chromatographed by TLC (R_f 0.27, SiO_2, $CHCl_3$/MeOH/concentrated NH_4OH = 10/4/1).

Synthesis of Elaeokanine A (22). 1-Aza-5-[2-(1,3-dithianylidene)]bicyclo[4.3.0]nonane. To a solution of lithium aluminum hydride (0.12 g, 3.21 mmol) in THF (11 mL) was added a solution of **10b** (0.55 g, 2.15 mmol) in THF (11 mL). The resulting solution was stirred for 1 h and quenched with a mixture of H_2O–THF. The solution was basified with saturated aqueous Na_2CO_2 and extracted with ethyl acetate. The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to give 0.49 g (95%) of the amine as a yellowish solid: IR ($CDCl_3$) 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.17 (dd, J = 10.6 Hz, J = 7.0 Hz, 1 H) 2.70–3.10 (m, 7 H), 2.59 (m, 1 H), 2.48 (m, 1 H), 2.14 (m, 2 H), 1.50–2.00 (m, 7 H); MS (EI, 70 eV), m/e (relative intensity) 241 (M^+, 64), 167 (M - C_3H_7S, 69), 123 (M - $C_4H_6S_2$, 100), 122 (M - $C_4H_7S_2$, 85).

1-Aza-5-[2-(2-propyl-1,3-dithianyl)]bicyclo[4.3.0]nonene. *n*-Butyllithium (2.42 mL of a 2.15 M solution in hexane, 5.20 mmol) was added to a solution of diisopropylamine (0.73 mL, 5.21 mmol) in THF (4 mL). The resulting solution was stirred for 20 min at 0 °C and then was added to a solution of the product from the previous reaction (0.25 g, 1.04 mmol), hexamethylphosphoramide (0.90 mL, 5.17 mmol), and THF (7 mL) at -78 °C. After warming to -20 °C over 2 h, the dark red solution was cooled to -78 °C and *n*-propyl iodide (1 mL, 10.25 mmol) was added. This resulting solution was stirred at -78 °C for 1 h, quenched with 2 mL of methanol, diluted with 10 mL of ethyl acetate, and washed with water. The organic phase was dried (Na_2SO_4) and concentrated. Flash chromatography (silica gel, 8% triethylamine in ethyl acetate) of the crude product gave 0.13 g of the dithiane and 0.09 g of starting material (43% yield, or 68% yield based on recovery of starting material): ^1H NMR ($CDCl_3$) δ 6.30 (br s, 1 H), 3.19 (m, 1 H), 2.95 (m, 1 H), 2.80 (m, 1 H), 2.74 (m, 2 H), 2.62 (m, 4 H), 2.38 (m, 2 H), 2.22 (m, 2 H), 1.85 (m, 4 H), 1.50 (m, 2 H), 1.25 (m, 2 H), 0.83 (t, J = 6.8 Hz, 3 H); MS (EI, 70 eV), m/e (relative intensity) 283 (M^+, 3), 250 (M - 33, 4), 240 (M - 43, 3), 223 (M - 60, 3), 208 (M - 75, 100), 177 (M - 106, 47), 149 (M - 134, 64).

Elaeokanine A (22). A mixture of the dithiane from the previous reaction (162 mg, 0.57 mmol), mercuric chloride (0.31 g, 1.14 mmol), calcium carbonate (0.23 g, 2.30 mmol), and 80% aqueous acetonitrile (12 mL) was heated at 50 °C for 1 H. The cooled mixture was filtered, and the solid was washed with acetonitrile. The combined solutions were concentrated, diluted with dichloromethane (20 mL), and washed with saturated aqueous Na_2CO_3. The organic extract was treated with solid Na_2S, filtered, and then dried (Na_2SO_4). Flash chromatography (silica gel, 2% triethylamine in ethyl acetate) of the crude product gave 78 mg (70%) of **22** as an oil: IR ($CDCl_3$) 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.88 (br s, 1 H), 3.50 (m, 1 H), 2.20–3.00 (m, 10 H), 1.20–1.90 (m, 4 H), 0.93 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 200.8, 141.9, 136.9, 58.9, 52.9, 45.3, 39.4, 29.6, 25.6, 22.5, 18.3, 14.0; MS (EI, 70 eV), m/e (relative intensity) 193 (M^+, 15), 192 (M - 1, 11), 128 (M - 15, 9), 165 (M - 18, 8), 164 (M - 19, 14), 151 (M - 42, 11), 150 (M - 43, 100), 149 (M - 44, 12), 124 (M - 70, 23), 122 (M - 71, 42), 120 (M - 73, 16). Spectral data and chromatographic mobility (R_f 0.27, 8% Et_3N in ethyl acetate) are identical with an authentic sample of elaeokanine A.[18b]

Acknowledgment. This research was supported by the National Institutes of Health (GM 30073), to which we express our gratitude. We also thank the National Science Foundation for providing instrumentation funds.

Registry No. **7a**, 83177-75-7; **7b**, 89556-85-4; **7c**, 89556-86-5; **7d**, 89556-87-6; **7e**, 89556-88-7; (±)-**10a**, 83177-77-9; (±)-**10b**, 89556-89-8; (±)-**10c**, 89556-90-1; (±)-**10d**, 89556-91-2; (±)-**10e**, 89556-92-3; (±)-**11**, 85588-63-2; (±)-**12**, 486-72-6; (±)-**13**, 89556-93-4; (±)-**13** ethyl ester derivative, 77513-73-6; (±)-**14**, 18929-91-4; (±)-**17**, 89556-94-5; (±)-**18**, 89556-95-6; (±)-**19**, 89556-96-7; (±)-**20**, 89556-97-8; (±)-**21**, 23185-51-5; (±)-**22**, 73971-21-8; succinimide, 123-56-8; glutarimide, 1121-89-7; (±)-1-aza-4-formylbicyclo[3.3.0]oct-3-en-8-one, 83177-79-1; (±)-1-aza-5-[2-(2-propyl-1,3-dithianyl)]bicyclo[4.3.0]nonene, 89556-98-9; 1,3-propanedithiol, 109-80-8; butyrolactone, 96-48-0; valerolactone, 108-29-2; caprolactone, 502-44-3.

Total Synthesis of (±)-Nitramine. Development of a Ketene Equivalent in the Ene Reaction

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Received November 30, 1983

(±)-Nitramine (**1a**) was synthesized in seven steps from methylenecyclohexane in 33% overall yield. A three-step sequence was developed from methylenecyclohexane to aldehyde **4** in which methyl α-chloroacrylate was used as a ketene equivalent in the ene reaction. Aldehyde **4** was converted to nitrone **3** which cyclized to a 2.5:1 mixture of **2** and **9**. Hydrogenolysis of **2** gave **1a**. Lewis acid catalyzed cyclization of **4** gave a 3.5:1 mixture of hydrindanones **13** and **14** at 25 °C and a 12:1 mixture of **13** and **14** at -20 °C.

(+)-Nitramine (**1a**), isolated from *Nitraria schoberi*, is the first alkaloid to possess a 2-azaspiro[5.5]undecane skeleton.[2] More recently, the diastereomers of **1a** and **1b**, isonitramine[2a,b,3a] and sibirene,[3b] and (±)-nitramine[3c] (**1a**), have been isolated from *Nitraria sibirica*. The structures of nitramine and isonitramine were determined by X-ray crystallography.[2b] These alcohols are related to the neurotoxins histrionicotoxin and congeners, which are 2,7-disubstituted 1-azaspiro[5.5]undecan-8-ols.[4] The unusual carbon skeleton of **1a** and the potential for biological activity in this class of γ-amino alcohols made it an intriguing synthetic problem.

Our approach to nitramine was based on the intramolecular cycloaddition[5] of the nitrone **3** to give **2**, which can be converted to nitramine by hydrogenolysis. The relative

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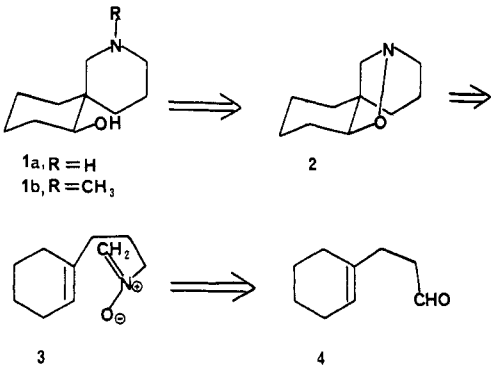
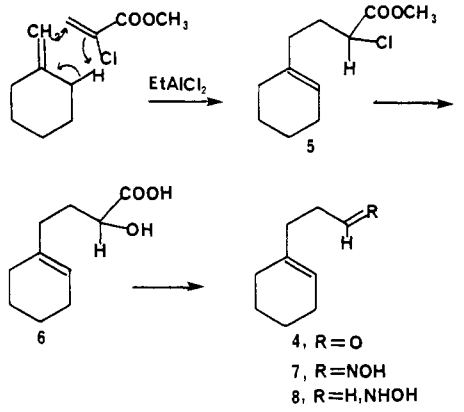


stereochemistry at the two chiral centers of nitramine will be established by the cycloaddition. Nitrone **3** should be available from aldehyde **4** by a standard sequence[5a]: oxime formation, reduction to the hydroxylamine, and condensation with formaldehyde. Surprisingly, aldehyde **4**, which is very simple, does not appear to be a known compound. While it can undoubtedly be made by a classical multistep synthesis,[6] we were interested in developing an efficient approach to **4** via the ene reaction of methylenecyclohexane with a ketene equivalent as the enophile. Although, the use of ketene equivalents as dienophiles in the Diels-Alder reaction has been entensively developed,[7] this concept has not been applied to the ene reaction.

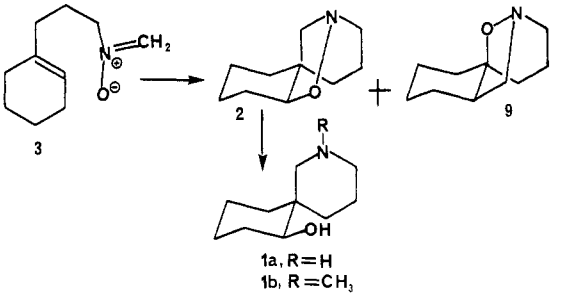
Results and Discussion

Ene reaction of methylenecyclohexane and methyl α-chloroacrylate catalyzed by $EtAlCl_2$ in benzene at 25 °C for 20 h gave a 95% yield of **5**.[8] Chloro ester **5** was converted to hydroxy acid **6** in 89% yield by hydrolysis in refluxing aqueous sodium carbonate solution.[9] Oxidation of **6** with lead tetraacetate in pyridine[10] for 2 h at 25 °C

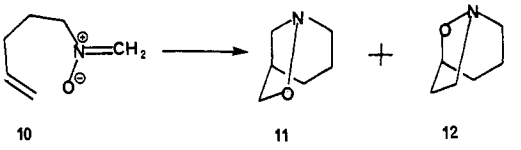


gave the desired aldehyde **4** in 84% yield. Aldehyde **4** is therefore available from methylenecyclohexane in a three-step sequence in 71% overall yield.[11] Methyl α-chloroacrylate functions as a ketene equivalent in the ene reaction in a manner similar to that of α-chloroacryloyl chloride[7a] or α-chloroacrylonitrile[7b] in the Diels-Alder reaction.

Aldehyde **4** was converted to the oxime **7** in 99% yield by reaction with hydroxylamine hydrochloride and sodium carbonate in aqueous ethanol.[12] Reduction of **7** with sodium cyanoborohydride at pH 3 by the procedure of Borch et al.[13] gave a 95% yield of the unstable hydroxylamine **8**, which was ~80% pure by NMR analysis. Due to the instability of **8**[14] it was used immediately without purification. Gaseous formaldehyde was bubbled into a solution of **8** in toluene containing anhydrous sodium sulfate at 0 °C to form the nitrone **3**.[5a] The resulting mixture was heated for 24 h at reflux to give a 70% yield, based on **7**, of a 2.5:1 mixture of **2** and **9**, which were separated by preparative GC. The hydroxylamine **8** could be stored as its stable hydrogen oxalate and liberated prior to reaction.[5a] This resulted in slightly lower yields of **2** and **9**.



Oppolzer has studied the cyclization of nitrone **10**, which gave a 2:1 mixture of **11** and **12** in 70% yield.[5a] This and



related results led him to suggest that C–C bond formation is more advanced than C–O bond formation in the transition state. Formation of **11** is favored since C–C bond formation results in an entropically favored six-membered rather than a seven-membered ring. Selectivity is moderate in this case since electronic effects favor C–C bond formation at the least substituted end of the double bond to give **12**. Cyclization of **3** leads to similar results. The formation of **2** is favored by entropic effects favoring C–C bond formation to give a six-membered ring. Selectivity is again only moderate since electronic effects favor the formation of **9**.

Hydrogenolysis of **2** with hydrogen over Pd gave (±)-nitramine (**1a**) in 96% yield (33% from methylenecyclohexane). The structure was established by comparison of the ^1H and ^{13}C NMR spectra with reported data.[2a] The ^{13}C NMR signal for C-1 of **1a** occurs at δ 52.7 as compared to δ 52.0 and 60.3 reported for nitramine and its diastereomer isonitramine, respectively. The signals for the protons α to the oxygen and nitrogen of **1a** are well-resolved in the NMR spectrum and are identical with the data reported for nitramine. Further confirmation was

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(11) An alternate approach that was considered was the ene reaction of nitromethylene with methylenecyclohexane to give 3-nitropropyl-1-cyclohexene, which could be reduced to **8**. Unfortunately the ene reaction did not proceed either thermally or with Lewis acid catalysis. For a related ene reaction, see: Ranganathan, D.; Rao, C. B.; Ranganathan, S.; Mehrotra, A. K.; Iyengar, R. *J. Org. Chem.* **1980**, *45*, 1185.
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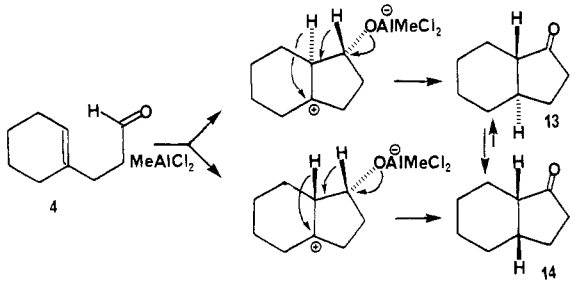
obtained by reaction of (±)-nitramine with methyl iodide to give (±)-*N*-methylnitramine (**1b**), whose structure was established by comparison of the ^1H NMR spectrum with reported data.[2a]

Cyclization of 4 to 13 and 14. Aldehyde **4** possesses a suitable substitution pattern for Lewis acid catalyzed cyclization to give a cyclopentanone.[15,16] Treatment of **4** with 0.8 equiv of $MeAlCl_2$ in CH_2Cl_2 at 25 °C for 1 h gave a 52% yield of a ≈3.5:1 mixture of **13** and **14** as determined by ^{13}C NMR and GC analysis.[17] The moderate yield is probably a result of the volatility of **13** and **14**.



$SnCl_4$-catalyzed cyclization of (*E*)-4-methyl-4-hexenal has been reported to give exclusively *trans*-2,3-dimethylcyclopentanone.[18] We have previously reported that the cyclization of the methyl ketone corresponding to **4** gives exclusively the trans-fused hydrindanone,[16a] although related ketones give small amounts of cis-fused hydrindanones.[16b] The lack of selectivity in the cyclization of **4** could result from direct formation of **13** and **14** or from isomerization of **13** to the more stable isomer **14**.[19] Cyclization of **4** at −20 °C proceeded slowly to give a ≈12:1 mixture of **13** and **14** as determined by GC analysis of aliquots. The reaction was 90% complete after 8 h at −20 °C, in contrast to related ketones, which require much harsher conditions.[16] These results suggest that the reaction is not stereospectific, although isomerization of **13** to **14** may also be occurring.

Attempted cyclization of 1-cyclopentene-1-propanal under similar conditions was unsuccessful. In view of the strain present in the trans-fused bicyclo[3.3.0]octane ring system, this is not surprising.

These studies demonstrate the utility of methyl α-chloroacrylate as a ketene equivalent in the ene reaction. The synthesis of (±)-nitramine from methylenecyclohexane in seven steps in 33% overall yield illustrates the value of this sequence in natural product synthesis.

Experimental Section

Materials and Methods. NMR spectra were taken on Varian EM-390, Perkin-Elmer R32, Bruker WH-90, and a homemade 500-MHz spectrometer. Analyses were performed by Galbraith Laboratories.

Methylene chloride and toluene were dried by distillation from CaH_2. Methyl α-chloroacrylate was purchased from Polysciences, Inc. $EtAlCl_2$ was purchased as a 25% solution in hexane (1.48 M) from Alfa. $MeAlCl_2$ was purchased as a 21.2% solution in hexane (1.40 M) from Texas Alkyls, Inc.

Methyl α-Chloro-1-cyclohexene-1-butanoate (5). $EtAlCl_2$ (18.2 mL of 1.48 M in hexane, 27 mmol) was added to a solution of methylenecyclohexane (3.17 g, 33 mmol) and methyl α-chloroacrylate (3.61 g, 30 mmol) in 80 mL of anhydrous benzene under nitrogen.[8] The reaction mixture was stirred for 20 h at 25 °C and poured into 100 mL of water. The layers were separated, and the aqueous layer was extracted with four 50-mL portions of ether. The combined organic layers were dried ($MgSO_4$) and evaporated to give 6.89 g of a yellow oil. Chromatography on silica gel (9:1 hexane–ether) gave 6.17 g (95%) of **5** as a colorless oil: NMR ($CDCl_3$) δ 5.43 (br s, 1), 4.37–4.07 (m, 1), 3.77 (s, 3), 2.20–1.77 (m, 7), 1.77–1.43 (m, 5); IR (neat) 1750, 1435, 1320, 1195, 1165 cm^{-1}.

α-Hydroxy-1-cyclohexene-1-butanoic Acid (6). α-Chloro ester **5** (3.16 g, 14.6 mmol) was added to a solution of sodium carbonate decahydrate (20.92 g, 73.1 mmol) in 250 mL of water.[9] The mixture was heated at reflux for 16 h and allowed to cool. The solution was acidified to pH 2 with 10% HCl. The precipitated α-hydroxy acid **6** was removed by filtration to give 1.093 g of crude **6**. The filtrate was extracted with three 40-mL portions of chloroform. The combined organic extracts were dried ($MgSO_4$) and evaporated to give an additional 1.405 g of crude **6**. The combined material was recrystallized from hexane to give 2.40 g (89%) of pure **6**: mp 93–95 °C; NMR ($CDCl_3$) δ 6.57 (br s, 2, OH) 5.40 (s, 1), 4.30–4.03 (m, 1), 2.17–1.83 (m, 6), 1.83–1.37 (m, 6); IR (KBr) 3460, 3420, 2920, 2820, 1720, 1435, 1225, 1090, 908 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.93; H, 8.58.

1-Cyclohexene-1-propanal (4). Lead tetracetate (4.46 g, 10.1 mmol) in 50 mL of anhydrous pyridine was added to a solution of α-hydroxy acid **6** (1.85 g, 10.07 mmol) in 50 mL of anhydrous pyridine.[10] The solution was stirred for 2 h at 25 °C during which time the color changed from dark brown to yellow. The solution was treated with 20 mL of saturated aqueous oxalic acid solution. The precipitate was removed by filtration, and the filtrate was diluted with ether and washed with 10% HCl until the pH of the aqueous layer was acidic. The organic layer was dried ($MgSO_4$) and evaporated to give 1.16 g (84%) of crude **4**. Evaporative distillation (100 °C, 1.5 torr) gave 1.12 g (81%) of pure **4**: NMR ($CDCl_3$) δ 9.77 (s, 1), 5.53–5.33 (br s, 1), 2.67–2.13 (m, 4), 2.13–1.80 (m, 4), 1.80–1.43 (m, 4); IR (neat) 2720, 1725, 1440, 1410, 1390, 1140, 920 cm^{-1}.

1-Cyclohexene-1-propanal Oxime (7). Hydroxylamine hydrochloride (0.600 g, 8.6 mmol) in 300 mL of water and aldehyde **4** (0.953 g, 6.9 mmol) in 15 mL of EtOH were placed in a flask equipped with an addition funnel.[12] The solution was cooled in an ice bath, and a solution of 1.233 g (4.3 mmol) of sodium carbonate decahydrate in 110 mL of water was added dropwise. After the addition was complete, the solution was stirred for 1 h at 25 °C and poured into 200 mL of saturated brine. This was extracted with three 30-mL portions of ether, which were combined, dried ($MgSO_4$), and evaporated to give 1.05 g (99%) of crude oxime as a colorless oil, which crystallized on cooling. This was used without further purification. The NMR spectra indicated a 1:1 mixture of *E* and *Z* isomers was present:[20] NMR ($CDCl_3$) δ 8.9–8.3 (br, 1), 7.40 (t, 0.5 × 1, J = 6 Hz, *E* isomer), 6.67 (t, 0.5 × 1, *J* = 6 Hz, *Z* isomer), 5.43 (br, 1), 2.60–2.27 (m, 2), 2.27–1.77 (m, 6), 1.77–1.43 (m, 4); IR (CCl_4) 3600, 3280, 2920, 2860, 2840, 1670, 1435, 1335, 1305, 1140, 920, 905 cm^{-1}. An analytical sample was prepared by recrystallization from hexane: mp 66–67 °C, pure *Z* isomer by NMR. Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.31; H, 9.91; N, 8.98.

***N*-Hydroxy-1-cyclohexene-1-propanamine (8).** Sodium cyanoborohydride (0.124 g, 2 mmol) was added to a solution of crude oxime **7** (0.454 g, 3 mmol) in 15 mL of MeOH.[13] A trace of methyl orange was added. A 1:1 mixture of concentrated hydrochloric acid–methanol was added dropwise with stirring to maintain an orange-red color (pH 3) for 1 h. The pH was adjusted to 9 with 6 N KOH. The solution was saturated with sodium chloride and extracted with five 10-mL portions of chloroform. The combined organic extracts were dried ($MgSO_4$) and evaporated to give 0.439 g (95%) of ≃80% pure **8**, which was used immediately for the next step since it decomposed on standing: NMR ($CDCl_3$) δ 6.40 (br s, 2), 5.40 (br s, 1), 2.93 (t, 2, *J* = 6 Hz), 2.17–1.83 (m, 6), 1.83–1.40 (m, 6). The presence of ≈10% of the corresponding amine is indicated by a peak at δ 2.63 (t, 2, *J* = 6 *Hz*) in the NMR spectrum.

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(20) McCarty, C. G. In "The Chemistry of the Carbon–Nitrogen Double Bond"; Patai, S., Ed.; Interscience: London, 1970; pp 386–389.

Preparation of 2 and 9. Gaseous formaldehyde, prepared from paraformaldehyde (0.571 g, 19 mmol) by heating a flask containing the solid with a flame, was bubbled into a solution of hydroxylamine **8** (0.295 g, 1.9 mmol) in 50 mL of toluene containing 18 g of anhydrous sodium sulfate under nitrogen.[5a] The mixture was stirred for 15 min at 0 °C and then heated at reflux for 24 h. The mixture was cooled, filtered through Celite, and evaporated to give 0.327 g of an orange oil. Chromatography on silica gel (ether) gave 0.234 g (74%, 70% based on **7**) of a 2.5:1 mixture of **2** and **9** as determined by GC analysis. Pure samples of **2** and **9** were isolated by preparative GC on a 10 ft × $^1/_4$ in. 4% KOH, 15% Carbowax 20 M on 60/80 Chromosorb W column at 200 °C at a flow rate of 50 mL/min.

The data for **2** follow: NMR ($CDCl_3$) δ 3.93 (dd, 1, J = 6, 9 Hz), 3.38 (d, 1, J = 11 Hz), 3.27 (dd, 1, J = 12.5, 4.5 Hz), 2.63 (ddd, 1, J = 12.5, 12, 5 Hz), 2.57 (d, 1, J = 11 Hz), 1.17–2.17 (m, 12); IR (neat) 2940, 2865, 1460, 980, 920, 905, 900, 875, 765 cm^{-1}; MS, m/e (relative intensity) 167 (M^+, 39) 150 (70), 96 (28), 93 (36), 81 (40), 79 (53), 67 (33), 60 (31), 55 (31), 43 (30), 42 (28), 41 (35), 40 (100); GC (200 °C) t_R 13.8 min. Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.28, H, 10.18; N, 8.21.

The data for **9** follow: NMR ($CDCl_3$, 500 MHz) δ 3.29 (ddd, 1, J = 5, 8, 13.5 Hz), 3.27 (d, 1, J = 11.5 Hz), 2.94 (dd, 1, J = 11.5, 4 Hz), 2.75 (dd, 1, J = 13.5, 5.5 Hz), 2.39–2.25 (m, 1), 1.77–1.00 (m, 12); IR (neat) 2940, 2870, 1455, 1020, 955, 870, 830, 780, 620 cm^{-1}; MS, m/e (relative intensity) 167 (M^+, 43), 150 (100), 93 (41), 91 (42), 81 (47), 79 (58), 67 (38), 55 (62), 43 (42), 42 (58), 41 (95), 39 (48); GC (200 °C) t_R 11.1 min. Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.65; H, 10.15; N, 8.17.

(±)-Nitramine (1a). 10% Pd on carbon (0.017 g) was added to a solution of **2** (0.042 g, 0.25 mmol) in 6 mL of ethanol. The resulting mixture was stirred under 1 atm of hydrogen for 2 h, filtered through Celite, and evaporated to give 0.041 g (96%) of (±)-nitramine (**1a**): NMR ($CDCl_3$) δ 5.33 (br s, 2), 3.53 (dd, 1, J = 9, 4 Hz), 3.37 (d, 1, J = 12 Hz), 3.17–2.83 (m, 1), 2.65 (ddd, 1, J = 11.5, 11.5, 3 Hz), 2.43 (d, 1, J = 12 Hz), 2.2–0.8 (m, 12); ^{13}C NMR (C_6D_6) δ 78.5 (C-7), 52.7 (C-1), 47.3 (C-3), 39.0, 37.5, 36.3, 33.2, 24.7, 24.2, 21.5; IR (CCl_4) 3300, 2940, 2870, 2820, 1455, 1440, 1125, 1080, 1050 cm^{-1}. The ^1H and ^{13}C NMR data correspond closely to those reported for the natural product.[2a]

An acetone solution of nitramine was mixed with an ethanolic solution of hydrogen chloride. The solvent was evaporated to give a yellowish solid, mp 180–185 °C, which was recrystallized twice from acetone to give pure (±)-nitramine hydrochloride, mp 225–228 °C.

(±)-*N*-Methylnitramine (1b). A solution of **1a** (40 mg, 0.28 mmol) in 0.5 mL of EtOH and 0.5 mL of methyl iodide was heated for 2 h at 90 °C in a sealed tube. The solvent and excess methyl iodide were evaporated. The residue was treated with ice water, and the solution was made alkaline with 5% sodium hydroxide solution and extracted with three portions of ether. The combined organic layers were dried (Na_2SO_4) and evaporated to give 0.029 g (68%) of pure (±)-**1b**: NMR ($CDCl_3$) δ 4.77 (br s, 1), 3.53 (dd, 1, J = 9, 4 Hz), 3.17 (d, 1, J = 12 Hz), 3.00–2.63 (m, 1), 2.27 (s, 3), 2.2–1.1 (m, 14); ^{13}C NMR ($CDCl_3$) δ 78.0 (C-7), 61.4 (C-1), 56.1 (C-3), 46.4 (N-Me), 37.4 (2 carbons), 36.9, 32.7, 24.3, 23,4, 21.1; IR ($CDCl_3$) 3230, 2940, 2860, 2800, 1455, 1265, 1160, 1065, 1020 cm^{-1}. The ^1H NMR and IR data correspond closely to those previously reported.[2a]

***trans*- and *cis*-Hexahydro-1-indanone (13 and 14).** $MeAlCl_2$ (1 mL of 1.4 M in hexane, 1.4 mmol) was added to a solution of aldehyde **4** (0.234 g, 1.69 mmol) in 20 mL of CH_2Cl_2 at 0 °C under nitrogen. The solution was stirred for 5 min at 0 °C and 1.5 h at 20 °C. The reaction mixture was poured into water and treated with 10% HCl to dissolve the precipitate. The mixture was extracted with three portions of CH_2Cl_2, which were combined, dried ($MgSO_4$), and evaporated to give 0.181 g of a brown oil. Chromatography on silica gel (9:1 hexane–ether) gave 0.121 g (52%) of a ≈3.5:1 mixture of **13** and **14** as determined by GC analysis and ^{13}C NMR spectroscopy: NMR ($CDCl_3$) δ 0.7–2.5 (m, 14); ^{13}C NMR ($CDCl_3$) δ **13** 217.9, 55.4, 43.2, 36.9, 32.5, 27.6, 25.8, 25.5, 24.9; **14** 49.3, 34.7, 28.1, 23.9, 22.8, 22.4, three carbons were not observed; IR (neat) 2930, 2850, 1740, 1450, 1085 cm^{-1}; GC (9 ft; $^1/_4$ in.; 10% Carbowax 20 M on Chromosorb PNAW 60/80, 50 mL/min, 150 °C) t_R 20.9 (**13**) and 21.9 (**14**) min, partially overlapping. The ^{13}C NMR data are identical with those previously reported.[17]

An identical reaction was carried out at −20 °C and monitored by GC. Ketones **13** and **14** were formed as a ≈12:1 mixture. The reaction was worked up after 8 h, at which time it was 90% complete.

Acknowledgment. We are grateful to the National Institues of Health for financial support. The 500-MHz spectrometer was purchased with funds provided by NIH Grant GM 20168. C.P.C-M. gratefully acknowledges a fellowship support from CONICIT (Venezuela).

Registry No. (±)-**1a**, 82227-98-3; (±)-**1a**·HCl, 89398-21-0; (±)-**1b**, 89460-82-2; (±)-**2**, 89398-19-6; **4**, 60416-25-3; (±)-**5**, 89398-16-3; (±)-**6**, 89414-11-9; (*E*)-**7**, 89398-17-4; (*Z*)-**7**, 89398-24-3; **8**, 89398-18-5; (±)-**9**, 89398-20-9; (±)-**13**, 89398-22-1; (±)-**14**, 89398-23-2; methylenecyclohexane, 1192-37-6; methyl α-chloroacrylate, 80-63-7.

Asymmetric Diels–Alder Reactions with Sulfines Derived from Proline

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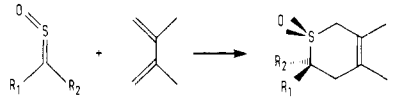
Received September 13, 1983

The synthesis of a variety of sulfines **8** derived from *S*-proline, utilizing the reaction of α-silyl carbanions with sulfur dioxide, is described. Reaction of the thus prepared sulfines **8** with 2,3-dimethyl-1,3-butadiene gave dihydrothiopyran *S*-oxides **9**. During these cycloaddition reactions asymmetric inductions up to 40% were observed. From one pure diastereomeric form of cycloadduct **9d** an X-ray analysis was carried out in order to provide insight in the steric course of the cycloaddition reaction.

Sulfines (thione *S*-oxides) are sulfur-centered heterocumulenes that can undergo a variety of cycloaddition reactions,[2] e.g., with carbon 1,3-dienes, heterodienes, diazo compounds, nitrile oxides, and nitrilimines. The Diels–Alder type reactions with 1,3-butadienes lead to dihydrothiopyran *S*-oxides (Scheme I). An interesting feature of this cycloaddition is that geometrically isomeric sulfines

Scheme I



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