Acknowledgment. This research was supported by faculty research funds granted by the University of California, Santa Cruz. We would also like to thank the Dow Chemical Company for their financial support.

Registry No. 2-Ethylbutanal, 97-96-1; morpholine, 110-91-8; 2-ethyl-1-morpholino-1-butene, 28478-26-4; pyrrolidine, 123-75-1; 2-ethyl-1-pyrrolidino-1-butene, 66685-15-2; 1,1-diphenyl-2-pyrrolidinoethylene, 13150-54-4; 1,1-diphenylethene, 530-48-3; (*E*)-2-methyl-1-pyrrolidino-1-pentene, 135310-61-1; (*Z*)-2-methyl-1-pyrrolidino-1-pentene, 135285-83-5; 2-methyl-1-pentene, 763-29-1; (*E*)-2-methyl-1-morpholino-1-pentene, 135285-84-6; (*Z*)-2-methyl-1-morpholino-1-pentene, 135285-85-7; 2-methyl-1-morpholinopentan-2-ol, 135285-86-8; 1-(cyclohexylidenemethyl)pyrrolidine, 6815-55-0; 1-(1-pyrrolidinomethyl)cyclohexanol, 25363-24-0; 2-methyl-1-pyrrolidinopentan-2-ol, 135285-87-9; 2-methylundecanal, 110-41-8; 1-(diethylamino)-2-methylpentan-2-ol, 58124-08-6; 2-methylvaleraldehyde, 123-15-9; 1-(4-morpholinomethyl)cyclohexanol, 116886-08-9; (*E*)-2-phenyl-1-pyrrolidino-1-propene, 66217-90-1; (*Z*)-2-phenyl-1-pyrrolidino-1-propene, 66217-97-8; (*E*)-1-morpholino-2-phenyl-1-propene, 39166-22-8; (*Z*)-1-morpholino-2-phenyl-1-propene, 39173-00-7; 4-(cyclohexylidenemethyl)morpholine, 16963-29-4; (*E*)-2-methyl-1-pyrrolidino-1-undecene, 135285-88-0; (*Z*)-2-methyl-1-pyrrolidino-1-undecene, 135285-89-1; diphenylacetaldehyde, 947-91-1; 2-phenylpropionaldehyde, 93-53-8; cyclohexanecarboxaldehyde, 2043-61-0; cyclooctanecarboxaldehyde, 6688-11-5.

Supplementary Material Available: Physical properties and the spectra of the enamines, alkenes, aminoboranes, and amino alcohols (40 pages). Ordering information is given on any current masthead page.

Synthesis of (±)-Ferruginine and (±)-Anhydroecgonine Methyl Ester by a Tandem Cyclopropanation/Cope Rearrangement

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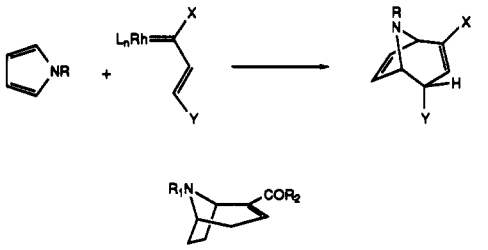
Rhodium(II) acetate catalyzed decomposition of vinyldiazomethanes in the presence of *N*-(alkoxycarbonyl)pyrroles led to the synthesis of 8-azabicyclo[3.2.1]octa-2,6-dienes. The vinylcarbenoids generated from vinyldiazomethanes with a single electron-withdrawing group exhibited competing reactivity at the vinyl terminus in addition to the carbenoid site. Good regiocontrol was possible, however, by appropriate choice of catalyst and solvent. The practicality of this new approach to tropane alkaloids was demonstrated through short syntheses of (±)-ferruginine, (±)-anhydroecgonine methyl ester, and the lower homologue of (±)-anatoxin *a*.

Due to the important bioactivity of the tropane alkaloids, the development of general synthetic procedures to these compounds has been extensively studied.[1] The most notable work in this area has been the pioneering studies of Willstatter[2] and Robinson.[3] Indeed, Robinson's approach based on the condensation of a dialdehyde with methylamine and an acetone derivative is still commonly used.[4] New approaches have been developed such as Noyori's [3 + 4] cycloaddition of iron oxyallyl cations with pyrroles,[5] Tufariello's intramolecular 1,3-dipolar cycloaddition,[6] Kibayashi's nitroso cycloaddition,[7] and Rapoport's imine condensation.[8]

Scheme I



1a $R_1 = H$, $R_2 = OMe$
1b $R_1 = Me$, $R_2 = OMe$
1c $R_1 = H$, $R_2 = Me$
1d $R_1 = Me$, $R_2 = Me$

As part of a program to produce compounds with novel neurochemical activity, we required a general and potentially enantioselective method for the synthesis of tropane derivatives. A new approach based on a tandem cyclopropanation/Cope rearrangement between metal-stabilized vinylcarbenoids and pyrroles[9] appeared to be an attractive strategy as shown in Scheme I. We have previously reported that seven-membered rings may be selectively formed in the reaction of vinylcarbenoids with furans[10] and

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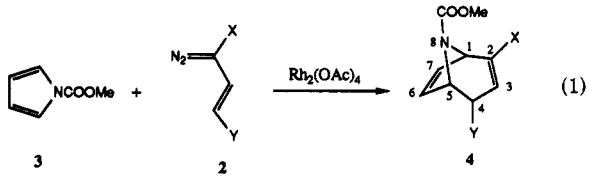
dienes[11] and have communicated our preliminary results with pyrroles.[12] In this paper, we report our completed studies on the reaction of vinylcarbenoids with pyrroles. Short syntheses of two tropane natural products, (±)-anhydroecgonine methyl ester (**1b**) and (±)-ferruginine (**1d**), are described as illustratory examples of the potential of this chemistry.

In our preliminary studies on the rhodium(II) acetate catalyzed decomposition of vinyldiazomethanes **2** in the presence of *N*-(methoxycarbonyl)pyrrole (**3**) we observed that 8-azabicyclo[3.2.1]octa-2,6-dienes **4** were readily formed when vinylcarbenoids containing two electron-withdrawing groups were used (eq 1.)[12] The transfor-



(1)

a: X = COOEt, Y = COOEt (62%)
b: X = COOEt, Y = SO_2Ph (61%)
c: X = COOMe, Y = Ph (53%)
d: X = COOEt, Y = CH=CHPh (18%)

mations proceeded cleanly, as seen in the NMR spectra of the concentrated crude reaction mixtures. The moderate isolated yields, however, were due to the slight instability of these compounds to chromatography. The proton at C-4 in these compounds was quite acidic, and consequently, decomposition initiated by elimination of the aza bridge appeared to be a facile process. The lability of the proton at C-4 was very apparent for **4a** and **4b** because on chromatographic purification significant equilibration of the initially formed endo products to the exo isomers occurred.

Extension of this chemistry to vinylcarbenoids with a single electron-withdrawing group would be necessary for the direct synthesis of ferruginine and anhydroecgonine methyl ester. All of our initial studies on vinylcarbenoids were carried out with systems containing two electron-withdrawing groups. The reason for this was to avoid any potential side reactions due to electrocyclization of vinyldiazomethanes to 3*H*-pyrazoles.[13] Since then, the synthesis of vinyldiazomethanes with a single electron-withdrawing group has been shown to be feasible.[14] As anticipated, these vinyldiazomethanes were very prone to cyclization to 3*H*-pyrazoles, but if rhodium-catalyzed decomposition of the vinyldiazomethanes was carried out immediately after preparation and isolation, effective formation of vinylcarbenoid intermediates was still possible.

Initially, the reaction between vinyldiazomethanes with a single electron-withdrawing group and pyrroles was only partially successful. Decomposition of methyl 2-diazo-3-butenoate (**5**) in the presence of *N*-(methoxycarbonyl)-pyrrole (**3**) under standard conditions (rhodium(II) acetate/dichloromethane) gave a mixture of products from which only a low yield of the azabicyclooctadiene **6** was

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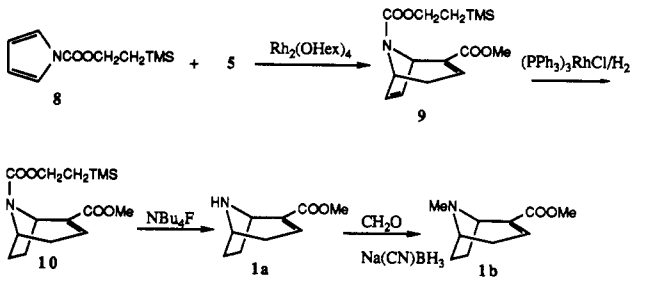
Table I. Product Distribution in the Rhodium(II)-Catalyzed Decomposition of 5 in the Presence of *N*-(Methoxycarbonyl)pyrrole (3)

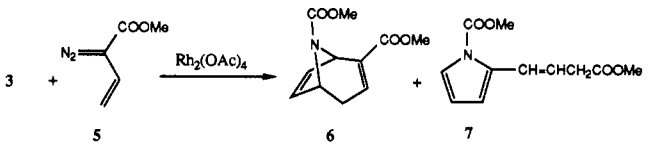
catalyst	solvent	ratio 6:7[a]	6, % yield[b]
rhodium(II) acetate	CH_2Cl_2	55:45	35
rhodium(II) mandelate	CH_2Cl_2	40:60	20
rhodium(II) trifluoroacetate	CH_2Cl_2	15:85	16
rhodium(II) hexanoate	$C_2H_4Cl_2$	86:14	34
rhodium(II) hexanoate	benzene	>95:5	68
rhodium(II) hexanoate	hexane	>95:5	75
rhodium(II) pivalate	hexane	>95:5	67
rhodium(II) trifluoroacetate	hexane	26:74	29

[a] Ratio determined from the NMR spectra of the concentrated reaction mixtures. [b] Represents isolated yield of purified material.

Scheme II



obtained. On careful analysis, the crude reaction mixture was shown to consist of a 55:45 mixture of **6** and the alkylated pyrrole **7**. The generation of **7** is an intriguing



transformation because carbon–carbon bond formation occurred at the vinylogous position of the carbenoid. The product distribution in this reaction was determined from the proton NMR after removal of excess **3** by distillation. Control of reactivity was readily achieved through the use of an appropriate solvent and catalyst.[15] As shown in Table I, an electron-withdrawing ligand such as trifluoroacetate strongly enhanced the formation of the alkylated product **7**, but by changing to nonpolar solvents, this reaction could be totally suppressed. Thus, with rhodium(II) hexanoate in hexane a clean transformation was observed and the azabicyclooctadiene **6** was isolable in 75% yield.

Having developed suitable conditions for the reaction of monofunctionalized vinylcarbenoids with pyrroles, the chemistry was then applied to the synthesis of tropane alkaloids of biological interest. Anhydroecgonine methyl ester (**1b**) is an important synthetic precursor to 3-aryl derivatives of cocaine, which have been extensively used as molecular probes in cocaine drug abuse research.[16] A direct synthesis of **1b** was readily achieved as illustrated in Scheme II. Decomposition of **5** by rhodium(II) hexanoate in the presence of 5 equiv of *N*-((2-(trimethylsilyl)ethoxy)carbonyl)pyrrole (**8**) gave the bicyclic system **9** in 62% yield. Catalytic hydrogenation of **9** with Wil-

(15) For other examples of product control by changing ligands on the rhodium catalyst, see Doyle, M. P.; Pieters, R. J.; Taunton, J.; Pho, H. Q.; Padwa, A.; Hertzog, D. L.; Precedo, L. *J. Org. Chem.* **1991**, *56*, 820 and references cited therein.

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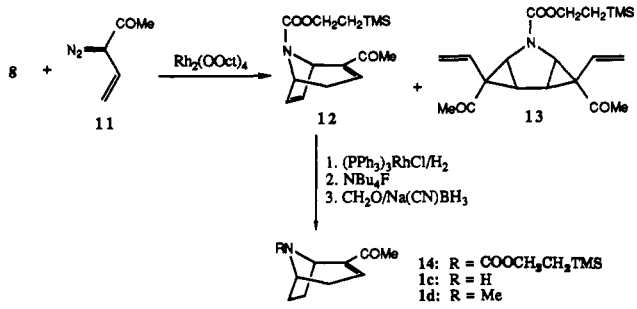
Scheme III

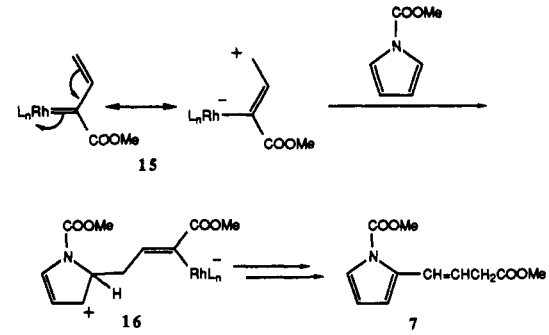


kinson's catalyst occurred exclusively at the less polar double bond to generate **10** in 92% yield. Deprotection of **10** by treatment with tetrabutylammonium fluoride gave **1a** in 95% yield. Finally, reductive methylation of **1a** with aqueous formaldehyde and sodium cyanoborohydride proceeded in 95% yield to generate anhydroecgonine methyl ester (**1b**).

Due to the intense interest in the potent nicotinic agonist, anatoxin *a*,[17] the tropane lower homologue of anatoxin *a* (**1c**)[18b] and the natural product ferruginine (**1d**)[18] seemed to be worthwhile synthetic targets. The approach parallels that used for the synthesis of anhydroecgonine methyl ester, except that 3-diazo-4-penten-2-one (**11**) was used as the vinylcarbenoid precursor (Scheme III). Once again, by use of the nonpolar solvent hexane, reaction at the vinyl terminus was inhibited, but the desired product **12** was generated in only moderate yield (57%) because the biscyclopropanated product **13** was also formed. Biscyclopropanation has been observed previously by us when the Cope rearrangement of the initially formed divinylcyclopropane was rather sluggish.[12] Optimization of this process was not possible by slow addition of **11** because of vinyldiazomethane instability. The use of higher boiling solvents such as toluene, however, did eliminate the formation of **13**, and the overall yield of **12** was improved to 73%. The further conversion of **12** to **1c** and ferruginine (**1d**) followed the approach used to synthesize **1b** and proceeded uneventfully.

Even though the formation of the alkylation product **7** could be avoided by use of appropriate reaction conditons, the unusual nature of this transformation merits further comment. A reasonable explanation for the formation of **7** would require electrophilic reactivity at the vinyl terminus of the vinylcarbenoid **15** as shown in Scheme IV. This could be achieved by pushing electron density into the metal, which is consistent with the observation that rhodium(II) trifluoroacetate is the most efficient catalyst at promoting the formation of **7**. Furthermore, the intermediates involved in the formation of **7** are dipolar, which would explain why the formation of **7** is strongly inhibited in nonpolar solvents. Similar behavior was proposed earlier by us to to explain the products formed in the reaction of **5** with cyclopentadiene.[14] The further conversion of the initial intermediate **16** to the final product **7** is also an unusual process. One possibility would be the generation of a new carbenoid species by rearomatization of the pyrrole and protonation of the vinylrhodium, which could then undergo a 1,2-hydride shift

Scheme IV



followed by isomerization of the newly formed double bond into conjugation with the aromatic ring to form **7**. Alternatively, rearomatization of **16** could be facilitated intramolecularly to generate a rhodium hydride species, which would then undergo reductive elimination and double-bond isomerization to generate **7**. The involvement of rhodium hydride species has been proposed in carbenoid C–H insertions,[19] and their intermediacy is an intriguing possibility because some dissociation of the carboxylate ligands would be required.

The reaction of vinylcarbenoids with *N*-(alkoxycarbonyl)pyrroles offers a direct route to tropane alkaloids as illustrated in the synthesis of (±)-ferruginine and (±)-anhydroecgonine methyl ester. Control of side reactions of vinylcarbenoids with a single electron-withdrawing group is readily achieved by use of nonpolar solvents and electron-donating ligands. Further applications of this chemistry to develop an enantioselective synthesis of tropane derivatives with novel neurochemical properties are in progress.

Experimental Section

Ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Diisopropylamine was distilled from calcium hydride. Hexane and toluene were dried over 4-Å molecular sieves. ^1H and ^{13}C NMR spectra were recorded at 200 and 50.3 MHz, respectively. Mass spectral determinations were carried out at 70 eV. *N*-(Methoxycarbonyl)pyrrole (**3**),[20] methyl but-3-en-1-oate,[21] 4-penten-2-one,[22] dodecylbenzenesulfonyl azide,[23] and *p*-toluenesulfonyl azide[24] were prepared according to literature procedures.

Methyl 2-Diazobut-3-enoate (5). A solution of *n*-butyllithium (41.2 mL, 65.6 mmol, 1.6 M in hexane) was added to a solution of diisopropylamine (10.12 mL, 72.2 mmol) in ether under argon at −78 °C. The reaction was warmed to room temperature with stirring for 15 min and then cooled to −78 °C before HMPA (16.8 mL, 65.6 mmol) was added, and the mixture was stirred for 30 min. A solution of methyl but-3-en-1-oate[22] (3.28 g, 32.8 mmol) in ether (5 mL) was added, and the mixture was stirred for 30 min before *p*-toluenesulfonyl azide[24] (12.94 g, 75.6 mmol) in ether (10 mL) was added. The mixture was warmed to room temperature over a 12-h period. Water was then added, and the mixture was extracted with pentane; the organic layer was washed with water and saturated NaCl, dried ($MgSO_4$), and then concentrated under reduced pressure at 15-20 °C. The residue was rapidly purified by silica gel column chromatography with 1/9 ether/pentane to give **5** as an orange liquid (3.0 g, 73%): IR (neat)

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2082, 1695, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.15 (dd, 1 H, J = 17.4, 11.0 Hz), 5.01 (d, 1 H, J = 11.0 Hz), 4.94 (d, 1 H, J = 17.4 Hz), 3.79 (s, 3 H). Due to lack of stability, elemental analysis was not attempted and **5** was used immediately in subsequent reactions.

Methyl *N*-(Methoxycarbonyl)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (6) and Methyl 4-(2-(*N*-(Methoxycarbonyl)pyrrolyl))but-3-enoate (7). A solution of **5** (1–3 mmol) in solvent (5 mL) was added dropwise over a 2-h period by means of a syringe pump to a mixture of **3** (5 equiv) and rhodium(II) carboxylate[26] (0.01 equiv) in refluxing solvent (10 mL) under an argon atmosphere. The mixture was heated for a further 12 h, and then the solvent was removed under reduced pressure and excess **3** was removed by bulb-to-bulb distillation (80 °C (0.8 mmHg)). The ratio of **6** and **7** was determined by proton NMR analysis of the residue. The residue was purified by silica gel column chromatography (1/9–4/6 ether/petroleum ether) to give pure **6** and **7**.

6: IR (neat) 3100, 2970, 2910, 1730, 1715, 1635, 1458, cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.52 (m, 1 H), 6.46 (dd, 1 H, J = 5.9, 2.2 Hz), 5.93 (dd, 1 H, J = 5.9, 2.4 Hz), 5.07 (m, br, 1 H), 4.70 (m, br, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 2.84 (d, br, 1 H, J = 20.0 Hz), 1.93 (d, 1 H, J = 20.0, 4.0 Hz); ^{1}H NMR (toluene-d_8, 95 °C) δ 6.57 (m, 1 H), 6.51 (dd, 1 H, J = 6.5, 2.5 Hz), 5.77 (dd, 1 H, J = 6.2, 2.3 Hz), 5.54 (m, 1 H), 4.78 (d, br, 1 H, J = 5.5 Hz), 3.75 (s, 3 H), 3.72 (s, 3 H), 2.85 (d, br, 1 H, J = 19.9 Hz), 1.70 (dd, 1 H, J = 19.9, 3.9 Hz); MS m/z (rel intensity) 223 (1), 191 (10), 164 (20), 163 (24), 148 (59), 132 (29), 104 (49), 59 (64); HRMS calcd for $C_{13}H_{13}NO_4$ 223.0844, found 223.0847.

7: IR (neat) 2990, 1770, 1740, 1650, 1505, 1458, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.22 (dd, 1 H, J = 3.3, 1.8 Hz), 6.39 (dt, 1 H, J = 11.5, 7.1 Hz), 6.12 (dd, 1 H, J = 3.3, 3.3 Hz), 6.06 (m, 1 H), 5.84 (dt, 1 H, J = 11.5, 1.8 Hz), 4.25 (d, br, 2 H, J = 7.1 Hz), 3.93 (s, 3 H), 3.73 (s, 3 H); ^{13}C ($CDCl_3$) 166.6, 151.2, 146.7, 132.9, 121.0, 119.5, 112.4, 110.9, 77.2, 53.7, 51.1, 28.5; HRMS m/z (rel intensity) 223 (32), 191 (37), 164 (35), 132 (38), 104 (24), 69 (100), 59 (32), 57 (58); HRMS calcd for $C_{11}H_{13}NO_4$ 223.0844, found 223.0843.

***N*-(2-((Trimethylsilyl)ethoxy)carbonyl)pyrrole (8).** *N*-pyrrolecarboxylic acid chloride was prepared from *N*-pyrrolecarboxylic acid according to the procedure of Boger.[25] The crude acid chloride (4.66 g, 36 mmol) was dissolved in THF (30 mL), and 2-(trimethylsilyl)ethanol (5.10 g, 43 mmol) and pyridine (5.69 g, 72.0 mmol) were consecutively added. The reaction mixture was stirred overnight and then extracted with ether (2×). The organic phase was dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether) to give **8** as a clear liquid: 4.82 g (63%); IR (neat) 3160, 3120, 2980, 2860, 1745, 1475, 1410 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 2 H), 6.23 (m, 2 H), 4.44 (t, 2 H, J = 8.6 Hz), 1.14 (t, 2 H, J = 8.6 Hz), 0.08 (s, 9 H); ^{13}C NMR ($CDCl_3$) 150.5, 120.0, 112.3, 65.9, 17.6, -1.5; MS m/z (rel intensity) 211 (43), 167 (12), 124 (31), 73 (100); HRMS calcd for $C_{10}H_{17}NO_2S$ 211.1028, found 211.1027.

Methyl 8-((2-(Trimethylsilyl)ethoxy)carbonyl)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (9). A solution of **5** (1.0 g, 8 mmol) in hexane (20 mL) was added over 2 h by means of a syringe pump to a stirred solution of **8** (3.0 g, 24 mmol) and rhodium(II) hexanoate (0.027 g, 0.04 mmol) in refluxing hexane (10 mL) under an argon atmosphere. The mixture was heated for a further 12 h, and then the solvent was removed under reduced pressure. Purification of the product by silica gel column chromatography (1/9–4/6 ether/petroluem ether) gave **9** as an orange liquid (1.54 g, 62%): IR (neat) 3000, 1710 (br), 1620, 1590 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.49 (m, 1 H), 6.42 (dd, 1 H, J = 5.8, 1.7 Hz), 5.89 (dd, 1 H, J = 5.8, 2.3 Hz), 5.05 (m, br, 1 H), 4.66 (m, br, 1 H), 4.14 (m, 2 H), 3.71 (s, 3 H), 2.84 (d, br, 1 H), 1.89 (dd, 1 H, J = 19.9, 3.8 Hz), 0.91 (t, br, 2 H, J = 7.4 Hz), 0.01 (s, 9 H). Anal. Calcd for $C_{15}H_{23}O_4NSi$: C, 58.22; H, 7.49, N, 4.53. Found: C, 58.33; H, 7.53; N, 4.58.

Methyl 8-((2-(Trimethylsilyl)ethoxy)carbonyl)-8-azabicyclo[3.2.1]oct-2-ene-2-carboxylate (10). A mixture of **9** (0.50 g, 1.6 mmol) and $RhCl(PPh_3)_3$ (0.015 g, 0.016 mmol) in ethanol (50 mL) was pressurized with 45 psi H_2 and shaken for 12 h. The solvent was then evaporated, and the residue was purified by silica gel column chromatography (3/7 ether/petroluem ether) to give **10** as an orange liquid (0.46 g, 92%): IR (neat) 2985, 1710, 1630, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.74 (m, 1 H), 4.87 (m, br, 1 H), 4.37 (m, br, 1 H), 4.15 (t, br, 2 H, J = 7.8 Hz), 3.69 (s, 3 H), 2.81 (d, br, 1 H, J = 19.4 Hz), 1.99 (dd, 1 H, J = 19.4, 5.2 Hz), 1.80–1.21 (m, 4 H), 1.02 (t, br, 2 H, J = 7.8 Hz), 0.01 (s, 9 H). Anal. Calcd for $C_{15}H_{25}NO_4Si$: C, 57.84; H, 8.09; N, 4.49. Found: C, 57.92; H, 8.10; N, 4.55.

Methyl 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylate (1a). A mixture of **10** (0.830 g, 2.66 mmol) and tetrabutylammonium fluoride (5.32 mL, 5.32 mmol, 1 M in THF) was stirred under argon at room temperature for 12 h. The reaction was purified by chromatography on basic alumina (1/1 ether/petroluem ether; 1/1 ethyl acetate/hexane) followed by bulb-to-bulb distillation (60 °C (0.6 mmHg)) to give **1a** as a yellow liquid (0.42 g, 95%): IR (neat) 3400 (br), 2940, 1695, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.65 (t, 1 H, J = 3.1 Hz), 4.05 (m, 1 H), 3.71 (s, 3 H), 3.64 (m, 1 H), 2.59 (d, br, 1 H, J = 18.4 Hz), 1.94 (dd, 1 H, J = 18.4, 2.9 Hz), 1.92–1.65 (m, 4 H), 1.55–1.45 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 166.1, 138.0, 135.9, 53.1, 52.2, 51.5, 36.4, 36.1, 30.3. Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.38; H, 7.92; N, 8.14.

Methyl 8-Methyl-8-azabicyclo[3.2.1]oct-2-ene-2-carboxylate (1b).[16a] To a stirred mixture of **1a** (0.1013 g, 0.606 mmol) and aqueous formaldehyde (0.24 mL, 3.0 mmol, 37%) in acetonitrile (15 mL) was added sodium cyanoborohydride (0.06 g, 1.0 mmol), and the reaction was stirred for 15 min. The solution was made neutral by the addition of glacial acetic acid and then stirred for 45 min. The mixture was made basic by the slow addition of concentrated NH_4OH, extracted with ethyl acetate (3×), dried (Na_2SO_4), and then concentrated under reduced pressure. Purification of the residue by chromatography on neutral aluminum oxide (7/3 ether/petroleum ether) gave **1b** as a yellow liquid (0.1045 g, 95%): IR ($CDCl_3$) 2940, 1700, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.78 (t, 1 H, J = 3.0 Hz), 3.76 (d, 1 H, J = 5.6 Hz), 3.72 (s, 3 H), 3.20 (t, 1 H, J = 5.4 Hz), 2.62 (d, br, 1 H, J = 19.8 Hz), 2.32 (s, 3 H), 2.20–2.07 (m, 2 H), 1.81 (d, 1 H, J = 19.8, 4.0 Hz), 1.82–1.35 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 166.5, 135.8, 133.9, 58.4, 56.8, 51.5, 36.2, 34.3, 31.6, 29.9; MS m/z (rel intensity) 181 (38), 166 (13), 152 (100), 138 (10), 122 (20), 106 (6), 94 (13), 82 (33); HRMS calcd for $C_{10}H_{15}O_2N$ 181.1102, found 181.1100. Anal. Calcd for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.43; H, 8.40; N, 7.59.

3-Diazo-4-penten-2-one (11). To a stirred solution of 4-penten-2-one[21] (0.91 g, 11 mmol) and dodecylbenzylsulfonyl azide[23] (4.62 g, 13.2 mmol) in pentane (50 mL) was added DBU (1.66 g, 11 mmol) at 0 °C. After being stirred for 8 min the mixture was purified by silica gel column chromatography (4/96 ether/petroleum ether) to give **11** as an orange liquid (0.79 g, 66%): IR ($CDCl_3$) 2920, 2250, 1650, 1610, 1300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.25 (dd, 1 H, J = 16.7, 11.0 Hz), 5.18 (d, 1 H, J = 11.0 Hz), 4.88 (d, 1 H, J = 16.7 Hz), 2.27 (s, 3 H). Due to lack of stability, elemental analysis was not attempted and **11** was used immediately in subsequent reactions.

2-Acetyl-8-((2-(trimethylsilyl)ethoxy)carbonyl)-8-azabicyclo[3.2.1]octa-2,6-diene (12). A solution of **11** (0.36 g, 3.27 mmol) in toluene (25 mL) was added over 2 h by a syringe pump to a stirred solution of **8** (7.0 g, 33 mmol) and rhodium(II) octanoate (0.025 g, 0.033 mmol) in refluxing toluene (10 mL) under an argon atmosphere. The mixture was refluxed for a further 12 h, and the solvent was then evaporated. The residue was purified by chromatography on silica gel (2/8–4/6 ether/petroleum ether) to give **12** as an orange liquid (0.70 g, 73%): IR ($CDCl_3$) 2960, 1690, 1650, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.46–6.38 (m, 2 H), 5.90 (dd, 1 H, J = 5.8, 2.2 Hz), 5.22 (s, br, 1 H), 4.71 (br, m, 1 H), 4.15 (m, 2 H), 2.87 (d, br, 1 H, J = 19.7 Hz), 2.32 (s, 3 H), 2.01 (dd, 1 H, J = 19.7, 4.1 Hz), 0.94 (m, 2 H), 0.01 (s, 9 H). Anal. Calcd for $C_{15}H_{23}O_3NSi$: C, 61.39; H, 7.90; N, 4.77. Found: C, 61.13; H, 7.72, N, 4.62.

2-Acetyl-8-((2-(trimethylsilyl)ethoxy)carbonyl)-8-azabicyclo[3.2.1]oct-2-ene (14). A solution of **12** (0.10 g, 0.34 mmol) and $RhCl(PPh_3)_3$ (0.009 g, 0.01 mmol) in ethanol (50 mL) was pressurized with 45 psi H_2 and shaken for 12 h. The solvent was then evaporated, and the residue was purified by silica gel column chromatography (3/7 ether/petroluem ether) to give **14** as an orange liquid (0.096 g, 96%): IR (neat) 2960, 1670 (br), 1630 cm^{-1};

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^{1}H NMR ($CDCl_3$) δ 6.63 (m, 1 H), 4.97 (d, 1 H, J = 5.6 Hz), 4.40 (m, br, 1 H), 4.14 (m, 2 H), 2.94 (d, 1 H, J = 19.5 Hz), 2.24 (s, 3 H), 2.04 (dd, 1 H, J = 19.5, 4.4 Hz), 2.00–1.50 (m, 4 H), 0.00 (s, 9 H). Anal. Calcd for $C_{15}H_{25}NO_3Si$: C, 60.98; H, 8.53; N, 4.74. Found: C, 61.14; H, 8.50; N, 4.67.

2-Acetyl-8-azabicyclo[3.2.1]oct-2-ene (1c).[18b] To a solution of **14** (0.074 g, 0.25 mmol) in THF (10 mL) was added tetrabutylammonium fluoride (0.25 mL, 0.25 mmol, 1 M), and the mixture was stirred under an argon atmosphere at room temperature for 12 h. The mixture was concentrated under reduced pressure and then purified by chromatography on neutral alumina (1/4 methanol/ether, R_f 0.37) followed by bulb-to-bulb distillation (50 °C (0.8 mmHg)) to give **1c** as a yellow liquid (0.028 g, 75%): IR (neat) 3160, 1660, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.63 (t, 1 H, J = 3.5 Hz), 4.25 (d, br, 1 H, J = 4.4 Hz), 3.70 (t, 1 H, J = 5.6 Hz), 2.69 (d, br, 1 H, J = 19.6 Hz), 2.24 (s, 3 H), 2.09–1.80 (m, 2 H), 2.03 (dd, 1 H, J = 19.6, 4.6 Hz), 1.76 (s, br, 1 H), 1.60–1.48 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 196.9, 146.8, 136.8, 52.4, 52.0, 36.7, 36.2, 30.5, 24.8; MS m/z (rel intensity) 151 (22), 136 (15), 122 (100), 108 (25), 91 (11), 80 (28), 68 (30); HRMS calcd for $C_9H_{13}NO$ 151.0997, found 151.0995.

8-Methyl-2-(methylcarbonyl)-8-azabicyclo[3.2.1]oct-2-ene (1d).[18b] To a stirred mixture of **1c** (0.1315 g, 0.87 mmol) and aqueous formaldehyde (0.35 mL, 4.35 mmol. 37%) in acetonitrile (15 mL) was added sodium cyanoborohydride (0.087 g, 1.39 mmol). After being stirred for 15 min the reaction was made acidic by addition of 1 M HCl (15 mL) over a 45-min period. The solution was extracted with ether, and the aqueous layer was then made basic by the addition of aqueous sodium hydroxide. The aqueous solution was extracted with ethyl acetate (3×); the organic layer was then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by chromatography on basic aluminum oxide (1/19 methanol/ether) followed by bulb-to-bulb distillation (70 °C (0.4 mmHg)) to give **1d** as a yellow liquid (0.1399 g, 97%): IR ($CDCl_3$) 2940, 1645, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.68 (t, 1 H, J = 3.6 Hz), 3.88 (d, 1 H, J = 5.2 Hz), 3.23 (br t, 1 H, J = 5.6 Hz), 2.67 (d, 1 H, J = 19.8 Hz), 2.29 (s, 3 H), 2.23 (s, 3 H), 2.20–2.00 (m, 2 H), 1.89 (dd, 1 H, J = 19.8, 4.4 Hz), 1.68 (t, 1 H, J = 9.3 Hz), 1.45 (t, br, 1 H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 197.5, 143.7, 136.7, 57.5, 57.4, 37.3, 33.7, 33.0, 29.5, 24.9; MS m/z (rel intensity) 165 (62), 150 (24), 136 (100), 122 (40), 107 (6), 94 (15), 82 (30). HRMS calcd for $C_{10}H_{15}O_2N$ 165.1133, found 165.1133.

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Notes

Reaction of Vinylboronic Acids with Iodine on γ-Alumina

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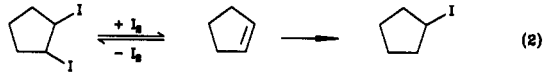
Introduction

For many years we have explored organic reactions on solid surfaces such as γ-alumina with the intent of discovering new reactions, improving reaction characteristics, and understanding how these processes occur.[1-8] Notable in this work are the reactions of unsaturated substrates with halogens.[3-7] Alumina, for example, catalyzes the facile iodination of aromatic compounds using molecular iodine,[3,4,7] a process that is difficult to carry out in solution. Alkynes, on the other hand, react with iodine on alumina by the stereospecific anti addition of the two iodine atoms to form (*E*)-diiodoalkenes.[6,7] Surprisingly, alkenes react with iodine to form monoiodoalkanes;[4,5,7] in this case, iodine adds reversibly to the double bonds, whereas hydrogen iodine (generated by reaction of iodine with surface hydroxyl groups) adds irreversibly to form the observed products.

$$I_2 + OH \rightleftharpoons HI + OI \qquad (1)$$



(2)

Other iodination reactions should also be catalyzed by alumina, and we decided to investigate the reaction of vinylboronic acids with iodine as a representative example. In solution halogenation only occurs when the boron is complexed with hydroxide.[9] Because activated alumina has exposed oxides on its surface[10] that could serve the same function as hydroxide in solution, its surface should provide a good environment for the iodination reaction. In this vein, the reaction of vinylboronic acids with iodine on alumina was examined. The reactions in fact do occur

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