silyl-*N*,*N*-dimethylanilines than for the *tert*-butyl compound. However, the total interaction of the d orbitals with the π system is significantly larger than the $p\pi$ interaction for the silicon compounds. The $p\pi$ and $d\pi$ interactions between silicon and the ring decrease as the π density at the carbon to which the trimethylsilyl group is attached decreases.

Our results are in substantial agreement with recently published results of Kawamura and Kochi.[29] These authors conclude from a study of hfcc's and *g* values for a series of neutral radicals [$(CH_3)_3MCH_2CH_2\cdot$, M = C, Si, Ge, Sn] that both p–d and hyperconjugative interactions provide delocalization of the odd electron to the β C–M σ bond. Further, both interactions are of the same order of magnitude and both increase with increasing atomic number of the metal.[29] On this basis we might suggest that the interactions in *p*-trimethylgermyl-*N*,*N*-dimethylaniline, for which we could not perform CNDO/2 calculations, are similar to those in the trimethylsilyl compounds. We do not agree with the conclusions of Symons and coworkers who, on the basis of coupling constants alone, ruled out p–dπ interactions for alkyl radicals containing Sn, P, or As in the β position.[30]

Although the CNDO/2 calculations indicate some contribution of the $p\pi$ orbital of silicon to the ground-state molecular orbitals, the larger coefficients for this orbital occur in the unoccupied molecular orbitals. The effect of group IV elements on the excited states of these molecules will be discussed in the following paper.

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(29) T. Kawamura and J. K. Kochi, *J. Amer. Chem. Soc.*, **94**, 648 (1972).

(30) A. R. Lyons and M. C. R. Symons, *Chem. Commun.*, 1068 (1971).

Interchange of Functionality in Conjugated Carbonyl Compounds through Isoxazoles

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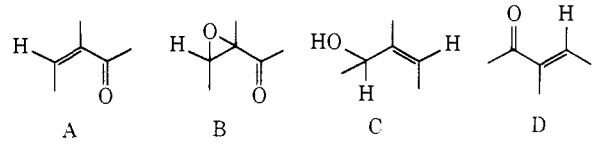
Abstract: Five isoxazoles were prepared in good to excellent yield by a new method involving oxidation of certain α,β-unsaturated ketoximes with iodine–potassium iodide in aqueous tetrahydrofuran in the presence of bicarbonate. Catalytic hydrogenation of the isoxazoles gave vinylogous amides while reduction with sodium and 3 equiv of *tert*-butyl alcohol in liquid ammonia yielded the β-aminocarbonyl compounds in excellent yields. The corresponding α,β-unsaturated carbonyl compounds were available from the crude amines by thermolysis or treatment with acidic catalysts. This new method for the transposition of functionality within α,β-unsaturated carbonyl compounds was used to convert the three ionones **1a**, **1b**, and **1d** to the corresponding damascones **4a**, **4b**, and **4d**. The method is also suitable for the preparation of unsaturated aldehydes, but the starting material cannot be an aldoxime because the resulting isoxazole is too unstable in the basic medium necessary for its creation.

Since the recognition of β-damascenone (**4c**)[1] as an important constituent of Bulgarian rose oil and raspberry aroma,[2] its chemical synthesis has received much attention.[1,3-5] Added impetus to develop efficient syntheses for this class of compounds was provided when β-damascone (**4a**) was found in Burley tobacco.[6] Both it and its α (**4b**)[7] and γ isomers[8] have been synthesized by multistep procedures from starting materials containing fewer carbon atoms. The readily available and inexpensive α- and β-ionones (**1b** and **1a**) represent ideal raw materials for the synthesis of the corresponding damascones (**4b** and **4a**). The hitherto most efficient method for the transposition of carbonyl group and double bond in conjugated ketones was discovered by Wharton.[9] He found that treatment with hydrazine of an epoxy ketone B, available by oxidation of the corresponding α,β-unsaturated ketone A, gave the allylic alcohol C, oxidizable, unless tertiary, to the transposed conjugated ketone D.



A B C D

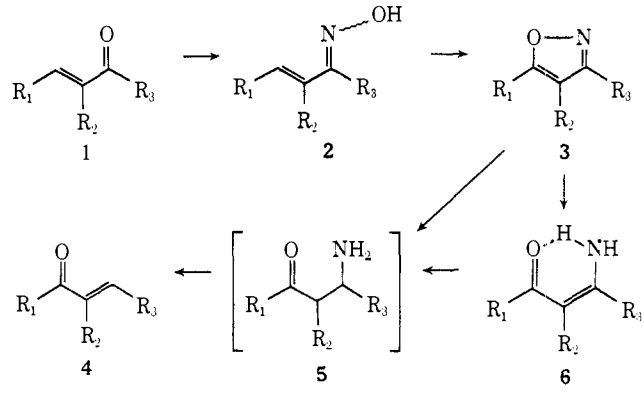
Both epoxydihydro-α-ionone and its γ isomer were submitted to the Wharton reaction, but the results were

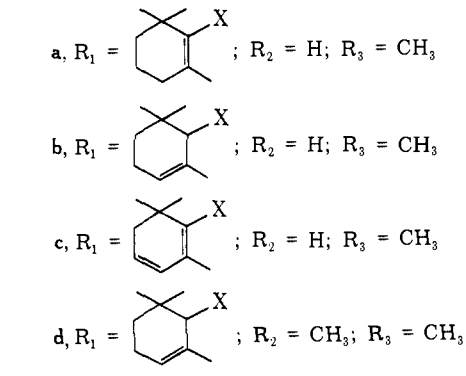
(1) E. Demole, P. Enggist, U. Säuberli, M. Stoll, and E. sz. Kováts, *Helv. Chim. Acta*, **53**, 541 (1970).
(2) M. Winter and P. Enggist, *ibid.*, **54**, 1891 (1971).
(3) G. Büchi and H. Wüest, *ibid.*, **54**, 1767 (1971).
(4) K. H. Schulte-Elte, B. L. Müller, and G. Ohloff, *ibid.*, **54**, 1899 (1971).
(5) K. H. Schulte-Elte, B. L. Müller, and G. Ohloff, *ibid.*, in press.
(6) E. Demole and D. Berthet, *Helv. Chim. Acta*, **54**, 681 (1971).
(7) G. Ohloff and G. Uhde, *ibid.*, **53**, 531 (1970).
(8) K. H. Schulte-Elte, V. Rautenstrauch, and G. Ohloff, *ibid.*, **54**, 1805 (1971).
(9) P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, 26, 3615 (1961).

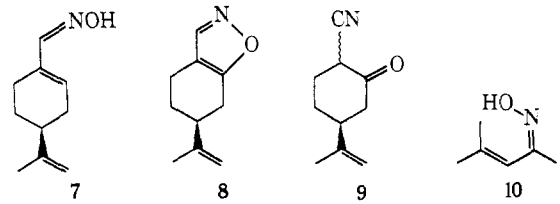
essentially negative in regards to damascones because hydrazinolysis led mainly to products resulting from a novel cyclization.[7,8]

We report herein a new and often efficient reaction sequence leading to an interchange of functionality within certain α,β-unsaturated carbonyl compounds. The three nuclear methyl groups in the ionones are expected to exert a serious rate retarding effect in any reaction delivering an external oxygen atom to the future carbonyl carbon atom, and consequently, attack by oxygen should be intramolecular. The underlying concept of our work is to accomplish this oxidatively with an oxime, and to transform the resulting isoxazole to the conjugated ketone by a reduction process. Although one-step ring closures to isoxazoles have been accomplished with acetylenic oximes,[10] α,β-dihalo oximes, monoximes of β-diketones, α,β-epoxy oximes,[11] and β-aminoacrolein oximes[12,13] no such cyclizations were known for α,β-unsaturated oximes. The first example of a two-step oxidative isoxazole synthesis from a conjugated oxime was reported by Crabbé.[14] A steroidal 16-en-20-one oxime on treatment with lead tetraacetate and iodine in wet benzene was converted to an iodoisoxazoline, from which an isoxazole was prepared by dehydrohalogenation with silver acetate. An attempt in these laboratories to utilize this method for the preparation of isoxazole **3a** from β-ionone oxime (**2a**) gave a multitude of unrecognizable products.

We found that when either (*E*)- or (*Z*)-β-ionone oxime (**2a**) is exposed to a mixture of iodine–potassium iodide in hot aqueous tetrahydrofuran containing sodium bicarbonate, the isoxazole **3a** is formed directly in high yield. Isoxazoles **3b**, **3c**, **3d**, and **3e** were prepared analogously from the corresponding oximes. Perillaldehyde oxime (**7**) consumed iodine readily under the usual conditions but no more than a few per cent of the 3-unsubstituted isoxazole **8** could be isolated. Even the weakly basic bicarbonate ion was capable of initiating the well-known isoxazole cleavage to the ketonitrile **9** which, not unexpectedly, had undergone further transformations. The pH of the reaction medium was found to be critical in all oxidations studied. Elemental iodine combines with iodide to form triiodide ions under neutral or slightly basic conditions, but the equilibrium is shifted to iodide and iodate in strong base.[15] Under the latter conditions the oximes were transformed to complex mixtures of products. The amount of expensive iodide added is not critical. Drs. G. Ohloff and K. H. Schulte-Elte, Firmenich et Cie., Geneva, kindly informed us that use of only catalytic amounts of iodide had no adverse effect on the yield of isoxazoles **3a** and **3b**. Efforts on our part to replace iodine with donors of "positive" chlorine or bromine failed without exception.



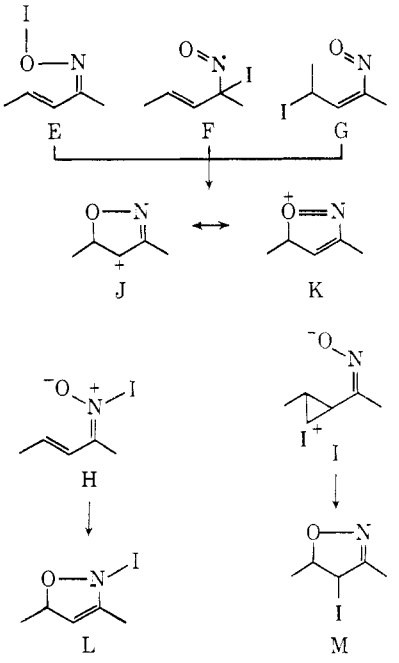




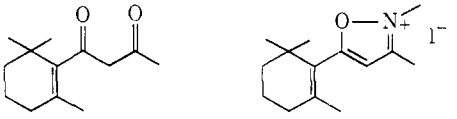
The mechanism of this new isoxazole synthesis is still unknown. Attack of iodine in a basic medium on an unsaturated oxime could yield one of five intermediates, E–I. Of these we eliminate three from being involved in isoxazole formation. Cyclization of E, F, and G would lead to the unlikely ion J ↔ K. Both H and I represent mechanistically reasonable intermediates leading to either *N*- or *C*-iodoisoxazolines L or M, and thence to isoxazoles. To test whether such iodoisoxazolines are isolable in cases where elimination of hydriodic acid without rearrangement is impossible, mesityl oxide oxime (**10**) was treated with triiodide. The compound proved to be remarkably stable and was recovered unchanged even after prolonged treatment at elevated temperature. This observation does not disprove the intermediacy of L and M and only demands return to starting material in cases where aromatization to isoxazoles cannot occur for structural reasons.

Catalytic reduction[10] of the three isoxazoles **3a**, **3b**, and **3d** proceeded smoothly to the vinylogous amides with ultraviolet absorption spectra expected for the chelated isomers.[16a] Facile hydrolysis of the enamino ketone **6a** to the diketone **11**[16b] demonstrated that the sequence is suited for conversion of α,β-unsaturated ketones to β-diketones. Somewhat unexpectedly, methylation of isoxazoles **3a** and **3b** with methyl iodide

(10) N. K. Kochetkov and S. D. Sokolov, *Advan. Heterocycl. Chem.*, 2, 365 (1963).
(11) L. I. Klimova and N. N. Suvorov, *Khim. Prir. Soedin.*, 2, 325 (1966); *Chem. Abstr.*, 67, 54332m (1967).
(12) H. Bredereck, H. Herlinger, and E. H. Schweizer, *Chem. Ber.*, **93**, 1208 (1960).
(13) H. V. Hansen, J. A. Caputo, and R. I. Meltzer, *J. Org. Chem.*, **31**, 3845 (1966).
(14) S. Kaufmann, L. Tökes, J. W. Murphy, and P. Crabbé, *ibid.*, **34**, 1618 (1969).
(15) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 2nd ed, Interscience, New York, N. Y., 1966, pp 570, 589; G. J. Hills in "Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. II, Supplement I, Longmans, Green and Co., London, 1956, p 836.
(16) (a) D. L. Ostercamp, *J. Org. Chem.*, **35**, 1632 (1970); (b) K. H. Schulte-Elte, unpublished.



gave the same isoxazolium salt **12**, indicating greater mobility of the cyclic double bond in the salt, and greater stability of the conjugated, yet surely not planar, isomer.



To continue with the transformation of β-ionone (**1a**) to β-damascone (**4a**) the vinylogous amide **6a** had to be reduced to the β-amino ketone **5a**. A number of such reductions have been accomplished with lithium aluminum hydride.[17] We reasoned that in analogy with the reduction of α,β-unsaturated to saturated ketones, dissolving metals should bring about this reduction. Indeed, reduction of **6a** with sodium and *tert*-butyl alcohol in liquid ammonia produced the β-amino ketone **5a**, which gave β-damascone (**4a**) by loss of ammonia when heated in toluene with a trace of an acidic catalyst. Even more interestingly, direct reduction of the isoxazole **3a** with sodium and 3 equiv of *tert*-butyl alcohol in liquid ammonia generated the enolate which was converted to the β-amino ketone **5a** on aqueous work-up. Generally we found it advantageous not to manipulate the somewhat sensitive β-amino ketones **5**, and to transform them without purification to the conjugated ketones **4** either by thermolysis or by treatment with acid. This mode of operation represents a practical method for the conversion of isoxazoles to α,β-unsaturated ketones, and the average yield in the transformations **3a** → **4a**, **3b** → **4b**, **3d** → **4d**, and **3e** → **4e** was 72%. β-Damascenone (**4c**) was not available by this sequence because the cyclohexadiene in **3c** was reduced about as rapidly as the isoxazole ring, resulting in a mixture of vinylogous amides **6a** and **6b**.

Much to our surprise we were unable to find literature references to the direct reduction of isoxazoles to saturated β-amino ketones, although Claisen already prepared vinylogous amides from isoxazoles by reduction with sodium in alcohol.[18]

Finally, examination of the scope of the new method for the transposition of functionality in α,β-unsaturated carbonyl compounds shows that it is applicable for the conversion of ketones to other ketones (**1a** to **4a**; **1b** to **4b**; **1d** to **4d**) and a ketone to an aldehyde (**1e** to **4e**), but that the starting carbonyl compound cannot be an aldehyde because of the instability of the derived isoxazole (*e.g.*, **8**) to base.

Experimental Section

Dry nitrogen or dry argon was used in reactions requiring an inert atmosphere. Anhydrous magnesium sulfate or sodium sulfate was employed as drying agent in all reaction work-ups. Progress of most reactions was followed by thin layer chromatography, using Merck silica gel GF 254 or Bakerflex aluminum oxide 1B. Visualization was by ultraviolet light (uv) or spray reagents such as phosphomolybdic acid, dinitrophenylhydrazine, or chromic acid. All melting points were determined on a Kofler hot stage microscope and are uncorrected, as are boiling points. The purity of isolated products was checked by gas chromatographic (gc) analysis on either an F & M 720 instrument (thermal detector) or a Perkin-Elmer 990 instrument (flame ionization detector), employing 6-ft gc columns packed with 15% SE30, 10% Carbowax 20M, 3% OV225, 3% OV17, or 3% HI-EFF-8BP. Uv spectra were recorded on Cary 14 and Perkin-Elmer 202 spectrophotometers. Infrared (ir) spectra were obtained on Perkin-Elmer 237B or 247 grating spectrophotometers. Nuclear magnetic resonance (nmr) spectra were measured on Varian T-60 or Hitachi Perkin-Elmer R20B instruments and are given in parts per million (δ) downfield from tetramethylsilane as an internal standard. Mass spectra were determined on a Hitachi Perkin-Elmer RMU 6E, and the molecular ion (M^+) is reported. Microanalyses were performed by the M.I.T. Microchemical Lab and Midwest Microlab, Inc., Indianapolis, Ind.

β-Ionone (1a). Commercially available β-ionone was purified either through its semicarbazone or by recrystallization from petroleum ether at −75°.

β-Ionone Oxime (2a). To a mixture of β-ionone (20.2 g, 0.105 mol) and hydroxylamine hydrochloride (7.35 g, 0.105 mol) in 25% water–ethanol (125 ml) was added dropwise a solution of potassium carbonate (7.5 g, 0.055 mol) in water (40 ml). When addition was complete, the mixture was refluxed for 25 min, cooled, and concentrated *in vacuo* to remove most of the ethanol. It was then diluted with water (20 ml) and extracted with ether (150 ml). The combined ether extracts were dried and concentrated *in vacuo* to give 18.1 g (86%) of a mixture of syn and anti oximes. Analytical samples were prepared by chromatography of the mixture (1.0 g) on silica gel (100 g), eluting with 1% methanol–chloroform to give 0.475 g of anti oxime: ir (neat) 3500, 2930, 1675, 1620 cm^{-1}; nmr ($CDCl_3$) δ 1.03 (s, 6), 1.71 (s. 3), 2.07 (s. 3), 6.33 (AB q, 2, J = 16 Hz), 10.00 (br s, 1); uv max (95% EtOH) 234, 268 nm. Also isolated was 63 mg of syn oxime: ir (neat) 3500, 2930, 1670, 1610 cm^{-1}; nmr ($CDCl_3$) δ 1.07 (s, 6), 1.83 (s. 3), 2.04 (s, 3), 6.5 (m, 2), 8.7 (br s, 1); uv max (95% EtOH) 235, 270 nm.

Isoxazole 3a. To a stirred solution of β-ionone oxime (**2a**) (85.0 g, 0.410 mol) in tetrahydrofuran (THF) (1500 ml) was added a solution of sodium bicarbonate (136 g, 1.62 mol) in water (1300 ml). The reaction mixture was protected from light, and a solution of potassium iodide (235 g, 1.41 mol) and iodine (109 g, 0.43 mol) in water (1000 ml) was added to it. After refluxing for 4 hr, the mixture was diluted with concentrated sodium bisulfite solution (1500 ml), extracted with ether (3 l.), dried, and concentrated *in vacuo*. Distillation gave 77.2 g of isoxazole **3a** (91%): bp 70–71° (0.03 mm); ir ($CHCl_3$) 2930, 1655, 1585, 1410 cm^{-1}; nmr ($CDCl_3$) δ 1.00 (s, 6), 1.50 (s, 3), 2.27 (s, 3), 5.86 (s, 1), 1.5 to 2.2 (br m, 6); uv max (95% EtOH) 226 nm (ε 8600); mass spectrum (70 eV) *m/e* 205 (M^+).

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.10; H, 9.27; N, 6.78. Found: C, 76.26; H, 9.53; N, 7.05.

Vinylogous Amide 6a. Isoxazole **3a** (30.75 g, 0.15 mol) was added in ethanol (50 ml) to a prehydrogenated mixture of 82.9% platinum oxide (1.396 g) in ethanol (600 ml). After hydrogenation was complete, the mixture was filtered through Celite and con-

(17) M. E. Kuehne in "Enamines," A. G. Cook, Ed., Marcel-Dekker, New York, N. Y., 1969, p 431.

(18) L. Claisen, *Ber.*, **24**, 3900 (1891).

centrated *in vacuo;* the residue was recrystallized from hexane containing a trace of ethanol to give 30.91 g (100%) of vinylogous amide **6a**, which exists in two interconvertible crystalline forms: mp 124.5–125.0°, 135–136°; ir ($CHCl_3$) 3490, 1610, 1510 cm^{-1}; nmr ($CDCl_3$) δ 1.09 (s, 6), 1.56 (s, 3), 1.92 (s, 3), 5.00 (br s, 1), 1.4 to 2.1 (br m, 6); uv max (95% EtOH) 303 nm (ϵ 20,100); mass spectrum (70 eV) *m/e* 207 (M^+).

Anal. Calcd for $C_{13}H_{21}NO$: C, 75.36; H, 10.15; N, 6.76. Found: C, 75.16; H, 10.39; N, 6.65.

β-Damascone (4a) from Isoxazole 3a. Sodium was added to a stirred mixture of liquid ammonia (200 ml), THF (30 ml), *tert*-butyl alcohol (2.796 g), and isoxazole **3a** (2.593 g, 12.65 mmol) until the solution remained dark blue. After the mixture was stirred for 15 min, solid ammonium chloride was added until decolorization, and the ammonia was evaporated under a stream of argon. Ether (50 ml) was added, followed by concentrated ammonium chloride solution (300 ml), and the mixture was extracted with ether (300 ml) and chloroform (150 ml). The material was dried and concentrated *in vacuo*, and one-half of it was redissolved in toluene (25 ml) containing a trace of *p*-toluenesulfonic acid. This mixture was refluxed for 24 hr, concentrated *in vacuo*, and distilled to give 1.037 g (84%) of β-damascone (**4a**): bp 55° (0.04 mm); ir ($CHCl_3$) 1670, 1645, 1630, 1615, 970 cm^{-1}; nmr ($CDCl_3$) δ 1.02 (s, 6), 1.50 (s, 3), 1.90 (d of d, 3, J = 7, 1 Hz), 1.3 to 2.2 (br m, 6), 5.9 to 6.9 (m, 2); uv max (95% EtOH) 227 (ϵ 12,900), 272 (2030) nm; mass spectrum (70 eV) *m/e* 192 (M^+).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.25; H, 10.42. Found: C, 81.22; H, 10.65.

β-Damascone (4a) from Vinylogous Amide 6a. Sodium was added to a stirred mixture of liquid ammonia (250 ml), THF (15 ml), *tert*-butyl alcohol (0.358 g), and vinylogous amide **6a** (1.002 g, 4.84 mmol) until the solution remained dark blue. The mixture was stirred for 15 min, solid ammonium chloride was added until decolorization, and the ammonia was evaporated under a stream of argon. Ether (25 ml) was added followed by concentrated ammonium chloride solution (75 ml), and the mixture was extracted with ether (200 ml) and chloroform (100 ml). The material was dried and concentrated *in vacuo* to give 1.038 g of crude material, and a portion of this (0.230 g) was refluxed in toluene (10 ml) overnight. Concentration *in vacuo* was followed by distillation to give 0.177 g of β-damascone (**4a**) (85%), identical with material obtained by one-step reduction of isoxazole **3a** and hydrogenation of damascenone (**4c**).

Isoxazolium Salt 12 from Isoxazole 3a. Methyl iodide (5.0 ml) and isoxazole **3a** (0.270 g, 1.31 mmol) were sealed in an evacuated glass tube. The material was then heated at 100° overnight, cooled, and opened. Evaporation of excess methyl iodide followed by recrystallization of the residue from chloroform–carbon tetrachloride and from acetone gave 0.230 g (50%) of isoxazolium salt **12**: mp 208–209°; ir ($CHCl_3$) 1595, 1520 cm^{-1}; nmr ($CDCl_3$) δ 1.07 (s, 6), 1.4 to 2.3 (br m, 6), 1.73 (s, 3), 3.03 (s, 3), 4.54 (s, 3), 6.89 (s, 1); uv max (95% EtOH) 221 nm (ϵ 21,500), 275 (4,860).

Anal. Calcd for $C_{14}H_{22}NOI$: C, 48.41; H, 6.34; N, 4.03. Found: C, 48.09; H, 6.54; N, 4.34.

Isoxazolium Salt 12 from Isoxazole 3b. Methyl iodide (10.0 ml) and isoxazole **3b** (1.62 g, 7.82 mmol) were sealed in a glass tube and heated at 110° overnight. After cooling and evaporation of excess methyl iodide, the material was recrystallized twice from acetone to give 1.13 g (41%) of isoxazolium salt **12** with melting point and spectral properties identical with those of the salt prepared from **3a**.

Isoxazole 3b. To a stirred solution of α-ionone oxime (**2b**) (53.0 g, 0.260 mol) in tetrahydrofuran (THF) (750 ml) was added a solution of sodium bicarbonate (88.9 g) in water (750 ml). The reaction mixture was protected from light, and a solution of potassium iodide (148.6 g) and iodine (69.2 g, 0.270 mol) in water (500 ml) was added to it. After refluxing for 7 hr and standing overnight, the mixture was diluted with concentrated sodium bisulfite solution (500 ml), extracted with ether (750 ml), dried, and concentrated *in vacuo*. Distillation gave 28.75 g of isoxazole **3b** (54%): bp 69–70° (0.04 mm); ir ($CHCl_3$) 2960, 1595, 1445, 1415 cm^{-1}; nmr ($CDCl_3$) δ 0.73 (s, 3), 0.99 (s, 3), 1.55 (m, 3), 2.22 (s, 3), 2.92 (br s, 1), 5.49 (m, 1), 5.68 (s, 1), 1.2 to 2.2 (br m, 4); uv max (95% EtOH) 218 nm (ϵ 9750); mass spectrum (70 eV) *m/e* 205 (M^+).

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.10; H, 9.27; N, 6.78. Found: C, 76.10; H, 9.40; N, 6.88.

Vinylogous Amide 6b. Isoxazole **3b** (4.10 g, 0.020 mol) was added in ethanol (5 ml) to a prehydrogenated mixture of 83.6% platinum oxide (0.173 g) in ethanol (30 ml). After hydrogenation was complete, the mixture was filtered through Celite, concentrated *in vacuo*, and chromatographed on Florisil (250 g). Elution with 25% $CHCl_3$–hexane gave 3.73 g (90%) of gummy vinylogous amide **6b**: ir ($CHCl_3$) 3485, 2950, 1615, 1590, 1520 cm^{-1}; nmr ($CDCl_3$) δ 0.89 (s, 6), 1.58 (m, 3), 1.90 (s, 3), 2.38 (br s, 1), 5.06 (br s, 1), 5.50 (*m*, 1), 1.2 to 2.3 (br m, 4); uv max (95% EtOH) 301 nm (ϵ 18,400); mass spectrum (70 eV) *m/e* 207 (M^+).

α-Damascone (4b). Sodium was added to a stirred mixture of liquid ammonia (500 ml), THF (100 ml), *tert*-butyl alcohol (14.0 ml), and isoxazole **3b** (10.11 g, 49.3 mmol) until the solution remained dark blue. After stirring for 15 min, solid ammonium chloride was added until decolorization, and the ammonia was evaporated under a stream or argon. Ether (100 ml) was added, followed by concentrated ammonium chloride solution (500 ml), and the mixture was extracted with ether (500 ml) and chloroform (250 ml). The material was dried, concentrated *in vacuo*, and split into two portions. One portion (41% of the crude material) was dissolved in toluene (200 ml) and passed down a Pyrex column (13 mm × 150 mm) packed with glass helices ($^3/_{32}$ in.) (previously washed with sulfuric acid and then water) heated to 225°. During the pyrolysis a slow stream of argon was passed through the system from above, and the product was collected in a flask cooled with Dry Ice. Concentration *in vacuo* followed by distillation afforded 3.198 g of almost pure α-damascone (**4b**) (82%). Further purification was effected by chromatography on Florisil (250 g) with 25% $CHCl_3$–hexane and distillation to give 2.880 g of α-damascone (**4b**) (74%): bp 55–56° (0.04 mm); ir ($CHCl_3$) 1675, 1660, 1650, 1620, 1435, 965 cm^{-1}; nmr ($CDCl_3$) δ 0.86 (s, 3), 0.96 (s, 3), 1.56 (m, 3), 1.89 (d of d, 3, J = 6.5, 1 Hz), 5.59 (m, 1), 6.30 (d of q, 1, J = 16, 1 Hz), 2.89 (m, 1), 6.92 (d of q, 1, J = 16, 6.5 Hz), 1.3 to 2.3 (br m, 4); uv max (95% EtOH) 229 nm (ϵ 12,200); mass spectrum (70 eV) *m/e* 192 (M^+).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.25; H, 10.42. Found: C, 81.53; H, 10.66.

3,4-Dehydro-β-ionone (1c). The procedure of Findlay and MacKay[19] was used to convert β-ionone (**1a**) to 3,4-dehydro-β-ionone (**1c**): uv max (95% EtOH) 226 nm (ϵ 6120), 347 (12,200) [lit.[20] (EtOH) 224 (5300), 345 (12,200)].

3,4-Dehydro-β-ionone Oxime (2c). To a stirred mixture of 3,4-dehydro-β-ionone (**1c**) (4.180 g, 0.022 mol), hydroxylamine hydrochloride (1.750 g, 0.025 mol), ethanol (40 ml), and water (25 ml) was added solid sodium bicarbonate (3.0 g). The reaction was refluxed for 90 min, poured into water (250 ml), and extracted with ether (375 ml) and chloroform (125 ml). The combined organic extracts were dried, concentrated *in vacuo*, and distilled to give 2.695 g (60%) of 3,4-dehydro-β-ionone oxime (**2c**): bp 110° (0.1 mm); ir ($CHCl_3$) 3580, 3240, 2960, 960 cm^{-1}; nmr ($CDCl_3$) δ 1.07 (s, 6), 1.86 (br s, 3), 2.08 (m, 5), 5.7 to 7.2 (br m, 4); uv max (95% EtOH) 236 nm (ϵ 11,800), 317 (14,000); mass spectrum (70 eV) *m/e* 205 (M^+).

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.10; H, 9.27; N, 6.78. Found: C, 75.79; H, 9.43; N, 6.53.

Isoxazole 3c. This substance was prepared from dehydro-β-ionone oxime (**2c**) in 29% yield as described for isoxazoles **3a** and **3b**: bp 80° (0.1 mm); ir ($CHCl_3$) 2955, 1645, 1590, 1405 cm^{-1}; nmr ($CDCl_3$) δ 1.07 (s, 6), 1.71 (s, 3), 2.20 (d, 2, J = 1 Hz), 2.33 (s, 3), 5.92 (br s, 3); uv max (95% EtOH) 281 nm (ϵ 7300); mass spectrum (70 eV) *m/e* 203 (M^+).

Anal. Calcd for $C_{13}H_{17}NO$: C, 76.85; H, 8.37; N, 6.90. Found: C, 76.83; H, 8.51; N, 6.88.

Reduction of Isoxazole 3c to Vinylogous Amides 6a and 6b. Sodium was added to a stirred mixture of isoxazole **3c** (0.390 g, 1.92 mmol), *tert*-butyl alcohol (0.142 g), THF (20 ml), and liquid ammonia (100 ml) until the solution remained dark blue. The mixture was stirred for 10 min, solid ammonium chloride was added until decolorization took place, and ether (20 ml) was added. The ammonia was evaporated, concentrated ammonium chloride solution (100 ml) was added, and the resulting solution was extracted with ether (75 ml). The extracts were dried, concentrated *in vacuo*, and chromatographed on Florisil 100–200 mesh (50 g) with chloroform. In addition to starting material (100 mg), the vinylogous amides **6a** and **6b** were isolated in the approximate ratio of 1:5.

α-Isomethylionone oxime (2d) was prepared from the ketone **1d** in 93% yield following the procedure described above for the preparation of **2c**: bp 110–112° (0.05 mm); ir ($CHCl_3$) 3560, 3250, 2900, 1630 cm^{-1}; nmr ($CDCl_3$) δ 0.79 (s, 3), 0.92 (s, 3), 1.53 (m, 3), 1.94 (br s, 3), 2.06 (s, 3), 2.66 (br d, 1, J = 10 Hz), 5.41 (m, 1), 5.69 (d of

(19) J. A. Findlay and W. D. MacKay, *Can. J. Chem.*, **49**, 2369 (1971).
(20) H. B. Henbest, *J. Chem. Soc.*, 1074 (1951).

q, 1, J = 10, 0.5 Hz), 9.85 (br, 1), 1.2 to 2.2 (br m, 4); uv max (95% EtOH) 236 nm (ε 22,800); mass spectrum (70 eV) *m/e* 221 (M^+).

Anal. Calcd for $C_{14}H_{23}NO$: C, 76.02; H, 10.41; N, 6.33. Found: C, 75.87; H, 10.69; N, 6.04.

Isoxazole 3d. Following the procedure outlined for the synthesis of **1a**, this isoxazole was prepared from oxime **2d** in 57% yield: bp 72–74° (0.04 mm); ir ($CHCl_3$) 2910, 1620, 1440, 1414 cm^{-1}; nmr ($CDCl_3$) δ 0.72 (s, 3), 1.00 (s, 3), 1.50 (m, 3), 1.90 (s, 3), 2.14 (s, 3), 2.96 (br s, 1), 5.63 (m, 1), 1.2 to 2.2 (br m, 4); uv max (95% EtOH) 225 nm (ε 8150); mass spectrum (70 eV) *m/e* 219 (M^+).

Anal. Calcd for $C_{14}H_{21}NO$: C, 76.71; H, 9.59; N, 6.39. Found: C, 76.43; H, 9.60; N, 6.22.

Vinylogous Amide 6d. When the isoxazole **3d** was reduced with a limited amount of sodium (see preparation of **3c**), the enamino ketone **6d** was obtained in 81% yield: mp 93–94° after recrystallization from acetone: ir ($CHCl_3$) 3485, 1605, 1575, 1480 cm^{-1}; nmr ($CDCl_3$) δ 0.86 (s, 3), 0.92 (s, 3), 1.2 to 1.6 (br m, 2), 1.59 (m, 3), 1.97 (s, 3), 2.01 (s, 3), 2.0–2.3 (br m, 2), 3.25 (br s, 1), 5.66 (m, 1); uv max (95% EtOH) 318 nm (ε 11,500); mass spectrum (70 eV) *m/e* 221 (M^+).

Anal. Calcd for $C_{14}H_{23}NO$: C, 76.02; H, 10.41; N, 6.33. Found: C, 75.76; H, 10.12; N, 6.30.

Methyl-α-damascone (4d). The crude β-amino ketone **5d** obtained by reduction of isoxazole **3d** with sodium, as described for the preparation of **1a** and **1b**, was dissolved in toluene and the solution passed down a Pyrex column (13 mm × 150 mm) packed with glass helices ($^3/_{32}$ in.) kept at 230–250° while a slow stream of argon was passed through the system. Work-up and distillation gave methyl-α-damascone (**4d**) (59%): bp 70–71° (0.05 mm); ir ($CHCl_3$) 2920, 1655, 1640 cm^{-1}; nmr ($CDCl_3$) δ 0.80 (s, 3), 0.97 (s, 3), 1.56 (m, 3), 1.86 (br s, 3), 2.00 (m, 3), 3.54 (br s, 1), 5.63 (m, 1), 6.85 (br q, 1, J = 6.5 Hz), 1.2 to 2.2 (br m, 4); uv max (95% EtOH) 233 nm (ε 12,600); mass spectrum (70 eV) *m/e* 206 (M^+).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.55; H, 10.68. Found: C, 81.67; H, 10.69.

Isopropenyl Ethyl Ketone (1e). Diethyl ketone and formaldehyde were condensed by the method of Colonge and Cumet[21] to form isopropenyl ethyl ketone (**1e**): bp 116–118° (lit.[21] bp 117–119°).

(21) J. Colonge and L. Cumet, *Bull. Soc. Chim. Fr.*, 838 (1947).

Isopropenyl Ethyl Ketoxime (2e). This oxime was prepared in 89% yield following the procedure described for the preparation of **2c**: bp 30–32° (10 mm); ir ($CHCl_3$) 3575, 3270, 2970, 960, 900 cm^{-1}; nmr ($CDCl_3$) δ 1.13 (t, 3, J = 7 Hz), 2.00 (br s, 3), 2.64 (q, 2, J = 7 Hz), 5.36 (br s, 1), 5.48 (br s, 1); uv max (95% EtOH) 227 nm (ε 7500); mass spectrum (70 eV) *m/e* 113 (M^+).

3-Ethyl-4-methylisoxazole (3e). Oxidation of oxime **2e** with triiodide as described above, followed by evaporation of the solvents at atmospheric pressure and distillation, gave isoxazole **3e** in 55% yield: bp 75–77° (50 mm); ir ($CHCl_3$) 2960, 1615, 1455, 1120 cm^{-1}; nmr ($CDCl_3$) δ 1.30 (t, 3, J = 7 Hz), 2.02 (s, 3), 2.67 (q, 2, J = 7 Hz), 8.17 (br s, 1); uv max (95% EtOH) 217 nm (ε 4520); mass spectrum (70 eV) *m/e* 111 (M^+).

Anal. Calcd for C_6H_9NO: C, 64.86; H, 8.11; N, 12.61. Found: C, 65.15; H, 8.22; N, 12.74.

2-Methylpent-2-enal (4e). Sodium was added to a stirred mixture of liquid ammonia (100 ml), THF (30 ml), *tert*-butyl alcohol (0.210 g), and 3-ethyl-4-methylisoxazole (**3e**) (1.041 g, 9.35 mmol) until the solution remained dark blue. The reaction was stirred for 15 min, decolorized with solid ammonium chloride, and treated with dry ether (50 ml). After evaporation of the ammonia with a stream of nitrogen, the material was cooled to 0°, and dry HCl was bubbled in rapidly. The precipitate was filtered, washed with ether (25 ml) and pentane (25 ml), and stored over potassium hydroxide overnight. A portion amounting to 35% of the total precipitate was pyrolyzed in a short-path distillation apparatus at 100° (130 mm) to yield 0.235 g (72%) of 2-methylpent-2-enal (**4e**): ir ($CHCl_3$) 2965, 1675, 1635 cm^{-1}; nmr ($CDCl_3$) δ 1.16 (t, 3, J = 7 Hz), 1.73 (br s, 3), 2.41 (d of q, 2, J = 7, 7.5 Hz), 6.43 (t of q, J = 7, 0.5 Hz), identical with that reported in ref 22.

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(22) K. Mori, S. K. Roy, and D. M. S. Wheeler, *J. Chem. Soc.*, 5815 (1964).

Enamine Formation and Hydrolysis. Ethyl β-Cyanomethylaminocrotonate[1]

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Abstract: Rate constants for the hydrolysis of the enamine ethyl β-cyanomethylaminocrotonate (**1**) have been studied as a function of pH and buffer concentration. At high buffer concentration, from pH 4 to pH 7, the rate-determining step is the acid-catalyzed addition of water to the imine tautomer. At very low buffer concentrations, tautomerization is rate determining. Equilibrium constants have been measured as a function of pH, so that rate constants for enamine formation may be calculated. The equilibrium constant for the formation of **1** from free aminoacetonitrile and ethyl acetoacetate is 0.94 M^{-1}.

As part of an investigation[4,5] of the amine-catalyzed decarboxylation of acetoacetic acid, the reaction of aminoacetonitrile (AAN) with ethyl acetoacetate (EAA) was studied. It was hoped that this reaction, leading to reversible formation of the enamine ethyl β-cyanomethylaminocrotonate (ECC), would serve as a model for the reaction of aminoacetonitrile with acetoacetic acid, without the complication of irreversible decarboxylation. The immediate purpose was to evaluate rate constants for imine formation from EAA and AAN for comparison with the rate constants for the AAN-catalyzed decarboxylation of acetoacetic acid. This proved to be more difficult than was an-

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