Commercially available compounds were used without further purification.

General Procedure for GLC Monitored Reactions of 12 with 1 and Varying Quantities of Pyridine or 2–5. A mixture of **12** (42 μL, 34 mg, 0.2 mmol) and an appropriate amount of pyridine or **2–5** was dissolved in 2 mL of dimethoxyethane. To this stirred solution was added 62 mg of **1** (0.2 mmol), and stirring was continued overnight. Anhydrous ether (10 mL) and $LiAlH_4$ (50 mg, 1.3 mmol) were added, and stirring was continued 1 h. The reactions were quenched by sequential addition of 50 μL of H_2O, 50 μL of 15% NaOH, and 150 μL of H_2O. After addition of a weighed amount of *n*-docosane, as an internal standard, the yields of **13** and **14** were determined by GLC analysis, using previously determined response factors.

General Procedure for Reaction of 12 and (*Z*)-5-Decene with 1 and 2. A mixture of the olefin (3 mmol) and **2** (1.67 g, 15 mmol) was dissolved in 20 mL of dimethoxyethane. Complex **1** (1.16 g, 3.75 mmol)[10] was added with stirring, and the reactions were stirred 36 h. After dilution with 30 mL of anhydrous ether, $LiAlH_4$ (400 mg, 10.5 mmol) was carefully added, and stirring was continued 1 h. The reactions were quenched by sequential addition of 400 μL of H_2O, 400 μL of 15% NaOH, and 1.2 mL of H_2O. The solutions were filtered, and the filtrate was washed with three portions of H_2O and one portion of brine and dried over Na_2SO_4. Filtration and evaporation of solvent gave the crude product. Residual **2** was removed from the crude product under high vacuum. Bulb-to-bulb distillation then gave the pure products which were identified by comparison with authentic samples.[2]

General Procedure for Preparation of 7–11. Each complex was prepared by mixing the ligand with 1 or 2 molar equiv of **1** (depending on the stoichiometry of the product) in tetrahydrofuran (10 mL/mmol of **1**). Heptane (20 mL/mmol of **1**) was added, and the complexes were crystallized by slow evaporation of the solvent with a stream of nitrogen.

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Registry No. **1**, 50381-48-1; **7**, 73384-36-8; **8**, 73384-37-9; **9**, 73395-64-9; **10**, 73384-38-0; **11**, 73384-39-1; **12**, 55915-70-3; **13**, 55915-77-0; **14**, 65760-61-4; (*Z*)-5-decene, 7433-78-5; (R*,S*)-6-[(1,1-dimethylethyl)amino]-5-decanol, 55915-74-7; (R*,S*)-5,6-decanediol, 3266-25-9.

(10) We have observed that **2** slowly reacts with **1** at room temperature and rapidly in refluxing dimethoxyethane to give an as yet unidentified purple osmium complex which probably is a complex of Os(VI). Because of this side reaction, we have used 1.25 molar equiv of **1** to ensure that all the olefin is consumed. A similar reaction was observed between OsO_4 and **2** and affords a green complex.

Convenient Stereoselective Syntheses of the Three Isomeric 2,6-Octadienes

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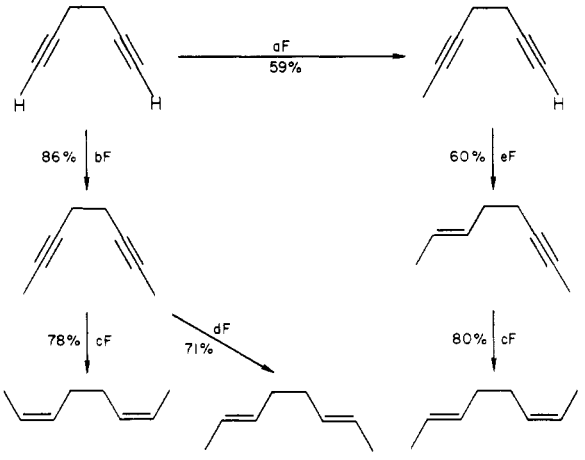
In connection with a mechanistic study,[1] we required multigram quantities of (*Z,Z*)-, (*E,E*)-, and (*E,Z*)-2,6-octadienes. These simple dienes are well-known in the literature and have been shown to be useful mechanistic probes.[2] In this sense they are the 1,5-diene analogues

Scheme I[a]



[a] (a) 1.8 molar equiv of NaH, THF/1% HMPA (v/v), 4 molar equiv of CH_3I, 72 h. (b) 3.6 molar equiv of NaH and as for a above. (c) P-2 Ni catalyst, ethylenediamine, H_2. (d) Na/liquid NH_3. (e) i, $NaNH_2$, liquid NH_3; ii, addition of Na^0; iii, addition of CH_3I.

of (*E*)- and (*Z*)-2-butene. The *Z,Z* isomer has been conveniently obtained in an isomerically pure state by catalytic hydrogenation of 2,6-octadiyne.[2b] The *E,E* isomer has been obtained by the nickel carbonyl promoted coupling of 1-chloro-2-butene and careful fractional distillation for removal of regioisomers.[2b] To date, the *EZ* isomer has only been obtained by preparative GC separation from the mixture of regio- and stereoisomers obtained from magnesium-promoted coupling of 1-chloro-2-butene.[2a]

Since we required relatively large quantities of all three dienes, we chose to devise a rational synthetic approach that would afford isomerically pure dienes without separation of regio- or stereoisomers. In this paper we report our approach, outlined in Scheme I, that utilizes the symmetrical diyne 1,5-hexadiyne[3] (**1**) as a common precursor of (*Z,Z*)-, (*E,E*)-, and (*E,Z*)-2,6-octadienes (**5**, **6**, and **7**, respectively) and allows their stereoselective preparation in a total of six synthetic steps.

Synthesis of the symmetrical dienes **5** and **6** is readily accomplished via the symmetrical diyne 2,6-octadiyne (**3**). Diyne **3**, in turn, is prepared by dialkylation of 1,5-hexadiyne (**1**). Thus, treatment of 1,5-hexadiyne (**1**) with *n*-BuLi in THF with 10% (v/v) HMPA followed by addition of methyl iodide to the resulting suspension readily affords 2,6-octadiyne (**3**) in 75% yield. Alternatively, the alkylation may be conveniently accomplished by a method developed in our laboratory where a reaction mixture containing the diyne, methyl iodide, and sodium hydride in the THF/HMPA (1% v/v) is stirred for 72 h at room temperature. Workup and simple distillation afford 2,6-octadiyne (**3**) in 86% yield. Though we have not optimized on the quantity of HMPA required for the reaction, deletion of this component decidedly lowers the reaction rate. We feel that this rate is determined by the rate of direct deprotonation of acetylene by solid sodium hydride and speculate that the HMPA acts by surface activation.

Hydrogenation of 2,6-octadiyne utilizing Lindlar catalyst as previously reported[2b] or P-2 nickel poisoned with ethylenediamine as catalyst[4] affords (*Z,Z*)-2,6-octadiene (**5**) in good yield. In our hands the product isolated by simple distillation contains ~5% of (*Z*)-2-octene, identified

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(2) (a) Doering, W. v. E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67 74. (b) Ulery, H. E.; Richards, J. H. *J. Am. Chem. Soc.* **1964**, *86*, 3113–7 and references therein.

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in the ^1H and ^{13}C spectra of diene **5**. Separation of diene **5** from octene is accomplished by chromatography on silver nitrate impregnated silica gel. However, recovery of the diene is low, presumably due to polymerization. For our purposes, this small amount of 2-octene impurity was not deleterious, and the distilled diene **5** proved satisfactory in our mechanistic studies.[1]

Dissolving-metal reduction of 2,6-octadiyne (**3**) proceeds normally. No compounds resulting from cyclization of radical anion intermediates could be detected in the product. Thus, treatment of diyne **3** with sodium metal in liquid ammonia, followed by extractive workup and simple distillation, affords (*E,E*)-2,6-octadiene (**6**) in good yield as the only volatile product.

Our synthesis of unsymmetrical (*E,Z*)-2,6-octadiene (**7**), as shown in Scheme I, involves the necessary desymmetrization of 1,5-hexadiyne (**1**) via monoalkylation. Experiments involving attempted selective monoalkylation of the mono- or dilithio salt of 1,5-hexadiyne in several aprotic solvent systems appeared to give greater than statistically random amounts of 2,6-octadiyne (**3**) by NMR. We feel that problems encountered in the experiments on the monolithio salt were the result of a tendency for this species to disproportionate to the very slightly soluble dilithio salt and hexadiyne. Similar behavior is well-known to occur with lithium acetylide.[5] Once the dilithio salt is formed, the reaction rate for the first alkylation is limited by the dissolution rate of the dianion, the second alkylation being faster. This type of behavior also explains the large amount of octadiyne formed when the dilithio salt is treated with 1 molar equiv of methyl iodide. The required monoalkylation of diyne **1** was quite conveniently accomplished by utilizing the sodium hydride procedure described above for preparation of 2,6-octadiyne. Use of a limiting amount of sodium hydride allows a statistically random alkylation affording the desired 1,5-heptadiyne (**2**) in 59% isolated yield along with 28% of 2,6-octadiyne (**3**) and a trace of hexadiyne. In this case precipitation of a disodium salt is not a problem as only a small amount of the sodium salt is present at any one time during the reaction. Though this procedure does not give selective monoalkylation, it is quite efficient for these purposes, considering the ease of separation of the two major products. Of course, the octadiyne isolated from this reaction may be used for preparation of the symmetrical dienes as described above.

Our strategy now calls for protection of the monosubstituted acetylene moiety of diyne **2** as its sodium salt,[6] dissolving-metal reduction of the disubstituted triple bond, and then alkylation of the resulting enyne salt with methyl iodide. In the event this one-pot procedure proved quite satisfactory. Thus, treatment of 1,5-heptadiyne (**2**) with sodium amide in liquid ammonia, followed by addition of sodium metal and then methyl iodide, affords (*E*)-2-octen-6-yne (**4**) in 60% yield. Catalytic hydrogenation of enyne **4** utilizing ethylenediamine-poisoned P-2 nickel as catalyst as described above allows isolation of (*E,Z*)-2,6-octadiene (**7**) contaminated with a small amount of a mixture of (*E*)- and (*Z*)-2-octene. With diene **7** in hand, the stereoselective synthesis of the title compounds is completed.

Though our immediate goal in this work was the synthesis of the octadienes **5**, **6**, and **7**, some of the methodology that we have developed would appear to offer potential for more general applications. Specifically, we report an efficient and convenient method for the alkylation of sodium acetylides in aprotic media under mild conditions. Direct deprotonation of the acetylene [in this case 1,5-hexadiyne (**1**)] by sodium hydride in the presence of alkylating agent over long time periods avoids problems associated with insolubility that arise if quantitative generation of the acetylide is attempted.[7] Application of this method to hexadiyne followed by either catalytic hydrogenation or dissolving-metal reduction could allow easy access to a variety of symmetrical *Z,Z*- and *E,E*-1,5-dienes. Statistically random monoalkylation with a limiting amount of NaH, coupled with the deprotonation–reduction–alkylation sequence reported above, may be imagined as a general route to unsymmetrical 1,5-bis-disubstituted dienes from 1,5-hexadiyne. This flexibility makes 1,5-hexadiyne, in principle, a useful general precursor to 1,5-dienes. Recently this unique diyne has been utilized for the synthesis of complex 3-substituted 1,5-diynes via the 1,3,6-trianion.[8]

Experimental Section

All boiling points are uncorrected and were obtained at ambient pressure in Boulder, CO (~630 mm), unless otherwise indicated. 1,5-Hexadiyne[9] was obtained from the Farchan Division, Chemical Samples Co., and was distilled prior to use (bp 81 °C). ^1H and ^{13}C NMR spectra were recorded on Varian EM 390 and JEOL 100 spectrometers, respectively, with tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer Model 927 spectrometer. Dry tetrahydrofuran (THF) was freshly distilled from a purple solution of sodium/benzophenone. Liquid ammonia was freshly distilled from a blue solution of lithium. Dry methyl iodide was freshly distilled from P_2O_5. Hexamethylphosphoramide (HMPA) was distilled from CaH_2 at reduced pressure and stored in a stoppered flask in a desiccator. All reactions except the hydrogenations were run under a slightly positive pressure of argon with a silicone oil or mercury bubbler.

1,5-Heptadiyne (2). To a magnetically stirred oil-free suspension of 2.76 g (0.115 mol) of sodium hydride in 200 mL of dry THF were added 6.2 mL (5.0 g, 0.064 mol) of 1,5-hexadiyne (**1**), 2.5 mL (2.58 g, 0.014 mol) of HMPA, and 16.0 mL (36 g, 0.257 mol) of dry methyl iodide, via syringe. After 72 h the reaction was quenched by addition of 100 mL of water. The products were isolated by extraction into pentane followed by fractional distillation through a 10-cm Vigreux column, affording 3.45 g (59%) of 1,5-heptadiyne (**2**) as a colorless liquid: bp 85–90 °C (140 mm) [lit.[9] bp 65.5 °C (90 mm)]; H NMR ($CDCl_3$) δ 1.78 (s, 3 H, RCH_3), 2.05 (s, 1 H, HC≡CR), 2.37 (m, 4 H, RCH_2CH_2R); IR (neat) 3290, 2915, 2850, 2230, 2120, 1440 cm^{-1}. Anal. Calcd for C_7H_8: C, 91.25; H, 8.75. Found: C, 91.44; H, 8.44. Reduction of the pressure to 90 mm and continuation of the distillation gave 1.91 g (28%) of 2,6-octadiyne [**3**; bp 90–95 °C (90 mm)] with spectral properties identical with diyne **3** prepared as described below.

2,6-Octadiyne (3). Diyne **3** was prepared from 6.2 mL (5.0 g, 0.064 mol) of 1,5-hexadiyne (**1**) exactly as described above for the preparation of 1,5-heptadiyne (**2**) except that 5.51 g (0.23 mol) of sodium hydride was used. Distillation through a short-path still head gave 5.86 g (86%) of 2,6-octadiyne (**3**) as a colorless liquid, bp 98–100 °C (100 mm) [lit.[9] bp 81.5–82 °C, (47 mm)], which solidified on standing at −15 °C: H NMR ($CDCl_3$) δ 1.78 (br s, 6 H, RCH_3), 2.31 (br s, 4 H, RCH_2CH_2R), identical with the NMR of a commercial sample obtained from Farchan. During the distillation 2,6-octadiyne (**3**) may freeze in the condenser. This problem may be remedied by turning off the condenser cooling water and gently heating the condenser with a heat gun if necessary.

(*Z,Z*)-2,6-Octadiene (5). An all-glass automatic borohydride hydrogenator set up for external hydrogen generation[10] was used for the hydrogenations described here: P-2 nickel[11] was generated

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(10) Brawn, C. A.; Brown, H. C. *J. Org. Chem.* **1966**, *31*, 3989–95.

in the reactor flask by addition of 21 mL (21 mmol) of a 1 M solution of ethanolic sodium borohydride stabilized with sodium hydroxide to a magnetically stirred suspension of 5.28 g (21 mmol) of nickel(II) acetate tetrahydrate in 170 mL of 95% ethanol. After 3 min hydrogen evolution ceased, and 2.84 mL (2.55 g, 42 mmol) of ethylenediamine was added as a catalyst poison.[4] To the resulting black suspension was added 9.0 g (84.8 mmol) of 2,6-octadiyne (3). Hydrogen uptake commenced immediately. After 3 h hydrogen uptake ceased, and 2 g of decolorizing carbon was added to the reaction mixture, which was then filtered through a Celite pad. The purple filtrate was diluted with 450 mL of water, and the product was isolated by pentane extraction and distillation to afford 7.30 g (78%) of (*Z,Z*)-2,6-octadiene (5) as a colorless liquid: bp 120–122 °C; ^{1}H NMR ($CDCl_3$) δ 1.60 (m, 6 H, RCH_3), 2.07 (m, 4 H, RCH_2CH_2R), 5.43 (m, 4 H, RCH=CHR); ^{13}C NMR ($CDCl_3$) δ 12.81, 26.94, 124.11, 130.18; IR (neat) 1650, 1440, 1400, 1365, 710 cm^{-1}, identical with that reported in the literature.[2a] Inspection of the ^{1}H and ^{13}C NMR spectra of diene 5 prepared in this manner shows the presence of ~5% of *cis*-2-octene. For our study,[1] that required stereochemical purity, this material was quite satisfactory. However, the diene was readily separated from octene by chromatography on silica gel impregnated with 10% by weight of silver nitrate. Thus, 1 g of distilled product was chromatographed through 100 g of silver nitrate–silica gel. Elution with 500 mL of pentane and then 400 mL of 10% ether/pentane gave a small amount of (*Z*)-2-octene, identified by its ^{1}H NMR. Elution with 400 mL of ether, followed by distillation, gave 270 mg (27%) of (*Z,Z*)-2,6-octadiene (5) that contained no trace of 2-octene by ^{1}H NMR.

(*E,E*)-2,6-Octadiene (6). To a mechanically stirred solution of 11.0 g (480 mmol) of sodium metal in dry liquid ammonia was added a solution of 8.5 g (80 mmol) of 2,6-octadiyne (3) in 20 mL of dry THF. After 30 min the reaction was quenched by careful addition of 26 g (480 mmol) of ammonia chloride, and most of the ammonia was allowed to evaporate slowly through a glass helices packed column with a slow stream of argon. The resulting slurry was diluted with 400 mL of water, and the product was isolated by pentane extraction and distillation to give 6.72 g (71%) of (*E,E*)-2,6-octadiene (6) as the only pentane-soluble product: colorless liquid; bp 115–117 °C; ^{1}H NMR ($CDCl_3$) δ 1.63 (m, 6 H, RCH_3), 2.02 (br s, 4 H, RCH_2CH_2R), 5.42 (m, 4 H, RCH=CHR); ^{13}C NMR ($CDCl_3$) δ 17.91, 32.76, 124.89, 131.00; IR (neat) 1440, 1378, 962 cm^{-1}, identical with that reported in the literature.[2a]

(*E*)-2-Octen-6-yne (4). Dry ammonia (200 mL) was distilled into a flask containing 1.67 g (70 mmol) of oil-free sodium hydride. Mechanical stirring was commenced, and the gray suspension was cooled with a bath at −60 °C (dry ice/2-propanol). After 30 min a solution of 4.0 g (43.4 mmol) of 1,5-heptadiyne (2) in 1 mL of dry THF was added, dropwise, via syringe. After an additional 30 min 2.99 g (130 mmol) of sodium metal was added in small pieces. The resulting blue solution was stirred for 20 min, and then 14.6 mL (33.3 g, 235 mmol) of dry methyl iodide was added dropwise. The solution decolorized to a white suspension immediately upon addition of the first few drops of methyl iodide. After an additional 20 min at −60 °C the reaction mixture was allowed to warm slowly to the boiling point of ammonia. Evaporation of most of the ammonia with a slow stream of argon, dilution of the resulting slurry with 200 mL of water, and isolation of the product by pentane extraction and simple vacuum distillation afforded 3.14 g of crude product, bp 85–87 °C (150 mm). The ^{1}H NMR spectrum of the material obtained in this manner revealed that the desired product was ~90% pure (60% yield of enyne 4). The only impurities were THF and 1,5-heptadiene. This crude product was used for the preparation of (*E,Z*)-2,6-octadiene as described below. Refractionation of an aliquot of the crude product through a Vigreux column gave analytically pure (*E*)-2-octen-6-yne (4): colorless liquid; bp 85–87 °C (150 mm); ^{1}H NMR ($CDCl_3$) δ 1.67 (m, 3 H, R=CHCH$_3$), 1.78 (br s, 3 H, R≡CCH$_3$), 2.17 (m, 4 H, RCH_2CH_2R), 5.53 (m, 2 H, RCH=CHR); IR (neat) 3005, 2980, 2900, 2840, 1450, 1435, 965 cm^{-1}. Anal. Calcd for C_8H_{12}: C, 88.82; H, 11.18. Found: C, 88.45; H, 11.28.

(*E,Z*)-2,6-Octadiene (7). (*E*)-2-Octen-6-yne (4; 2.30 g of material ~90% pure by NMR, 2.1 g of enyne, 19.4 mmol) was hydrogenated by using the procedure described above for the preparation of (*Z,Z*)-2,6-octadiene (5) and utilizing 0.44 g (1.77 mmol) of $Ni(OAc)_2 \cdot 4H_2O$ and 0.30 mL (0.27 g, 4.42 mmol) of ethylenediamine for generation of the catalyst. Extractive workup and distillation afforded 1.38 g (65%) of (*E,Z*)-2,6-octadiene (7): colorless liquid; bp 116–120 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (m, 6 H, RCH_3), 2.06 (br s, 4 H, RCH_2CH_2R), 5.42 (m, 4 H, RCH=CHR); ^{13}C NMR ($CDCl_3$) δ 12.77, 17.91, 27.04, 32.57, 123.91, 124.98, 130.13, 131.00; IR (neat) 1650 (w), 1440, 905, 700 cm^{-1}, identical with that reported in the literature.[2a] The ^{1}H and ^{13}C spectra of diene 7 prepared in this manner show the presence of ~5% of a mixture of (*E*)- and (*Z*)-2-octene.

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Registry No. 1, 628-16-0; 2, 764-56-7; 3, 764-73-8; 4, 73368-54-4; 5, 18680-11-0; 6, 18152-31-3; 7, 18152-32-4; (*Z*)-2-octene, 7642-04-8; (*E*)-2-octene, 13389-42-9.

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Reaction of α-Amino Ketone Hydrochlorides with Ortho Esters: An Oxazole Synthesis

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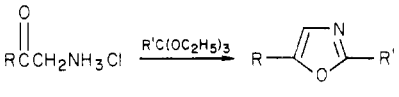
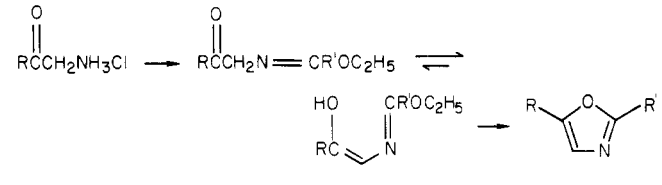
The synthesis of oxazoles by a variety of methods has recently been extensively reviewed.[1,2] Among these methods, the conceptually facile reaction of α-amino ketone hydrochlorides with ortho esters has received scant attention and, in fact, only one example of this reaction has been reported.[3] The work described herein demonstrates this approach to be both simple and general, thereby providing a variety of 2,5-disubstituted oxazoles from readily available α-amino ketone hydrochlorides.[4] The results are summarized in Table I.



It should be noted that substrates 1, 5, and 7 all react more rapidly than 3. This is apparently due to the ability of these substrates to more easily undergo enolization and subsequent cyclization, since the initial imino ether formation is quite rapid (<0.25 h) for all substrates. It would appear then that this procedure is limited to α-amino ketone hydrochlorides in which the R group is electron deficient.



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