25-8; **4,** x = H, 707-98-2; **4,** x = CN, 21708-27-0; **6,** n = 2, 21708-28-1; **6,** n = 3, 21708-29-2; **6,** n = 6, 21708-30-5; **7,** n = 3, 21708-31-6; **7,** n = 6, 21708-32-7; **10,** n = 2, 21708-33-8; **10,** n = 3, 21708-34-9; **10,** n = 6, 21708-35-0; Ad-C_3-NAn, 21708-36-1; DMNAn-C_3, 21708-37-2; NAn-C_3-NAn, 21708-38-3; DMNAn-C_1-TMB, 21708-39-4; DMNAn-C_2-TMB, 21708-40-7; DMNAn-C_2-Ind, 21708-41-8; DMNAn-C_3-Ind, 21708-42-9; 9-benzylisoalloxazine, 21708-43-0; 9-(3-bromopropyl)adenine, 21708-44-1; 9-[3-(3,4-dimethylanilino)propyl]adenine, 21766-51-8; 9-[3-(3,5-dimethoxyanilino)propyl]adenine, 21708-45-2; 9-[3-(aden-9-yl)-propyl]isoalloxazine, 21708-46-3.

Acknowledgment.—We are pleased to acknowledge the support of this work by a research grant (USPHS-GM-05829) from the National Institutes of Health, U. S. Public Health Service. We wish to thank Professor G. Weber of this department for his many helpful suggestions and for his guidance in the attendant spectroscopic investigation of the compounds in the series **1a–d.**

Reaction of Hydroxylamine with 3,3-Disubstituted 2,4-Pentanediones. Formation of Novel Isoxazole Derivatives

David T. Manning and Harold A. Coleman

Research and Development Department, Union Carbide Corporation, Chemicals and Plastics, South Charleston, West Virginia

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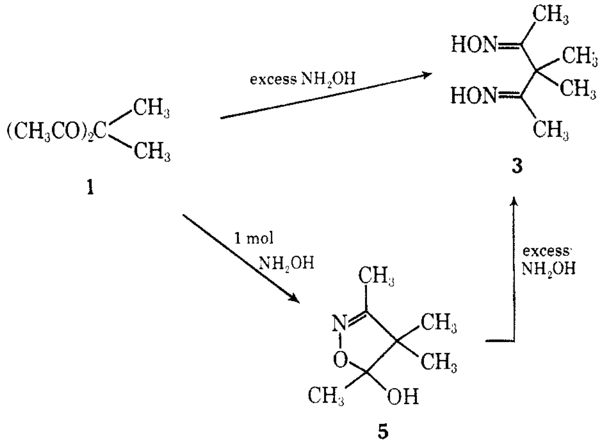
3,3-Disubstituted 2,4-pentanediones reacted with hydroxylamine to give good yields of novel 2-isoxazolin-5-ols. 3,4,4,5-Tetramethyl-2-isoxazolin-5-ol (**5**), prepared in this manner, underwent ring opening on treatment with excess hydroxylamine, forming 3,3-dimethyl-2,4-pentanedione dioxime (**3**). By contrast, all efforts to isolate a dioxime by hydroxylamine treatment of the 4,4-dipropargyl analog (**7**) of **5** failed. 3,5-Dimethyl-4,4-di(2-propynyl)-2-isoxazolin-5-ol (**7**) reacted with alcohols, in the presence of acids, to form the corresponding 5-alkoxy derivatives. Dehydration of **7** by treatment with thionyl chloride and pyridine gave a 5-methylene-2-isoxazoline (**15**) whose high stability contrasts markedly with analogous *exo*-methylene enamines of the related pyrazole series. Upon heating to 145°, **15** underwent exothermic isomerization to an allene, 5-(2,3-butadienyl)-3-methyl-4-(2-propynyl)isoxazole (**16**); a novel Claisen–Cope-type rearrangement is evidently involved. Attempted purification of **16** by alumina column chromatography caused an unexpected isomerization to a new, highly cross-conjugated allene, 5-(1,3-butadienyl)-3-methyl-4-(1,2-propadienyl)isoxazole (**18**), in near-quantitative yield.

Our interest in simple derivatives of 3,3-disubstituted 2,4-pentanediones led to a study of their reaction products with hydroxylamine. Gnichtel and Schönherr have reported[1] that 3,3-dimethyl-2,4-pentanedione (**1**) and 3,3-diethyl-2,4-pentanedione (**2**) react with hydroxylamine to give the expected dioximes **3** and **4**. This contrasted with our observation of cyclic (pyrazole) products resulting from reaction of 3,3-disubstituted 2,4-pentanediones with methylhydrazine, an isostere of hydroxylamine.[2] At the same time, we employed approximately equimolar amounts of diketones and methylhydrazine whereas Gnichtel and Schönherr used a substantial excess of hydroxylamine. Some other standard carbonyl derivatives of 3,3-disubstituted 2,4-pentanediones have been reported[3–8] although it is not evident, in all cases, whether cyclic or acyclic derivatives were obtained.

Results

Reaction of a 1:1 mol ratio of hydroxylamine with 3,3-dimethyl-2,4-pentanedione (**1**) afforded the novel 3,4,4,5-tetramethyl-2-isoxazolin-5-ol (**5**) in 61% yield. Treatment of **5** with excess hydroxylamine then gave Gnichtel and Schönherr's dioxime **3** in a yield of 48% (Scheme I). The reaction of 3,3-di(2-propynyl)-2,4-pentanedione (**6**) with hydroxylamine was then studied under various conditions. Treatment of **6** with a 4:1 mol ratio of hydroxylamine in refluxing aqueous ethanol produced only the 2-isoxazolin-5-ol (**7**) in yields as high as 85%. Examination of **7** showed it to be an acid, soluble in aqueous NaOH, and recoverable as an insoluble precipitate on adjustment to pH 6. Use of Gnichtel and Schönherr's conditions (2.88 mol of hydroxylamine hydrochloride in ethanol-pyridine) gave **7** (29%) along with its ethoxy derivative **8** (32%) (Scheme II) but not the dioxime. On the other hand, reaction of **6** with a high (10:1) excess of hydroxylamine gave **7** along with a minor unidentified impurity appearing, in the nmr spectrum, as a singlet at δ 1.8 ppm. Such a resonance is about what would be expected for a methyl group of the unknown dioxime of **6**.

Scheme I



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[1] H. Gnichtel and H. Schönherr, *Chem. Ber.*, **99**, 618 (1966).

[2] D. T. Manning, H. A. Coleman, and R. A. Langdale-Smith, *J. Org. Chem.*, **33**, 4413 (1968).

[3] A. E. Favorskii and A. S. Onischenko, *J. Gen. Chem. USSR*, **11**, 1111 (1941).

[4] M. F. Ansell, W. J. Hickinbottom, and A. A. Hyatt, *J. Chem. Soc.*, 1592 (1955).

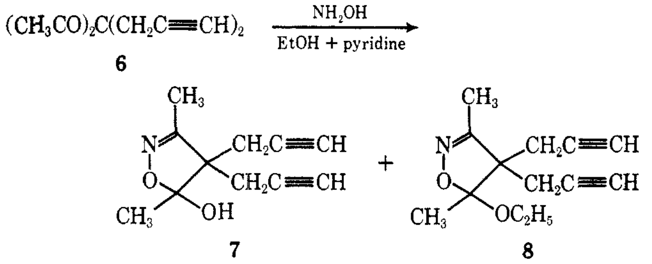
[5] R. B. Davis and P. Hurd, *J. Amer. Chem. Soc.*, **77**, 3284 (1955).

[6] E. Detilleux and J. Jadot, *Bull. Soc. Roy. Sci. Liege*, **24**, 366 (1955).

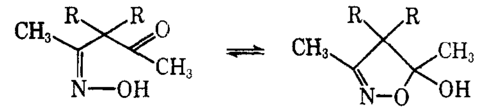
[7] T. A. Favorskaya, A. V. Marshueva, and Ting-Yü Hsü, *J. Gen. Chem. USSR*, **30**, 2499 (1960).

[8] J. J. Bloomfield, *J. Org. Chem.*, **26**, 4112 (1961).

SCHEME II



Nevertheless there is a clear divergence here between the behavior of **1** (and **2**) and **6** which has no ready explanation. While one would expect bulky R substituents to shift the equilibrium, below, to the right (the "*gem*" effect[9]) it is not evident, assuming that such an equilibrium is important, why R = propargyl should stabilize the heterocycle **10**, with respect to **9** (or the corresponding dioxime) more than would methyl or ethyl groups.



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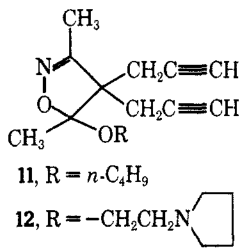
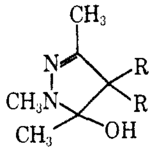
10

Formation of 5-alkoxy derivatives of 2-isoxazolin-5-ols, such as **8**, is facilitated by the expected ability of the C-5 ring position to accommodate a positive charge. Compound **7** reacted with alcohols, in the presence of HCl, giving 5-alkoxy-2-isoxazolines, exemplified by **11** and **12**, in fair to good yields.

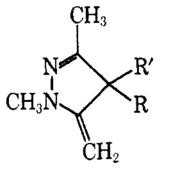


11, R = *n*-C$_4$H$_9$

12, R = -CH$_2$CH$_2$N



13

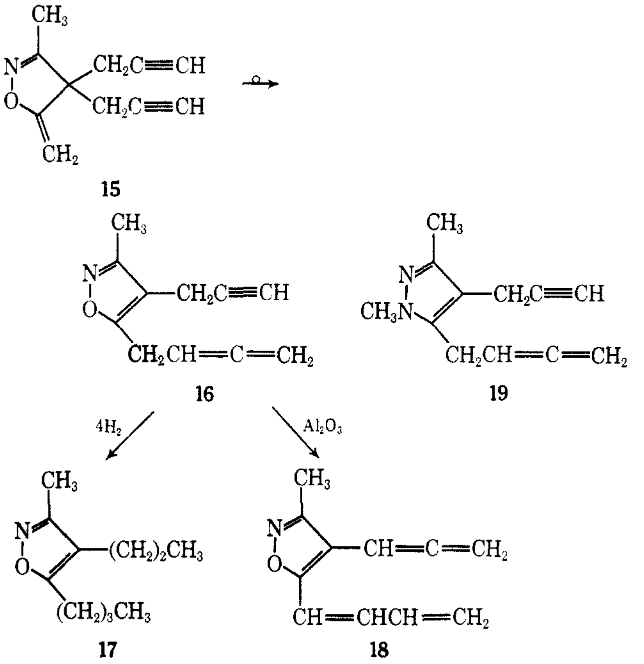


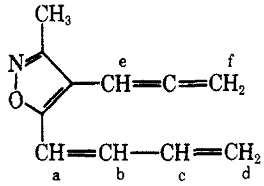
14

Preparation of 2-isoxazolin-5-ols from 3,3-disubstituted 2,4-pentanediones and hydroxylamine contrasts sharply with the behavior of these diketones with methylhydrazine. The latter reactions did not give isolable 5-hydroxypyrazolines (**13**) but, instead, either 5-methylene enamines (**14**) or pyrazoles were formed, depending upon the C-4 substituents.[2] It was of interest then to note that **7** can be dehydrated by treatment with thionyl chloride in pyridine to give the stable *exo*-methylene-2-isoxazoline **15**. The methylene protons of this compound lie in nonequivalent magnetic environments and appear as an AB pattern of doublets (nmr in CDCl$_3$), $J = 3.5$ Hz, centered at δ 4.30 and 4.72. Compound **15** proved relatively inert toward water at pH 7 and 25° but addition of acid to an aqueous slurry caused rehydration to **7**. Although **15** is stable and can be stored at room temperature, heating to *ca.* 145° caused exothermic rearrangement to the air-sensitive allene **16** in 77% yield. The ir and uv spectra of **16**, 6.11 and 6.28 μ and λ_{max} 220 (ϵ 6680), are characteristic[10] of the isoxazole ring and, along with the nmr data, are also in accord with the spectral features of the conventionally prepared model isoxazole **20**. Except for lack of an CH$_3$N signal the nmr spectrum of **16** is almost identical with that of the pyrazole analog **19**.[2] The energetics of the **15** → **16** conversion, presumably a novel type of Claisen-Cope rearrangement,[2] differ markedly from those of the pyrazole series, however. By contrast, rearrangements of 4-propargyl-5-methylene-2-pyrazolines (**14**, R or R′ = CH$_2$C≡CH) occur fairly rapidly even at 0°, hampering isolation of these enamine intermediates.[2,11]

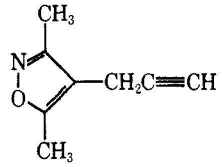
Further characterization of **16** was obtained by catalytic hydrogenation into 5-butyl-3-methyl-4-propylisoxazole (**17**) and by an unexpected isomerization into the cross-conjugated allene **18** (Scheme III). This step occurred in nearly quantitative yield upon attempted purification of **16** by alumina column chromatography at 25°. The polyene **18** is a white crystalline solid which undergoes fairly rapid polymerization on storage, at temperatures as low as −25°, with relatively little change in appearance. The nmr spectrum of **18** shows the eight protons lining the conjugated chains as a series of lines at δ 5.05–7.10 (Figure 1).

SCHEME III





18



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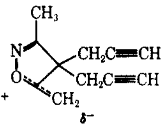
[9] G. Hammond, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley & Sons, Inc., New York, N. Y., 1956.

[10] W. L. Meyer, R. W. Huffman and P. G. Schroeder, *Tetrahedron*, **24** (18), 5959 (1968).

[11] The less facile rearrangement of **15**, compared with the 2-pyrazoline analogs, probably reflects a decreased capacity for electron donation from the more electronegative oxygen (as in **15A**) compared with donation from nitrogen in the corresponding pyrazoline enamines.



15A

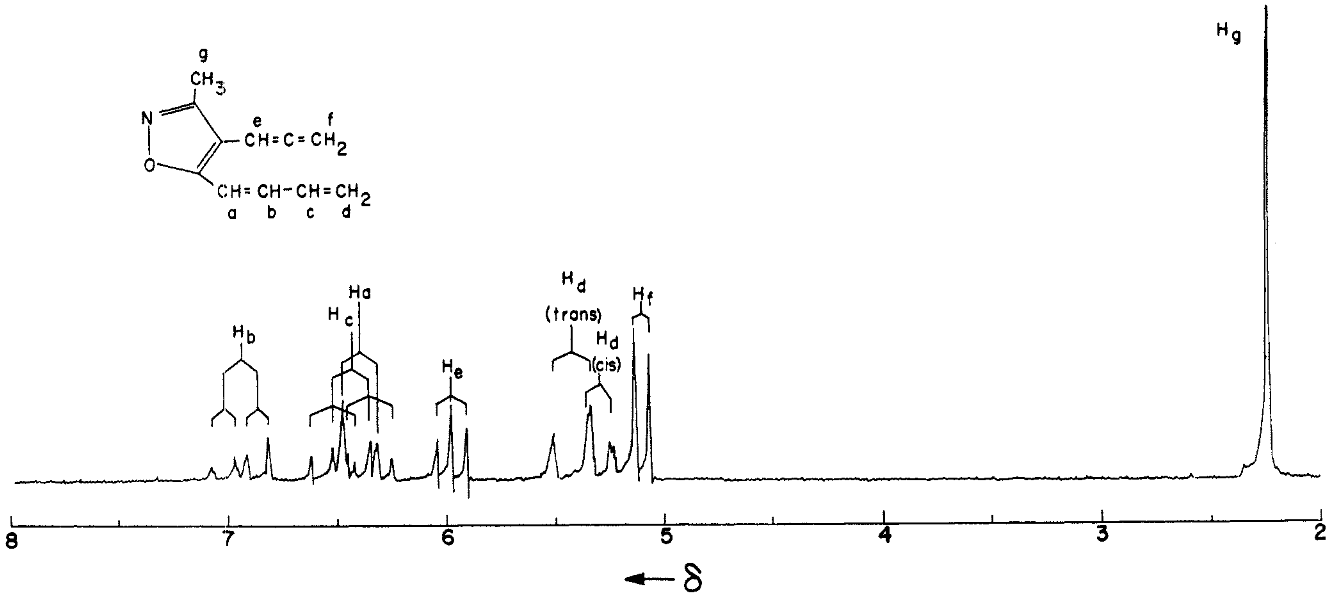


Figure 1.—The 100-Mc spectrum of 5-(1,3-butadienyl)-3-methyl-4-(1,2-propadienyl)isoxazole (**18**) in $CDCl_3$ solution.

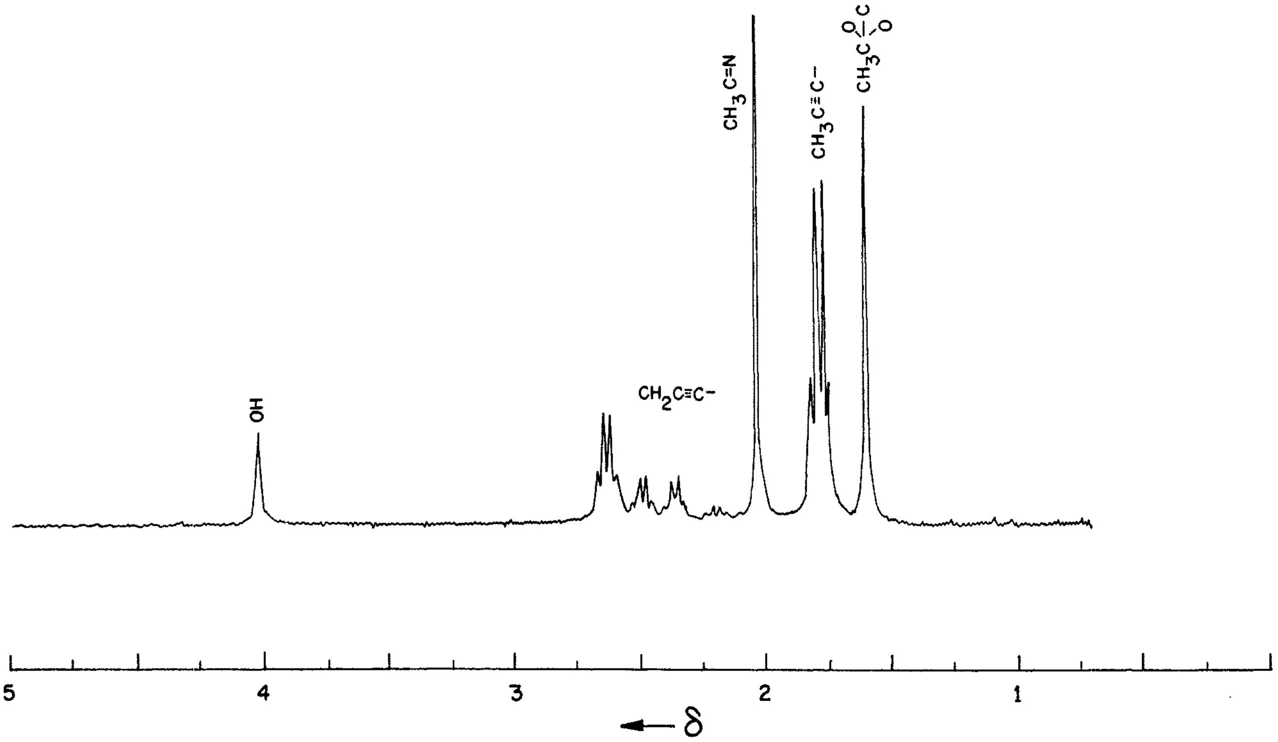
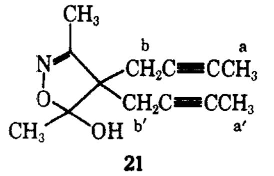


Figure 2.—The 100-Mc spectrum of 4,4-di(2-butynyl)-3,5-dimethyl-2-isoxazolin-5-ol (**21**) in $CDCl_3$.

Proton H_b of the butadienyl group is farthest downfield (δ 6.93) appearing as a doublet of doublets; J_{ba} = 16 Hz, J_{bc} = 10 Hz. Rather surprisingly H_a appears upfield (δ 6.40) as a doublet, J_{ab} = 16 Hz. Unlike **16**, the model compound **20** showed only a trace of propargyl → allene isomerization upon contact with alumina under identical conditions.[12]

The nmr spectra of **7** and particularly of **21** reveal magnetically nonequivalent protons, both between and within the methylene groups. Examination of **21** in deuteriochloroform at 100 Mc (Figure 2) revealed magnetically nonequivalent butynyl methyl groups as a 6 H pseudoquartet of overlapping triplets at δ 1.78. The methylene protons (b, b′) are spin coupled with the methyl protons (a, a′) and are also present in unlike environments with one methylene appearing as a quartet at δ 2.63. While the geminal protons of both methylene groups are diastereotopic,[13] only the protons of the high field group display internal nonequivalence and appear as an AB pattern of quartets (geminal and long-



21

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[12] We have noted that 5-(2,3-butadienyl)pyrazoles analogous to **16** are stable to alumina chromatography under these conditions.

[13] K. Mislow and M. Raban, in "Topics in Stereochemistry", Vol. I, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1967.

range methyl coupling) centered at about δ 2.43. One outlying quartet falls beneath the 2 H quartet of the low field CH_2 at δ 2.63 increasing its apparent magnitude.[14] A scan in benzene-d_6 showed similar methylene resonances but the a, a′ proton lines were shifted upfield to δ 1.48 with a remarkable maintenance of the pseudoquartet pattern.

Experimental Section

Nuclear magnetic resonance spectra were determined with Varian A-60 and HA-100 instruments employing TMS as the internal reference. An Aerograph Model 202 B dual-column gas chromatograph was used for vpc analysis. Molecular weight determinations were performed either by a modification of Neumayer's thermistor method[15] or by mass spectrometry, employing a Bendix Model 12-101 time-of-flight instrument. All melting point values are corrected. Boiling points are not corrected.

Preparation of 3,3-Disubstituted 2,4-Pentanediones.—Alkylation of 2,4-pentanedione by previously described methods[8,16] provided 3,3-dimethyl-2,4-pentanedione (**1**),[8] 3,3-di(2-propynyl)-2,4-pentanedione (**6**),[17] and 3,3-di(2-butynyl)-2,4-pentanedione.[16]

3,3-Di(2-butynyl)-2,4-pentanedione had mp 40–41°.

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.13; H, 7.69.

3,4,4,5-Tetramethyl-2-isoxazolin-5-ol (**5**).—A mixture of 3,3-dimethyl-2,4-pentanedione (12.1 g, 0.094 mol), hydroxylamine hydrochloride (6.1 g, 0.094 mol), sodium acetate (7.32 g, 0.089 mol), ethanol (100 ml), and water (100 ml) was refluxed for a 5-hr period. After evaporation of the volatile constituents from the mixture, the reaction residue crystallized upon storing at 0–5°. Recrystallization from hexane gave 7.0 g of **5**, mp 52–54°, and a 1.23-g second crop (61%): ir (KBr) 3.05 (O–H), 6.15 (C=N), 8.9 μ (*t*-C–OH); nmr ($CDCl_3$) δ 0.97 and 1.12 (two singlets, 6, CH_3CCH_3), 1.46 [s, 3, $CH_3C(OH)$], 1.88 (s, 3, $CH_3C{=}N$), 4.33 (s, 1, exchangeable OH).

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.46; H, 9.19; N, 10.09.

3,3-Dimethyl-2,4-pentanedione Dioxime (**3**).—A mixture of **5** (1.40 g, 0.01 mol), hydroxylamine hydrochloride (2.0 g, 0.029 mol), pyridine (2 ml), and ethanol (2 ml) was refluxed for 3.5 hr and then evaporated to dryness under reduced pressure. The residue was water washed and dried and then recrystallized from ethanol giving 0.75 g (47.5%) of **3**: mp 183–186° (lit.[1] mp 188°); ir (KBr) 3.05 (O–H), 6.01 (C=N), 10.75 μ (N–OH); nmr (deuterioacetone) δ 1.20 (s, 6, CH_3CCH_3), 1.65 (s, 6, $2CH_3$-$C{=}N$). Location of the exchangeable oxime protons was not established.

Anal. Calcd for $C_7H_{14}N_2O_2$: N, 17.71. Found: N, 17.71.

3,5-Dimethyl-4,4-di(2-propynyl)-2-isoxazolin-5-ol (**7**).—A mixture of 3,3-di(2-propynyl)-2,4-pentanedione (8.81 g, 0.05 mol), hydroxylamine hydrochloride (13.9 g, 0.20 mol), sodium acetate (16.7 g, 0.20 mol), ethanol (70 ml), and water (45 ml) was refluxed for 8.25 hr and the solution was then evaporated to near dryness. The solid residue was collected, water washed and recrystallized from benzene giving 6.47 g (67.7%) of crystalline **7**: mp 111.5–113°; ir (KBr) 2.95 (COH), 3.11 ($C\equiv CH$), 4.76 ($RC\equiv CH$), 6.15 (C=N), 8.60 (*t*-COH); nmr ($CDCl_3$) δ 1.63 (s, 3, CH_3CO), 2.05–2.15 (overlapping triplets, 2, $2C\equiv CH$), 2.06 (s, 3, $CH_3C{=}N$), and 4.06 (s, 1, exchangeable OH). The four propargyl methylene doublets appeared at δ 2.30, 2.47, 2.58, and 2.76 (J = 2.6 Hz).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33; mol wt, 191.2. Found: C, 69.17; H, 7.03; N, 7.41; mol wt, 186.

A small sample of **7** proved to be readily soluble in concentrated aqueous NaOH. Adjustment of the solution to pH 6 with HCl caused precipitation of **7**, unchanged as indicated by comparative ir spectra. Subsequent preparations of **7** afforded yields as high as 85.0%.

Action of Excess Hydroxylamine on 6. A. Employing Conditions of Gnichtel and Schönherr.—The diketone **6** (17.7 g, 0.1 mol) was treated with $NH_2OH \cdot HCl$ (20.0 g, 0.29 mol) in 60 ml of ethanol–pyridine (1:1) as described by Gnichtel and Schönherr.[1] Evaporation of the reaction mixture and water washing of the resulting residue gave 13.1 g of a pale yellow oil. When this was stirred with petroleum ether, 7.1 g of a solid, mp 87–115°, separated. The nmr spectrum (deuterioacetone) of this material showed it to be **7** (28.9%) containing the 5-ethoxy derivative **8** as an impurity. The content of **8** was estimated as 20 mol % from the integral of the ethoxy CH_3 triplet. Evaporation of the above petroleum ether wash solution left 5.4 g of **8**, mp 47–55.5°. The total yield of **8** was 31.8%. Recrystallization from hexane gave 4.4 g of analytical material: mp 55–58°; nmr ($CDCl_3$) δ 1.10 (t, 3, J = 7 Hz, CH_3CH_2), 1.53 (s, 3, CH_3CO), 2.03 (s, 3, $CH_3C{=}N$), 2.03–2.16 (m, 2, $2C\equiv CH$), 2.26–2.80 (series of doublets, 4, $2CH_2C\equiv C$), 3.43–3.74 (m, 2, CH_2CH_3). The series of doublets at δ 2.26–2.80 was similar to that shown by **7**.

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.81; N, 6.39. Found: C, 70.89; H, 7.72; N, 6.47.

B. With a 10:1 Hydroxylamine–6 Ratio.—A mixture of **6** (17.7 g, 0.1 mol), $NH_2OH \cdot HCl$ (69.5 g, 1.0 mol), sodium acetate (83.5 g, 1.02 mol), and 250 ml of ethanol–water (1:4) was refluxed for 3 hr after which the volatile constituents of the mixture were evaporated and the organic residue taken up in methylene chloride. The solution was dried ($MgSO_4$) and freed of solvent giving 20.1 g (105%) of crude product, mp 88–97°, shown by comparative nmr spectra to be **7** with a small amount of unknown impurities. An 18.1-g sample was dissolved in ether and chromatographed on alumina, successively eluting fractions with ether, acetonitrile and methanol. Work-up of these fractions gave only **7** along with an 3.5-g fraction of oil whose nmr spectrum ($CDCl_3$) was that of **7** with an unknown substance having a band at δ 1.8 ppm. Assuming the impurity to be the dioxime of **6**, its integral corresponded to *ca.* 35 mol % concentration.

5-Butoxy-3,5-dimethyl-4,4-di(2-propynyl)-2-isoxazoline (**11**).—A stream of anhydrous HCl was bubbled, for a 1-min period, into a mixture of **7** (3.00 g, 0.0157 mol), butanol (10 ml), and 100 ml of benzene after which the resulting solution was refluxed under a Dean–Stark trap. Formation of water ceased after 37 min and the reaction solution was stripped of the volatile constituents leaving a syrupy residue. This was taken up in ether and extracted with cold, saturated aqueous $NaHCO_3$ and the ether solution dried ($MgSO_4$) and evaporated giving 3.43 g (88.3%) of **11**. Vacuum distillation gave an analytical sample: bp 108–111° (0.6 mm); $n^{26}D$ 1.4786; ir (KBr) 3.07 ($C\equiv CH$), 4.74 ($C\equiv C$), 6.15 (C=N), 9.05 and 9.20 μ (COC).

Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56. Found: C, 72.54; H, 8.44.

3,5-Dimethyl-5-(2-pyrrolidinoethoxy)-4,4-di(2-propynyl)-2-isoxazoline (**12**).—Into a mixture of **7** (5.0 g, 0.026 mol), N-(2-hydroxyethyl)pyrrolidine (3.02 g, 0.026 mol), benzene (65 ml), and dioxane (50 ml) was passed a stream of dry HCl until the precipitate, initially formed, became a dense oil. The mixture was then refluxed for *ca.* 17 hr under a Dean–Stark trap. Upon cooling, 5.5 g of a deliquescent solid was recovered after washing with hot benzene and drying. The solid was dissolved in water and the pH adjusted to *ca.* 12 causing separation of an oil which crystallized. This material, apparently a hydrate of **12**, liquefied upon vacuum drying resulting in 1.64 g of crude product. This was purified by repeated cycles of cold water washing (conversion to solid hydrate), followed by vacuum drying with a final drying over P_2O_5 giving a pale yellow syrup: ir (KBr) 3.0 ($C\equiv CH$), 3.55 (OCH_2 and NCH_2), 4.7 ($C\equiv C$), 6.16 (C=N), 9.05 and 9.24 μ (COC).

Anal. Calcd for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N, 9.71. Found: C, 70.31; H, 8.42; N, 9.71.

4,4-Di(2-propynyl)-3-methyl-5-methylene-2-isoxazoline (**15**).—To a stirred solution of **7** (4.79 g, 0.025 mol) and pyridine (4.35 g, 0.055 mol) in 150 ml of benzene was added 3.21 g (0.027 mol) of thionyl chloride over 11 min, maintaining a temperature of 6–8° by external cooling. The reaction mixture was allowed to warm, slowly, to room temperature, stored overnight and the resulting white solid collected and washed repeatedly with hot benzene. Evaporation of benzene from the filtrate gave 4.0 g of crude **15**, mp 78–85°. Two recrystallizations from toluene gave 1.0 g of large, flat plates: mp 84–86.5°; ir (KBr) 3.03 ($C\equiv CH$), 4.7 ($C\equiv C$), 5.94, 6.03, 6.13 (C=C, C=N), 10.85 μ ($C{=}CH_2$); nmr ($CDCl_3$) δ 2.10 (s, 3, $CH_3C{=}N$), 2.16 (t,

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[14] The 100-Mc spectrum of the dipropargyl analog **7** shows a similar situation at the propargyl CH_2 groups. In this case, long range coupling splits the lines into doublets.

[15] J. J. Neumayer, *Anal. Chim. Acta*, **20** (6), 519 (1959).

[16] A. W. Johnson, E. Markham, and R. Price, *Org. Syn.*, **42**, 75 (1962).

[17] K. E. Schulte, J. Reisch, and A. Mock, *Arch. Pharm.* (Weinheim), **295**, 627 (1962).

2, J = 2.7 Hz, $2C\equiv C\mathbf{H}$), 2.55 and 2.70 (overlapping AB pair, 4, J = 2.7 Hz, $2C\mathbf{H}_2C\equiv C$), 4.30 (d, 1, J = 3.3 Hz, $=C\mathbf{H}_aH_b$), 4.72 (d, 1, J = 3.3 Hz, $=CH_a\mathbf{H}_b$); uv (C_6H_6) λ_{max} 274 (ϵ 170).

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.49; H, 6.52; N, 7.82.

A second crop of product, 1.32 g (mp 75–82°), brought the total yield to 53.6%. A yield of 67.2% was obtained in a subsequent preparation.

Action of Water on 15.—A 170-mg portion of **15** was ground with 20 drops of water at 25°, allowed to stand for 5 hr, then collected and air dried. The material melted at *ca.* 72–80° or close to that of the starting material. Sublimation occurred on vacuum drying and the ir spectrum of the sublimate was identical with that of **15**.

Another portion (200 mg) of **15** was stirred for 10 hr at 25–30° with 10 ml of water containing 5 drops of 5% HCl. The suspended solid was collected, water washed, and air dried giving 90 mg of **7**, mp 110.5–113.5°, as indicated by the comparative ir spectra.

5-(2,3-Butadienyl)-3-methyl-4-(2-propynyl)isoxazole (16).—A 6.1-g sample of **15** was heated under nitrogen at 140–145° for 15 min during which time a vigorously exothermic reaction required application of cooling for control. The resulting **16** was distilled through a short-path system to give 4.7 g (77.0%) of product, bp 96–97° (0.4 mm). Redistillation through a short column gave a 1.9-g main fraction: bp 106–107° (1.2 mm); ir (KBr) 3.06 ($C\equiv CH$), 4.74 ($C\equiv C$), 5.11 ($C{=}C{=}C$), 6.11 and 6.28 ($C{=}C$, $C{=}N$), 11.7 μ ($=CH_2$ allene wagging); nmr ($CDCl_3$) δ 2.14 (t, 1, J = 2.8 Hz, $C\equiv C\mathbf{H}$), 2.26 (s, 3, $C\mathbf{H}_3C{=}N$), 3.28 (d, 2, J = 2.8 Hz, $C\mathbf{H}_2C\equiv C$), 3.35–3.60 (m, 2, $C\mathbf{H}_2C{=}C{=}C$), 4.65–4.90 (m, 2, $C{=}C{=}C\mathbf{H}_2$), 5.04–5.50 (m, 1, $C\mathbf{H}{=}C{=}C<$); uv (acetonitrile) λ_{max} 220 (ϵ 6680).

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.06; H, 6.17; N, 7.89.

The distilled product discolored rapidly on exposure to air.

In large-scale preparations of **16** it proved advantageous to conduct the rearrangement in xylene solution to enable control of the strongly exothermic process.

5-Butyl-3-methyl-4-propylisoxazole (17).—A solution of 2.0 g (0.0115 mol) of **16** in 50 ml of ethanol was hydrogenated at 25° and *ca.* 1 atm in the presence of 5% Pd on carbon (0.1 g) for a period of 5 hr after which the residue was distilled through a short column. The main fraction was found to consist of two principal components by vpc analysis, suggesting incomplete hydrogenation. Hydrogen treatment was therefore continued, as above, for an additional 6 hr giving, on distillation, 1.2 g (57.6%) of **17**: bp 89° (1.0 mm); 98.7% pure by vpc; nmr ($CDCl_3$) δ 0.82–1.05 [t, 6, $C\mathbf{H}_3(CH_2)_2$, $C\mathbf{H}_3(CH_2)_3$], 1.13–1.83 (m, 6, $C\mathbf{H}_2CH_2C{=}C$, $C\mathbf{H}_2C\mathbf{H}_2CH_2C{=}C$), 2.18 (s, 3, $C\mathbf{H}_3C{=}N$), 2.20–2.75 (m, 4, $C\mathbf{H}_2C{=}CC\mathbf{H}_2$).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 73.05; H, 10.54; N, 7.92.

5-(1,3-Butadienyl)-3-methyl-4-(1,2-propadienyl)isoxazole (18).—A solution of **16** (11.1 g, 0.064 mol) in 250 ml of ether was passed, at room temperature, through a 23 × 1.25 in. column of aluminum oxide (Merck, Reagent Grade) and the effluent liquid evaporated, giving 10.4 g (93.8%) of crystalline **18** in fractions of varying purity, melting from 62 to 79.5°. Analytical data was obtained for a white crystalline fraction: mp 77–79.5°; ir (KBr) 5.12 ($C{=}C{=}C$), 5.5 (11.02-μ overtone), 6.11, 6.17, 6.3 ($C{=}C$, $C{=}N$), 11.05 ($CH{=}CH_2$ wagging), 11.6 μ ($=CH_2$ allene wagging); uv (benzene) λ_{max} 312 (ϵ 43,200); *m/e* 173 (parent). The nmr spectrum of **18** is described in Figure 1 and in the above discussion of results.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.01; H, 6.50; N, 7.83.

A sample of **18**, recrystallized from isopropyl ether, had an initial mp 78–80°. After standing 6 days the material was unchanged in appearance but melted above 250° and was insoluble in chloroform.

3,5-Dimethyl-4-(2-propynyl)isoxazole (20).—A 27.6-g (0.2 mol) sample of 3-(2-propynyl)-2,4-pentanedione was treated with a slight excess of hydroxylamine hydrochloride under conditions similar to those used in preparing **5**. Distillation of the solvent-free reaction residue gave 15.9 g (58.8%) of **20**: bp 51–52° (0.6 mm); ir (KBr) 6.06 μ ($C{=}N$ or $C{=}C$); nmr ($CDCl_3$) δ 2.06 (t, 1, J = 2.6 Hz, $C\equiv C\mathbf{H}$), 2.23 (s, 3, $C\mathbf{H}_3C{=}N$), 2.33 (s, 3, $C\mathbf{H}_3C{=}C$), 3.22 (d, 2, J = 2.6 Hz, $C\mathbf{H}_2C\equiv C$); uv (acetonitrile) λ_{max} 218 (ϵ 4500); *m/e* 135 (parent).

Anal. Calcd for C_8H_9NO: N, 10.36. Found: N, 10.05.

An ethyl ether solution of **20** was chromatographed on an alumina column as in the isomerization of **16** into **18**. Infrared examination of the principal fraction of eluted material showed it to be unchanged **20** containing a trace of an allene as indicated by a weak band at 5.24 μ.

4,4-Di(2-butynyl)-3,5-dimethyl-2-isoxazolin-5-ol (21).—A 20.4-g (0.10 mol) sample of 3,3-di(2-butynyl)-2,4-pentanedione was refluxed with a 300% excess (0.40 mol) of hydroxylamine in aqueous ethanol in a manner similar to the preparation of **7**. The stripped organic residue was dissolved in benzene and chromatographed on alumina. After unreacted diketone was removed by washing with benzene, methanol elution gave crude **21**, mp 80–88°, which was crystallized from isopropyl ether to give 10.7 g (48.8%) of white crystals: mp 87.5–88.5°; ir (KBr) 2.95 (COH), 4.5 ($C\equiv C$), 6.15 ($C{=}N$), 8.56 μ (COH).

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.81; N, 6.39. Found: C, 70.88; H, 7.74; N, 6.56.

Registry No.—**3**, 5363-39-3; **5**, 21708-01-0; **7**, 21708-02-1; **8**, 21708-03-2; **11**, 21708-04-3; **12**, 21708-05-4; **15**, 21708-06-5; **16**, 21708-07-6; **17**, 21708-08-7; **18**, 21708-09-8; **20**, 21708-10-1; **21**, 21708-11-2; 3,3-di(2-butynyl)-2,4-pentanedione, 21708-12-3; hydroxylamine, 7803-49-8.

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