tensities of the methyl resonances). The mixture had ir ($CHCl_3$) 5.78 μ (C=O); 11c nmr ($CDCl_3$) 1.82 (d, J = 8.5 Hz, 3 H), 3.2–3.7 (m, 3 H), 5.38 (dd, J = 3.7, 7.0 Hz, 1 H), 5.5–6.4 ppm (m, 5 H); 11d 1.68 (d, J = 8.5 Hz, 3 H), 3.2–3.7 (m, 3 H), 5.15 (dd, J = 3.7, 7.0 Hz, 1 H), 5.5–6.4 ppm (m, 5 H).

Preparation of 11e and 11f from 6-Phenylfulvene and α-Pyrone.—A 0.154-g (1 mmol) quantity of 6-phenylfulvene was added to a solution containing 0.096 g (1 mmol) of 2-pyrone, 3 drops of triethylamine, and 3 ml of benzene. Refluxing under nitrogen for 16 hr followed by plc (5% ethyl acetate–petroleum ether, two elutions) resulted in 0.220 g (88%) of a light yellow solid. The nmr spectrum of the crude solid indicated the presence of relatively pure adduct 11e contaminated with what appeared to be a small amount (<10%) of isomeric adduct 11f (no further purification was attempted): ir ($CHCl_3$) 5.76 μ (C=O); nmr ($CDCl_3$) 3.3–3.7 (m, 3 H), 5.27 (dd, J = 3.5, 7.0 Hz, 1 H), 5.7–6.4 (m, 4 H), 6.70 (d, J = 5.5 Hz, 1 H), 7.3 ppm (m, 5 H).

Preparation of 14 from 2,4-Cycloheptadienone and 6,6-Dimethylfulvene.—A solution containing 1.06 g (10 mmol) of 6,6-dimethylfulvene, 0.507 g (4.7 mmol) of 3,5-cycloheptadienone, 50 mg of hydroquinone, and 2 ml of tetrachloroethylene was heated under nitrogen at 85° for 5 days. The solvent and excess fulvene were removed under reduced pressure, and 0.409 g (41%) of a single 1:1 adduct was isolated by plc (5% ethyl acetate–petroleum ether, three elutions). Vacuum distillation of the yellow liquid at 190–205° (0.2 mm) led to increased impurity because of some decomposition. Slow redistillation (2 hr) at a pot temperature of 84° (0.2 mm) gave a deposit of light yellow crystals, mp about 25°, 14, on the condenser. This material was adequate for characterization except elemental analysis: mass spectrum m/e (rel intensity) 214 (30), 106 (100), 91 (30); ir (CCl_4) 5.85 μ (C=O).

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Research Corporation for financial support of this research.

Registry No.—1a, 29183-07-1; 1b, 2175-90-8; 1c, 2320-32-3; 1e, 3839-50-7; 1h, 7338-50-3; 1i, 4727-24-6; 1j, 15972-55-1; 1k, 4479-62-3; 1l, 35516-21-3; 2, 26307-17-5; 3a, 41727-87-1; 3b, 41727-88-2; 3c, 41762-74-7; 3d, 41727-89-3; 3e, 41727-90-6; 3f, 41727-91-7; 3h, 41727-92-8; 3i, 41727-93-9; 3j, 41727-94-0; 3k, 41727-95-1; 3l, 41727-96-2; 3m, 41727-97-3; 5, 41718-21-2; 6a, 41727-98-4; 6b, 41727-99-5; 6c, 41728-00-1; 11a, 41728-01-2; 11b, 41728-02-3; 11c, 41728-03-4; 11d, 41728-04-5; 11e, 41728-05-6; 11f, 41728-06-7; 14, 41728-07-8; cyclopentadiene, 542-92-7; α-pyrone, 504-31-4.

The [2 + 2] Cycloaddition Dimer from 1,2-Nonadien-4-yne

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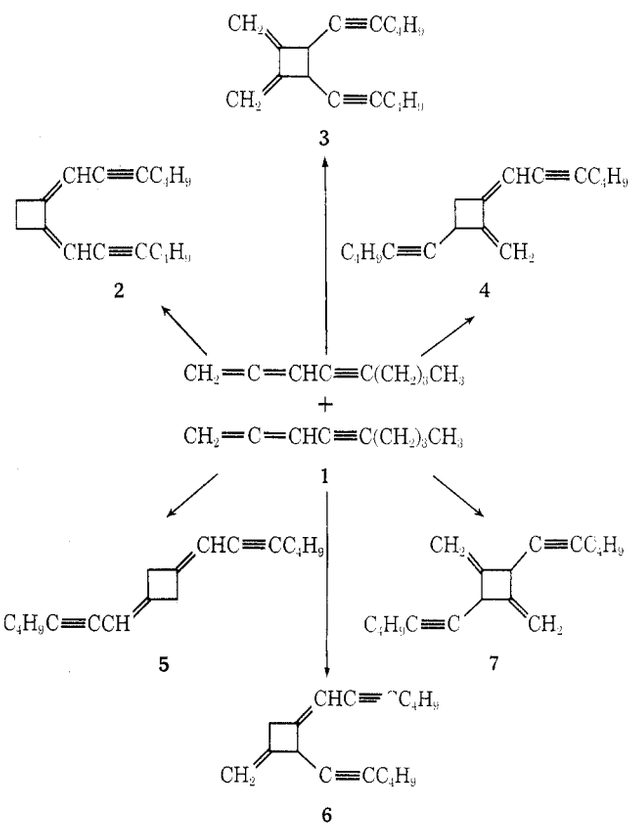
1,2-Nonadien-4-yne, a conjugated acetylenic allene, condenses with itself to form a short-lived dimer, which was not obtained as such but instead was trapped and isolated as a bis adduct with maleic anhydride. The proved structure of the bis adduct derivative provides evidence that the dimer is the product of a thermal [2 + 2] cycloaddition process. The structure of the derivative also serves to limit the allene dimer to two possibilities, namely, 1,2-bis(hexynylmethylene)cyclobutane or 3,4-bis(hexynyl)-1,2-bis(methylene)cyclobutane, with the former preferred.

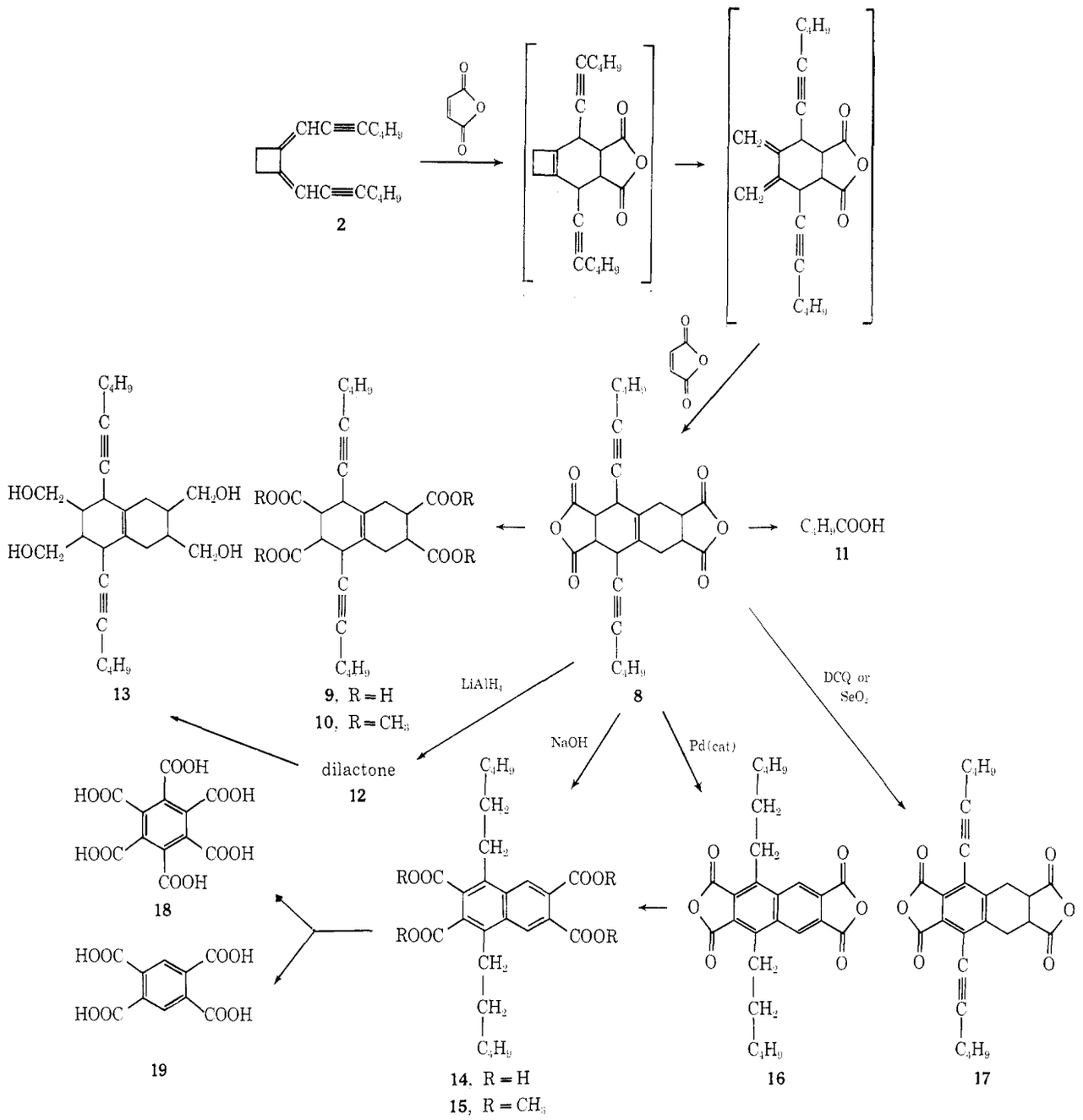
Allenes are known to dimerize by thermal [2 + 2] cycloaddition to give dimethylenecyclobutanes.[1] Among the compounds studied, we could find no example of an allene conjugated to an acetylenic group. To determine whether and how this kind of conjugation might affect the reaction, we undertook to examine the behavior of 1,2-nonadien-4-yne (**1**),[2] an allene that can lead to six *a priori* possible isomeric dimers, **2**–**7**.

1,2-Nonadien-4-yne (**1**) was found to be thermally unstable at temperatures above 100°. A variety of reaction conditions were tried in an effort to isolate dimers, but in every case only mixtures of unchanged starting material with intractable, nondistillable resins were obtained. The high boiling point together with the fact that the product showed no nuclear magnetic resonance signals attributable to vinylic protons suggested that the reaction had gone past the dimer stage, presumably at least to the level of tetramers ($C_{36}H_{48}$; ~4.1% vinylic H's) or pentamers ($C_{45}H_{60}$; 3.4%). Attempts to determine the molecularity of the process by following the decrease in the concentration of 1,2-nonadien-4-yne furnished data that, over the first 40% of the reaction, could be fitted equally well to first- as



(1) Reviews have been published by D. R. Taylor, *Chem. Rev.*, **67**, 317 (1967); T. F. Rutledge, "Acetylenes and Allenes," Reinhold, New York, N. Y., 1969; J. E. Baldwin, *Fortschr. Chem. Forsch.*, **15**, 281 (1970); and D. Seebach, "Methoden der Organischen Chemie (Houben-Weyl)," Vol. IV, 4th ed, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, 1971, p 151. Also see R. Maurin, G. Leandri, and M. Bertrand, *Bull. Soc. Chim. Fr.*, 530 (1971); T. L. Jacobs and O. L. Muscio, Jr., *Tetrahedron Lett.*, 4829 (1970).

(2) W. J. Gensler and J. Casella, Jr., *J. Amer. Chem. Soc.*, **80**, 1376 (1958).



to second-order rate expressions.[3] Thereafter, the data followed no simple kinetic order.

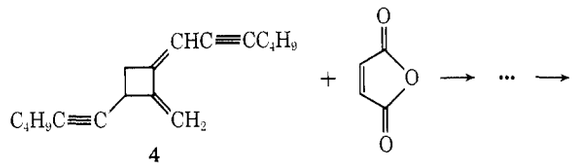
Failing to isolate dimers or lower oligomers, we resorted to trapping the dimer(s) by condensation with maleic anhydride.[4] Taking structure **2** as representing the allene dimer, the anticipated sequence of steps leading to a bis adduct may be formulated as **2** → **8**. This device proved successful, with the desired product **8** isolable in modest yield. Large amounts of gummy products were routinely obtained also; further, when the maleic anhydride was added to the allene reaction not during but immediately after the heating period, no trace of bis adduct **8** was formed. The bis adduct, therefore, must arise by action of maleic anhydride with the reactive, short-lived allene dimer **2** in competition with a more rapid oligomerization to high molecular weight products. The maleic anhydride plays no role in the initial dimerization step, **1** → **2**, since the rate of disappearance of allene was the same in the presence as in the absence of maleic anhydride.

All the properties of the bis adduct can be accommodated by formulation **8**. For example, hydrolysis gives tetraacid **9**, esterification gives the corresponding tetraester **10**, and oxidative cleavage affords more than 1 mol of valeric acid (**11**). Although 1-hexenyl side chains could account for the valeric acid, the absence of vinylic hydrogen signals in the nuclear magnetic resonance spectrum of **8** excludes this possibility.

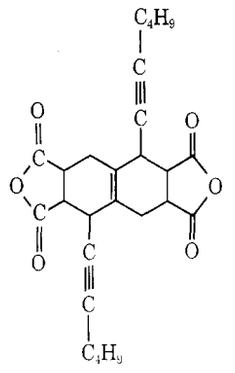
(3) N. Detzer and A. Roedig, *Tetrahedron Lett.*, 5697 (1971), find second-order kinetics for the dimerization of several tetrasubstituted allenes. This paper gives references to other kinetic studies.

(4) This approach has been used with allene itself [K. Alder and O. Ackermann, *Chem. Ber.*, **57**, 1567 (1954); A. T. Blomquist and J. A. Verdol, *J. Amer. Chem. Soc.*, **78**, 109 (1956)] and with a cyclic allene [L. Skattebøl and S. Solomon, *ibid.*, **87**, 4506 (1965)]. Another kind of reaction occurs between maleic anhydride and ethylallene, *sym*-dimethylallene, or *unsym*-dimethylallene [K. Alder and O. Ackermann, *Chem. Ber.*, **90**, 1697 (1957)].

An alternate structure for bis adduct **8** is the one derived from cycloaddition dimer **4**, namely **20**. To



4



20

distinguish between isomers **8** and **20**, we attempted to convert the bis adduct to a recognizable naphthalene bearing substituents either at positions 1, 2, 3, 4, 6, 7 (related to **8**) or at positions 1, 2, 3, 5, 6, 7 (derived from **20**). Although lithium aluminum hydride reduction to an intermediate dilactone **12** and further to the tetrahydroxymethyl compound **13** was possible, the subsequent transformation to the desired tetramethyl compound presented difficulties and was not pursued. In an alternative approach, in which the substituents remained at the carboxylic stage of oxidation, bis adduct **8** was aromatized to naphthalene **14** by the action of alkali. Bis adduct **8** and naphthalene **14** are at the same stage of oxidation, so that the conversion may be regarded as occurring through a series of alkali-catalyzed prototropic shifts.[5] Heating bis adduct **8** in the presence of a palladium catalyst caused disproportionation to naphthalene dianhydride **16**. Esterification converted both **14** and **16** to the same tetraester **15**. Dehydrogenation of bis adduct **8** with dichlorodicyanoquinone or with selenium dioxide gave product **17**, with intact hexynyl side chains attached to a benzene ring. The choice between bis adduct structures **8** and **20** was made possible by oxidatively degrading the naphthalene tetraacid **14** with permanganate to a mixture of 1,2,4,5-benzenetetracarboxylic acid (**19**) and benzenehexacarboxylic acid (**18**). Both of these acids can originate in naphthalene **14**, but only benzenepentacarboxylic acid can come from **20**. With this result, the structure of the maleic anhydride bis adduct could be accepted as **8**.

Discussion

Although eliminating structure **20** for the bis adduct serves to eliminate structure **4** for the dimer precursor, this still does not permit an unequivocal assignment for the dimer. Inspection will show that the same bis adduct **8** can arise not only from dimer **2** but, by a parallel series of steps, from dimer **3** as well. The reported structures for the cycloaddition dimers from various other monosubstituted allenes[6] suggest that the 1,2–1,2 mode of combination is preferred over the 2,3–2,3 mode;[7] and, in our case, the 1,2–1,2 combination leads to dimer **2** rather than **3**. Further, a special factor may be operating that favors **2** over **3**. Cycloaddition dimer **2** is the only one of the six possible dimers (**2**–**7**) that has an extended chain of conjugation. If the attendant resonance stabilization contributes significantly to the transition state for formation of dimer **2**, it could be produced faster than any of the others.

So far as 1,3-dimethylenecyclobutane structures **5**, **6**, and **7** are concerned, the literature offers little support for allene dimerizations to this kind of product. In fact, the only example of a 1,3-dimethylenecyclobutane from [2 + 2] cycloaddition refers to allene itself.[8]

With these considerations, we conclude that acetylenic conjugation does not change the mode of allene cycloaddition, although it does produce a 1,2-dimethylenecyclobutane dimer of high reactivity.

Experimental Section

General.—Boiling points and melting points are uncorrected. Nuclear magnetic resonance spectra were taken at 60 MHz. Galbraith Laboratories, Knoxville, Tenn., and Scandinavian Microanalytical Laboratories, Herlev, Denmark, performed the analyses for elements.

1,2-Nonadien-4-yne (1) from 1,4-Nonadiyne.[9]—A solution of 4 g (0.1 mol) of sodium hydroxide in 5 ml of water and 500 ml of 95% ethyl alcohol through which nitrogen was bubbling was cooled to 0° and was treated with 100 g (0.83 mol) of 1,4-nonadiyne containing less than 1% of the isomeric 2,4-diyne. The tightly stoppered mixture was stored at 0° for 15–18 hr. The cold alkaline mixture was shaken with 10 ml of concentrated hydrochloric acid plus 200 ml of petroleum ether (bp 30–60°), and the separated aqueous layer, after dilution with water to 4 l., was extracted further with petroleum ether. The combined petroleum ether layers were washed with water to pH 6–7, dried, and concentrated under reduced pressures at temperatures no higher than 45°. So far as possible throughout the entire preparation, a protective nitrogen atmosphere was kept above the solutions.

Unchanged 1,4-nonadiyne was removed as its insoluble copper derivative as follows. The product mixture was added to a cold (0°), stirred solution of cuprous chloride (45 g, 0.5 mol) in 200 ml of concentrated aqueous ammonia and 500 ml of ethyl alcohol. After about 15–20 min, when gas–liquid chromatography with a suitably processed small test sample showed that no 1,4-nonadiyne remained in solution, the mixture, diluted with 4 l. of water, was extracted several times with petroleum ether. Filtration through Kieselguhr, drying, and concentration at temperatures below 45° left a residue, which was distilled through a 9-in. vacuum-jacketed Vigreux column to give 44.2 g (44%) of water-white 1,2-nonadien-4-yne (**1**). Gas–liquid chromatography at 110° through a 4-ft column packed with silicone rubber on diatomaceous earth showed an intense peak at 3.1 min corresponding to the desired product **1** and a trace peak (less than 0.1%) at 4.0 min corresponding to 2,4-nonadiyne. Further exposure of the allene product **1** to alkali easily isomerized it to 2,4-nonadiene.[2] Half the starting material could be recovered from the copper precipitate as pure 1,4-nonadiyne, bp 82–83° (32 mm), by treat-

(5) R. J. Bushby, *Quart. Rev., Chem. Soc.*, **24**, 585 (1970).

(6) See especially the tabulation by D. R. Taylor in ref 1. Also *cf.* J. R. McClenon, *Diss. Abstr.*, **25**, 101 (1964).

(7) The one exception we could find refers to methylallene, which in the gas phase at 170° gives a mixture, including dimers, which consist of about twice as much of the 2,3–2,3 as the 1,2–1,2-isomer [J. J. Gajewski and C. N. Shih, *J. Amer. Chem. Soc.*, **91**, 5901 (1969)].

(8) S.-H. Dai and W. R. Dolbier, Jr., have recently reexamined the thermal dimerization of allene [*J. Org. Chem.*, **37**, 950 (1972); *J. Amer. Chem. Soc.*, **92**, 1774 (1970)].

(9) W. J. Gensler, A. P. Mahadevan, and J. Casella, Jr., *J. Amer. Chem. Soc.*, **78**, 163 (1956); H. Taniguchi, I. M. Mathai, and S. I. Miller, *Tetrahedron Lett.*, **22**, 867 (1966).

ment with cold aqueous hydrochloric acid,[2] so that the yield of allene 1 based on 1,4-nonadiyne consumed came to 86%.

Polymerization of 1,2-Nonadien-4-yne (1). A. Polymerization without Solvent.—When a flask provided with a reflux condenser and containing 2 g of 1,2-nonadien-4-yne (1) under a nitrogen atmosphere was lowered into a bath at 165°, the liquid boiled after 15 sec and darkened; after 1 min only a black tar remained. The same experiment at 140° showed bubbling in 30 sec. A black tar resulted even when the flask was removed as soon as boiling began.

Since 2,4-nonadiyne was almost certainly present in the 1,2-nonadien-4-yne (1), although in very low concentration, the possible involvement of the diyne had to be checked. A mixture of allene 1 and 2,4-nonadiyne (92:8) was held at 110°, with 0.5-μl samples analyzed at intervals by gas–liquid chromatography. The only two peaks appearing corresponded to those of the starting mixture, but, while the peak for the allene decreased steadily from 94 to 29 mm in 3 hr and to 3 mm after 17 hr, the diyne peak stayed about the same at about 5–8 mm. Distillation from a short-path still at temperatures gradually raised from 100 to 240° (0.01 mm) gave only a very small amount of distillate, which consisted of the starting components. A solution of the residue in carbon tetrachloride showed a broad nuclear magnetic resonance signal at δ 0.41–2.28 ppm and nothing else downfield as far as 11 ppm. This was also true when the attempted distillation was done with bath temperatures no higher than 110°.

B. Polymerization in the Gas Phase.—A sample of 1,2-nonadien-4-yne (1) containing 12% 2,4-nonadiyne was volatilized at 70° (10 mm), and the vapors at the reduced pressure were passed through a 24-in. Pyrex tube heated to 350°. Practically all the starting weight could be recovered as condensate at Dry Ice temperatures. Gas–liquid chromatography with the column temperature programmed to range from 110 to 300° gave only two peaks corresponding to the starting materials still in the same ratio. A similar gas-phase experiment at 420° furnished 65% of water-white condensate, again consisting only of starting materials. The hard yellow gum (30%) remaining in the tube showed no signals between δ 2.3 and 11 ppm.

C. Polymerizations in Solution.—The experiments were performed using 4.07 g of allene 1 containing 8.4% of 2,4-nonadiyne dissolved in 50 ml of refluxing pure solvent under a blanket of nitrogen. Aliquots, withdrawn by hypodermic needle through a septum, were analyzed by gas–liquid chromatography (110°) with the stable 2,4-nonadiyne serving as an internal reference. The only other peak observed was that for allene. A sampling of the data follows. In boiling *n*-decane (174°), the allene content dropped from 0.57 to 0.33 *M* after 5 min and to 0.082 *M* after a total time of 15 min. In *p*-xylene (130°), the allene content went from 0.57 to 0.424 *M* in 35 min and to 0.084 *M* in 160 min. In *n*-octane (125°), the change was from 0.57 to 0.49 *M* in 0.5 hr, and to 0.12 *M* in 6 hr. In toluene (110°) the change was from 0.57 to 0.51 *M* in 5 hr, and to 0.10 *M* after 48 hr. Plots of log *C* or of $1/C$ against time were linear before but not after the first 40% of reaction.

When a xylene solution of the allene containing *both* 2,4-nonadiyne (8%) and the skipped 1,4-nonadiyne (8%) was refluxed, the allene content decreased as before while the amounts of the two diynes remained about the same. At no time did gas–liquid chromatography show more than the three peaks corresponding to the initial components.

D. Exposure to Ultraviolet Light.—A 0.25 *M* stock solution of 1,2-nonadien-4-yne (1) containing 2,4-nonadiyne (15%) was prepared with oxygen-free pentane as solvent. Samples of this stock solution in 0.5-in. quartz tubes under a nitrogen atmosphere were tightly stoppered with rubber serum caps. The three ultraviolet sources used were a Sylvania blue-black lamp, a Sylvania H37/5KB lamp, and a high-intensity 253.7-nm source. During irradiation periods of up to 66 hr, no gas–liquid chromatography peaks other than the two corresponding to the starting materials were observed. Since the height of the peaks changed little and not regularly, only a minimal amount of photochemistry could have occurred.

Polymerization of Allene 1 in the Presence of Maleic Anhydride.—1,2-Nonadien-4-yne (14 g, 0.20 mol) containing about 3% of 2,4-nonadiyne was added over a period of 5 min to a solution of maleic anhydride (19.6 g, 0.20 mol) in pure *p*-xylene (200 ml) refluxing in a nitrogen atmosphere. After 3.5 hr, gas–liquid chromatography showed that no allene 1 remained. Distillation removed the solvent, followed by 11.3 g (56.5% recovery) of unchanged maleic anhydride, bp 100° (5 mm), mp 51–52°. Recrystallizations of the brown, viscous residue from ether–petroleum ether and from ethyl acetate gave 5.8 g (13%) of white, crystalline bis adduct **8**, mp 231–235°. The presence of a small quantity of hydroquinone did not change the yield significantly. Use of an excess of maleic anhydride resulted in a somewhat lower yield. Changing the solvent to *n*-octane gave the same yield (14%), but a longer reaction time in refluxing toluene lowered the yield.

When two parallel reactions were run with 1.2 g (0.01 mol) of allene in 20 ml of refluxing xylene, one with and the other without 0.98 g (0.01 mol) of maleic anhydride, the decrease in allene concentration in each tube followed the same curve to within 4%. Adding maleic anhydride to an octane solution of allene that had been boiled for 9 hr and in which allene could no longer be detected, and then refluxing the mixture gave none of the bis adduct and allowed recovery of 97.5% of the maleic anhydride.

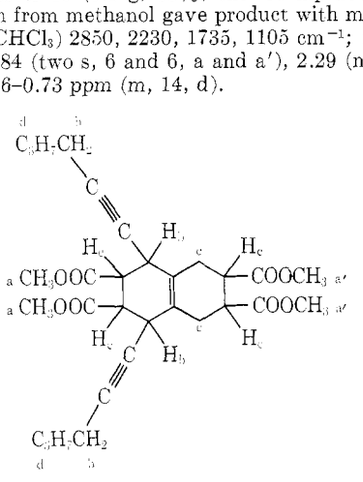
Further crystallization brought the melting point of bis adduct **8** to 235–236°: mass spectrum *m/e* (rel intensity) 436 (37), 364 (84), 279 (100), 45 (90), 42 (100); ir (mineral oil mull) 2220 (C≡C), 1870, 1790 cm^{-1}; nmr (CF_3CCOOH) δ 2.32–1.90 (m, 14, ring protons plus 2 $CH_2C{\equiv}C$), 1.10–0.55 ppm (m, 14, 2 C_3H_7).

Anal. Calcd for $C_{26}H_{28}O_8$: C, 71.54; H, 6.47. Found: C, 71.33; H, 6.49.

Tetracarboxylic Acid 9 and Ester 10 Derived from Bis Adduct 8.—A mixture of 2.5 g of bis adduct **8** and 10 ml of 2 *N* sodium hydroxide solution was heated at steam-bath temperatures until the solids dissolved. Acidification with 2 *N* hydrochloric acid to pH 2 precipitated a white solid, which after washing with a small volume of cold water and drying *in vacuo* weighed 2.7 g (100%), mp 213–216°. Recrystallization from ethanol gave 1.9 g (70%) of white, needlelike tetraacid **9**, mp 216.5–217.5°, ir (mineral oil mull) 3600, 2500, 2220, 1700 cm^{-1}.

Anal. Calcd for $C_{26}H_{32}O_8$: C, 66.72; H, 6.71. Found: C, 66.45; H, 6.93.

To form the tetraester **10**, bis adduct **8** (3.0 g, 0.0069 mol) was dissolved in refluxing absolute methanol (25 ml). The solution was cooled to 0°, and diazomethane in ether was added until the yellow color persisted. After a drop of 2 *N* acetic acid was added, the solution was concentrated to a volume of 10 ml and then held at 0–5° for 1 day. The resulting precipitate of colorless cubes of tetramethyl ester **10** (3.2 g, 88%) showed mp 207–209°. One crystallization from methanol gave product with mp 210.5–211° (2.6 g): ir ($CHCl_3$) 2850, 2230, 1735, 1105 cm^{-1}; nmr ($CDCl_3$) δ 3.76 and 3.84 (two s, 6 and 6, a and a′), 2.29 (m, 6, b), 1.91 (m, 8, c), 1.06–0.73 ppm (m, 14, d).



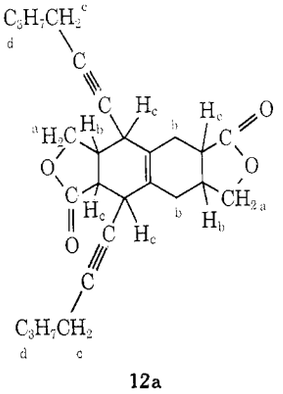
Anal. Calcd for $C_{30}H_{40}O_8$: C, 68.15; H, 7.64. Found: C, 68.32; H, 7.79.

Oxidative Cleavage of Bis Adduct 8. A. Ozonolysis.—Over a 3-hr period, ozonized oxygen was bubbled into a −78° solution of bis adduct **8** (0.215 g, 0.493 mmol) in methanol (100 ml). After the excess ozone had been swept out with oxygen (1 hr, 0°), the solution was treated with 2 g of zinc dust and 20 ml of ice–water, and the mixture was stirred for 18 hr. Solids were removed, and the filtrate, to which 10 ml of 2 *N* sodium hydroxide was added, was distilled *in vacuo* in a 40–50° heating bath to remove methanol. The remaining aqueous solution was acidified to pH 2, saturated with sodium chloride, and extracted continuously with ether for 24 hr. The dried extract was treated at room temperature with 5 mmol of diazomethane in ether (25 ml). Removal of low-boiling material left 96 mg of a yellow, oily residue. Gas–liquid chromatography (110° column) showed only a single peak even when the column temperature was

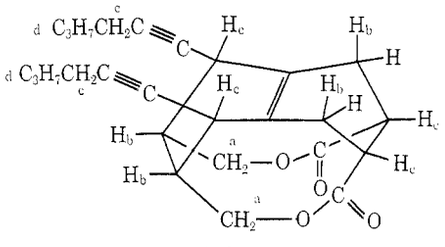
brought to 210°; direct gas–liquid chromatography comparisons with authentic samples of methyl butyrate, methyl valerate, and methyl hexanoate identified this product as methyl valerate. After column chromatography through a silica gel column with ether as eluent, 88 mg (79% assuming a 2-mol yield) of pure methyl valerate was obtained, which was identified by gas–liquid chromatography and by thin layer chromatography (silica gel with 39:1 *n*-pentane–ether) comparisons.

B. Oxidative Cleavage with Permanganate.—A solution of 1.00 g (2.29 mmol) of bis adduct **8** in 50 ml of 2% aqueous sodium bicarbonate was titrated at 50° with 0.100 *M* permanganate. A permanent pink color persisted only after adding 125.5 ml of the reagent. If each of the acetylenic carbon atoms in **8** is oxidized to carboxyl, and if the two carbon atoms of the double bond are oxidized to the ketone stage, the equivalence point may be calculated to be 121.8 ml, in good agreement with that found. A steam-volatile acid (3.17 mmol by alkali titration of the steam distillate) could be obtained by processing the oxidation mixture. Further treatment gave pure methyl valerate (3.02 mmol) as assayed by gas–liquid chromatography, so that the yield of valeric acid **11** here too comes to about 70%.

Dilactone 12 by Lithium Aluminum Hydride Reduction of Bis Adduct 8.—Over a 5-min period, a solution of 1.5 g (3.4 mmol) of bis adduct **8** in 5 ml of tetrahydrofuran was added to a cooled, stirred suspension of lithium aluminum hydride (0.56 g, 14 mmol) in 10 ml of tetrahydrofuran. After 2 hr, water (1 ml) was carefully added followed by enough 2 *N* hydrochloric acid to dissolve the solids. Product was taken up in ether, and the ether extract was dried and stripped of solvent. Cooling the residue gave a precipitate, which was collected by centrifugation and recrystallized from methylene chloride–benzene. The dilactone **12**, mp 141.5–142.5°, was obtained in this way in 0.24-g yield: ir ($CHCl_3$) 2870, 2230, 1745 cm^{-1}; nmr ($CDCl_3$) δ 4.05 (distorted t, 4, a), 2.29 (*ca.* t, 6, b), 1.81 (m, 8, c), 1.09–0.83 ppm (m, 14, d). Formulations **12a** and **12b** are both possible, but, since the



12a



12b

observed 1745-cm^{-1} lactone carbonyl absorption is low for a five-membered lactone, we favor **12b**.

Anal. Calcd for $C_{26}H_{32}O_4$: C, 76.46; H, 7.90. Found: C, 76.59; H, 7.81.

Naphthalenes from Bis Adduct 8. A. Base-Catalyzed Prototropy.—A stoppered mixture of 1.5 g (3.44 mmol) of bis adduct **8** and 10 ml of 10% aqueous sodium carbonate was stored at room temperature for 5 weeks. Acidification with 6 *N* hydrochloric acid followed by extraction of organic material into ether, etc., afforded 1.6 g of naphthalenetetracarboxylic acid **14** as a white solid. The corresponding tetraester **15** was formed by refluxing a solution of this solid in 10 ml of methanol containing 1 ml of boron trifluoride etherate. After dilution of the reaction mixture with 20 ml of cold water, shaking with ether extracted the product, which was isolated in the usual way to give 1.71 g of white tetramethyl ester **15**, mp 196–201°, showing a dark thin layer chromatographic spot at R_f 0.37 (2:1 chloroform–ether) and a light spot at R_f 0.42. Recrystallization from methanol afforded 0.95 g (52%) of white, crystalline product **15**: mp 204.5–206°; R_f 0.37 (note, this is slower running than tetramethyl ester **10**, with R_f 0.49); uv (10^{-3}–10^{-5} *M* in CH_3OH) λ_{max} 242 nm (log ϵ 4.87), 304 (3.82), 342 sh (2.87), 387 (2.25); blue fluorescence under ultraviolet light; ir ($CHCl_3$) 3010, 1725, 1628, 1105 cm^{-1}; nmr ($CDCl_3$) δ 7.91 (s, 2, aromatic H), 3.97 (s, 12, OCH_3), 2.24 (t, J = 6–7 Hz, 4, benzylic H's), 1.19–0.65 (m, 22, all other H's).

Anal. Calcd for $C_{30}H_{40}O_8$: C, 68.15; H, 7.64. Found: C, 68.06; H, 7.49.

The same product was obtained on refluxing a solution of the bis adduct **8** in 1 *N* aqueous sodium hydroxide under nitrogen for 12 days. Exposing the bis adduct to hot sodium methoxide in methanol for 3 days, however, proved not to be particularly effective.

B. Catalytic Disproportionation.—A mixture of bis adduct **8** (2.2 g), 50 ml of peroxide-free *p*-cymene (bp 177°), and 5 g of 10% palladium on carbon was refluxed under nitrogen for 3 hr. Removal of solids and then solvent left an off-white solid (2.06 g, mp 272–277°), which on recrystallization from ethyl acetate and tetrahydrofuran furnished white, needlelike bis anhydride **16** (1.5 g, 66%), mp 281–281.5°, ir (mineral oil mull) 3010, 1850, 1780, 1615 cm^{-1}.

Anal. Calcd for $C_{26}H_{28}O_6$: C, 71.54; H, 6.49. Found. C, 71.63; H, 6.45.

When *p*-cymene was replaced with *p*-xylene (bp 138°), no reaction occurred over a 17-hr period. The process was not simply thermal, since 96% of unchanged starting material could be recovered after refluxing a cymene solution of bis adduct **8** in the absence of palladium catalyst.

To form the tetramethyl ester, a methanol solution of bis anhydride **16** (1.1 g in 15 ml) containing 1 ml of boron trifluoride etherate solution was refluxed overnight. The brown residue, obtained on removing volatiles, could be crystallized from methanol to give 0.91 g (69%) of tetramethyl ester **15**, mp 204.5–205.5°, showing the same properties as those described above.

Dehydrogenation of Bis Adduct 8 to Tetralin 17.—Dry dioxane (25 ml) containing 2.2 g (5.0 mmol) of bis adduct **8** plus 4.5 g (20 mmol) of 2,3-dichloro-5,6-dicyanoquinone was refluxed for 6 hr. Filtration gave 2.6 g of insoluble 2,3-dichloro-5,6-dicyanohydroquinone, an amount corresponding to the consumption of 11.4 mmol of reagent. Refluxing the filtrate further for 17 hr precipitated no more hydroquinone. Thin layer chromatography at this point demonstrated the presence of quinone, hydroquinone, and product **17**, but not of starting material **8**. After the remaining 2,3-dichloro-5,6-dicyanoquinone was destroyed by adding 2 ml of tetralin and boiling the mixture, the mixture was cooled and filtered and the filtrate was stripped of volatile materials. The brown residue, crystallized from ethyl acetate, afforded 1.4 g of white, crystalline product **17**: mp 267.5–268.5°; ir (mineral oil mull) 2230, 1870, 1765, 1620 cm^{-1}; nmr (DMSO-d_6) δ 2.26 (m, 8, benzylic H's plus $C{\equiv}CCH_2$), 1.86 (m, 2, $HCC{=}O$), 1.60 ppm (m, 14, all other H's).

Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.20; H, 5.59. Found: C, 72.42; H, 5.80.

The same product **17** was formed when bis adduct **8** was dehydrogenated with selenium dioxide in acetic anhydride. Chloranil failed to effect dehydrogenation.

Benzenecarboxylic Acids 18 and 19 by Oxidative Degradation of Naphthalene Derivative 14.—When a mixture of naphthalene **14** (2.2 g, 5 mmol), 5 g of sodium hydroxide, 15 ml of water, and 7.9 g of potassium permanganate was held at 70–80° for 4–5 hr, all the oxidant was converted to manganese dioxide. The filtrate from this mixture was acidified to pH 2 with 25% sulfuric acid, cooled, and filtered to collect solids. Treatment with methanol dissolved the organic material and allowed the inorganics to be separated by decanting. To methylate the carboxylic acid groups, ethereal diazomethane was added until the yellow color persisted. Removing all volatiles left a mixture of white solids (0.49 g).

For separation, the product mixture dissolved in ethyl acetate (50 mg in 0.5 ml) was streaked onto a plate covered with a 2-mm layer of silica gel, and the plate was developed with 1:1 ether–benzene. The resulting three bands were scraped off, each was extracted with ethyl acetate, and the solvent was then removed to isolate the separated compounds. The respective fractions from three such preparative plates (*i.e.*, from a total of 150 mg of

mixed oxidation products) were combined and examined individually. The fastest moving material (22 mg) showed R_f 0.76 on thin layer chromatography (1:2 ether–benzene), melted at 247–249°, and produced a pale-blue fluorescence under ultraviolet light. This product, which could be the naphthalene hexacarboxylate, was not investigated further. The fraction with R_f 0.51 weighed 16 mg and showed mp 138–140°; the fraction with R_f 0.35 weighed 44 mg and showed mp 187–188°. Direct thin layer chromatographic and mixture melting point comparisons with authentic samples of the methyl esters of 1,2,4,5-benzenetetracarboxylic acid, benzenepentacarboxylic acid (R_f 0.44), and benzenehexacarboxylic acid identified the material with R_f 0.51 as the tetraester of acid **19**, and the material with R_f 0.35 as the hexaester of acid **18**. No pentaester could be detected among the oxidation products.

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Synthesis of DL-Slaframine

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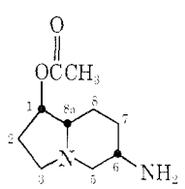
A stereoselective synthesis of slaframine is described. Ethyl *N*-(β-carbethoxyethyl)-5-oxopyrrolidine-2-carboxylate was obtained conveniently from glutamic acid and acrylonitrile. Dieckmann cyclization of this pyrrolidine diester followed by hydrolysis, decarboxylation, and catalytic hydrogenation furnished 2-(β-carbomethoxyethyl)-3-hydroxypyrrolidine hydrochloride. *N*-Alkylation with methyl bromoacetate led to a mixture of the lactone and the methyl ester of *N*-(carbomethoxymethyl)-2-(β-carboxyethyl)-3-hydroxypyrrolidine, which could be cyclized by a second Dieckmann process. Subsequent hydrolysis, decarboxylation, and acetylation gave 1-acetoxy-6-oxoindolizidine, which, after conversion into the oxime, was hydrogenated to DL-slaframine.

Slaframine (**1**), an alkaloid first detected as the result of its property of stimulating excess salivation in livestock foraging on fungus-infected red clover, has been isolated in low yield from cultures of *Rhizoctonia leguminicola*.[1,2] The proposed indolizidine structure **1**,[3,4] as revised in 1968,[5] has been confirmed by synthesis.[6] Since slaframine is of interest as a possible research tool for locating acetylcholine receptor sites and as an agent relieving the symptoms of cystic fibrosis,[7-9] we were led to investigate alternative approaches. The present paper describes our work on a direct and stereoselective synthesis of DL-slaframine (**13**).



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The starting point was ethyl *N*-(β-carbethoxyethyl)-5-oxopyrrolidine-2-carboxylate (**3**), which can be prepared conveniently from L-(+)-glutamic acid (**2**) and acrylonitrile.[10] Cyclization with sodium ethoxide produced ethyl 1,5-dioxopyrrolizidine-2-carboxylate (**4**). Although pyrrolidone **3** still showed optical activity, pyrrolizidine **4** was completely racemized. Decarboxylation of the pyrrolizidine **4** in hot hydrochloric acid was accompanied by lactam ring hydrolysis, so that the product was the 3-oxopyrrolidine acid **5**. The corresponding alcohol methyl ester **6** was obtained (46% from **3**) by hydrogenating the keto group over a platinum catalyst in methanol solvent.

To attach the fused six-membered rings as in slaframine (**1**), the sequence continued by alkylating hydroxypyrrolidine **6** on nitrogen with methyl bromoacetate. The expected diester **7** was obtained mixed with the equally useful lactone **8** (40 and 23%, respectively). The relation between the two products was established by allowing lactone **8** to methanolize, whereupon dimethyl ester **7** was produced. Dieckmann cyclization of a mixture of diester **7** and ester lactone **8** gave rise to indolizidine **9**. Although there is no steric barrier to direct ring closure of lactone **8** as a first step, whether this occurs or whether there is prior *in situ* methanolysis that converts the lactone into the diester **7** was not ascertained. The unstable Dieckmann product **9** was decarboxylated with acid to give 1-hydroxy-6-oxoindolizidine hydrochloride (**10**), which was first acetylated to **11** and then converted into the relatively stable oxime **12**.

With the hope of providing milder conditions in the decarboxylation stage (**9** to **10**), *tert*-butyl bromoacetate was substituted for methyl bromoacetate in the *N*-alkylation of pyrrolidine **6**. Although a pair of products analogous to diester **7** and lactone **8** was obtained in good yield, the next two steps with these *tert*-butyl esters was found to offer no advantages over the methyl esters.

The oxime **12** emerged as a mixture of syn and anti forms, which could be separated and characterized. The last step proceeded by hydrogenating the mixed

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