Pergamon

Tetrahedron, Vol. 52, No. 41, pp. 13181-13188, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00785-5

Radical Cyclization of α-Allenic Ketone: A New Approach to the Synthesis of (±)-α-Chamigrene

Yao-Jung Chen*, Chi-Ying Wang, and Wen-Yuan Lin

Department of Chemistry, National Chung Hsing University, Taichung, Taiwan 402

Abstract : A regioselective cyclization of ε-alkyl radicals attacking on the sp-carbon of α-allenic ketone to construct a spiro[5.5]undecane skeleton has been studied, and a new approach to the synthesis of (±)-α-chamigrene **22** is also reported. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

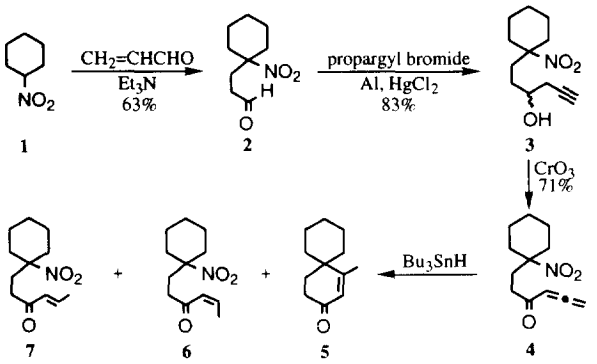
Recently radical cyclization reactions have been extensively studied and successfully applied to organic synthesis.[1] A good radical acceptor plays an important role for insuring an efficient process of radical cyclizations.[2] While most of radical acceptors used are such as olefins and acetylenes,[1] relatively little attention has been paid to studies of allenes,[3] especially electron-deficient allenes.[4] Up to date, there are two noticeable examples reported by Crandall and Gillmann for the radical cyclization of allenes bearing radical-stabilizing substituents such as $P(O)Ph_2$, SOPh, SO_2Ph,[4a] and COOMe,[4b] respectively. According to their studies, results indicated that the regiochemical outcome of radical cyclizations were controlled by radical acceptors used. For instances, Crandall[4a] found the cyclization of ε-alkyl radicals add exclusively to the sp-carbon of α-allenic sulphoxide, sulphone, and phosphine oxide, but Gillmann[4b] observed ε-ketyl radicals prefer the proximal sp^2-carbon of α-allenic ester. However, the study in the regiochemistry of cyclizations of ε-alkyl radicals adding to α-allenic ketones has not been reported before.

(±)-α-Chamigrene **22**[5] is one kind of spirocyclic sesquiterpenes containing a spiro[5.5]undecane nucleus. From a synthetic standpoint, the construction of the spiro[5.5]undecane nucleus turns out to be a synthetic challenge. Although many methods[6] have been recorded for syntheses of chamigrenes through Diels-Alder reactions,[6a] carbocations,[6b,6c,6d] carbanions,[6e] or carbenes etc,[6f,6g] no study dealing with radical cyclization reaction appeared. As parts of our studies on radical cyclizations towards syntheses of natural products,[7] we now demonstrate the radical cyclization for the above system is highly regioselective to construct a spiro[5.5]undecane skeleton and describe a new approach to the synthesis of (±)-α-chamigrene **22** based on this strategy.

RESULTS AND DISCUSSION

Our model study is shown in Scheme 1. The radical cyclization precursor **4**, an α-allenic ketone, was readily prepared by Michael addition of nitrocyclohexane **1** and acrolein, followed by propargylation with propargyl sesquialuminum bromide[8], and then by Jones oxidation with a yield of 37% in three steps. The radical cyclization

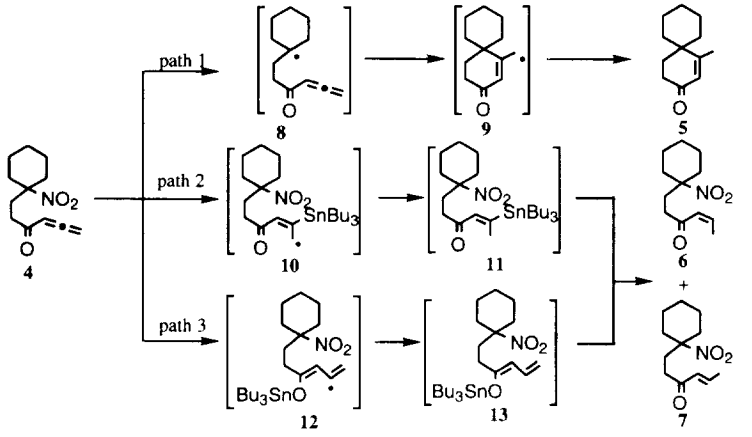
Scheme 1



of α-allenic ketone **4** was effected by treatment with tributyltin hydride in the presence of 20 mol% of azobisisobutyronitrile (AIBN) in 0.0015M of refluxing benzene for 12 h to give 53% yield of spiro[5.5]undecenone **5** and trace amount of nitroenone **6** and **7**. Like analogous allenes in Crandall's studies,[4a] only the *6-exo-dig* cyclization product spiro[5.5]undecenone **5** was observed, but none of the *6-endo-dig* cyclization product or the uncyclized allenic ketone appears from a direct reduction of nitro group. This result shows that the cyclization of an ε-alkyl radical added to the sp-carbon of an α-allenic ketone was regioselective and rapid, and a selective hydrogen abstraction at an unsubstituted exocyclic carbon was followed. The substituent of carbonyl group facilitates cyclization and promotes radical attack at the sp-carbon of an allene due to electronic effects that acts as a similar role as sulphoxide and sulphone groups in Crandall's studies.[4a] However, trace amount of undesired nitroenone **6** and **7** from a direct reduction of allene group were also observed. To circumvent the inconvenience of isolating these two minor products and testify a different reactivity of tin radical towards nitro group and allenic ketone, another cyclization reaction was carried out in the same condition except at 60 °C. Interestingly, only 47% yield of *cis*-enone **6** and 13% yield of *trans*-enone **7** were observed and none of cyclized enone **5** or uncyclized allenic ketone was detected. These results indicate that a tertiary nitro group is more reactive towards tin radical than an allene ketone in a sufficiently harsh condition such as refluxing benzene. Nevertheless, the generation of a desired tertiary radical via path 1, shown as in Scheme 2, was failed in a milder condition at 60 °C probably due to an inefficient fission of carbon-nitrogen bond. Instead, a direct reduction of the allenic ketone occurred. These unexpected nitroenone **6** and **7** possibly were generated by proceeding through path 2, which tin radical added selectively on a central carbon of allene, followed by hydrogen abstraction and destannylation. A similar mechanism has been reported by Hatem[9] in studies of the radical hydrostannylation of β-allenic oxime ethers and hydrazones. Unfortunately, the intermediate of vinyl tin **11** was not obtained after workup in our studies. Hence, the other path 3, which tin radical attacks directly on oxygen atom of allenic ketone via dienyl stannyl ether followed by destannylation after workup, was unable to be ruled out yet. Finally, the reason why a larger amount

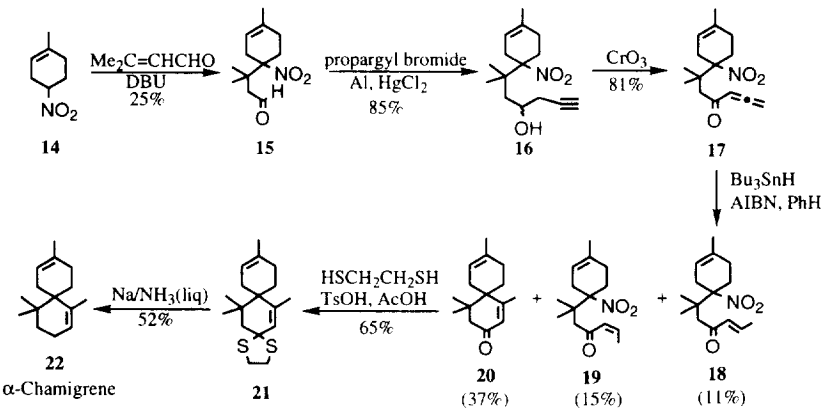
of a less stable *cis*-enone **6** relative to *trans*-enone **7** was obtained still remains unclear and more investigations for this reaction mechanism are needed.

Scheme 2



In terms of regioselectivity in an 6-exo-dig radical cyclization reaction, our results show that the above methodology is appropriate for the construction of a spiro[5.5]undecenone skeleton. Therefore, we now demonstrate a new approach for the synthesis of (±)-α-chamigrene based on this strategy shown in Scheme 3. The

Scheme 3



starting material **14**, 1-methyl-4-nitrocyclohexene, was readily prepared by a known procedure.[7a,10] The β-alkynyl nitroalcohol **16**, a precursor of α-allenic nitroketone, was obtained by Michael addition of **14** and 3-methyl-2-butenal followed by propargylation with propargyl sesquialuminum bromide in 21% yield for two steps. The low yield observed might be affected by steric effects, compared with the result in our model study. It must be mentioned, surprisingly, that a zero yield of Michael adduct from primary nitroethane and 4-methyl-3-penten-2-one was once reported.[11] The α-allenic nitroketone **17** was readily available in 81% yield by Jones oxidation of β-

alkynyl nitroalcohol **16** at 0~5 °C. Direct radical cyclization was carried out by treatment of precursor **17** with 1.5 eq tributyltin hydride in the presence of 20 mol% of azobisisobutyronitrile (AIBN) in 0.0015M of refluxing benzene for 15 h. Three major products, *trans*-enone **18**, *cis*-enone **19**, and spiroenone **20**, were afforded in yields of 11%, 15%, and 37%, respectively. The lower yield of cyclized enone **20** was obviously caused by more difficult generation of the radical from a tertiary neopentyl nitro group. Finally, the reduction of carbonyl group[12] of enone **20** was acheived by two steps as follows. Dithiolation of **20** with 1,3-ethanedithiol catalyzed by TsOH in acetic acid at room temperature, followed by dethiolation with Na/NH_3(liq) at -60 °C, gave a colorless liquid of (±)-α-chamigrene **22** in 34% yield for two steps, based on the data from ^1H NMR, ^{13}C NMR, IR, and HRMS studies.[6b]

In conclusion, a regioselective cyclization of an ε-alkyl radical attacking on the sp-carbon of α-allenic ketone to construct a spiro[5.5]undecane skeleton has been described and a new route to the synthesis of (±)-α-chamigrene **22** has been also accomplished. Further investigations, involving reaction mechanisms and other usefully synthetic applications of α-allenic ketones, are undergoing.

EXPERIMENTAL SECTION

Melting points (Buchi 535 capillary melting point apparatus) are uncorrected. Infrared spectra were recorded on a Hitachi 270-30 spectrometer. Nuclear magnetic resonance spectra were recorded on a Varian VXR-300S or a Varian VXR-200S spectrometer. NMR data are reported as follows: chemical shift [multiplicity (*s*=singlet, *d*=doublet, *t*=triplet, *q*=quartet, *m*=multiplet), coupling constant, integration] in units of ppm. Mass spectra were recorded on JOEL JMS-HX 110 and JEOL NMS-SX/SX 102A mass spectrometers. Silica-gel plates (Merck 60 F-254) were used for analytical thin-layer chromatography. Column chromatography was performed on SiO_2 (70-230 mesh) with elution of gradients of EtOAc and hexane. CH_2Cl_2 was distilled over P_2O_5 under nitrogen. THF and benzene were distilled over sodium under nitrogen.

1-(2'-Formylethyl)nitrocyclohexane (2). To a solution of nitrocyclohexane (1.2 mL, 10 mmol) and Et_3N (0.14 mL, 1 mmol) in acetonitrile (3.5 mL) was added acrolein (1 mL, 16 mmol) in acetonitrile (2.5 mL) within 5 min at room temperature. After stirred for 15 h, the reaction mixture was evaporated and purified by column chromatography with hexane/EtOAc (2:1) as eluent to give a pale yellow liquid **2** (1.174 g, 63%): IR (neat) 1732 (C=O), 1534 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 ~1 74 (m, 8H), 2.10~2.22 (m, 2H), 2.32~2.54 (m, 4H), 9.77 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.2 (t), 24.6 (t), 31.8 (t), 34.0 (t), 37.9 (t), 90.4 (s), 199.9 (d); MS m/z 139 (M^+-NO_2), 121 (base); HRMS Calcd for $C_9H_{15}O$ (M^+-NO_2) 139.1123, Found 139.1124.

1-(3'-Hydroxyl-5'-hexynyl)nitrocyclohexane (3). A mixture of $HgCl_2$ (60 mg, 0.22 mmol) and Al (156 mg, 5.79 mmol) in dry THF (2 mL) was vigorously stirred for 1 h. To this was then added dropwise a solution of propargyl bromide (0.69 mL, 7.72 mmol) in THF (1 mL). The reaction mixture was kept warm and stirred untill aluminium disappeared. After additional 20 min, the solution of propargyl sesquialuminium bromide[8] was prepared. To a solution of compound **2** (357 mg, 1.93 mmol) in ether (16 mL) was added 1.5 mL of the above prepared solution at -78 °C. After stirred for 2 h, the reaction mixture was poured into 40 mL of ice water and extracted with ether (25 mL x 3). The combined organic layer was rinsed with 40 mL of saturated NaCl aqueous

solution, dried over $MgSO_4$, and then evaporated *in vacuo*. The residue was purified by column chromatography with hexane/EtOAc (6:1) as eluent to give a pale yellow liquid **3** (359 mg, 1.6 mmol, 83%): IR (neat) 3448 (OH), 2116 (C≡C), 1536 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20~1.75 (m, 10H), 1.75~2.15 (m, 4H), 2.26~2.48 (m, 4H), 3.62~3.76 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 22.2(t), 22.3(t), 24.8(t), 27.4(t), 29.7(t), 33.6(t), 34.5(t), 36.4(t), 69.3(d), 71.4(d), 80.1(s), 91.2(s); MS m/z 179 (M^+- NO_2), 161, 139 (base); HRMS Calcd for $C_{12}H_{19}O$ (M^+-NO_2) 179.1436, Found 179.1434

1-(3'-Oxo-4',5'-hexadienyl)nitrocyclohexane (4). A solution of **3** (1.394 g, 6.2 mmol) in acetone (60 mL) at 0~5 °C was stirred for 5 min and to this was then added dropwise 2.3 mL of Jones reagent (1.34 g of CrO_3 and 1.15 mL of H_2SO_4 were diluted by water up to 5 mL). After additional for 10 min, the reaction mixture was quenched by adding EtOAc (50 mL) and water (50 mL), and the organic layer was separated. The aqueous layer was extracted by EtOAc (50 mL x 2). The combined organic layer was dried over $MgSO_4$ and then evaporated *in vacuo*. After chromatography by using hexane/EtOAc (6:1) as eluent, 986 mg of **4** was obtained as a pale yellow liquid in 71% yield: IR (neat) 1962, 1934 (C=C=C), 1680 (C=O), 1534 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20~1.70 (m, 8H), 2.10~2.20 (m, 2H), 2.30~2.45 (m, 2H), 2.50~2.65 (m, 2H), 5.27 (d, J = 6.3 Hz, 2H), 5.77 (t, J = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.2 (t), 24.7 (t), 32.8 (t), 34.0 (t), 80.2 (t), 90.8 (s), 96.5 (d), 198.5 (s), 216.7 (s); MS m/z 223 (M^+), 154 (base); HRMS Calcd for $C_{12}H_{17}O_3N$ (M^+) 223.1209, Found 223.1204.

1-Methylspiro[5.5]undec-1-en-3-one (5). To a solution of **4** (33.5 mg, 0.15 mmol) in refluxing benzene (100 mL) was added by syringe pump a solution of Bu_3SnH (67 mg, 0.23 mmol) and AIBN (6 mg, 0.04 mmol) in dry benzene (10 mL). After the addition completed in 12 h, the reaction mixture was cooled and evaporated to give a pale yellow liquid. The crude product was purified by chromatography using hexane and then changed to hexane/ethyl acetate (10:1) as eluent to remove tin compounds. After the further purification by TLC method using hexane/ethyl acetate (10:1) as eluent to give **5** (14 mg, 0.08 mmol, 53%): IR (neat) 1674, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12~1.30 (m, 2H), 1.40~1.80 (m, 8H), 1.93 (d, J = 1.5 Hz, 3H), 1.98~2.06 (m, 2H), 2.34~2.41 (m, 2H), 5.80 (q, J = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1(q), 21.3(t), 25.7(t), 29.2(t), 32.5(t), 33.4(t), 38.5(s), 127.2(d), 170.4(s), 199.5(s); MS m/z, 178 (M^+, base); HRMS Calcd for $C_{12}H_{18}O$ (M^+) 178.1358, Found 178.1359.

1-(3'-Oxo-4'*Z*-hexenyl)nitrocyclohexane (6) and 1-(3'-oxo-4'*E*-hexenyl)nitrocyclohexane (7). To a solution of **4** (33.5 mg, 0.15 mmol) in 60 °C benzene (100 mL) was added by syringe pump a solution of Bu_3SnH (134 mg, 0.46 mmol) and AIBN (14 mg, 0.09 mmol) in dry benzene (20 mL). After the addition completed in 24h, the reaction mixture was cooled and evaporated to give a pale yellow liquid. The crude product was purified by chromatography using hexane and then changed to hexane/ethyl acetate (10:1) as eluent to remove tin compounds. After the further purification by TLC method using hexane/ethyl acetate (10:1) as eluent to give **6** (16 mg, 0.07 mmol, 47%) and **7** (5 mg, 0.02 mmol, 13%). Compound **6**: IR (neat) 1694 (C=O), 1533 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22~1.80 (m, 8H), 2.11 (dd, J = 1.2, 6.9 Hz, 3H), 2.10~2.20 (m, 2H), 2.32~2.48 (m, 4H), 6.08~6.29 (m, 2H) ; ^{13}C NMR ($CDCl_3$) δ 15.9(q), 22.2(t), 24.7(t), 33.7(t), 34.1(t), 37.7(t), 90.8(s), 127.2(d), 144.0(d), 199.4(s); MS m/z, 179 (M^+-NO_2), 69(base); HRMS Calcd for $C_{12}H_{19}O$ (M^+-NO_2) 179.1436, Found 179.1443. Compound **7**: IR (neat) 1678 (C=O), 1538 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22~1.80 (m, 8H), 1.90 (dd, J = 1.8, 6.9 Hz, 3H), 2.10~2.20 (m, 2H), 2.34~2.54 (m, 4H), 6.10 (dq, J = 1.8, 15.6 Hz, 1H), 6.85 (dq, J = 6.9, 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.2(q), 22.2(t), 24.7(t), 33.5(t), 33.9(t),

34.1(t), 90.9(s), 131.6(d), 143.5(d), 198.2(s); MS m/z, 179 (M^+-NO_2), 69(base); HRMS Calcd for $C_{12}H_{19}O$ (M^+-NO_2) 179.1436, Found 179.1431.

4-(1',1'-Dimethyl-2'-formylethyl)-1-methyl-4-nitrocyclohexene (15). 1-Methyl-4-nitrocyclo hexene **14** (705 mg, 5 mmol), readily prepared from nitroethylene and isoprene,[7a,10] was treated with DBU (2.2 mL, 15 mmol), and acetonitrile (2.5 mL) at 0 °C. After 2 min, 3-methyl-2-butenal (490 mg, 5.8 mmol) was added and the mixture was stirred for 30 min. Another one equivalent of compound **14** (705 mg, 5 mmol) was added and stirred for 10 min at room temperature. Another two equivalent of DBU (1.7 mL, 11.6 mmol) was added. The reaction mixture was stirred for 20 min and then poured into 30 mL of ice water. After diluted with 20 mL of ether, the mixture was acidified with 1N HCl aqueous solution and the organic layer was separated. The aqueous layer was extracted with ether (30 mL x 2). The combined organic layer was dried over MgSO4 and evaporated *in vacuo*. The residue was purified by column chromatography with hexane/EtOAc (1:5) as eluent. The crude product was further purified by MPLC with 20:1 hexane/EtOAc as eluent to afford a pale yellow liquid **15** (330 mg, 25%): IR (neat) 1722 (C=O), 1534 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (s, 3H), 1.19 (s, 3H), 1.61 (s, 3H), 1.79 (ddd, J = 6.6, 11.1, 13.5 Hz, 1H), 1.96~2.22 (m, 2H), 2.30~2.44 (m, 2H), 2.46~2.58 (m, 2H), 2.96~3.10 (m, 1H), 5.25~5.33 (m, 1H), 9.82 (t, J = 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.8 (q), 23.0 (q), 23.1 (q), 25.7 (t), 27.4 (t), 29.0 (t), 39.5 (s), 50.1 (t), 96.1 (s), 117.0 (d), 134.0 (s), 201. 41 (d); MS m/z 225 (M^+), 135 (base); HRMS Calcd for $C_{12}H_{19}NO_3$ (M^+) 225.1364, Found 225.1360.

4-(1',1'-Dimethyl-3'-hydroxyl-5'-hexynyl)-1-methyl-4-nitrocyclohexene (16). A mixture of $HgCl_2$ (30 mg, 0.11 mmol) and Al (215 mg, 7.95 mmol) in dry THF (2 mL) was vigorously stirred for 40 min. To this was then added dropwise a solution of propargyl bromide (0.95 mL, 10.6 mmol) in THF (2 mL). The reaction mixture was kept warm and stirred untill aluminium disappeared. After additional 10 min, the solution of propargyl sesquialuminium bromide[8] was prepared. To a solution of compound **15** (597 mg, 2.65 mmol) in THF (15 mL) was added 3 mL of the above prepared solution at -78 °C. After stirred for 3 h, the reaction mixture was poured into 40 mL of ice water and extracted with ether (25 mL x 3). The combined organic layer was rinsed with 40 mL of saturated NaCl aqueous solution and dried with $MgSO_4$ and then evaporated *in vacuo*. The residue was purified by column chromatography wiht hexane/EtOAc (8:1) as eluent to give a pale yellow liquid **16** (598 mg, 85%): IR (neat) 3564 (OH), 2120 (C≡C), 1534 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04~1.16 (m, 6H), 1.44~1.70 (m, 6H), 1.74~1.90 (m, 1H), 1.92~2.20 (m, 3H), 2.26~2.60 (m, 4H), 2.98~3.12 (m, 1H), 3.82~3.94 (m, 1H), 5.26~5.32 (m, 1H); MS m/z 265 (M^+), 135 (base); HRMS Calcd for $C_{15}H_{23}NO_3$ (M^+) 265.1678, Found 265.1669.

4-(1',1'-Dimethyl-3'-oxo-4',5'-hexadienyl)-1-methyl-4-nitrocyclohexene (17). A solution of **16** (106 mg, 0.4 mmol) in acetone (8 mL) at 0~5 °C was stirred for 5 min and to this was then added dropwise 0.5 mL of Jones reagent (2.67 g of CrO_3 and 2.3 mL of H_2SO_4 were diluted by water up to 10 mL). After stirred for 5 min, the reaction monitored by TLC was incomplete and 0.2 mL of Jones reagent was added again. After stirring for 10 min, to the reaction mixture was added EtOAc (10 mL) and water (10 mL) and the organic layer was separated. The aqueous layer was extracted by EtOAc (20 mL x 2). The combined organic layer was dried over $MgSO_4$ and then evaporated *in vacuo*. After chromatography by using hexane/EtOAc (10:1) as eluent, 85.4 mg of **17** was obtained as a pale yellow liquid in 81% yield. Compound **17**: IR (neat) 3072 (=CH), 1964, 1934 (C=C=C), 1672 (C=O), 1536 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (s, 3H), 1.14 (s, 3H), 1.61 (s, 3H), 1.81

(ddd, J = 6.6, 11.7, 13.5 Hz, 1H), 1.94~2.20 (m, 2H), 2.32~2.58 (m, 2H), 2.50 (d, J = 13.2 Hz, 1H), 2.83 (d, J = 13.2 Hz, 1H), 2.96~3.10 (m, 1H), 5.27~5.30 (m, 3H), 5.78 (t, J = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.3 (q), 22.4 (q), 22.8 (q), 25.7 (t), 27.5 (t), 29.0 (t), 39.9 (s), 43.2 (t), 80.1 (t), 96.7 (s), 99.1 (d), 117.2 (d), 133.8 (s), 199.3 (s), 217.4 (s); MS (FAB) m/z 264 (M^++1), 217, 154, 135 (base); HRMS Calcd for $C_{15}H_{21}O$ (M^+-NO_2) 217.1592, Found 217.1597.

1,5,5,9-Tetramethylspiro[5.5]undec-1,8-dien-3-one (20). To a solution of **17** (26.2 mg, 0.1 mmol) in refluxing benzene (67 mL) was added by syringe pump a solution of Bu_3SnH (0.04 mL, 0.15 mmol) and AIBN (5 mg, 0.03 mmol) in dry benzene (10 mL). After the addition completed in 15 h, the reaction mixture was cooled and evaporated to give a brown liquid. The crude product was purified by chromatograpgy using hexane (250 mL) and then changed to hexane/ethyl acetate (5:1) as eluent to remove tin compounds. After the further purification by TLC using hexane/ethyl acetate (10:1) as eluent, three pale yellow liquids, **18** (3 mg, 11%), **19** (4 mg, 15%), and **20** (8 mg, 37%) were obtained, respectively. Compound **18**: IR (neat) 1690 (C=O), 1626 (C=C), 1534 (NO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 3H), 1.14 (s, 3H), 1.62 (s, 3H), 1.89 (dd, J = 1.8, 6.9 Hz, 3H), 1.76~1.92 (m, 1H), 1.94~2.20 (m, 2H), 2.42 (d, J = 13.8 Hz, 1H), 2.71 (d, J = 13.8 Hz, 1H), 2.34~2.60 (m, 2H), 2.96~3.10 (m, 1H), 5.25~5.33 (m, 1H), 6.12 (dq, J = 1.5, 15.6 Hz, 1H), 6.80 (dq, J = 6.9, 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.2 (q), 22.5 (q), 22.5 (q), 22.8 (q), 25.7 (t), 27.5 (t), 29.1 (t), 39.8 (s), 44.8 (t), 96.9 (s), 117.3 (d), 133.6 (d), 133.9 (s), 143.3 (d), 199.0 (s); MS (FAB) m/z, 266 (M^++1), 135 (base); HRMS Calcd for $C_{15}H_{23}O$ (M^+-NO_2) 219.1749, Found 219.1757. Compound **19**: IR (neat) 1688 (C=O), 1616 (C=C), 1534 (NO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (s, 3H), 1.16 (s, 3H), 1.61 (s, 3H), 1.81 (ddd, J = 6.6, 11.7, 13.8 Hz, 1H), 2.09 (d, J = 5.7 Hz, 3H), 1.90~2.20 (m, 2H), 2.37 (d, J = 13.8 Hz, 1H), 2.58 (d, J = 13.8 Hz, 1H), 2.30~2.60 (m, 2H), 2.95~3.10 (m, 1H), 5.22~5.34 (m, 1H), 6.06~6.24 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 15.8 (q), 22.3 (q), 22.4 (q), 22.8 (q), 25.7 (t), 27.5 (t), 29.0 (t), 40.0 (s), 49.0 (t), 96.8 (s), 117.3 (d), 129.5 (d), 133.9 (s), 143.4 (d), 200.5 (s); MS m/z, 265 (M^+), 135 (base); HRMS Calcd for $C_{15}H_{23}NO_3$ (M^+) 265.1678, Found 265.1685. Compound **20**: IR (neat) 1666 (C=O), 1612 (C=C); ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 3H), 1.03 (s, 3H), 1.68 (s, 3H), 1.97 (s, 3H), 1.70~2.15 (m, 6H), 2.16~2.32 (m, 1H), 2.54~2.70 (m, 1H), 5.50 (br s, 1H), 5.87 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 23.3 (q), 23.9 (q), 24.2 (q), 24.8 (q), 28.0 (t), 28.2 (t), 30.6 (t), 40.4 (s), 43.4 (s), 49.0 (t), 121.7 (d), 127.1 (d), 134.2 (s), 170.6 (s), 198.8 (s); MS m/z, 218 (M^+), 147 (base); HRMS Calcd for $C_{15}H_{22}O$ (M^+) 218.1671, Found 218.1667.

1,5,5,9-Tetramethyl-3-spiro[1,3-dithiolane]spiro[5.5]undec-1,8-diene (21). To a stirring mixture of **20** (40 mg, 0.18 mmol), TsOH (17 mg, 0.09 mmol), and AcOH (0.5 mL) was added 1,2-ethanedithiol (0.02 mL, 0.23 mmol) at room temperature. After 45 h, 10 mL of water was added to the reaction mixture and the aqueous layer was extracted with dichloromethane. The combined organic layers were rinsed with 10 mL of 4M NaOH aqueous solution and 10 mL of water, dried over $MgSO_4$, and evaporated *in vacuo*. The crude product was purified by column chromatography (hexane) to give a colorless liquid of **21** (34.6 mg, 65%): IR (neat) 3020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H), 0.97 (s, 3H), 1.64 (s, 3H), 1.69 (s, 3H), 1.58~1.74 (m, 2H), 1.78~2.00 (m, 3H), 2.02~2.22 (m, 2H), 2.63 (d, J = 15.0 Hz, 1H), 3.22~3.46 (m, 4H), 5.40~5.48 (m, 1H), 5.55 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 23.3 (q), 23.9 (q), 24.9 (q), 28.4 (t), 28.6 (t), 30.0 (t), 38.3 (s), 38.9 (t), 40.0 (s), 40.5 (t), 50.5 (t), 63.3 (s), 122.2 (d), 128.2 (d), 134.0 (s), 140.2 (s); MS m/z, 294 (M^+, base), 233, 211, 198, 165; HRMS Calcd for $C_{17}H_{26}S_2$ (M^+) 294.1476, Found 294.1477.

1,5,5,9-Tetramethylspiro[5.5]undec-1,8-diene (α-Chamigrene, 22). A solution of **21** (54 mg, 0.18 mmol) in ether (10 mL) was cooled to -60 °C and to this was then condensed 5 mL of liquid NH_3. To the vigorously stirred solution were added small pieces of sodium metal until the blue color persisted. The cooling bath was removed, and the blue solution was kept at reflux for 45 min. To the reaction solution was added slowly methanol until it turned white, and the ammonia was allowed to evaporate overnight. Water (10 mL) was added to the residue, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by TLC plate (hexane) to yield 19 mg (52%) of **22** as a colorless liquid: IR (neat) 3020, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (s, 3H), 0.89 (s, 3H), 1.13~1.29 (m, 2H), 1.58~2.03 (m, 13H), 2.05~2.19 (m, 1H), 5.33 (br s, 1H), 5.42~5.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 22.9 (t), 23.3 (q), 23. 4 (q), 25.1 (q), 28.8 (t), 29.0 (t), 30.6 (t), 32.8 (t), 35.9 (s), 40.5 (s), 122.5 (d), 122.8 (d), 133.9 (s), 140.4 (s); MS m/z, 204 (M^+), 136 (base), 121; HRMS Calcd for $C_{15}H_{24}$ (M^+) 204.1878, Found 204.1877.

Acknowledgement: We thank the National Science Council of the Republic of China for financial support under Grant No. NSC83-0208-M005-011.

REFERENCES

1. (a) Curran, D. P. *Synthesis* **1988**, 417 and 489. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, **1986**.(d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.
2. Giese, B. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 753.
3. (a) Burnett, D. A.; Choi, J. K.; Hart, D. J.; Tsai, Y. M. *J. Am. Chem. Soc.* **1984**, *106*, 8201. (b) Apparu, M.; Crandall, J. K. *J. Org. Chem.* **1984**, *49*, 2125. (c) Crandall, J. K.; Mualla, M. *Tetrahedron Lett.* **1986**, *27*, 2243. (d) Myers, A. G.; Condroski, K. R. *J. Am. Chem. Soc.* **1993**, *115*, 7926.
4. (a) Crandall, J. K.; Ayers, T. A. *Tetrahedron Lett.* **1991**, *32*, 3659. (b) Gillmann, T. *Tetrahedron Lett.* **1993**, *34*, 607. (c) Pasto, D. J.; L'Hermine, G. *J. Org. Chem.* **1990**, *55*, 685.
5. (a) Ito, S.; Endo, K.; Yoshida, T.; Ytatagui, M.; Kodama, M. *J. Chem. Soc., Chem. Commun.* **1967**, 186. (b) Ohata, Y.; Hirose, Y. *Tetrahedron Lett.* **1968**, *9*, 2483.
6. (a) Tanaka, A.; Uda, H.; Yoshikoshi, A. *J. Chem. Soc., Chem. Commun.* **1967**, 188. (b) Kanno, S.; Kato, T.; Kitahara, Y. *J. Chem. Soc., Chem. Commun.* **1967**, 1257. (c) Kitagawa, Y.; Hashimoto, S.; Iemura, S.; Yamamoto, H.;Nozaki, H.*J. Am. Chem. Soc.* **1976**, *98*, 5030. (d) Martin, J. D.; Perez, C.; Ravelo, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 7801. (e) Plamondon, J.; Canonne, P. *Tetrahedron Lett.*, **1991**, *32*, 589. (f) White, J. D.; Torii, S.; Nogami, J. *Tetrahedron Lett.*, **1974**, *15*, 2879. (g) Iwata, C.; Yamada, M.; Shinoo, Y. *Chem. Pharm. Bull.*, **1979**, *27*, 274.
7. (a) Chen, Y. J.; Lin, W. Y. *Tetrahedron Lett.* **1992**, *33*, 1749. (b) Chen, Y. J.; Chen, C. M.; Lin, W. Y. *Tetrahedron Lett.* **1993**, *34*, 2961. (c) Chen, Y. J.; Lin, W. Y. *Tetrahedron* **1993**, *45*, 10263.
8. Janardhanam, S.; Shanmugam, P.; Rajagopalan, K. *J. Org. Chem.* **1993**, *58*, 7782.
9. (a) Hatem, J.; Henriet-Bernard, C. ; Grimaldi, J. ; Maurin, R. *Tetrahedron Lett.* **1992**, *33*, 1057. (b) Bernard-Henriet, C. D. ; Grimaldi, J. R. ; Hatem, J. M. *Tetrahedron Lett.* **1994**, *35*, 3699.
10. Ono, N.; Miyake, H.; Kamimura, A.; Tsukui, N.; Kaji, A. *Tetrahedron Lett.* **1982**, *23*, 2957.
11. Bergbreiter, D. E.; LaLonde, J. J. *J. Org. Chem.* **1987**, *52*, 1601.
12. Orru, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; Groot, A. *J. Org. Chem.* **1994**, *59*, 374.

(*Received in China* 2 *February* 1996; *revised* 19 *April* 1996; *accepted* 5 *August* 1996)