Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 23 Sep 2006.

To cite this article: Michael A. Brodney , Justin P. O'Leary , Jeffrey A. Hansen & Raymond J. Giguere (1995) Tandem Intramolecular Diels-Alder (Timda) Reactions: Branched Substrate Studies and New Synthetic Pathways, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:4, 521-531, DOI: 10.1080/00397919508011386

To link to this article: http://dx.doi.org/10.1080/00397919508011386

SYNTHETIC COMMUNICATIONS, 25(4), 521-531 (1995)

TANDEM INTRAMOLECULAR DIELS-ALDER (TIMDA) REACTIONS: BRANCHED SUBSTRATE STUDIES AND NEW SYNTHETIC PATHWAYS

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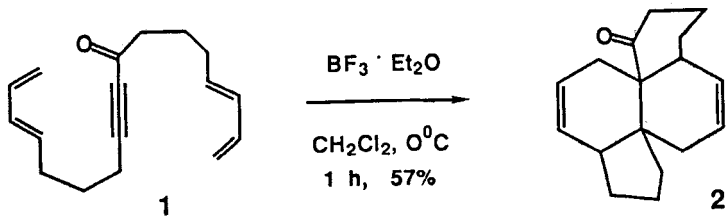
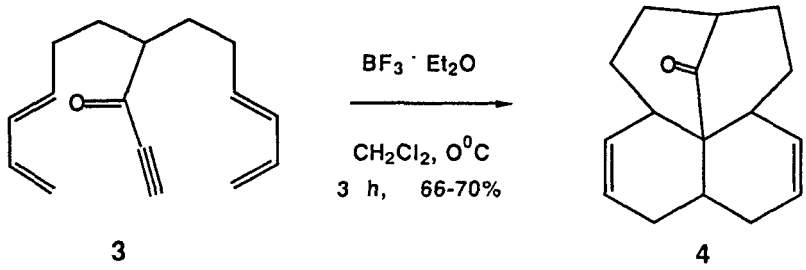
Abstract: *Using a malonic ester route, the first* branched *tandem intramolecular Diels-Alder (TIMDA) precursor, **3**, was synthesized from sorbic acid in seven steps (15 % overall yield). Treatment with Lewis acid catalysts (e.g., boron trifluoride etherate) affects the TIMDA reaction to afford a new fused-tetracyclic, **4**, as two diastereomers (1:1). An alternative synthetic route to key intermediates used in the synthesis of linear TIMDA precursors has also been achieved.*

Since 1990 we have been investigating the tandem intramolecular Diels-Alder (TIMDA) reaction,[2] a process that employs the triple bond as a double dienophile to permit two [4+2] cycloadditions in a single transformation. We recently reported the successful synthesis of tetracyclic ketone **2** from linear precursor **1** (prepared from 1,5-pentanediol), the first example of a TIMDA reaction (Scheme 1).[3]



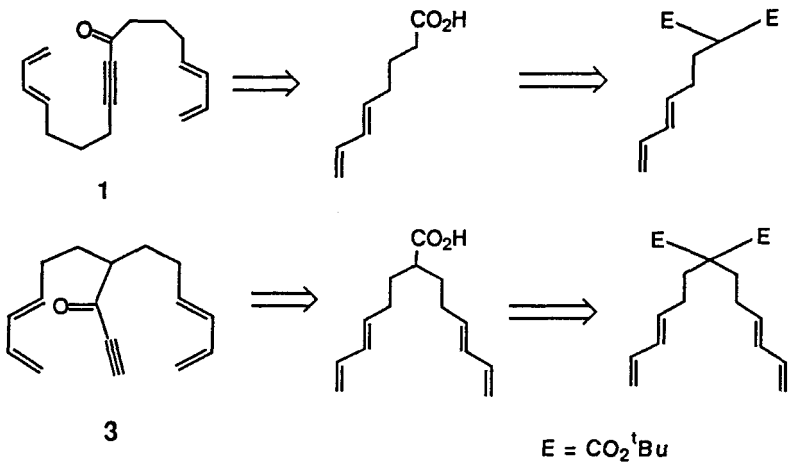
Scheme 1

Now the synthesis of TIMDA precursor **3** and its reaction to fused-tetracyclic **4**, the first example of the *branched* TIMDA process is described. In addition, a new synthetic pathway to key intermediates used in the synthesis of linear TIMDA adduct **2** has been developed.



Scheme 2

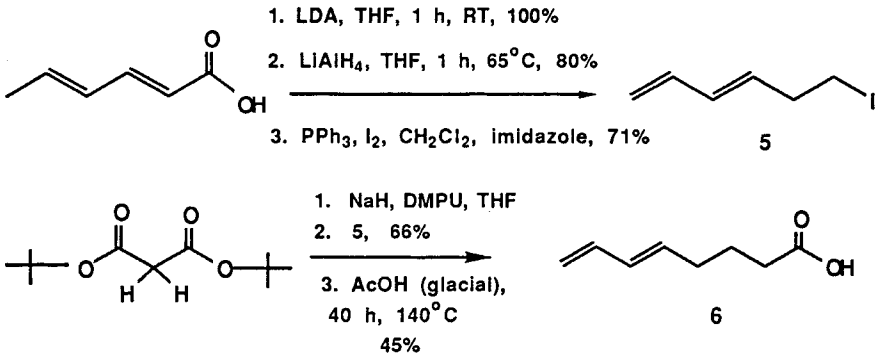
The syntheses of both TIMDA precursors employs a classic malonic ester route, retrosynthetically outlined in Scheme 3. The respective acids obtained are converted to the TIMDA precursors via their corresponding Weinreb amides. The requisite alkylating agent, E-3,5-iodohexadiene, **5** (Scheme 4), is conveniently prepared from sorbic acid in three steps.



Scheme 3

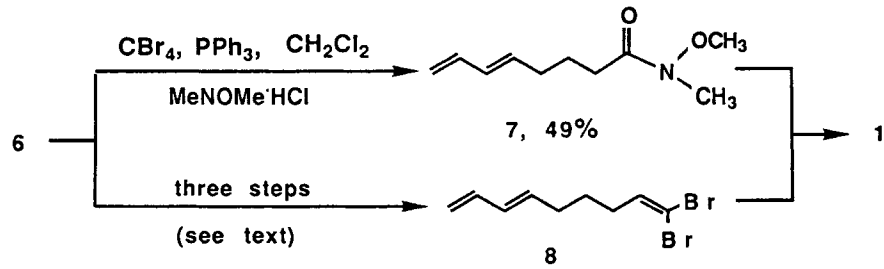
The improved synthesis of diene acid **6**, an important intermediate in the synthesis of linear TIMDA precursor **1**,[3] is also described in Scheme 4. Sorbic acid is isomerized to the deconjugated acid by treatment with LDA followed by an acid quench.[4] Conversion to diene iodide **5** is achieved by lithium aluminum hydride (LAH) reduction and iodination of

the resulting primary alcohol by the method of Lange.[5] Conditions for optimal alkylation of t-butyl malonate were established by model studies with diethyl malonate and n-butyl bromide, indicating that sodium hydride was a more effective base than sodium ethoxide for the reaction. Hydrolysis and decarboxylation of the alkylated malonate to diene acid **6** was effected by refluxing in glacial acetic acid.



Scheme 4

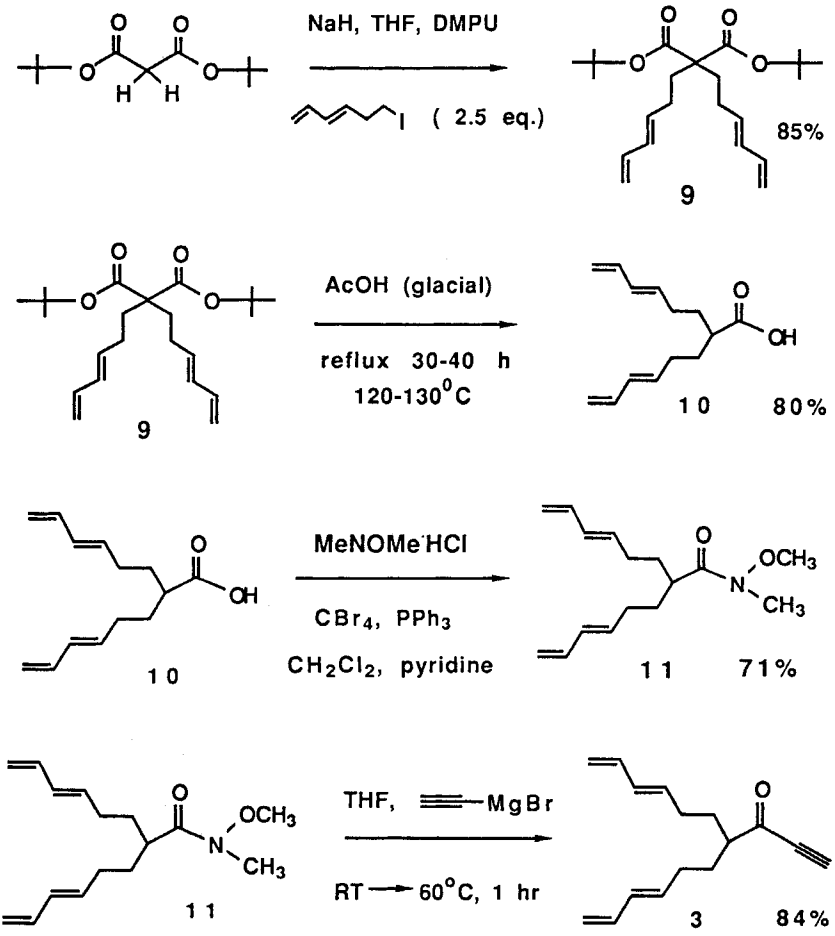
Diene acid **6** is converted to Weinreb amide **7** in one subsequent step.[6] Furthermore, **6** can serve as a precursor for triene dibromide **8** by a direct three step process: LAH reduction, PCC oxidation, and Wittig reaction by the method of Corey and Fuchs (Scheme 5).[7] Previously these intermediates have been convergently coupled to provide the linear TIMDA precursor **1**.[3] Compared with our initial route to **1** (from 1,5-pentanediol), this improved sequence has the advantage of avoiding several low-yielding reactions as well as a THP protection and deprotection operation (cf. reference 3).



Scheme 5

Synthesis of branched precursor **3** (Scheme 6) is accomplished analogously to that of the linear one. Bis-alkylation[8] of t-butyl malonate proceeds smoothly to diester **9**. Routine hydrolysis and decarboxylation of **9** provides key tetraene acid **10**. Conversion of acid **10** to Weinreb amide **11**[6] is followed by nucleophilic acyl substitution using excess ethynyl magnesium bromide to afford TIMDA precursor **3**.

Dilute solutions (0.005 M) of **3** readily undergo TIMDA cyclization under our standard conditions[3] to afford tetracyclic adduct **4** in 66-70% isolated yield (Scheme 2).



Scheme 6

The diastereoselectivity of this branched TIMDA reaction is less selective than in the linear case, providing two of four possible diastereomers in nearly equal amounts (GC-MS). Conducting the TIMDA reaction at -78°C unfortunately did not effect the diastereoselectivity at all. At -95°C, reaction diastereoselectivity improved slightly (ca. 65:35). The reaction could also be effected by zinc chloride under similar conditions, but reaction diastereoselectivity remained essentially the same.

The fused-tetracyclic TIMDA adduct **4** was characterized by high field NMR, FT-IR, GC-MS and UV-Vis and found to be a equal mixture of two diastereomers. Several features of the spectral data are noteworthy. For example, the two ^{13}C-NMR signals of the carbonyl groups resonate at 219.9 and 219.7 ppm, indicating the strained ring system. The carbonyl stretches in the IR are at 1730 and 1712 cm^{-1} along with isolated C=C stretches and bends at 3015 and 708 cm^{-1}, respectively. The ^{1}H-NMR is quite complex at 200 MHz, although bridgehead hydrogens are discernible within the multiplet at 3.20 - 2.65 ppm. The mass spectra of adducts **4** exhibit large molecular ion peaks and an M^{+}- 28 fragment presumably resulting from loss of the carbonyl group as CO.

Summary

The first branched TIMDA precursor, **3** , is synthesized by a malonic ester route in 15% overall yield from sorbic acid in seven steps. Eynone **3** undergoes Lewis acid-catalyzed TIMDA cyclization readily at low temperatures and affords tetracyclic adduct **4** as an equal mixture of two diastereomers. A new synthetic pathway to important intermediates (**6** -**8**) for the syntheses of linear TIMDA precursors has also been developed.

Experimental

General:

^{1}H and ^{13}C-NMR spectra were recorded on a Varian Gemini 200 instrument as solutions in $CDCl_3$ with TMS as an internal standard referenced to 0.00 ppm. IR spectra were recorded on a Perkin Elmer 1600 FT-IR.[9] GC-MS was performed on a Hewlett Packard, Model 5890/5971 using a 12 meter, HP-1 column (0.25 micron). The temperature program used for the GC-MS was 50°C for 2 minutes initially, then a rate increase of 10°C per minute to 250°C and finally 250°C for 6 minutes.

Thin layer chromatography (TLC) was performed on Kieselgel precoated (0.2 mm) silica gel 60 F_{254} plates. Visualization of the TLC plates was accomplished by UV, PMA, and/or *p*-Anisaldehyde. Reaction products were purified using flash chromatography with Kieselgel 0.063-0.200 mm silica gel. All reactions were performed in glassware that was

flame-dried and under an atmosphere of dry nitrogen or argon, unless otherwise noted. Tetrahydrofuran (THF) was distilled under N_2 from sodium/benzophenone and stored over 3^{o}A molecular sieves before use. Ethyl acetate, methylene chloride and hexanes were distilled in glass before use. Brine, used in extractive work-ups, refers to saturated aqueous NaCl solutions.

E-3,5-Hexadienoic acid: [4] In a 3-neck, 100 ml round bottom flask under nitrogen was generated a solution of LDA from diisopropyl amine, dry THF and n-BuLi at -10°C. The LDA was prepared by the addition of 8 ml of 2.5 M BuLi (0.02 mole) to a 1.0 M solution of diisopropyl amine (2.02 g, 0.02 mole) in 20 ml of dry THF. The reaction was allowed to stir at -10°C for 30 minutes at which time a 1.8 M solution of sorbic acid (1.0 g, 8.9 mmole) in dry THF was added dropwise to the LDA solution. The light green/yellow solution instantly forms a white precipitate and gradually turns orange. The white precipitate dissolves as the reaction is raised to RT and held there for one hour. The flask is fitted with a reflux condenser and then the reaction solution is rapidly quenched by addition of 20 ml of 3 M HCl. (Caution: heat is evolved - best to place the flask in a cold water bath and carry out the quench under a hood). The reaction is worked up with three 30 ml ethyl ether extractions, one brine wash, and dried over anhydrous sodium sulfate to yield, upon concentration, a yellow oil (1.0 g, 8.9 mmole, 100%), R_f = 0.18 in 50% ethyl acetate/hexanes. ^{1}H-NMR: [9.4 (br s 1H, OH)], 6.10-6.45 (m, 2H), 5.78 (dt, 1H), 5.18 (dd, 1H), 5.10 (d, 1H), 3.18 (d, 2H). ^{13}C-NMR: 178.6, 136.5, 135.3, 125.0, 117.7, 37.7.

E-3,5-Hexadienol: E-3,5-Hexadienoic acid from the previous step (0.50 g, 4.5 mmole) is added as a 0.7 M solution in dry THF at RT to a 2.0 M solution of lithium aluminum hydride (142 mg, 3.7 mmole) in 6.2 ml of dry THF and allowed to reflux for 1 hr at 60°C. The reaction is checked for completion by TLC (product R_f = 0.50 in 50% ethyl acetate/hexanes). The mixture is quenched by adding in order: 0.15 ml of water, 0.15 ml of 15% NaOH, and 0.45 ml of water with vigorous stirring during the additions. The mixture is passed through a sintered glass funnel containing a two inch pad of silica gel moistened with ethyl ether. Elution with 200 ml of ether and concentration of the filtrate gives E-3,5-hexadienol (343 mg, 3.5 mmole, 73%). If desired, further purification may be accomplished by vacuum distillation (Kugelrohr) at 0.2 torr to afford the pure diene alcohol, bp = 79°-80°C. ^{1}H-NMR: 6.43-6.08 (m, 2H), 5.70 (dt, 1H), 5.11 (dd, 1H), 5.03 (d, 1H), 3.70 (q, 2H), [2.52 (br s, 1H, OH)] 1.25 (t, 2H). ^{13}C-NMR: 137.2, 133.9, 131.0, 116.1, 61.9, 35.9.

E-3,5-Iodohexadiene (5): [5] To a stirring 11 ml solution of dry CH_2Cl_2 at room temperature is added in the following order: triphenyl phosphine (794 mg, 3.0 mmole), imidazole (206 mg, 3.0 mmole) and iodine (768 mg, 3.0 mmole) forming an dark orange

solution. E-3,5-hexadienol (220 mg, 2.2 mmole) from the previous step is added and the solution immediately turns bright yellow. Shortly thereafter it becomes two phases: a blood-red solution and a white precipitate. After 15 minutes the reaction is complete by TLC. The solution is poured through a sintered glass funnel containing two inches of silica gel moistened with pentane. Elution with 150 ml of pentane affords a bright pink solution. The solution is decolorized by washing three times with 10 ml of 10% aqueous sodium bisulfite. The organic layer is washed with brine and dried over anhydrous sodium sulfate. Concentration on a rotory evaporator gives **5** as a yellow oil (308 mg, 1.5 mmole, 66%) having an R_f = 0.7 in 50% ethyl acetate/hexanes. ^{1}H-NMR: 6.42-6.06 (m, 2H), 5.62 (dt, 1H), 5.16 (dd, 1H), 5.10 (d, 1H), 3.17 (t, 2H), 2.67 (q, 2H). ^{13}C-NMR: 136.9, 133.5, 132.9, 116.9, 36.6, 4.8. GC-MS (70eV): R_t = 6.3 min; m/e: 208 (M^+, 19), 127 (21), 81 (100), 79 (42), 65 (5), 53 (24), 41 (18).

E-t-butylmalonate-3,5-hexadiene: To a dry 25 ml flask is added sodium hydride (28 mg, 1.15 mmole), 2.5 ml of dry THF, and t-butylmalonate (214 mg, 1.0 mmole). The solution is stirred for 10 minutes and 0.4 ml of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU) is added. The solution is stirred for 20 minutes and diene iodide **5** (200 mg, 0.96 mmole) in 1 ml of dry THF is added dropwise. Upon addition, the reaction solution turns a turbid yellow and after 90 minutes becomes a clear yellow/brown solution. The reaction is monitored by GC-MS; the mono-alkylation product has R_t=14.8 minutes. The reaction is quenched with hexanes/water (1:1), and worked up by extraction with hexanes, washed with brine and dried over anhydrous sodium sulfate to give the crude product. The monoalkyled product is isolated by silica gel column chromatography using 10% ethyl acetate/hexanes as eluent which, upon concentration, gives a light yellow oil (188 mg, 0.90 mmole, 66%). ^{1}H NMR: 6.3 (dt, 1H), 6.07 (m, 1H), 5.75-5.6 (m, 1H), 5.1 (dd, 1H), 4.98 (dd, 1H), 3.15 (t, 1H), 2.20-1.85 (m, 4H), 1.45 (s, 18H). ^{13}C-NMR: 169.3, 137.4, 133.7, 132.5, 115.8, 81.6, 53.3, 30.1, 28.0, 27.1. GC-MS (70eV): R_t = 14.8 min; m/e: 281 (1) [M+ -15], 240 (4), 184 (19), 149 (8), 80 (91), 57 (100), 41 (31).

E-5,7-Octadienoic acid (6]: A 0.01 M solution of monoalkylated product in glacial acetic acid (188 mg, 0.63 mmole) is refluxed under argon for 24 h at 135°C in a sand bath. The reaction, monitored by GC-MS, shows the product at R_t = 8.7 minutes. After the reaction is complete, it is cooled to room temperature, and quenched by slow addition of saturated sodium bicarbonate. The reaction mixture is extracted with methylene chloride, washed with brine, dried over anhydrous sodium sulfate and purified by column chromatography using 30% ethyl acetate/hexanes as eluent to give, upon concentration, E-5,7-octadienoic acid, **6** (40.1 mg, 0.29 mmole, 45%; R_f = 0.38 in 50% ethyl

acetate/hexanes). ^{1}H NMR: 11.1 (br s, 1H, OH), 6.32 (dt, 1H), 6.08 (m, 1H), 5.75-5.6 (m, 1H), 5.12 (dd, 1H), 5.0 (dd, 1H), 2.40 (t, 2H), 2.25-2.05 (m, 2H), 1.78 (m, 2H). ^{13}C-NMR: 180.7, 137.3, 133.9, 132.4, 115.8, 33.5, 31.8, 24.1. GC-MS (70eV): Rt = 8.7 min; m/e: 140 (M^+, 31), 80 (100), 77 (17), 67 (41), 55 (13), 54 (29), 41 (56).

E-5,7-Octadienamide (7)[6]**:** In a 10 ml dry flask, a solution of acid **6** (79 mg, 0.57 mmole), N,O-dimethyl hydroxylamine·HCl (60.6 mg, 0.62 mmole), pyridine (49 mg, 0.62 mmole), and carbon tetrabromide (206 mg, 0.62 mmole), is stirred in 1.4 ml of dry methylene chloride. Triphenylphosphine (163 mg, 0.62 mmole) is added portionwise over a 5 minute period at room temperature. The clear yellow solution is allowed to stir for 20 minutes. The reaction is monitored for completion by TLC (R_f = 0.40 in 50% ethyl acetate/hexanes), and the solution is concentrated on a rotory evaporator. The residue is taken up in 50% ethyl acetate/hexanes, and vacuum filtered through a sintered glass funnel containing one inch of silica gel moistened with the eluent. Several 25 ml fractions are collected; upon concentration fractions 2 and 3 give **7** (50.9 mg, 0.28 mmole, 49%). ^{1}H NMR: 6.32 (dt, 1H), 6.08 (m, 1H), 5.78-5.60 (m, 1H), 5.1 (dd, 1H), 4.97 (dd, 1H), 3.69 (s, 3H), 3.19 (s, 3H), 2.43 (t, 2H), 2.29-2.05 (dt, 2H), 1.82-1.67 (m, 2H). ^{13}C-NMR: 174.9, 137.6, 134.7, 132.0, 115.4, 61.4, 32.1, 31.2, 24.3, 24.0. GC-MS (70eV): R_t = 11.6 min: m/e: 183 (M^+, 39), 152 (19), 123 (13), 103 (72), 95 (74), 79 (58), 67 (100), 61 (58), 45 (12), 41 (48).

Bis-E,E-di-t-butylmalonate-3,5-hexadiene (9): To a dry 50 ml, three neck flask is added sodium hydride (69 mg, 2.9 mmole), 9 ml of dry THF, and t-butylmalonate, (535 mg, 2.5 mmole). The solution is allowed to stir for 10 minutes and charged with 1.0 ml of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU). The solution stirs for an additional 10 minutes and one equivalent of E-3,5-iodohexadiene **5** (500 mg, 2.4 mmole) is added dropwise. After 15 minutes GC-MS shows mono product is 85% formed with minor amounts of bis-alkylation and starting material remaining. To the yellow/golden solution is added a second equivalent of NaH (69 mg, 2.9 mmole), followed by one more equivalent of E-3,5-iodohexadiene **5** (500 mg, 2.4 mmole). A second GC-MS after 30 minutes shows an approximately 50:50 bis to mono product ratio, with mono-alkylation R_t = 14.8 minutes and bis-alkylation R_t =19.5 minutes. To push the reaction to completion 0.5 equivalents of E-3,5-iodohexadiene **5** (250 mg, 1.2 mmole) is added. The reaction is quenched with hexanes/water (1:1) and worked-up by extraction with hexanes, washed with brine and dried over sodium sulfate to give **9** as a golden brown oil, (791 mg, 2.1 mmole, 85%). ^{1}H-NMR: 6.40-5.96 (m, 4H), 5.68 (dt, 2H), 5.08 (dd, 2H), 5.02 (d, 2H), 2.10-1.70 (m, 8H), 1.44 (s, 18H). ^{13}C-NMR: 171.2, 137.4, 134.4, 131.6, 115.7, 81.4, 58.0, 31.4, 27.3, 27.1. GC-

MS (70eV): R_f = 19.5 min; m/e: 320 (4), [M^+ - 56], 264 (19), 229 (6), 186 (7), 166 (8), 117 (100), 80 (42), 57 (88), 41 (32).

E,E-1,3,10,12-tridecatetraene-7-oic acid (10): A 0.01 M solution of bis-alkylated product **9** (62 mg, 0.017 mmole) in glacial acetic acid is heated under argon at 120-130°C for 30-40h in a sand bath. At higher temperatures the reaction fails and unidentified products of decomposition are obtained. The reaction is monitored by GC-MS, product R_f = 15.6 min. Upon completion, the solution is quenched with saturated sodium bicarbonate, extracted with ethyl ether, washed with brine, and dried over sodium sulfate. The desired product is purified by column chromatography with 5% ethyl acetate/ hexanes as the eluent, and concentrated to give **10**, (29 mg, 0.13 mmole, 80%). The product R_f = 0.8 in 10% ethyl acetate/hexanes. ^{1}H-NMR: [11.5 0 (br s 1H, OH)], 6.40-5.95 (m, 4H), 5.68 (dt, 2H), 5.09 (dd, 2H), 5.01 (dd, 2H), 2.51-2.32 (m, 1H), 2.30-1.95 (m, 4H), 1.9-1.5 (m, 4H). ^{13}C-NMR: 182.0, 137.4, 134.1, 132.2, 115.8., 44.2, 30.3, 29.8. ^{13}C-APT NMR: peaks up (C-quat. & CH_2): 182.0 115.8, 30.3, 29.8; peaks down (CH & CH_3): 37.4, 134.1, 132.2, 44.2. GC-MS (70eV): R_f =15.6 min; m/e: 220 (M^+, 4), 179 (5), 175 (6), 131 (10), 121 (10), 91 (19), 80 (66), 73 (100), 68 (68), 55 (37), 41 (98).

Weinreb amide (11)[3]**:** A solution of mono-acid **10**, (15 mg, 0.07 mmole), N,O-dimethylhydroxylamine·HCl (7 mg, 0.07 mmole), pyridine (5.8 mg, 0.07 mmole), and carbon tetrabromide (24 mg, 0.07 mmole) in 0.2 ml of methylene chloride is stirred at RT. Over a five minute period at room temperature, triphenylphosphine (19 mg, 0.07 mmole) is added portionwise. The reaction is complete by TLC after ten minutes and the solution is concentrated on a rotory evaporator. The residue is taken up in 4 ml 50% ethyl acetate/hexanes and poured through a sintered glass funnel containing 1/2 inch of silica gel moistened with the eluent. Elution with 35 ml of 50% ethyl acetate/hexanes (product R_f = 0.6) followed by concentration of the filtrate affords the crude product. Purification on a silica gel pipette column with 30% ethyl acetate/hexanes as the eluent gave **11** (12 mg, 0.05 mmole, 71%). ^{1}H-NMR: 6.40-5.96 (m, 4H), 5.65 (dt, 2H), 5.04 (dd, 2H), 4.98 (dd, 2H), 3.65 (s, 3H), 3.18 (s, 3H), 2.20-2.00 (m, 5H), 1.88-1.41 (m, 4H). ^{13}C-NMR: 177.5, 137.5, 134.9, 131.9, 115.4, 61.6, 39.7, 31.8, 30.5, 25.7. GC-MS (70eV): R_f =17.0 min; m/e: 263 (M^+, 4), 232 (3), 203 (3), 185 (4), 175 (3), 116 (100), 107 (6), 91 (14), 67 (94), 61 (24), 41 (44).

TIMDA precursor (3): A dry 25 ml three neck flask under argon is fitted with a reflux condenser and is charged with amide **11**, (18 mg, 0.07 mmole), 0.2 ml of dry THF, and 2.7 ml of 0.5 M (1.4 mmol) ethynyl magnesium bromide. The solution is stirred for 30 minutes at RT and heated for one hour at 60°C (reflux). TLC in 50% ethyl acetate/hexanes

show product R_f = 0.70. The reaction is worked up by pouring onto 5 ml of 5% HCl and 5 ml of 1:1 CH_2Cl_2/ethyl ether. The organic layer is washed once each with 0.1 M HCl, saturated sodium bicarbonate and brine. The organic layer is dried over sodium sulfate and concentrated. Silica gel column chromatography with 10% ethyl acetate/hexanes as the eluent yields precursor **3**, (13 mg, 0.06 mmole, 84%) with product R_f = 0.73 in 50% ethyl acetate/hexanes. ^{1}H-NMR: 6.40-5.96 (m, 4H), 5.65 (dt, 2H), 5.08 (dd, 2H), 5.02 (dd, 2H), 3.22 (s, 1H), 2.53 (m, 1H), 2.25-2.00 (m, 4H), 1.95-1.50 (m, 4H). ^{13}C-NMR: 191.3, 137.3, 133.9, 132.3, 115.9, 79.5, 77.4, 53.2, 30.4, 30.0. GC-MS (70eV): R_t = 17.9 min; m/e: 228 (M^+, 9), 210 (3), 159 (5), 148 (100), 133 (21), 120 (8), 105 (11), 91 (32), 77 (16), 65 (8), 55 (10), 41 (20).

TIMDA adduct (4): To a solution of precursor **3** (13 mg, 0.06 mmole, 0.005 M), in 12 ml of CH_2Cl_2 at 0°C is added 0.23 ml (263 g; 1.85 mmol) of 0.5 M $BF_3{\cdot}Et_2O$ in methylene chloride. The clear yellow solution is stirred for three hours at 0°C (overnight at 0°C is also OK). The solution is quenched at 0°C with saturated $NaHCO_3$, extracted with hexanes, brine, and dried over sodium sulfate. Silica gel column chromatography with 15% ethyl acetate/hexanes as eluent yields TIMDA adduct **4** as a mixture (1:1) of two diastereomers (8-9 mg, 0.04 mmole, 66-70%) with product R_f = 0.68 in 50% ethyl acetate/hexanes. ^{1}H-NMR: 5.81-5.68 (m, 2H), 5.50-5.71 (m, 2H), 5.48-5.10 (m, 4H), 3.20-2.65 (m, 8H), 2.60-2.20 (m, 8H), 2.15-1.22 (m, 16H). ^{13}C-NMR: 219.9, 219.7, 132.0, 129.4, 128.9, 127.3, 126.8, 125.9, 51.3, 50.9, 49.8, 47.8, 45.0, 42.9, 38.2, 35.1, 33.9, 32.1, 31.0, 30.4, 30.2, 29.9, 29.7, 29.5, 29.0, 28.8, 28.6, 25.3. FT-IR (CH_2Cl_2; cm^{-1}): 3015 (m), 2913 (vs), 2827 (vs), 1730, 1713 (both vs; C=O), 1278 (s), 708 (m). GC-MS (70eV): R_t = 19.94 min; m/e: 228 (M^+, 32), 200 (8), 159 (100), 146 (63), 133 (37), 129 (31), 115 (23), 105 (16), 91 (63), 77 (29), 65 (19), 55 (31), 41 (35); R_t = 19.98 min; m/e: 228 (M^+, 42), 210 (37), 200 (11), 182 (10), 159 (100), 146 (71), 133 (44), 129 (39), 117 (38), 105 (21), 91 (79), 77 (37), 67 (23), 65 (23), 55 (32), 41 (42). UV-Vis (CH_2Cl_2): λ max = 234. HRMS: Calc. Mass ($C_{16}H_{20}O$): 228.151415; Found: 228.151482 (-0.3 PPM).[10]

Acknowledgments

We gratefully acknowledge the Research Corporation (sponsored by the Olin Corporation Charitable Trust) and The Camille and Henry Dreyfus Foundation for generous financial support of our undergraduate research. We also thank the Hewlett-Packard Company for donation of Skidmore's HP 5891 GC/MS.

References and Notes

1. Selected as one of six projects in national competition for presentation by MAB at the 16th Annual *Semon Undergraduate Research Symposium,* Kent State University, Kent, Ohio, April 18, 1994.

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8. Excess E-3,5-iodohexadiene (2.5 equivalents) is required to force the alkylation to completion.

9. We thank Professor Les Hull (Union College) for recording the FT-IR of **4** for us.

10. We thank Mr. Rich Milberg of the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign for conducting the HRMS analysis of TIMDA adduct **4**.

(Received in the USA 04 August 1994)