The Oxygenation of 2-Oxazolin-5-ones: A New Synthesis of Imides[1]

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In the presence of mild base such as triethylamine, the two 4-alkylidene-2-phenyl-2-oxazolin-5-ones, **1** and **8**, rapidly absorb oxygen at room temperature with the loss of carbon dioxide and the formation of the imides **4** and **10**. The imide probably arises by decomposition of a hydroperoxide resulting from the reaction of oxygen and the anion of the oxazolinone. A hydroperoxide intermediate will also account for the origin of the acidic by-products **6***a* and **11***a*. The 2-methyl-2-oxazolin-5-one **14** did not react with oxygen at room temperature; at 60° some reaction occurred but no imide was formed.

Lorsque mis en présence d'une base faible comme la triéthylamine, les deux alkylidène-4 phenyl-2 oxazolin-5-ones, **1** et **8** absorbent rapidement de l'oxygène à la température ambiante pour ensuite libérer du gaz carbonique et conduire aux imides **4** et **10**. La formation d'un imide peut être attribuée à la décomposition d'un hydroperoxyde issu de la réaction entre l'oxygène et l'anion de l'oxazolinone. L'intermédiaire hydroperoxyde peut aussi expliquer l'origine des produits secondaires acidiques **6***a* et **11***a*. La méthyl-2-oxazolin-5-one **14** ne réagit pas avec l'oxygène à la température ambiante: toutefois à 60° une transformation fut observée mais non la formation d'un imide.

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In the course of synthetic approaches to peptide alkaloid derivatives (1), a conjugate addition of a phenol to the isobutylidene-2-oxazolin-5-one (isobutylidene azlactone) **1** was attempted (2). When *N*-(*N'*-carbobenzoxyphenylalanyl)-tyramine and **1** were allowed to react in acetonitrile solution containing some triethylamine, instead of the desired addition product there was isolated a colorless solid, $C_{12}H_{13}NO_2$, m.p. 113°, which contained no feature of the protected phenylalanyltyramine group. It was established that the product, whose formula was that of the azlactone minus one carbon atom, arose from the azlactone when it was found that **1** alone in acetonitrile–triethylamine became bright yellow at room temperature and rapidly gave the same compound in up to 58% yield. The suspicion that oxygen was also involved was confirmed when the product was not formed in an attempted reaction in CH_3CN–Et_3N solution under a nitrogen atmosphere. Moreover, oxygen was presumably reacting with the anion **2** of the azlactone since no reaction occurred when an acetonitrile solution of **1** was exposed to oxygen in the absence of base. The choice of solvent was not critical since the same product was formed in acetone and dimethylformamide solutions.

The oxidation product absorbed 1 mol of hydrogen to form the dihydro derivative, m.p. 83°. Comparison of the n.m.r. spectra of these two compounds uniquely defined the dihydro derivative to be benzoyl isovaleryl imide **5**, and the oxidation product itself to be benzoyl β,β-dimethylacrylyl imide **4** with which structure the u.v. and i.r. spectra were in agreement. Final proof of identity was obtained by comparison with an authentic specimen of **4** prepared by reaction of the *N*-lithio salt of benzamide with β,β-dimethylacrylyl chloride.

The reaction probably occurs (Scheme 1) through electron transfer (3) from the resonance stabilized anion **2** of the oxazolinone to oxygen and either recombination of the resulting radical and radical anion, or else reaction of the radical with oxygen and **2**, to produce a peroxide which could have a number of formulations, **3***a*, *b*, or *c*.[3,4] Involvement of the

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[3]It is recognized that in principle oxygen could become attached at three other positions to produce hydroperoxides **i**, **ii**, and **iii** or their cyclic peroxide addition products, two of which can readily explain the carboxylic acid by-products. However, since a peroxide of type **3** most readily explains the formation of imide, and since the carboxylic

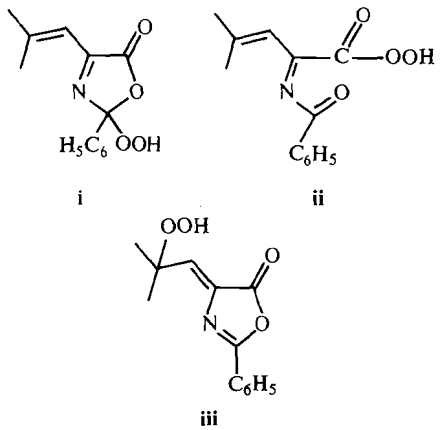
anion **2** is supported not only by the failure of **1** to react in the absence of base, but also by the ready exchange of the allylic methine hydrogen of **1** when D_2O was added to the CH_3CN–Et_3N solution in the absence of oxygen. The oxazolinone **1** also exchanges this tertiary hydrogen slowly at room temperature in acetone-d_6–Et_3N solution. Breakdown of the peroxide (Scheme 1) with loss of carbon dioxide would yield the imide **4** directly, and in fact carbon dioxide was isolated as $BaCO_3$ in a yield almost equal to that of the imide **4**.

A peroxide intermediate can also explain the formation of a major carboxylic acid by-product. The bicarbonate soluble portion of the oxygenation reaction was esterified with diazomethane, and the predominant one of seven compounds isolated by t.l.c. Since this product was clearly a dienoic ester from its u.v. absorption, the structure **6***b* follows and is in agreement with the n.m.r. spectrum. Hydrogenation of the ester gave racemic *N*-benzoylleucine methyl ester **7** whose i.r. and n.m.r. spectra were identical with those of authentic *N*-benzoyl-L-leucine methyl ester. The possible origin of the dienoic acid **6***a* by an elimination reaction of the peroxide[5] followed by acylimine ⇌ enamide tautomerism is depicted for **3***b* in Scheme 2.[5]

To test the generality of this new oxidation, two other oxazolinones were treated with oxygen in CH_3CN–Et_3N solution. The azlactone **8** from hippuric acid and phenylacetone also rapidly absorbed oxygen with the formation of the imide **10** in 43% yield (Scheme 3). In fact the uptake of oxygen was faster than with **1** as would be expected from the greater acidity of the methylene hydrogens in **8** which are both allylic and benzylic. The product was identical with an authentic specimen made by the reaction of the *N*-lithio salt of benzamide and the acid chloride of (*E*)-α-methylcinnamoyl chloride. Also in this oxygenation there was a carboxylic acid by-product formed in 36% yield. The n.m.r. and u.v. spectra identified the methyl ester of the acid to be methyl 3-benzylidene-2-oxobutyrate **11***b*. Oxidative degradation of the α-keto acid **11***a* gave (*E*)-α-methylcinnamic acid. The α-keto acid **11***a* could also have arisen from the hydroperoxide, *e.g.* **9**, which could not in this case give a dienoic acid of the **6***a* type because of the absence of a δ-hydrogen atom. However, the hydroperoxide (*e.g.* **9**) could undergo ring opening[5] and hydrolysis of the benzoylimine **9** → **12** → **11***a*.

The final azlactone tested was the 4-isobutylidene-2-methyl derivative **14**. At room temperature under the same conditions resulting in rapid oxygen absorption by both 2-phenyloxazolinones **1** and **8**, the 2-methyl compound did not react. At 60° over a period of 3 days the azlactone was consumed but no imide **15** was produced. Apparently additional stabilization such as provided by a 2-phenyl substituent is required for facile oxygenation, and the reaction may not be as general as first thought.[6]

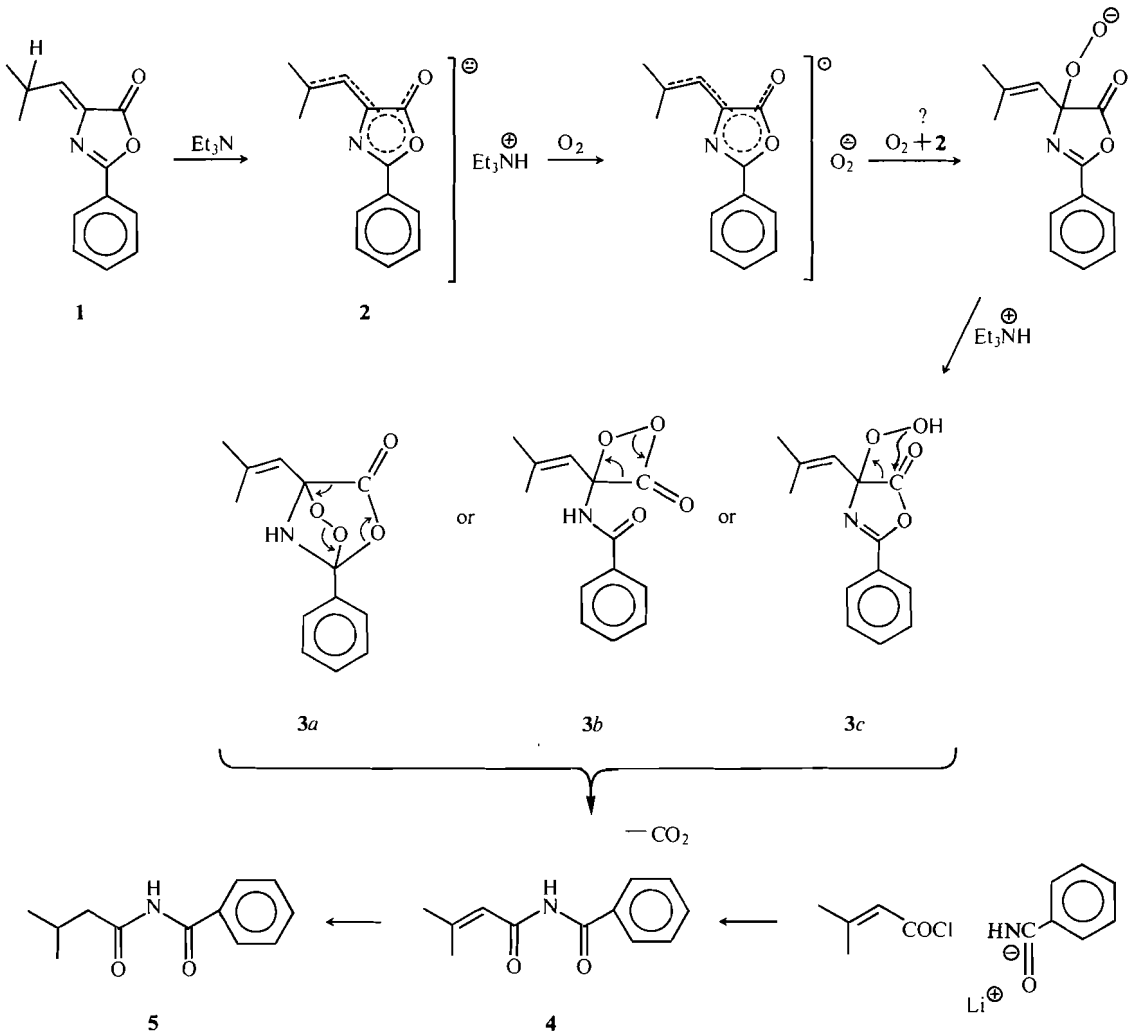
acid by-products can be rationalized on the basis of **3***a*–*c*, there is no need to invoke the alternative peroxide formulations in the absence of evidence for them.



[4]The oxygenation of Schiff base anions (4*a*) and 3,7-dihydroimidazo[1,2-*a*]pyrazin-3-ones (4*b*) follows a similar path. In these cases the breakdown of cyclic four-membered peroxides often radiates visible light, but the absence of observable visible *luminescence* in the present oxygenations (the reactions did become bright yellow) does not necessarily exclude a structure such as **3***b*.

[5]The peracid so formed would break down to the carboxylic acid either by exchange or oxygen loss. Although the formation of the carboxylic acid by-products is shown for one of the possible peroxide structures, similar mechanisms can be written for the other peroxide formulations, and no preference is intended. Some of the other compounds present in the acid fraction may result from attack of the peracid on double bonds.

[6]The apparent failure to form any hydroperoxide which would lead to **15** is probably not due to the acidity of the 2-methyl group. Although in 2-alkyloxazolin-5-ones the α-hydrogens of the 2-alkyl group are acidic enough to be removed to some extent by triethylamine, the pK_a's of the



SCHEME 1

Experimental

General

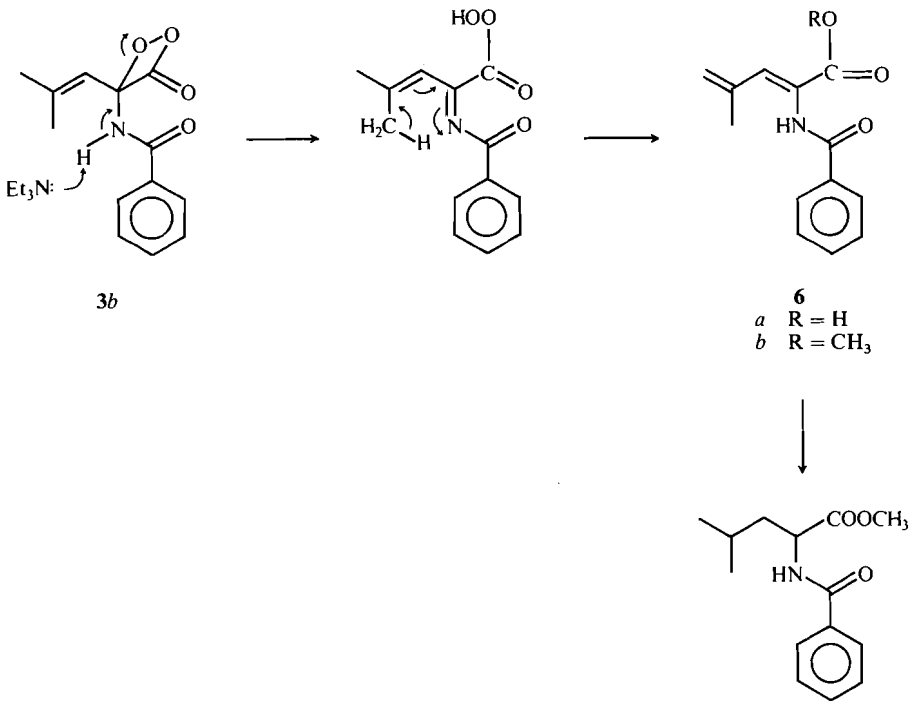
Melting points were determined on a Reichert–Kofler microscope hot stage and are corrected.

I.r. spectra were recorded on a Beckman IR-10 instrument with chloroform solutions. N.m.r. spectra were recorded on Varian A-60 and T-60 spectrometers with deuteriochloroform solutions. Peak positions are given in p.p.m. from internal tetramethylsilane = 0(δ); s = singlet, d = doublet, m = multiplet, b = broad. Aromatic peaks are not reported for most spectra. U.v. spectra were recorded on a Cary 14 spectrometer with methanol solutions.

Silica gel GF_{254} (Merck, Germany) was used for thin and thick layer (20 g/20 × 20 cm plate) chromatography. Thin layer plates were visualized by u.v. and/or by charring (H_2SO_4:HNO_3, 4:1). B.D.H. silica gel was used for column chromatography.

Organic solutions from work-up of reactions were washed to neutrality with aqueous $NaHCO_3$ and water, dried over anhydrous $MgSO_4$ and then evaporated to dryness under reduced pressure on a rotary evaporator. Petroleum ether refers to the fraction boiling at 60–80°.

allylic and 2-methyl hydrogens of **14** are probably close enough to allow formation of both monoanions in which case the allylic anion could lead to some imide **15**. However, the ability of oxygen to abstract an electron from the allylic anion will depend on the energy difference between the anion and its corresponding radical. Provided that phenyl stabilizes the radical more than the anion, a 2-phenyl group may serve to lower the activation energy enough for electron abstraction to occur, while the effect of the 2-alkyl group may not be sufficient to make electron abstraction by oxygen facile.



SCHEME 2

(Z?)-4-Isobutylidene-2-phenyl-2-oxazolin-5-one (1)

The procedure of Galantay *et al.* (5) was used. A mixture of hippuric acid (17.9 g, 0.10 mol), $Pb(OAc)_2 \cdot 3H_2O$ (16.0 g, 0.04 mol), acetic anhydride (30 g, 0.30 mol), isobutyraldehyde (7.7 g, 0.12 mol), and tetrahydrofuran (230 ml) was stirred magnetically at reflux temperature for 5 h. After cooling, the mixture was filtered and concentrated under vacuum. The residue was diluted with 350 ml of benzene and treated with an excess of H_2S. The filtered solution was evaporated to leave an orange oil that crystallized at room temperature. Recrystallization from petroleum ether to constant melting point gave 5.75 (26%) of pure oxazolinone **1**, m.p. 86–87° (lit. (6) 87°); ν_{max} 1800 (C=O) and 1675 cm^{-1} (C=N); δ 1.19 (Me_2CH, d, $J = 7$ Hz), 3.30 (Me_2CH, m), and 6.51 p.p.m. (=CH—, d, $J = 10$ Hz).

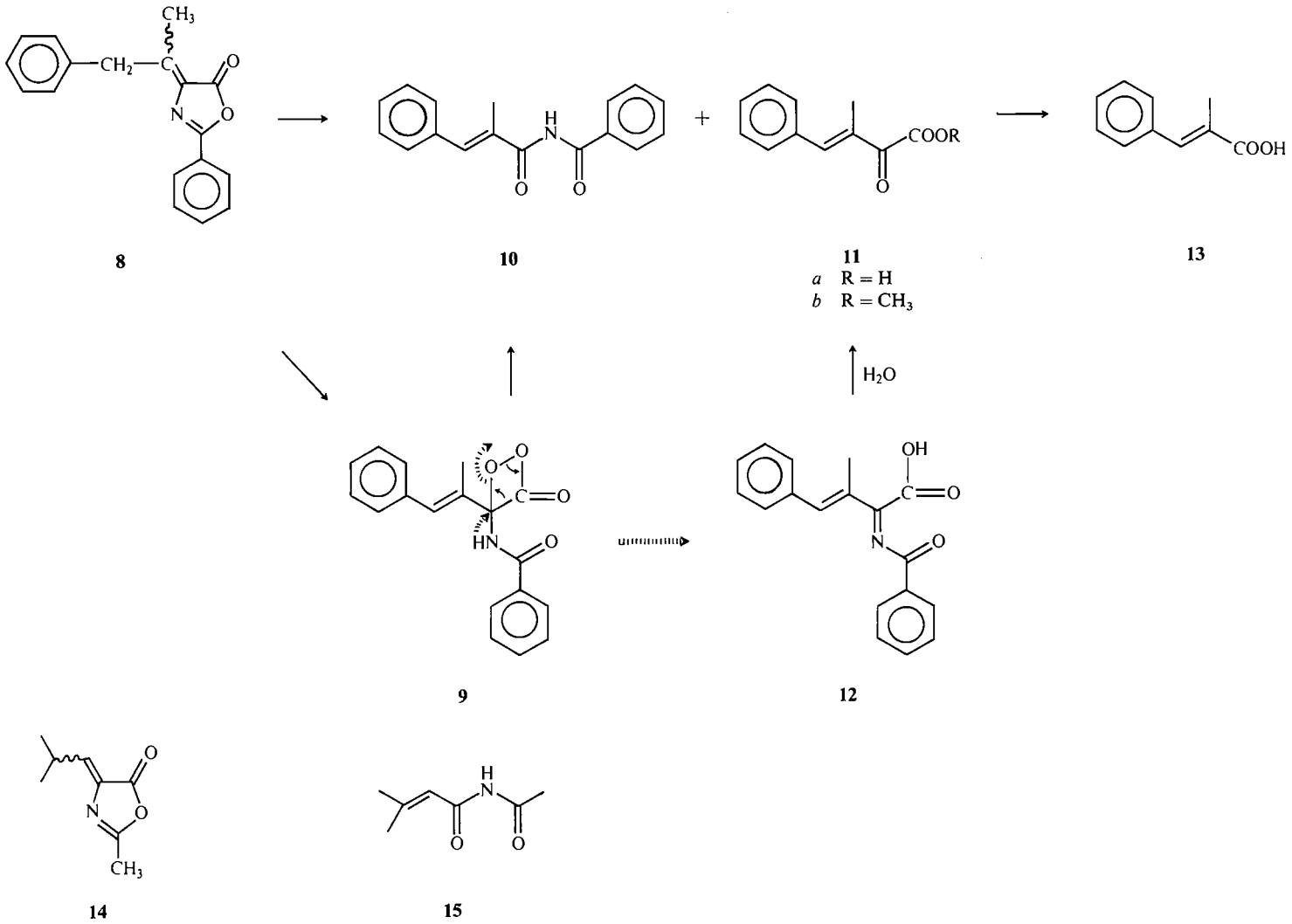
(E) or *(Z)-4-(2'-Phenylisopropylidene)-2-phenyl-2-oxazolin-5-one (8)*

A mixture of hippuric acid (18.6 g, 0.10 mol), $Pb(OAc)_2 \cdot 3H_2O$ (16 g, 0.04 mol), acetic anhydride (40 g, 0.40 mol), phenylacetone (16.6 g, 0.12 mol), and tetrahydrofuran (240 ml) was stirred magnetically during 8 h at reflux temperature and then left overnight. The ether soluble material after concentration under vacuum was distilled under reduced pressure to allow the recovery of 11.7 g (70%) of phenylacetone. Column chromatography of the distillation residue on silica gel gave 1.4 g (14%) of crude oxazolone **8** (mixture of stereoisomers) in the petroleum ether:ether (97:3) eluate. Recrystallization from petroleum ether afforded 536 mg (5%) of silky needles of pure (*E*)- or (*Z*)-oxazolinone **8**, m.p. 88–89°, ν_{max} 1790, 1760 shoulder (C=O), and 1665 cm^{-1} (C=N); δ 2.28 (CH_3, s) and 4.00 ($—CH_2—$, s).

Anal. Calcd. for $C_{18}H_{15}NO_2$ (277.3): C, 77.96; H, 5.45. Found: C, 77.97; H, 5.47.

(Z?)-4-Isobutylidene-2-methyl-2-oxazolin-5-one (14)

The experimental procedure followed was patterned closely on that of Herbst and Shemin (7). A mixture of *N*-acetylglycine (14.6 g, 0.12 mol), anhydrous NaOAc (7.5 g, 0.09 mol), isobutyraldehyde (13.0 g, 0.18 mol), and acetic anhydride (31 g, 0.45 mol) was stirred magnetically at 105° for 2 h. The mixture was stirred at room temperature for 2 h more, then diluted with water and extracted with ether. After washing and drying, the combined ether layers were concentrated under vacuum to leave 20.3 g of reddish brown oil (acetic anhydride still present). Fractional distillation through an 8-cm Vigreux column under reduced pressure gave the following four fractions: (*i*) b.p. 30–47° (0.9 Torr), 3.8 g, Ac_2O and *i*-$PrCH(OAc)_2$; (*ii*) b.p. 47–48° (0.9 Torr), 3.8 g, *i*-$PrCH(OAc)_2$ (mostly) and **14**; (*iii*) b.p. 50–75° (0.9 Torr), 3.7 g, mostly **14**; and (*iv*) b.p. 78–80° (0.9 Torr), 3.8 g, unknown mixture. The oxazolinone **14** was not readily purified in quantity and decomposed on standing in a sealed tube. However, successive preparative layer chromatography in petroleum ether:ether (85:15) afforded enough **14** (mixture of *cis* and *trans* isomers) for spectroscopic characterization, b.p. ~48° (0.8 Torr) (lit.



SCHEME 3

(8) 68–69° (0.15 Torr)), ν_{max} 1800 (C=O) and 1675 cm^{-1} (C=N); δ 1.09 and 1.11 (Me_2CH, d, $J \sim 6$ Hz), 2.23 and 2.28 (Me—C=, s), 2.9–3.8 (Me_2CH), b.m.), and 6.32 and 6.40 p.p.m. (—CH=, d, $J \sim 10$ Hz); *m/e* 153 (molecular ion).

Oxygenation of Oxazolinone ***1***

Oxygen was bubbled through a solution of oxazolinone **1** (538 mg, 2.5 mmol) and triethylamine (513 mg, 6.3 mmol) in acetonitrile (30 ml) at room temperature for 4 h at which point t.l.c. showed the absence of **1**. The yellow reaction mixture was evaporated to dryness to leave 683 mg of brownish solid whose t.l.c. (petroleum ether:ether, 70:30) gave a spot corresponding to the imide **4** and a spot near the application point. The crude product was partitioned between ether and 10% aqueous $NaHCO_3$. From the ether layer was recovered 295 mg (58%) of brownish solid which after recrystallization from cyclohexane gave colorless flat prisms of ***N*-benzoyl-β,β-dimethylacrylamide (4)**, m.p. 112.5–113°, λ_{max} 246 nm (36 000), found to be identical with the authentic sample whose preparation is described below.

Anal. Calcd. for $C_{12}H_{13}NO_2$ (203.2): C, 70.92; H, 6.45; N, 6.89; O, 15.74. Found: C, 70.82; H, 6.37; N, 6.88; O, 15.86.

Acidification of the $NaHCO_3$ solutions and extraction with ether gave 230 mg of yellowish solid amorphous carboxylic acids which were esterified with ethereal diazomethane. The 270 mg of methyl esters gave seven spots on t.l.c. (petroleum ether:ether, 70:30). The major compound (R_f 0.13) was separated by preparative t.l.c. in the same solvent system, and after two recrystallizations from ether–petroleum ether there was obtained 37 mg (6%) of colorless crystals of **2-benzamido-4-methyl-2,4-pentadienoic acid methyl ester (6*b*)**, m.p. 123–124°; λ_{max} 235 (10 400) and 260 nm (11 500); ν_{max} 3400 (NH), 1710 (ester C=O), and 1675 cm^{-1} (amide C=O; δ 1.97 (CH_3, s), 3.80 (CH_3O, s), 5.30 (=CH_2, b.s), and 7.10 p.p.m. (=CH—, s) (NH not apparent).

The ratio of the imide **4** to the acid **6*a*** in the crude oxygenation mixture was about 3:1 from n.m.r. integration.

In an experiment to measure the volume of oxygen absorbed, a solution of **1** (107 mg, 0.50 mmol) and triethylamine (102 mg, 1.0 mmol) in 6 ml of acetonitrile gently shaken under an atmosphere of oxygen at 25° absorbed 11.8 ml (theor. 12.5 ml) in 27 h at 745 Torr. Most of this absorption occurred during the first 9 h. From the 127 mg of crude oxygenation product there was obtained 50 mg (50%) of **imide 4** by preparative layer chromatography.

Trapping of the Carbon Atom Lost from ***1***

Oxygen freed from carbon dioxide by passage through Ascarite was bubbled through a solution of oxazolinone **1** (215 mg, 1.00 mmol) and triethylamine (205 mg, 2.5 mmol) in acetonitrile (12 ml), and the exiting gas was passed through a clear saturated aqueous solution of $Ba(OH)_2$. At the end of the reaction 93 mg (47%) of precipitated $BaCO_3$ was collected by filtration. Preparative t.l.c. (petroleum ether:ether, 70:30) of the crude product and recrystallization from cyclohexane gave 93 mg (45%) of **imide 4**.

Hydrogenation of Oxygenation Product from ***1***

A solution of 36 mg of the oxygenation product from **1** in 5 ml of ethanol absorbed 4.28 ml (1.0 mol) of hydrogen in the presence of 8 mg of 10% Pd/C catalyst at 29° and 743 Torr. Filtration, evaporation, and recrystallization from ether–petroleum ether gave colorless crystals of **benzoyl isovaleryl imide 5**, m.p. 82–83°; ν_{max} 3400 (NH), 1715 (imide C=O), and 1690 cm^{-1} (imide C=O); δ 1.03 (Me_2CH, d, $J \sim 6$ Hz), 1.8–2.7 (Me_2CH, m), 2.92 (CH—CH_2, d, $J \sim 6$ Hz), and 9.07 p.p.m. (NH, b.s.).

Anal. Calcd. for $C_{12}H_{15}NO_2$ (205.3): C, 70.22; H, 7.37; N, 6.82. Found: C, 69.93; H, 7.15; N, 6.80.

Hydrogenation of Methyl Ester ***6b***

A solution of ester **6*b*** (37 mg) in methanol (6 ml) was shaken for 1.5 h under a hydrogen atmosphere in the presence of 5% Pd/C (10 mg). Filtration and concentration left 29 mg (78%) of **(±)-*N*-benzoylleucine methyl ester (7)**, m.p. 94–95° (lit. (9) 95–95.5°) after recrystallization from petroleum ether, whose i.r. and n.m.r. spectra were identical with an authentic specimen of *N*-benzoyl-L-leucine methyl ester, m.p. 102–102.5° (lit. (10) 102°); ν_{max} 3440 (NH), 1740 (ester C=O), and 1660 cm^{-1} (amide C=O); δ 0.99 (Me_2CH, d, $J \sim 5$ Hz), 1.5–2.1 (3H, m), 3.78 (CH_3O, s), 4.93 (O=C—N—CH—C=O, m) and 6.66 p.p.m. (NH, b.d., $J \sim 8$ Hz).

*N-Benzoyl-β,β-dimethylacrylamide (****4****)*

β,β-Dimethylacrylic acid, prepared from mesityl oxide as reported by Smith *et al.* (11), was converted into the acyl chloride by treatment with PCl_5 according to the procedure of Feuer and Pier (12).

A solution of benzamide (500 mg, 4.1 mmol) in tetrahydrofuran (20 ml) was placed in a septum-sealed flask into which was injected a solution of *n*-butyllithium in hexane (2 ml, 4 mmol). The precipitated *N*-lithio salt was washed with three portions (10 ml) of tetrahydrofuran and then suspended in the same solvent (10 ml). A solution of β,β-dimethylacrylyl chloride (450 mg, 3.8 mmol) in tetrahydrofuran (4 ml) was injected into the *N*-lithio salt suspension. The reaction mixture was diluted with ether, washed with saturated aqueous NaCl, dried, and evaporated at reduced pressure to leave 700 mg of yellow solid. Recrystallization from cyclohexane gave 117 mg (15%) of colorless crystals, m.p. 110–111.5°, ν_{max} 3430 (NH), 1705 (imide C=O), 1675 (imide C=O), and 1630 cm^{-1} (C=C); δ 2.02 (CH_3, d, $J \sim 1$ Hz), 2.22 (CH_3, b.s.), 6.97 (C=CH, b.s.), and 9.53 (NH, b.m.).

Oxygenation of Oxazolinone ***8***

Oxygen was bubbled through a mixture of **8** (348 mg, 1.26 mmol) and triethylamine (260 mg, 2.5 mmol) in acetonitrile (16 ml) during 0.5 h at which point t.l.c. showed the absence of starting material **8**. The reaction mixture was concentrated under reduced pressure to leave 540 mg of dark yellow oil whose t.l.c. (petroleum ether:ether, 70:30) gave two spots, one corresponding to the imide **10** and the other at the point of application. The product was partitioned between ether containing a little chloroform and 10% aqueous $NaHCO_3$ solution. Evaporation of the dried ethereal layer left 148 mg (43%) of crude yellow imide. Preparative layer chromatography and recrystallization from petroleum ether–chloroform gave 60 mg of pure **(*E*)-*N*-benzoyl-2-methylcinnamamide (10)**, identical (mixed m.p., t.l.c., i.r., and n.m.r.) with the authentic sample prepared as described below.

Acidification of the $NaHCO_3$ solution and ether extraction gave 239 mg of greenish oily carboxylic acid mixture. Esterification with ethereal diazomethane and preparative

t.l.c. of the methyl esters (petroleum ether–ether, 80:20) yielded 97 mg (36%) of yellow liquid **methyl (*E*)-3-benzylidene-2-oxobutyrate (11*b*)**, λ_{max} 222 (4200) and 292 nm (19 400); ν_{max} 1735 (ester C=O), 1665 (ketone C=O), and 1615 cm^{-1} (C=C); δ 2.13 (CH_3, b.s.), 3.97 (CH_3O, s), 7.28 (=CH—, b.s.), and 7.43 p.p.m. (5 phenyl H, s). Some **benzamide** was also isolated from the crude methyl ester.

In another oxygenation the crude acidic fraction (263 mg) was esterified with diazomethane and the crude methyl ester mixture was recrystallized from chloroform–petroleum ether to give 25 mg of **benzamide**, m.p. 125–126°, identical (i.r. and n.m.r.) with an authentic specimen.

Trapping of the Carbon Atom Lost from 8

With the same procedure for trapping CO_2 used for oxazolinone **1**, the oxygenation of a solution of oxazolinone **8** (277 mg, 1.00 mmol) and triethylamine (205 mg, 2.0 mmol) in acetonitrile (12 ml) gave 47 mg (24%) of $BaCO_3$ and 80 mg (30%) of **imide 10**.

(E)-N-Benzoyl-2-methylcinnamamide (10)

The procedure of Perkin (13) was used to prepare (*E*)-2-methylcinnamic acid from benzaldehyde and propionic acid. The acid was converted into its acid chloride by treatment with PCl_5 according to the procedure of Feuer and Pier (12).

Into a suspension of the *N*-lithio salt of benzamide, prepared from benzamide (500 mg, 4.1 mmol) in the same manner described for the preparation of **4**, in tetrahydrofuran (4 ml) was injected a solution of (*E*)-2-methylcinnamoyl chloride (508 mg, 2.8 mmol). The reaction mixture was diluted with ether, washed with three portions of water, dried, and evaporated at reduced pressure to leave an orange residue. Recrystallization of the ether soluble material from chloroform–ether yielded 28 mg (4%) of long feathery needles, m.p. 128.5–129.5°; ν_{max} 3390 (NH), 1740 (imide C=O), 1675 (imide C=O), and 1625 cm^{-1} (C=C); δ 2.14 (CH_3, d, $J \sim 1.5$ Hz) and 9.20 (NH, b.s.) (the olefinic H was hidden in the aromatic proton absorption).

Anal. Calcd. for $C_{17}H_{15}NO_2$ (265.7): C, 76.96; H, 5.70; N, 5.28. Found: C, 76.45; H, 5.69; N, 5.31.

Oxidative Cleavage of α-Keto Acid 11a

In a procedure similar to the one outlined by Stecher and Gelblum (14), crude α-keto acid **11*a*** (130 mg, 0.68 mmol) was dissolved in dioxane (6 ml) and treated at room temperature alternately with small portions (magnetic bar stirring) of 1% aqueous Na_2CO_3 solution and a total of 8 ml of 30% aqueous H_2O_2. Care was taken to maintain a p*H* of ~8 in the reaction mixture which was stirred for 4 h. Acidification and ether extraction yielded an oily residue after removal of ether. The residue was further purified by solution in petroleum ether. Evaporation of the petroleum ether soluble portion left 80 mg of yellowish oil whose t.l.c. (petroleum ether:ether:acetic acid, 86:10:4) revealed the presence of *(E)*-α-methylcinnamic acid. Preparative t.l.c. in the same solvent system yielded 31 mg (28%) of **(*E*)-α-methylcinnamic acid**, m.p. 79.5–80.5° (lit. (13) 81°) after recrystallization from petroleum ether; λ_{max} 207 (14 300) and 267 nm (17 400); ν_{max} 1685 (C=O) and 1630 cm^{-1} (conj. C=C); δ 2.12 (CH_3, d, $J \sim 1.5$ Hz), 7.30 (5 phenyl H, s), 7.73 (=CH—, b.s.), and 11.63 (—COOH, b.s.).

Oxygenation of Oxazolinone 14

When a solution of oxazolinone **14** (153 mg, contaminated with *i*-PrCH$(OAc)_2$) and triethylamine (225 mg) in acetonitrile (25 ml) was shaken under an oxygen atmosphere in a mercury sealed burette system for 3 h no uptake of oxygen occurred. However, after oxygen was bubbled through the same solution at 60° with stirring for 3 days, the reaction mixture no longer contained **13**. T.l.c. comparison of the crude product with authentic ***N*-acetyl-β,β-dimethylacrylamide (15)** prepared as described below, showed the absence of this imide. When this oxygenation was carried out at room temperature to check the evolution of any CO_2 in an experiment similar to the ones with **4** and **8**, no $BaCO_3$ precipitated.

N-Acetyl-β,β-dimethylacrylamide (15)

A mixture of sublimed acetamide (540 mg, 9.1 mmol), sodium hydride (430 mg, 56% oil suspension, ~9 mmol), and dioxane (20 ml) was stirred magnetically for 30 min and then treated with a solution of β,β-dimethylacrylyl chloride (1.18 g, 10 mmol) in dioxane (10 ml). The resulting mixture was stirred magnetically at reflux temperature for 30 min. The cooled reaction mixture was diluted with chloroform, filtered, and evaporated to leave 1.07 g of brownish solid. Several recrystallizations from ether–petroleum ether afforded 173 mg (13%) of white needles, m.p. 92–93°; ν_{max} 3400 (NH), 1720 (imide C=O), 1680 (imide C=O), and 1640 cm^{-1} (C=C); δ 1.95 (CH_3, d, $J \sim 1.5$ Hz), 2.21 (CH_3, d, $J \sim 1.5$ Hz), 2.41 (CH_3, s), 6.10 (=CH—, b.s.), and 9.43 p.p.m. (NH, b.s.).

Anal. Calcd. for $C_7H_{11}NO_2$ (141.2): C, 59.56; H, 7.85; N, 9.92. Found: C, 59.83; H, 7.87; N, 10.16.

Hydrogen Exchange of Oxazolinone 1

(a) In CD_3CN–D_2O

To a solution of **1** in CD_3CN used for recording of the n.m.r. spectrum was added a drop of Et_3N and a drop of D_2O. The 1-H multiplet near δ 3.3 decreased rapidly and a sharp singlet from DOH appeared at δ 3.6 before much of the **1** had been changed by the D_2O.

(b) In Acetone-d_6

A solution of 50 mg of **1** in 0.25 ml of acetone-d_6 gave an n.m.r. spectrum unchanged by time. One drop of Et_3N was added (solution became yellow) and the n.m.r. spectrum was recorded periodically during 2 days. The methine hydrogen gradually disappeared, and the expected simplification of the methyl (d → b.s.) and olefinic (d → b.s.) signals slowly occurred at room temperature.

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