyl azide (15.65 g, 65.2 mmol), and sodium acetate (0.42 g, 5.2 mmol) in dry acetonitrile (60 mL) over a 30 min period.[24] The resulting mixture was cooled to rt and stirred for a further 7 h. Water was added, and the mixture was extracted with ether. The ether extract was quickly washed with 15% KOH solution, dried ($MgSO_4$) and then the solvent was evaporated under vacuum. Flash column chromatography on silica gel using petroleum ether/ether (4:1) as eluting solvent gave **2a** as an oil (7.18 g, 46% yield): IR ($CDCl_3$) 3162, 2933, 2873, 2150, 1722, 1644, 1138 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.28 (dd, J = 3.2, 1.8 Hz, 1 H), 6.30 (dd, J = 3.2, 1.8 Hz, 1 H), 6.13 (t, J = 3.2 Hz, 1 H), 5.42 (s, 2 H), 2.45 (s, 3 H), 1.54 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.2, 161.2, 148.7, 127.9, 123.2, 116.3, 110.2, 87.5, 84.3, 60.0, 28.2, 27.9, (*C*=N$_2$ not observed). Anal. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.58; H, 5.62; N, 13.59.

[1-(1,1-Dimethylethoxycarbonyl)-5-methyl-2-pyrrolyl]-methyl 2-diazo-3-oxobutanoate (2b) was prepared from **1b** (10.0 g, 47.4 mmol), in 43% yield by treatment with diketene and *p*-acetamidobenzenesulfonyl azide according to the procedure described for the synthesis of **2a**: IR ($CDCl_3$) 3173, 2984, 2147, 1708, 1658, 1596 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.17 (d, J = 3.3 Hz, 1 H), 5.87 (d, J = 3.3 Hz, 1 H), 5.37 (s, 2 H), 2.45 (s, 3 H), 2.39 (s, 3 H), 1.57 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.2, 161.2, 149.6, 134.3, 127.8, 115.1, 110.6, 84.2, 61.0, 28.2, 27.9, 16.5, (*C*=N$_2$ not observed). Anal. Calcd for $C_{15}H_{19}N_3O_5$: C, 56.07; H, 5.96; N, 13.08. Found: C, 56.17; H, 6.03; N, 12.99.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-Diazo-3-butenoate (3a). $NaBH_4$ (0.80 g, 21.1 mmol) was added over 30 min to a solution of **2a** (2.16 g, 7.0 mmol) in methanol (50 mL) at 0 °C under argon. The mixture was stirred for a further 1 h, and then ice cold water was added. The mixture was then extracted with CH_2Cl_2 (3 × 50 mL), the extract was washed with $NaHCO_3$ and brine, dried ($MgSO_4$), and the solvent was then evaporated to give the alcohol. The alcohol was used in the next step without purification. To a solution of the alcohol and triethylamine (2.83 g, 28.0 mmol) in dry CH_2Cl_2 (60 mL) at 0 °C under argon was added $POCl_3$ (1.61 g, 10.6 mmol) in dry CH_2Cl_2 (2 mL) over a period of 30 min. The resulting mixture was left to stir at 0 °C overnight. The solution was then washed with ice cold water until there was no color in the aqueous layer, washed with cold brine, and dried (Na_2SO_4), and then the solvent was evaporated at a

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reduced pressure. The residue was purified by column chromatography on silica gel using pentane:ether (19:1) as eluting solvent to give **3a** as an oil (1.60 g, 78% yield): IR (neat) 2981, 2088, 1748, 1743, 1716, 1616 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.29 (dd, J = 3.3, 1.9 Hz, 1 H), 6.30 (m, 1 H), 6.12 (m, 1 H), 6.12 (dd, J = 17.4, 11.0 Hz, 1 H), 5.39 (s, 2 H), 5.09 (d, J = 11.0 Hz, 1 H), 4.83 (d, J = 17.4 Hz, 1 H), 1.57 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **3a**.

[1-(1,1-Dimethylethoxycarbonyl)-5-methyl-2-pyrrolyl]-methyl 2-diazo-3-butenoate (3b) was prepared from **2b** (2.00 g, 6.2mmol) in 43% yield by treatment with $NaBH_4$ followed by $POCl_3$ according to the procedure described for the synthesis of **3a**: IR (neat) 3089, 2982, 2926, 2088, 1744, 1699, 1621, 1542, 1458, 1390, 1378 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.18 (dd, J = 17.4, 11.0 Hz, 1 H), 6.16 (m, 1 H), 5.87 (m, 1 H), 5.36 (s, 2 H), 5.11 (d, J = 11.0 Hz, 1 H), 4.85 (d, J = 17.4 Hz, 1 H), 2.42 (s, 3 H), 1.59 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **3b**.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-Diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-butenoate (4). Triethylamine (2 mL, 14.3 mmol) was added to a stirring solution of **2a** (3.1 g, 10.1 mmol) in CH_2Cl_2 (26 mL) at 0 °C under argon. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (2.8 mL, 12.2 mmol) was added after 5 min, and the mixture was further stirred for 30 min at 0 °C. The reaction mixture was diluted with hexanes (100 mL), and the organic phase was washed with dilute aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried (Na_2SO_4), and the solvent was removed under reduced pressure to yield **4** as a yellow oil which was used without further purification: IR (neat) 2955, 2928, 2858, 2107, 1748, 1710, 1612, 1476 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.34 (m, 1 H), 6.32 (m, 1 H), 6.17 (t, J = 3.2 Hz, 1 H), 5.43 (s, 2 H), 5.04 (d, J = 2.1 Hz, 1 H), 4.27 (d, J = 2 Hz, 1 H), 1.62 (s, 9 H), 0.94 (s, 9 H), 0.25 (s, 6 H). Due to lack of stability, elemental analysis was not attempted on **4**.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 4-Phenyl-3(*E*)-butenoate (5a). A solution of 4-phenyl-3-butenoyl chloride (4.38 g, 24.3 mmol) in dry CH_2Cl_2 (50 mL) was added to stirred solution of **1a** (5.00 g, 25.4 mmol) and pyridine (2.16 g, 27.3 mmol) in CH_2Cl_2 (30 mL) at 0 °C, under argon. The ice bath was then removed, and the mixture was stirred at rt overnight. The mixture was then washed with a saturated aqueous NH_4Cl and dried ($MgSO_4$), and the solvent was removed at reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether/ether (9:1) as eluting solvent to give **5a** as an oil (5.60 g, 68% yield): IR (neat) 3032, 2972, 2929, 1743, 1504, 1411, 1373, 1352 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.25−7.50 (m, 6H), 6.58 (d, J = 16.0 Hz, 1 H), 6.39 (dt, J = 16.0, 6.7 Hz, 1 H), overlapping broad doublet at δ 6.39 (1 H), 6.23 (t, J = 3.3 Hz, 1 H), 5.40 (s, 2 H), 3.36 (d, J = 6.7 Hz, 2 H), 1.65 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.1, 148.8, 136.9, 133.6, 128.6, 128.5, 127.5, 126.3, 122.9, 121.7, 115.7, 110.2, 84.1, 59.9, 38.4, 27.9. Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.25; H, 6.80; N, 4.09.

[1-(1,1-Dimethylethoxycarbonyl)-5-methyl-2-pyrrolyl]-methyl 4-phenyl-3(*E*)-butenoate (5b) was prepared from **1b** (5.93 g, 28.1 mmol) in 52% yield by treatment with 4-phenyl-3-butenoyl chloride and pyridine according to the procedure described for the synthesis of **5a**: IR (neat) 3065, 3027, 2983, 2834, 1743, 1667, 1602, 1537, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.25−7.50 (m, 6 H), 6.57 (d, J = 15.7 Hz, 1 H), 6.36 (dt, J = 15.7, 6.6 Hz, 1 H), 6.26 (d, J = 3.3 Hz, 1 H), 5.96 (d, J = 3.3 Hz, 1 H), 5.34 (s, 2 H), 3.34 (d, J = 6.6 Hz, 2 H), 2.50 (s, 2 H), 1.65 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.2, 149.7, 136.8, 134.2, 133.4, 128.5, 128.3, 127.5, 126.3, 121.8, 114.6, 110.6, 84.0, 60.8, 38.5, 27.9, 16.4. Anal. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.68; H, 7.24; N, 3.77.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-Diazo-4-phenyl-3(*E*)-butenoate (6a). DBU (2.79 g, 18.3 mmol) was added dropwise to a solution of **5a** (5.21 g, 15.3 mmol) and *p*-acetamidobenzenesulfonyl azide (4.39 g, 18.3 mmol) in acetonitrile (100 mL) at 0 °C under argon. The mixture was stirred overnight, and then ether was added. The resulting mixture was washed with saturated aqueous NH_4Cl and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel using petroleum ether:ether (9:1 to 8:2) as solvent gradient to give **6a** as a red oil (3.35 g, 60% yield): IR (CCl_4) 2979, 2081, 1742, 1716, 1699, 1686 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.12−7.37 (m, 6 H), 6.47 (d, J = 15.6 Hz, 1 H), 6.31 (brs, 1 H), 6.18 (d, J = 15.6 Hz, 1 H), 6.15 (brs, 1 H), 5.44 (s, 2 H), 1.58 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **6a**.

[1-(1,1-Dimethylethoxycarbonyl)-5-methyl-2-pyrrolyl]-methyl 2-diazo-4-phenyl-3(*E*)-butenoate (6b) was prepared from **5b** (4.57 g, 12.9 mmol) in 29% yield by treatment with DBU and *p*-acetamidobenzenesulfonyl azide according to the procedure described for the synthesis of **6a**: IR (CCl_4) 2961, 2081, 1743, 1701, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.10−7.36 (m, 5 H), 6.46 (d, J = 16.3 Hz, 1 H), 6.17 (d, J = 3.2 Hz, 1 H), 6.16 (d, J = 16.3 Hz, 1 H), 5.88 (d, J = 3.2 Hz, 1 H), 5.38 (s, 2 H), 2.41 (s, 3 H), 1.58 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **6b**.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 3-Oxopentanoate (8). A solution of **1a** (5.18 g, 26.2 mmol), **7** (5.26 g, 26.2 mmol), and pyridine (2.2 mL, 27.2 mmol) in benzene (70 mL) was heated at 65 °C for 14 h under argon. The mixture was then cooled to rt and diluted with ether (50 mL), and the resulting mixture was washed with saturated aqueous NH_4Cl (100 mL) and dried (Na_2SO_4). The solvent was removed under pressure, and the residue was purified by chromatography on silica gel with 1:4 ether:hexanes as solvents to yield **8** as an oil (6.45 g, 83% yield): R_f = 0.55 in 1:1 ether:pentane; IR (neat) 2977, 2939, 1743, 1710, 1650, 1623 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 1.8 Hz, 1 H), 6.22 (brs, 1 H), 6.05 (m, 1 H), 5.24 (s, 2 H), 3.36 (s, 3 H), 2.47 (q, J = 7.2 Hz, 2 H), 1.50 (s, 9 H), 0.95 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1, 167.0, 148.8, 128.8, 122.8, 115.8, 110.1, 83.9, 59.9, 48.6, 35.6, 27.4, 7.0. Anal. Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 61.10; H, 7.21; N, 4.81.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-Diazo-3-oxopentanoate (9). Triethylamine (3.3 mL, 23.7 mmol) was added to a stirred solution of *p*-acetamidobenzenesulfonyl azide (5.5 g, 22.9 mmol) and **8** (6.45 g, 21.9 mmol) in acetonitrile (50 mL) at rt under argon. The reaction mixture was stirred overnight at room temperature and then diluted with 1:2 ether:pentane (100 mL). The resulting precipitate was filtered and rinsed with 1:2 ether:pentane (50 mL). The filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica gel with 1:3 ether:hexanes as solvent to yield **9** as an oil (6.32 g, 90% yield): R_f = 0.81 in ether:pentane; IR (neat) 2972, 2939, 2123, 1743, 1716, 1650, 1313 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 2 Hz, 1 H), 6.29 (brs, 1 H), 6.11 (t, J = 3.4 Hz, 1 H), 5.31 (s, 2 H), 2.54 (q, J = 6.8 Hz, 2 H), 1.56 (s, 9 H), 1.03 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 161.8, 149.3, 128.5, 127.7, 116.7, 110.7, 84.6, 60.2, 33.9, 28.1, 8.3 (C=N_2 not observed). Anal. Calcd for $C_{15}H_{19}N_3O_5$: C, 56.07; H, 5.96; N, 13.08. Found: C, 56.12; H, 6.00; N, 13.01.

[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]methyl 2-diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-pentenoate (10) was prepared from **9** (1.05 g, 3.27 mmol) by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **5**: IR (neat) 2960, 2934, 2862, 2091, 1744, 1708, 1662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 1 H), 6.27 (brs, 1 H), 6.13 (m, 1 H), 5.37 (s, 1 H), 5.27 (q, J = 8.0 Hz, 1 H), 1.65 (d, J = 8.0 Hz, 3 H), 1.58 (s, 9 H), 0.94 (s, 9 H), 0.13 (s, 6 H). NOE data: irradiation at δ 0.12, enhancements at δ 0.94 (1.4%) and 1.65 (0.5%); irradiation at δ 1.65, enhancements at δ 0.12 (1.4%), 0.94 (0.8%), and 5.27 (3.6%). Due to lack of stability, elemental analysis was not attempted on **10**.

2-(2-Pyrrolyl)ethyl 4-phenyl-3(*E*)-butenoate (12) was prepared from **11** (1.95 g, 17.6 mmol) in 46% yield by treatment with 4-phenyl-3-butenoyl chloride and pyridine according to the procedure described for the synthesis of **5a**: IR (neat) 3386, 3027, 2961, 2912, 1732, 1650, 1580, 1450, 1270, 1168 cm^{-1};

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.20 (brs, 1 H), 7.20−7.45 (m, 5 H), 6.53 (d, J = 17 Hz, 1 H), 6.53 (m, 1 H), 6.30 (dt, J = 17, 6.4 Hz, 1 H), 6.22 (m, 1 H), 5.98 (m, 1 H), 4.33 (t, J = 6.4 Hz, 2 H), 3.28 (d, J = 7.2 Hz, 2 H), 2.95 (t, J = 6.4 Hz, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.3, 136.6, 133.8, 128.6, 128.1, 127.7, 126.3, 121.5, 117.1, 108.3, 106.4, 64.6, 38.5, 27.2; MS (M + 1, 256.2); HRMS calcd for $C_{16}H_{18}NO_2$ 256.1338, found 256.1329.

2-[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]ethyl 2-diazo-4-phenyl-3(*E*)-butenoate (13) was prepared from **12** (2.00 g, 7.8 mmol) in 36% overall yield by treatment with di-*tert*-butyl dicarbonate according to the procedure described for the synthesis of **1a** followed by treatment with DBU and *p*-acetamidobenzenesulfonyl azide according to the procedure described for the synthesis of **6a**. The product was purified by column chromatography on silica gel using petroleum ether: ether (9:1) as eluting solvent: IR (neat) 3059, 3021, 2989, 2945, 2086, 1743, 1705, 1629, 1602, 1503, 1450 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.15−7.45 (m, 6 H), 6.48 (d, J = 16.3 Hz, 1 H), 6.19 (d, J = 16.3 Hz, 1 H), 6.12 (t, J = 3.3 Hz, 1 H), 6.07 (m, 1 H), 4.51 (t, J = 6.7 Hz, 2 H), 3.29 (t, J = 6.7 Hz, 2 H), 1.61 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **13**.

2-[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]ethyl 2-Diazo-3-oxobutanoate (14). 2-[2-Hydroxyethyl]pyrrole (**11**) (3.0 g, 27 mmol) was dissolved in acetonitrile (50 mL) under argon. Diketene (3.4 g, 40.4 mmol) in acetonitrile (50 mL) and pyridine (1 mL) were added, and after stirring for a further 15 min, the mixture was heated under reflux for 4 h. The solvent was removed under reduced pressure, and the residue was purified by columnn chromatography on silica gel using 1:2 ether:pentane as solvent to give 2-(2-pyrrolyl)ethyl 3-oxobutanoate in 65% yield: R_f = 0.13 in 1:4 ethyl acetate: pentane; IR (neat): 3385, 3096, 2962, 2922, 1737, 1712, 1649, 1571 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.71 (brs, 1 H), 6.73 (dd, J = 2.6, 4.2 Hz, 1 H), 6.12 (dd, J = 2.8, 5.7 Hz, 1 H), 5.96 (brs, 1 H), 4.35 (t, J = 6.1 Hz, 2 H), 3.52 (s, 2 H), 2.97 (t, J = 6.1 Hz, 2 H), 2.26 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.4, 166.6, 127.6, 117.0, 107.7, 105.8, 64.9, 49.6, 30.0, 26.7.

Compound **14** was prepared from 2-(2-pyrrolyl)ethyl 3-oxobutanoate (1.75 g, 8.97 mmol) in 66% overall yield by treatment with triethylamine and *p*-acetamidobenzenesulfonyl azide according to the procedure described for the synthesis of **9** followed by treatment with di-*tert*-butyl dicarbonate according to the procedure described for the synthesis of **1a**: R_f = 0.69 in 1:1 ether:pentane; IR (neat) 2978, 2934, 2871, 2140, 1738, 1660, 1493, 1478 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.19 (dd, J = 1.8, 3.3 Hz, 1 H), 6.07 (t, J = 3.3 Hz, 1 H), 6.00 (m, 1 H), 4.46 (t, J = 6.6 Hz, 2 H), 3.25 (t, J = 6.6 Hz, 2 H), 2.44 (s, 3 H), 1.58 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 189.7, 160.9, 149.0, 130.3, 121.3, 112.8, 109.8, 83.5, 63.8, 28.1, 27.9, 27.7, (C=N_2 not observed). Anal. Calcd for $C_{15}H_{19}N_3O_5$: C, 56.07; H, 5.96; N, 13.08. Found: C, 56.17; H, 6.02; N, 13.10.

2-[1-(1,1-Dimethylethoxycarbonyl)-2-pyrrolyl]ethyl 2-diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-butenoate (15) was prepared from **14** (0.50 g, 1.55 mmol) by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **3**: IR (neat) 2965, 2929, 2851, 2100, 1745, 1710, 1611, 1327 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (dd, J = 1.8, 3.1 Hz, 1 H), 6.05 (t, J = 3.3 Hz, 1 H), 5.98 (brs, 1 H), 4.39 (t, J = 6.6 Hz, 2 H), 4.19 (d, J = 2.0 Hz, 1 H), 3.20 (t, J = 6.6 Hz, 2 H), 1.55 (s, 9 H), 0.87 (s, 9 H), 0.17 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.0, 149.3, 140.7, 130.8, 121.3, 112.8, 110.0, 90.3, 83.6, 63.5, 27.9, 25.5, 18.0, 14.0, −3.0, −4.8, (C=N_2 not observed). Due to lack of stability, elemental analysis was not attempted on **15**.

[1-(1,1-Dimethylethoxycarbonyl)-3-pyrrolyl]methyl 2-diazo-3-oxobutanoate (16) was prepared from **1c** (5.0 g, 27.6 mmol) in 58% yield by treatment with diketene and *p*-acetamidobenzenesulfonyl azide according to the procedure described for the synthesis of **2a**: IR (CH_2Cl_2) 3150, 2984, 2937, 2143, 1712, 1654, 1590, 1458 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.28 (dd, J = 2.4, 1.7 Hz, 1 H), 7.19 (dd, J = 3.2, 2.4 Hz, 1 H), 6.22 (dd, J = 3.2, 1.7 Hz, 1 H), 5.10 (s, 2 H), 2.45 (s, 3 H), 1.57 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 189.9, 161.2, 148.3, 121.2, 120.7, 119.8, 112.2, 84.0, 60.2, 28.1, 27.8, (C=N_2 not observed). Anal. Calcd for $C_{14}H_{17}NO_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.80; H, 5.63; N, 13.59.

[1-(1,1-Dimethylethoxycarbonyl)-3-pyrrolyl]methyl 2-diazo-3-butenoate (17) was prepared from **16** (1.05 g, 3.42 mmol) in 37% yield by treatment with sodium borohydride followed by phosphorus oxychloride according to the procedure described for the synthesis of **3a**: IR (neat) 2983, 2933, 2087, 1748, 1710, 1623 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (brs, 1 H), 7.16 (brs, 1 H), 6.21 (d, J = 1.77 Hz, 1 H), 6.13 (dd, J = 11.1, 17.4 Hz, 1 H), 5.06 (m, 3 H), 4.81 (d, J = 17.4 Hz, 1 H), 1.55 (s, 9 H). Due to lack of stability, elemental analysis was not attempted on **17**.

[1-(1,1-Dimethylethoxycarbonyl)-3-pyrrolyl]methyl 2-diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-butenoate (18) was prepared from **16** (1.0 g, 3.25 mmol) by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **4**: IR (neat) 2955, 2928, 2858, 2102, 1754, 1716, 1612 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (brs, 1 H), 7.13 (brs, 1 H), 6.17 (brs, 1 H), 5.02 (brs, 2 H), 4.95 (brs, 1 H), 4.17 (brs, 1 H), 1.51 (s, 9 H), 0.84 (s, 9 H), 0.15 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 148.6, 140.8, 122.0, 120.6, 119.5, 112.3, 90.3, 83.6, 59.5, 27.5, 25.3, 17.7, −5.2, (C=N_2 not observed). Due to lack of stability, elemental analysis was not attempted on **18**.

***cis*-1,1-Dimethylethyl 1,5a,7,7a-Tetrahydro-1-oxoisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (20).** A solution of **3a** (2.00 g, 6.9 mmol) in hexane (100 mL) was added dropwise to a refluxing solution of rhodium(II) octanoate (0.054 g, 0.07 mmol) in hexane (100 mL) under argon. The resulting solution was refluxed for a further 1 h, and the solvent was removed and the residue was purified by column chromatography on silica gel using ether/petroluem ether (4:1) as solvent followed by recrystallization from petroleum ether/ether mixture to give **20** as colorless crystals (0.87 g, 49% yield): mp 112−114 °C; IR (CH_2Cl_2) 3054, 2979, 1752, 1695, 1599, 1473 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 95 °C) δ 6.35 (d, J = 9.8 Hz, 1 H), 6.26 (dd, J = 9.8, 4.2 Hz, 1 H), 5.16 (dd, J = 9.8, 4.3 Hz, 1 H), 4.80−5.05 (m, 2 H), 4.31 (t, J = 8.1 Hz, 1 H), 3.85 (dd, J = 8.1, 4.8 Hz, 1 H), 3.52 (m, 1 H), 1.40 (s, 9 H). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.94; H, 6.48; N, 5.27.

Phthalide 21. A solution of TFA (0.89 mL, 11.6 mmol) in CH_2Cl_2 (2 mL) was added dropwise to a stirred solution of compound **20** (0.31 g, 1.2 mmol) in CH_2Cl_2 (20 mL) at room temperature under argon. The resulting mixture was stirred for a further 30 min, and then the solvent was evaporated under reduced pressure. Aqueous NH_4Cl was added to the residue, and the mixture was extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4), and the solvent was removed under reduced presure. Purification by recrystallization from ether:petroleum ether gave **21** as a colorless solid (0.151 g, 80%), mp 73−75 °C, lit[25a] mp 73 °C. The ^{1}H and ^{13}C NMR spectra of **21** matched the literature data.[25b]

***cis*-1,1-Dimethylethyl 1,5a,7,7a-tetrahydro-5a-methyl-1-oxoisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (26)** was prepared from **3b** (0.82 g, 2.7 mmol) in 37% yield by treatment with rhodium(II) octanoate in hexane according to the procedure described for the synthesis of **20**: mp 106−109 °C; IR (CH_2Cl_2) 3070, 2933, 1753, 1691, 1597, 1474 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 95 °C) δ 6.28 (d, J = 9.9 Hz, 1 H), 6.18 (d, J = 9.9 Hz, 1 H), 4.79−5.02 (m, 2 H), 4.16 (t, J = 8.1 Hz, 1 H), 3.72 (dd, J = 8.1, 5.6 Hz, 1 H), 3.21 (m, 1 H), 1.60 (s, 3 H), 1.40 (s, 9 H). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 65.03; H, 6.95; N, 5.04.

6-Methylphthalide 27 was prepared from **26** (0.78 g, 2.8 mmol) in 82% yield by treatment with TFA according to the procedure described for the synthesis of **21**: mp 88−91 °C from ether; IR (neat) 3043, 2923, 1770, 1596, 1504, 1460, 1167, 1063, 1009 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60 (s, 1 H), 7.43 (d, J = 7.9 Hz, 1 H), 7.32 (d, J = 7.9 Hz, 1 H), 5.20 (s, 2 H), 2.38

(25) (a) Sunko, D. E. *Arkiv Kem.* **1955**, *27*, 183 (*Chem. Abstr. 50*, 11985b). (b) *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, 1st ed.; 1993; Vol. II, p 1306.

(s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.9, 143.7, 139.0, 135.0, 125.6, 125.3, 121.6, 69.4, 21.1. Anal. Calcd for $C_9H_8O_2$: C, 72.96; H, 5.44. Found: C, 73.02; H, 5.52.

1,1-Dimethylethyl 1,5aα,7,7aα-tetrahydro-1-oxo-7*β*-phenylisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (28a) and 1,1-dimethylethyl 1,5aα,7,7aα-tetrahydro-1-oxo-7α-phenylisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (29a) were prepared as an inseparable mixture (2:1) ratio from **6a** (0.21 g, 0.6 mmol) in 60% yield by treatment with rhodium(II) octanoate in benzene according to the procedure described for the synthesis of **20**: IR (neat) 2976, 2924, 1757, 1698, 1450, 1391, 1365, 1254, 1137 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 95 °C) **28a**, δ 7.25−7.45 (m, 5 H), 6.50 (dd, J = 9.9, 3,9 Hz, 1 H), 6.41 (d, J = 9.9 Hz, 1 H), 5.40 (dd, J = 9.8, 3.9 Hz, 1 H), 5.23 (d, J = 5.0 Hz, 1 H), 5.05 (brd, J = 17.9 Hz, 1 H), 4.90 (dd, J = 17.9, 2.4 Hz, 1 H), 3.40 (ddd, J = 9.8, 5.0, 2.4 Hz, 1 H), 1.27 (s, 9 H); **29a**, δ 7.25−7.45 (m, 5 H), 6.32 (m, 2 H), 5.70 (d, J = 8.6 Hz, 1 H), 5.20 (m, 1 H), 4.70 (dd, J = 17.8, 2.6 Hz, 1 H), 4.55 (brd, J = 17.8 Hz, 1 H), 4.05 (ddd, J = 8.6, 8.6, 2.6 Hz, 1 H), 1.27 (s, 9 H). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.62; H, 6.26; N, 4.10.

1,1-Dimethylethyl 1,5aα,7,7aα-tetrahydro-5a-methyl-1-oxo-7*β*-phenylisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (28b) and 1,1-dimethylethyl 1,5aα,7,7aα-tetrahydro-5a-methyl-1-oxo-7α-phenylisobenzofuro[5,4-*b*]azete-6(3*H*)-carboxylate (29b) were prepared as an inseparable mixture (3:1) from **6b** (0.83 g, 2.2 mmol) in 79% yield by treatment with rhodium(II) octanoate in toluene (maintained at 80−90 °C) according to the procedure described for the synthesis of **20**: IR (CH_2Cl_2) 3074, 2982, 2932, 1754, 1693, 1594, 1446 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 95 °C) **28b**, δ 7.11−7.43 (m, 5 H), 6.45 (d, J = 9.9 Hz, 1 H), 6.28 (d, J = 9.9 Hz, 1 H), 5.08 (d, J = 6.1 Hz, 1 H), 4.80−5.07 (m, 2 H), 3.09 (d, J = 6.1 Hz, 1 H), 1.66 (s, 3 H), 1.34 (s, 9 H); **29b**, δ 7.11−7.43 (m, 5 H), 6.23 (s, 2 H), 5.67 (d, J = 8.7 Hz, 1 H), 4.56−4.80 (m, 2 H), 3.68 (brd, J = 8.7 Hz, 1 H), 1.73 (s, 3 H), 1.34 (s, 9 H). Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.30; H, 6.57; N, 3.98.

1,1-Dimethylethyl 6,7-dihydro-8-[(1,1-dimethylethyl)-dimethylsiloxy]-1-oxo-1*H*-cyclohepta[*c*]furan-3*H*-3aα,6α-imine-9-carboxylate (30) was prepared from **4** (4.25 g, 10.1 mmol) by treatment with rhodium(II) octanoate in hexane according to the procedure described for the synthesis of **20**. After completion of the reaction, the mixture was cooled to room temperature and stirred for 16 h at room temperature. The solvent was then removed under reduced pressure, and the residue was washed with pentane (3 × 20 mL) on a fritted funnel which yielded the white solid **30** (2.5 g, 63% yield): mp (petroleum ether:ether) 136−38 °C; IR (neat) 2955, 2950, 2858, 1754, 1702, 1639, 1476 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.34 (d, J = 5.7 Hz, 1 H), 6.00 (dd, J = 5.8, 2.7 Hz, 1 H), 5.16 (m, 1 H), 4.75 (dd, J = 5.2, 2.6 Hz, 1 H), 4.49 (d, J = 9.9 Hz, 1 H), 2.78 (dd, J = 18.3, 5.6 Hz, 1 H), 1.84 (d, J = 18.3 Hz, 1 H), 1.41 (s, 9 H), 0.91 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 155.1, 141.1, 128.7, 110.8, 110.5, 81.5, 68.8, 66.7, 59.5, 31.4, 27.9, 25.2, 18.0, −4.3, −4.6. Anal. Calcd for $C_{20}H_{31}NO_5Si$: C, 61.04; H, 7.94; N, 3.56. Found: C, 60.85; H, 8.02; N, 3.58.

1,1-Dimethylethyl 6,7-dihydro-8-[(1,1-dimethylethyl)-dimethylsiloxy]-7α-methyl-1-oxo-1*H*-cyclohepta[*c*]furan-3*H*-3aα,6α-imine-9-carboxylate (31) was prepared from **10** (1.42 g, 3.26 mmol) by treatment with rhodium(II) octanoate in hexane according to the procedure described for the synthesis of **20**. After completion of the reaction, the mixture was cooled to rt and stirred for 16 h at rt. The solvent was removed under reduced pressure, and the residue was washed with pentane (3 × 20 mL) on a fritted funnel to yield **31** as a white solid (0.573 g, 44% yield): mp (hexane:ether) 170−71 °C; IR (neat) 2974, 2928, 2852, 1757, 1704, 1646 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (d, J = 4.8 Hz, 1 H), 5.98 (d, J = 2.8 Hz, 1 H), 5.01 (brs, 1 H), 4.66 (brs, 2 H), 1.97 (q, J = 6.8 Hz, 1 H), 1.42 (d, J = 7.8 Hz, 12 H), 0.92 (s, 9 H), 0.29 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 162.1, 156.0, 142.7, 129.4, 110.8, 81.3, 68.8, 67.4, 66.2, 38.0, 27.9, 25.3, 18.2, 17.2, −4.2, −5.0. Anal. Calcd for $C_{21}H_{33}NO_5Si$: C, 61.88; H, 8.16; N, 3.44. Found: C, 61.86; H, 8.12; N, 3.50.

1,1-Dimethylethyl 1,3,4,6aα,8,8aα-Hexahydro-1-oxo-8*β*-phenyl-7*H*-2-benzopyrano[7,8-*b*]azete-7-carboxylate (33), 1,1-Dimethylethyl 1,3,4,6aα,8,8aα-Hexahydro-1-oxo-8α-phenyl-7*H*-2-benzopyrano[7,8-*b*]azete-7-carboxylate (34), 1,1-Dimethylethyl 3,4,7,8-Tetrahydro-1-oxo-8*β*-phenyl-1*H*-cyclohepta[*c*]pyran-4aα,7α-imine-10-carboxylate (35) and 1,1-Dimethylethyl 3,4,7,8-Tetrahydro-1-oxo-8α-phenyl-1*H*-cyclohepta[*c*]pyran-4aα,7α-imine-10-carboxylate (36). 13 (0.57 g, 1.5 mmol) was decomposed by treatment with **32** in hexane according to the procedure described for the synthesis of **20**. The solvent was removed and purification achieved by column chromatography on silica gel using ether/petroleum ether (3.5:1.5 to 4:1) to give the following compounds in order of elution from the column. **Compound 35**: 0.09 g (16% yield), mp 158−159 °C; IR (CH_2Cl_2) 3029, 2980, 1805, 1715, 1620, 1603, 1584, 1496 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.24−7.36 (m, 3 H), 7.03−7.10 (m, 2 H), 7.02 (dd, J = 2.8, 1.2 Hz, 1 H), 6.42 (d, J = 6.1 Hz, 1 H), 5.51 (dd, J = 6.1, 2.8 Hz, 1 H), 4.92 (ddd, J = 5.3, 2.8, 1.2 Hz, 1 H), 4.60 (m, 1 H), 4.32 (ddd, J = 14.6, 9.6, 2.9 Hz, 1 H), 4.22 (dd, J = 5.3, 2.8 Hz, 1 H), 3.25 (ddd, J = 16.5, 9.6, 3.8 Hz, 1 H), 2.08 (ddd, J = 16.5, 5.8, 2.9 Hz, 1 H), 1.45 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.1, 153.5, 142.7, 141.9, 135.5, 134.5, 128.8, 128.0, 127.6, 96.3, 81.0, 65.9, 65.1, 63.1, 43.4, 28.4, 28.0. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.12; H, 6.67; N, 3.85. **Compound 36**: 0.04 g (8% yield); IR ($CDCl_3$) 3086, 2981, 1826, 1803, 1689, 1602, 1493, 1342, 1250, 1082 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.10−7.34 (m, 5 H), 6.88 (dd, J = 3.4, 1.8 Hz, 1 H), 6.36 (d, J = 6.0 Hz, 1 H), 6.24 (dd, J = 6.0, 2.8 Hz, 1 H), 4.73 (dd, J = 2.8, 1.8 Hz, 1 H), 4.66 (ddd, J = 14.0, 6.7, 3.5 Hz, 1 H), 4.36 (ddd, J = 14.0, 8.4, 2.9 Hz, 1 H), 3.33 (d, J = 3.4 Hz, 1 H), 3.30 (ddd, J = 14.8, 8.4, 3.5 Hz, 1 H), 2.16 (ddd, J = 14.8, 6.7, 2.9 Hz, 1 H), 0.99 (s, 9 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.1, 150.9, 142.1, 140.2, 140.0, 134.2, 129.5, 128.8, 128.5, 127.1, 79.9, 66.3, 64.9, 63.2, 45.1, 27.8, 27.7. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.14; H, 6.70; N, 3.93. **Compound 33**: 0.21 g (40% yield); IR (neat) 3059, 3032, 2978, 2929, 2902, 1700, 1596, 1460, 1422, 1389 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 95 °C) δ 7.20−7.45 (m, 5 H), 6.38 (dd, J = 9.6, 4.2 Hz, 1 H), 6.16 (d, J = 9.6 Hz, 1 H), 5.30 (dd, J = 10.2, 4.2 Hz, 1 H), 5.11 (d, J = 5.5 Hz, 1 H), 4.25−4.48 (m, 2 H), 3.45 (brdd, J = 10.2, 5.5 Hz, 1 H), 2.30−2.45 (m, 2 H), 1.25 (s, 9 H). Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.42; H, 6.60; N, 4.04. **Compound 34**: 0.06 g (11% yield); IR (neat) 3059, 2978, 2923, 1700, 1450, 1390, 1368, 1259, 1140 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.12−7.36 (m, 5H), 6.30 (dd, J = 9.7, 4.3 Hz, 1 H), 5.94 (d, J = 9.7 Hz, 1 H), 5.72 (d, J = 8.8 Hz, 1 H), 5.16 (dd, J = 10.8, 4.3 Hz, 1 H), 4.25 (ddd, J = 10.8, 8.8, 2.8 Hz, 2 H), 4.04 (ddd, J = 11.5, 5.5, 3.2 Hz, 1 H), 3.26 (ddd, J = 11.5, 11.5, 3.2 Hz, 1 H), 2.46 (dddd, J = 17.7, 11.5, 5.5, 2.8 Hz, 1 H), 1.99 (ddd, J = 17.7, 3.2, 3.2 Hz, 1 H), 1.37 (s, 9 H); HRMS calcd for $C_{21}H_{24}NO_4$ 354.1705, found 354.1689.

1,1-Dimethylethyl 3,4,7,8-tetrahydro-9-[(1,1-dimethylethyl)dimethylsiloxy]-1-oxo-1*H*-cyclohepta[*c*]pyran-4aα,7α-imine-10-carboxylate (38) was prepared from **15** (0.67 g, 1.55 mmol) by treatment with **32** in hexane according to the procedure described for the synthesis of **20**. Purification by silica gel chromatography using 1:4 diethyl ether:pentane as eluting solvent gave **38** as a white solid (0.2 g, 32% yield): R_f = 0.28 in 1:1 diethyl ether:hexanes, mp (pentane:diethyl ether) 139−41 °C; IR (neat) 2927, 2856, 1707, 1700, 1653 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.19 (d, J = 5.9 Hz, 1 H), 5.92 (dd, J = 2.6, 5.9 Hz, 1 H), 4.61 (m, 2 H), 4.22 (m, 1 H), 2.91 (m, 2 H), 2.09 (m, 1 H), 1.92 (d, J = 18.3 Hz, 1 H), 1.43 (s, 9 H), 0.91 (s, 9 H), 0.20 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.9, 152.9, 141.9, 126.1, 112.6, 80.4, 64.9, 62.6, 58.3, 34.1, 29.6, 29.2, 28.2, 25.6, 18.4, −4.1, −4.3. Anal. Calcd for $C_{21}H_{33}NO_5Si$: C, 61.88; H, 8.16; N, 3.44. Found: C, 61.86; H, 8.16; N, 3.44.

(*Z*)-6*H*-5-[2-[*N*-(1,1-Dimethylethoxycarbonyl)imino]ethylidene]-3-vinylpyran-2(5*H*)-one) (39) was prepared from **17** (0.36 g, 1.2 mmol) by treatment with rhodium(II) octanoate in hexane according to the procedure described for the synthesis of **20**. Purification by silica gel chromatography

using 1:3 diethyl ether:pentane as eluting solvent gave **39** as a white solid (0.242 g, 77% yield): R_f = 0.24 in 1:1 ether: hexanes, mp (hexane:ether) 117−20 °C; IR (neat) 2979, 2930, 2900, 1771, 1710, 1583, 1414 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.74 (d, J = 2.8 Hz, 1 H), 5.65 (d, J = 17.6 Hz, 1 H), 5.43 (d, J = 12 Hz, 1 H), 5.25 (m, 1 H), 5.19 (dd, J = 10.0, 17.6 Hz, 1 H), 4.51 (d, J = 8.8 Hz, 1 H), 4.42 (d, J = 9.6 Hz, 1 H), 4.16 (s, 1 H), 1.49 (s, 9 H). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.99; H, 6.55; N, 5.24.

11-(1,1-Dimethylethoxycarbonyl)-4α,10α-imino-2-[(1,1-dimethylethyl)dimethylsiloxy]-8-oxa-9-oxobicyclo[4.3.1]-deca-1,5-diene (41) was prepared from **18** (1.36 g, 3.25 mmol) by treatment with rhodium(II) octanoate in hexane according to the procedure described for the synthesis of **20**. The residue was washed with pentane (3 × 20 mL) on a fritted funnel to yield **41** as a colorless solid (0.68 g, 53% yield): mp (pentane) 156−57 °C; IR (neat) 2957, 2928, 2852, 1739, 1710, 1594, 1256 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.29 (brs, 1 H), 5.00 (d, J = 12.3 Hz, 1 H), 4.93 (brs, 1 H), 4.83 (d, J = 12.2 Hz, 1 H), 4.67 (brs, 1 H), 2.94 (brd, J = 18 Hz, 1 H), 1.70 (d, J = 18 Hz, 1 H), 1.40 (s, 9 H), 0.85 (s, 9 H), 0.17 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 153.0, 151.0, 146.7, 118.2, 115.9, 80.7, 66.1, 57.5, 57.3, 32.3, 28.0, 25.3, 18.0, −4.3, −5.1. Anal. Calcd for $C_{20}H_{31}NO_5Si$: C, 61.04; H, 7.94; N, 3.56. Found: C, 60.96; H, 7.92; N, 3.50.

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