

Unsaturated Macrocyclic Compounds. XL.¹

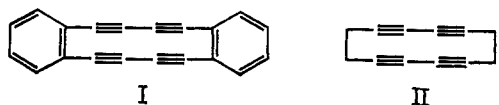
1,3,7-Cyclodecatriyne as an Intermediate in the Coupling of 1,5,9-Decatriyne

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Abstract: The oxidative coupling of 1,5,9-decatriyne (III) with cupric acetate in dilute pyridine-ether solution is shown to give rise to 1,3,7-cyclodecatriyne (IV) as an unstable intermediate, which immediately undergoes addition of the elements of acetic acid. The product, which appears to be a mixture of 1-acetoxycyclodecene-3,7-diyne (V) and the 2-acetoxy isomer (VI), on full hydrogenation leads mainly to cyclodecanol acetate (X), as well as to smaller amounts of cyclodecane (IXa) and bicyclic hydrocarbons.

The synthesis of a number of strained compounds incorporating 1,3-diyne groupings by the oxidative coupling of terminal diacetylenes has been reported. The most extreme examples are the dibenzo-1,3,7,9-cyclododecatetrayne derivative (I)³ and 1,3,7,9-cyclododecatetrayne (II)⁴ itself, both containing 12-membered rings. The strain in these substances is mani-

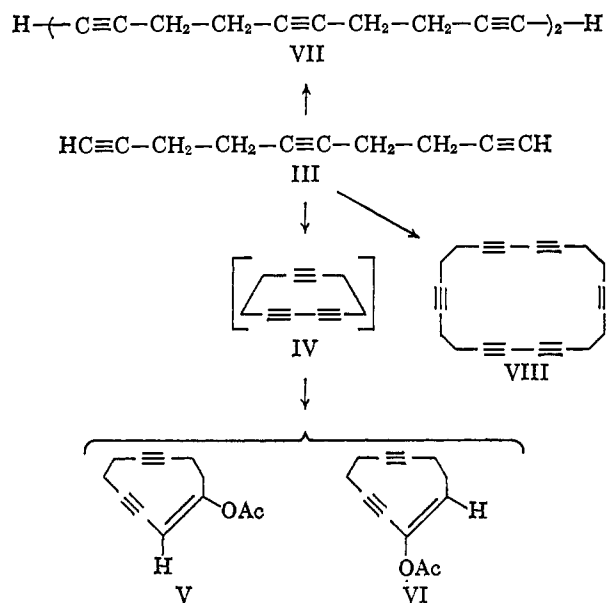


fest by the fact that the dibenzo compound I contains "bowed" diacetylenic bonds,⁵ and that II is an exceedingly unstable compound.⁴

It was decided to investigate whether even more strained 1,3-diacetylenes in the ten-membered ring series could be prepared, starting from linear C₁₀ terminal diacetylenes. The resulting unsaturated cyclodecane derivatives were expected to be of interest *per se*, as well as being potential intermediates for the synthesis of [10]annulene or dehydro[10]annulenes.

In the present paper, we describe the results of the attempted coupling of 1,5,9-decatriyne (III)⁶ to the cyclic monomer, 1,3,7-cyclodecatriyne (IV). The last-mentioned substance contains one acetylenic group less than the cyclododecatetrayne II, and should be even more strained than this compound. In a 1,3-diyne, six carbon atoms (the four acetylenic ones and one on each side) normally form a straight rod. In the cyclic triyne IV, only four additional carbon atoms are available for incorporating this six-carbon unit into a ring, and the acetylenic bonds must therefore be severely "bent." For this reason it was anticipated that if the cyclic monomer IV were indeed formed, it would be extremely unstable and decompose readily or undergo chemical reactions.

In practice, it has been found that under suitable conditions the monomer III can give rise to the cyclic



triyne IV as an unstable intermediate, which immediately undergoes addition of the elements of acetic acid. The product appears to consist of a mixture of the enol acetates V and VI, as evidenced by the spectral data and full hydrogenation results.

1,5,9-Decatriyne (III) was prepared from *trans*-1,5,9-decatriene by bromine addition and subsequent dehydrobromination with sodamide, as described previously.⁶ Ultraviolet examination of the resulting triyne III showed it to be contaminated with small amounts of materials containing a conjugated dienyne, as well as a conjugated tetraenyne⁷ chromophore (see the Experimental Section), but these impurities did not interfere in the following step.

It has been found previously that the oxidative coupling of the triyne III with cupric acetate in pyridine at 55° leads to the cyclic dimer VIII (*ca.* 6% yield) and the corresponding cyclic trimer (*ca.* 5% yield) when the usual dilution conditions are used [one part of triyne in 100 parts of pyridine (w/v)].⁶ No attempt had been made to isolate the cyclic monomer IV or substance derived from it. This experiment was now repeated under the previously described conditions,⁶ and an

(7) The prototropic rearrangement of the triyne III with potassium *t*-butoxide to a mixture of decatetraenyne has been described: F. Sondheimer, D. A. Ben-Efraim, and Y. Gaoni, *ibid.*, **83**, 1682 (1961).

(1) For Part XXXIX, see J. Mayer and F. Sondheimer, *J. Am. Chem. Soc.*, **88**, 603 (1966).

(2) University Chemical Laboratory, Cambridge, England.

(3) O. M. Behr, G. Eglinton, and R. A. Raphael, *Chem. Ind. (London)*, 699 (1959); O. M. Behr, G. Eglinton, A. R. Galbraith, and R. A. Raphael, *J. Chem. Soc.*, 3614 (1960).

(4) (a) R. Wolovsky and F. Sondheimer, *J. Am. Chem. Soc.*, **84**, 2844 (1962); (b) *ibid.*, **87**, 5720 (1965).

(5) W. K. Grant and J. C. Speakman, *Proc. Chem. Soc.*, 231 (1959).

(6) F. Sondheimer and Y. Gaoni, *J. Am. Chem. Soc.*, **84**, 3520 (1962).

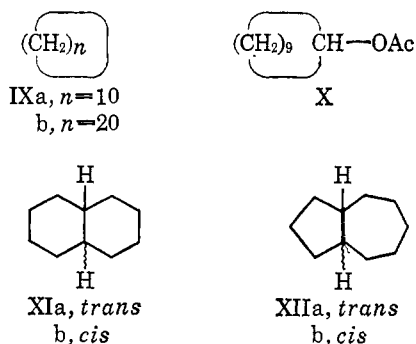
aliquot of the total unpurified product was submitted to full hydrogenation. Gas chromatographic analysis then showed that *ca.* 0.13% of cyclodecane (IXa) was present, in addition, of course, to a number of other substances. This result indicated that the cyclic monomer IV might indeed have been formed and encouraged us to investigate this reaction further.

It has been shown that the use of high-dilution conditions in the cupric acetate-pyridine coupling of terminal diacetylenes favors the formation of lower as against higher cyclic oligomers.⁸ The coupling of the triyne III was therefore carried out in a solution four times as dilute as that used previously, a mixture of pyridine and ether⁹ being employed. Full hydrogenation of an aliquot of the total product and gas chromatographic analysis then revealed the presence of *ca.* 1.3% of cyclodecane.

The coupling product from the high-dilution experiment was now submitted to careful chromatography on alumina, in order to isolate the material responsible for the cyclodecane. Unchanged starting material was eluted first, followed by the linear dimer VII.⁶ Mixtures of an unstable yellow oil (subsequently shown to consist of the enol acetates V and VI) and of the crystalline cyclic dimer VIII⁶ were eluted next, as evidenced by full hydrogenation of individual fractions (see below). The separation was poor, although the cyclic dimer was adsorbed slightly more strongly than the enol acetates. The pure cyclic dimer VIII was then eluted, and later fractions were not investigated further.

The yellow oil was separated from the cyclic dimer VIII as completely as possible by allowing the latter substance to crystallize from the mixture. In this way, *ca.* 8% of the enol acetates V and VI were obtained, contaminated with *ca.* 5% of the cyclic dimer.

The enol acetate mixture was fully hydrogenated in acetic acid over platinum. Gas chromatographic analysis of the product then showed five separate peaks. The main component (72%) was found to be cyclodecanol acetate (X) through isolation by preparative gas chromatography, followed by spectral examination and elemental analysis. This substance was eventually identified with an authentic sample, by direct comparison. The other hydrogenation products proved to be *trans*-decalin (XIa; 2%), a hydrocarbon (5%) which may be *cis*-decalin (XIb), *trans*-perhydroazulene



(XIIa) and/or *cis*-perhydroazulene (XIIb),¹⁰ cyclode-

(8) I. D. Campbell and G. Eglinton, *J. Chem. Soc.*, 1158 (1964), and unpublished observations with 1,5-hexadiyne from our laboratory.

(9) See G. Eglinton and A. R. Galbraith, *ibid.*, 889 (1959).

(10) Authentic samples of XIb, XIIa, and XIIb were found to have identical retention times under the conditions employed, making a dis-

cane (IXa; 16%), and cycloeicosane (IXb; 5%), as evidenced by comparison of the retention times with those of authentic samples.¹¹ The cycloeicosane is derived from the cyclic dimer VIII, while the C_{10} hydrocarbons must be derived from V and VI by hydrogenolysis and (for the bicyclic products) transannular reactions. This follows from the fact that hydrogenation of representative individual chromatography fractions containing the enol acetates gave the same relative ratios of cyclodecanol acetate and the various C_{10} hydrocarbons, but the relative amount of cyclodecane increased as the chromatogram progressed.

The fact that cyclodecanol acetate X was the major hydrogenation product of the yellow oil showed that the latter was derived from the anticipated 1,3,7-cyclodecatriyne (IV) by addition of the elements of acetic acid. The possibility that the oil was in fact the triyne IV itself, and that addition of acetic acid had occurred during the hydrogenation in acetic acid, was ruled out by the finding that cyclodecanol acetate was also the major product when the hydrogenation was carried out in ethanol or in hexane (acetic acid was generally used for the full hydrogenation, since the reaction did not always proceed to completion when the other solvents were employed).

The remaining question concerns the position of the acetoxy group. It was anticipated that addition of acetic acid to the intermediate triyne IV would occur at the 1,3-diyne grouping, and not at the isolated acetylene. This was confirmed by the ultraviolet spectrum of the enol acetates, which showed a maximum (in ether) at $244 \text{ m}\mu$ (ϵ 10,500). This value is compatible with the acetoxy-ene chromophore present in V and VI,¹² but not with a 1,3-diyne chromophore (which shows only low intensity maxima)¹⁴ in the presence of an isolated enol acetate. The infrared spectrum (in chloroform) showed a weak band at 4.48 (acetylene), strong bands at 5.67 and 8.35 (acetate), and a medium band at 6.11μ (double bond), in agreement with structures V and VI.¹⁵ The acetylene band was not split into a doublet, as is usual for 1,3-diyne,¹⁶ again confirming the absence of this chromophore.

The 60-Mc nuclear magnetic resonance spectrum (in carbon tetrachloride) of the enol acetate in the low-field region exhibited a narrow band at τ 3.87, as well as a much broader band centered at 4.23 (approximately equal integrated intensities), assigned to the vinylic protons in the structures V and VI, respectively. It is this spectrum which leads us to believe that both possible positional isomers are present, in about equal

tion between them impossible by gas chromatography; N. L. Allinger and V. B. Zalkow, *J. Am. Chem. Soc.*, **83**, 1144 (1961), have also been unable to separate the *trans* and *cis* isomers of perhydroazulene by gas chromatography.

(11) The percentage composition is approximate and is not corrected for variations in thermal conductivity.

(12) Linear conjugated enynes show a maximum at *ca.* $229 \text{ m}\mu$ (ϵ 11,500),¹³ and the acetoxy group as well as other factors may be responsible for the bathochromic shift.

(13) *Inter alia*, see M. Akhtar and B. C. L. Weedon, *Proc. Chem. Soc.*, 303 (1958).

(14) See J. B. Armitage, C. L. Cook, N. Entwistle, E. R. H. Jones, and M. C. Whiting, *J. Chem. Soc.*, 1998 (1952).

(15) See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen & Co., Ltd., London, 1958, Chapter 11; K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day Inc., San Francisco, Calif., 1962, p 44.

(16) *Inter alia*, see F. Sondheimer, Y. Amiel, and R. Wolovsky, *J. Am. Chem. Soc.*, **81**, 4600 (1959).

amounts. In the high-field region, a singlet at τ 7.97 appears (about triple the intensity of the combined low-field bands), due to the methyl protons of the acetate.

Thin layer chromatography of the yellow oil resulted in no separation of the isomers V and VI. An attempt was made to convert these substances to derivatives of the corresponding ketones by treatment of the mixture with 2,4-dinitrophenylhydrazine reagent, and then to effect separation by chromatography. However, this experiment led to a complex mixture, and this approach was not pursued further.

The effect of dilution on the coupling of the linear triyne III is as follows. The initial experiment, carried out with one part of triyne in 100 parts of pyridine (w/v), led to *ca.* 0.8% of the enol acetates (calculated by analysis of the mixture obtained by full hydrogenation). This is to be compared to the *ca.* 8% yield obtained in the above-described preparative experiment, using a dilution of one part of triyne in 400 parts of pyridine and ether. It was not determined whether the presence of ether in the latter experiment played a part in the markedly increased yield. Further dilution led to only a moderate increase in yield, an experiment employing one part of triyne in 1000 parts of pyridine and ether, giving rise to *ca.* 11.5% of the enol acetates.

The presently observed formation of both isomers V and VI from the intermediate cyclic 1,3-diyne IV is to be compared with the previously reported direction of addition to linear 1,3-dienes. Addition of methanol to such compounds under basic conditions leads to methoxy-enynes in which the methoxyl group is attached to the 1-position (type V), while hydration under acidic conditions gives rise to the α,β -acetylenic ketones, the oxygen becoming attached to the 2 position (type VI).¹⁷ The double bond in both isomers V and VI must possess the indicated *cis* configuration, for steric reasons, and *cis* addition of acetic acid must therefore have taken place. The exact mechanism of the addition has not been determined.

The ten-membered ring contained in V and VI is the smallest ring to be obtained so far by the acetylene coupling reaction. The substances V and VI are the most highly unsaturated, unbridged, ten-membered ring compounds known, and appear to be useful intermediates for the synthesis of [10]annulene and its derivatives. Further transformations of these enol acetates are now under investigation.

Experimental Section¹⁸

1,5,9-Decatriyne (III). 1,5,9-Decatriyne was prepared from *trans*-1,5,9-decatriene, as described previously.⁶ Crystallization from pentane gave material: mp 43–45°; $\lambda_{\text{max}}^{\text{pentane}}$ 257 m μ (ϵ 2020), 295 (165), 308 (255), and 327 (275). The 257-m μ maximum points to the presence of *ca.* 6% of impurity containing a conjugated monosubstituted diene chromophore (*cf.* the monosubstituted diene 3,5-octadien-7-yn-2-ol, $\lambda_{\text{max}}^{\text{EtOH}}$ 260 m μ (ϵ 34,000),¹⁹ while the other three maxima indicate the presence of *ca.* 0.6% of conjugated

decatetraene(s) (this chromophore has been shown to exhibit $\lambda_{\text{max}}^{\text{isoctane}}$ *ca.* 293 m μ (ϵ 34,500), 307 (40,000), and 327 (40,500)).⁷ The conjugated impurities could be removed by chromatography on alumina, but this material was used for the coupling experiment without further purification.

Oxidative Coupling of 1,5,9-Decatriyne (III). A three-necked 2-l. flask equipped with an efficient reflux condenser (on top of which was attached a cold finger filled with Dry Ice-acetone), stirrer, and dropping funnel was placed in a water bath. Cupric acetate monohydrate (37.5 g), pyridine (500 ml, commercial grade, previously distilled over sodium hydroxide), and ether (490 ml) were introduced, followed by a solution of 2.5 g of the triyne III in 10 ml of ether. The mixture was then heated to 55° and stirred at this temperature for 4 hr. The mixture was cooled to room temperature and poured into 5-l. of ice-cold 5% hydrochloric acid. The product was extracted with ether, and a small amount of insoluble, red-brown polymer was removed by filtration. The ether extract was washed with water (until all the copper salts were removed), sodium bicarbonate solution, and again with water. The dried extract was then concentrated to *ca.* 50 ml under reduced pressure in a water bath kept at room temperature. The resulting precipitate (80 mg, mp 228–230° dec) was collected; after crystallization from ether it showed mp 230–231° dec, and proved to be the cyclic dimer VIII as shown by direct comparison with an authentic sample.⁸ The filtrate was diluted with *ca.* 30 ml of benzene and evaporated at room temperature under reduced pressure to *ca.* 20 ml in order to remove the ether. The resulting solution was then chromatographed on a column of 500 g of alumina (Merck, acid washed), prepared with pentane. The column was washed with pentane and then with increasing amounts of ether in pentane, about 150 fractions (250 ml each) being collected.

Fractions 19–31, eluted with pentane and pentane-ether (99:1), contained 12 mg of unchanged 1,5,9-decatriyne, mp 42–44°, identified by direct comparison with starting material.

Fractions 61–72, eluted with pentane-ether (97:3), contained 92 mg of the linear dimer VII. Crystallization from pentane gave colorless plates, mp 141–142°, identified by direct comparison with an authentic specimen.⁸

Fractions 95–121, eluted with pentane-ether (95:5 to 93:7), consisted of the enol acetates V and VI, admixed with the cyclic dimer VIII.⁶ This follows from the fact that full hydrogenation of representatives on gas chromatographic examination yielded cyclodecanol acetate (X) and related compounds (see below), as well as cycloecosane (the relative amount of cycloecosane increased in later fractions, indicating the cyclic dimer to be slightly more strongly adsorbed than the enol acetates). The enol acetates and the cyclic dimer could not be separated by thin layer chromatography under the previously described conditions,^{4b} representatives of fractions 95–121 giving essentially one spot.

The fractions containing the enol acetates could be located conveniently by the fact that the light green thin layer chromatography spot given by this material (after being sprayed with cupric acetate-permanganate reagent) became brown-black after 1–2 days of storing without protection from daylight, or more rapidly by 1–2 hr of irradiation with a 150-w tungsten lamp. The similar light green spot given by the cyclic dimer was unchanged in color under these conditions. The enol acetates could also be located by the fact that thin layer chromatography of this material, followed by spraying with 2,4-dinitrophenylhydrazine in methanol and sulfuric acid, gave an intense orange-brown spot.

Representatives of fractions 95–121 all showed ultraviolet maxima at *ca.* 243–244 m μ (measured against pentane). They gave no precipitate with ammoniacal silver nitrate, indicating that substances containing a terminal acetylene were absent. Some cyclic dimer (uncontaminated with the enol acetates) was eluted after fraction 121.

Fractions 95–121 were combined and evaporated under reduced pressure to small volume (bath temperature below 40°), and the cyclic dimer, which had crystallized, was removed by filtration. Concentration of the filtrate yielded a second crop, which was removed. Finally, evaporation to dryness under reduced pressure at room temperature gave the enol acetates V and VI (295 mg, 8.2%) as a light yellow oil (yields in the range 6–9% were obtained in other experiments). This material, which gave essentially only one spot on thin layer chromatography, was contaminated with *ca.* 5% of the cyclic dimer VIII, as estimated by full hydrogenation and gas chromatography (see below). The ultraviolet, infrared, and nmr spectra are given in the theoretical section. The material was unstable; a sample on being kept in the neat state at room temperature without protection from diffuse daylight had decomposed

(17) See F. Bohlmann and H. G. Viehe, *Ber.*, **88**, 1017 (1955).

(18) Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Ultraviolet spectra were measured on a Cary Model 14 recording spectrophotometer. Infrared spectra were determined on a Perkin-Elmer Model 137 Infracord recording spectrophotometer with sodium chloride optics. Nuclear magnetic resonance (nmr) spectra were measured on a Varian A-60 spectrometer, tetramethylsilane being used as internal reference.

(19) I. M. Heilbron, E. R. H. Jones, and J. T. McCombie, *J. Chem. Soc.*, 134 (1944).

to a small extent after 0.5 hr, to a considerable extent after 24 hr, and almost completely after 48 hr (as determined by ultraviolet spectroscopy and by gas chromatography after full hydrogenation). Even solutions were unstable, as shown by the fact that chromatography fractions in pentane-ether had deposited a thin, opaque polymeric residue on the side of the flask after 1-2 weeks of standing. The material was stored most conveniently in pentane-ether solution in the dark at *ca.* 0°; under these conditions only small amounts had decomposed after several months.

Treatment of Enol Acetates with 2,4-Dinitrophenylhydrazine. The mixture of enol acetates (20 mg), dissolved in a few drops of methanol, was treated with 2 ml of 2,4-dinitrophenylhydrazine reagent (prepared by dissolving 1 g of the hydrazine in 40 ml of methanol and 4 ml of concentrated hydrochloric acid) at *ca.* 40° for 10 min. The resulting dark red precipitate was collected; it showed $\lambda_{\text{max}}^{\text{ether}}$ 368 m μ . Thin layer chromatography gave five separate spots, which exhibited the following ultraviolet maxima (in order of elution): $\lambda_{\text{max}}^{\text{ether}}$ 378, 352, 385, 365, and 382 m μ .

Full-Hydrogenation Experiments. The first hydrogenation experiments were carried out in pentane-ether over platinum and did not always lead to complete reduction (*e.g.*, *cis*-cyclodecene was occasionally formed, identified by gas chromatographic comparison with an authentic sample). Subsequent hydrogenations were therefore generally performed in glacial acetic acid over a pre-reduced platinum oxide catalyst (room temperature, atmospheric pressure, stirring for *ca.* 2 hr). The catalyst was removed, water and ether were added to the filtrate, and the ether layer was washed with sodium bicarbonate solution and water. The dried extract was evaporated to small volume through a short column and then submitted to gas chromatography.

Gas chromatographic analyses were carried out with a Research Specialties Model 600 instrument (argon ionization detector), using a glass column (6 ft \times 0.25 in. o.d.) filled with 5% SE 30 silicone rubber on Chromosorb W. The initial temperature was 75°, and the inlet pressure was 10 psi. After the cyclodecane had been eluted, the inlet pressure was raised to 30 psi and the temperature was programmed to 230° at the rate of 5°/min.

A sample of the 295 mg of enol acetates described above on full hydrogenation and gas chromatography by this method was found to give the following products (in order of elution): *trans*-decalin (2%), *cis*-decalin, *trans*-perhydroazulene, and/or *cis*-perhydroazulene (5%),¹⁰ cyclodecane (16%), cyclodecanol acetate (72%), and cycloeicosane (5%).¹¹ Each of these compounds was identified by comparison of the retention time with that of an authentic sample, and through nonseparation by gas chromatography after admixture with an authentic sample. Representatives of the chromatography fractions 95-121 from the above-described experiment on hydrogenation gave similar results, except that early fractions gave relatively less cycloeicosane, while late fractions gave relatively more of this hydrocarbon.

Before the cyclodecanol acetate was identified, this substance was isolated in pure form by preparative gas chromatography. This was carried out with an Aerograph Autoprep instrument,

using a column (20 ft \times 0.375 in.) filled with 10% SE 30 silicone rubber on Chromosorb W operated at 220°, and a gas flow rate of 300 ml/min. The resulting cyclodecanol acetate (shown to be homogeneous by analytical gas chromatography) formed a colorless liquid, n_D^{20} 1.4671 (lit n_D^{20} 1.4681,^{20a} 1.4689^{20b}); infrared bands (neat) at 5.76 and 8.01 μ (acetate); nmr bands (CDCl₃) at τ 4.91 (1 H), 8.10 (3 H), and 8.45 (18 H).

Anal. Calcd for C₁₂H₂₂O₂: C, 72.68; H, 11.18. Found: C, 72.75; H, 11.01.

The substance was identified with an authentic sample (n_D^{20} 1.4677; prepared from cyclodecanone by lithium aluminum hydride reduction to cyclodecanol²¹ and subsequent acetylation), through infrared spectral comparison and mixed gas chromatography. Saponification with boiling aqueous methanolic potassium hydroxide led to cyclodecanol, mp 38-40° (lit mp 40-41°^{20a,21}), identified with an authentic sample (mp 39-41°) by infrared comparison and mixture melting point determination.

In order to confirm that the acetic acid used as solvent played no part, the hydrogenation was repeated in ethanol, as well as in hexane (platinum catalyst, 24-hr reaction). Cyclodecanol acetate was formed as major product in all cases, as shown by as chromatographic analysis.

Effect of Concentration on Yield. A. Dilute Conditions. The coupling of 0.5 g of the triyne III was carried out with 7.5 g of cupric acetate in 250 ml of pyridine and 250 ml of ether (*i.e.*, dilution of one part of triyne in 1000 parts of solvent, w/v), the other conditions being unchanged. A measured aliquot of the product (without chromatography) was fully hydrogenated in acetic acid over platinum and submitted to gas chromatographic analysis after addition of a known amount of *n*-dodecane as internal standard. Comparison of the integrated areas of the various saturated hydrocarbons derived from the enol acetates V and VI showed that 11.6% of these substances had been formed.

B. Concentrated Conditions (Normal Coupling Conditions). The coupling of 0.5 g of the triyne III was performed with 7.5 g of cupric acetate in 50 ml of pyridine (*i.e.*, one part of triyne in 100 parts of solvent, w/v), under otherwise unchanged conditions. Hydrogenation and gas chromatographic analysis, as under A, showed that 0.8% of the enol acetates had been formed (yield of cyclodecane, 0.13%).

Acknowledgments. We are indebted to Professor N. L. Allinger (Wayne State University, Detroit) for kindly providing authentic samples of *trans*- and *cis*-perhydroazulene, as well as to Mrs. Rita Weitman for her capable technical assistance.

(20) (a) M. Kobelt, P. Barman, V. Prelog, and L. Ruzicka, *Helv. Chim. Acta*, **32**, 256 (1949); (b) A. T. Blomquist and A. Goldstein, *J. Am. Chem. Soc.*, **77**, 1001 (1955).

(21) See A. T. Blomquist, R. E. Burge, and A. C. Sucsy, *ibid.*, **74**, 3636 (1952).