2-Butenoic Acid (14), Alkanes, and $AlCl_3$. The acid 14 (20 mmol), *n*-hexane or ligroin (25 ml), and aluminum chloride (40 mmol) were refluxed during 4 hr to yield only a small transformation into butanoic acid (8). Most of the starting material did not react.

Cinnamic Acid (7), Ligroin, and $AlCl_3$. The acid 7 (20 mmol), ligroin (25 ml), and aluminum chloride (40 mmol) were refluxed during 4 hr to yield 1.99 g of acid material from which crystals of *p*-phenylenedipropanoic acid (12) separated on cooling. The recrystallized (water) solid showed mp 230° (lit. mp 230°,[6] 224° [7]); ir (KBr) 3030 m, 2924 m, 2858 m, 2728 w, 2649 w, 1703 s, 1520 w, 1434 s, 1405 m, 1362 w, 1312 m, 1275 m, 1222 s, 1189 m, 1133 w, 945 w, and 830 cm^{-1} m. Its methyl ester **15**, mp 120° (methanol) (lit.[7] mp 117–118°), was obtained by treatment with diazomethane in ether: ir (KBr) 3024 w, 2929 m, 2894 w, 2838 w, 1728 s, 1520 m, 1434 s, 1368 s, 1303 s, 1272 m, 1193 s, 1180 s, 1141 s, 1105 w, 1050 m, 1000 w, 976 m, 900 w, 838 s, and 793 cm^{-1} w; mass spectrum (80 eV) *m/e* (rel abundance) 117 (100), 91 (28), 130 (28), 190 (28), 131 (19), 115 (19), 77 (13), 176 (12), 118 (12), 59 (11), 250 (M^+, 11), and 39 (9); metastable ions *m/e* 144.5, 113.5, and 89; doubly charged ions (at half integer masses) *m/e* 95.5[8] and 88.5; ^1H NMR (60 MHz, $CDCl_3$, TMS) δ 2.74 (AA'BB' multiplet, 8 H), 3.67 (singlet, 6 H), and 7.13 ppm (singlet, 4 H). GLC quantitative analysis showed **12** to be present in 11% yield and **10** in 19% yield together with other unidentified materials. None of the starting acid **7** survived the treatment.

Registry No.—**1**, 504-85-8; **5**, 10321-71-8; **6**, 541-47-9; **7**, 621-82-9; **12**, 4251-21-2; **14**, 3724-65-0; **15**, 5312-03-8; $AlCl_3$, 7446-70-0; hexane, 110-54-3.

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(8) The peaks at *m/e* 95 and 96 are about of equal intensity and one-fourth as intense as *m/e* 95.5, after background subtraction.

A Novel Cyclization Catalyzed By Magnesium Methyl Carbonate

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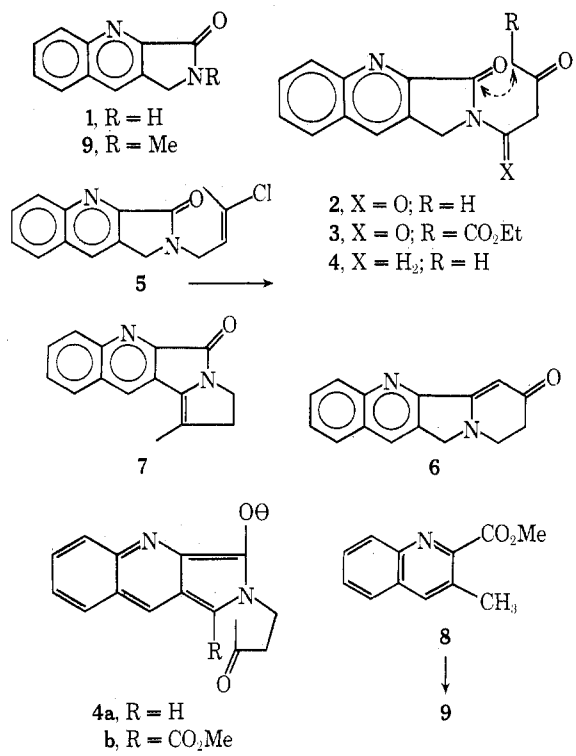
The synthesis of the tricyclic lactam **1** in 75% yield from 2-oxobutyric acid and *o*-aminobenzaldehyde has been described.[2,3] Its ready availability made it an attractive substrate for studying lactam annelation reactions with a view toward the syntheses of camptothecin and analog structures.[4,5] The strategy was based on acylation of the lactam nitrogen, followed by cyclization of a nucleophilic center in the side chain with the lactam carbonyl group.

Our original efforts were addressed to the acetoacetyl derivative **2** (X = O; R = H). This compound, mp 242–245°, was prepared (55%) by the reaction of **1** with *n*-butyllithium followed by diketene. In our hands, compound **2** could not be induced to undergo cyclodehydration in the sense indicated, under a variety of catalytic situations. Under mild conditions (e.g., boron trifluoride etherate or sodium acetate–acetic anhydride), **2** was recovered in high yield. Under more severe conditions (sodium ethoxide or potassium *tert*-butoxide) deacylation, leading to a high recovery of **1**, resulted. Parallel results have been reported by Sugasawa.[6] The eventual solution, which was discovered by the Japanese workers,[6] involved the use of the 3-ketoglutaryl system, **3** (X = O; R = CO_2Et). The added acidity conferred by the β-keto ester linkage allowed for smooth dehydration.



In the light of the serious competing reaction of deacylation in the case of **2**, we investigated the preparation and reactions of the β-acetoethyl derivative **4** (X = H_2; R = H). Lactam **1** was alkylated with 1,3-dichloro-2-butene to give **5**, mp 202–203°, in 57% yield. The chloroolefin linkage was smoothly cleaved (86%) with concentrated H_2SO_4 to give **4**, mp 184–185°.

Treatment of **4** with triethylamine resulted in high recovery of starting material. However, reaction of **4** with pyrrolidine gave (71%) lactam **1**. Presumably this transformation occurs by reversible formation of the trisubstituted enamine which suffers retro-Michael type elimination of **1**. Substantial β-elimination was also observed in the reaction of **4** with potassium *tert*-butoxide.

Treatment of **4** with sodium methoxide–methanol gave, in 2% yield, a yellow, crystalline product, mp 283–284°, whose mass spectrum and combustion analysis define it to be a dehydration product. The NMR spectrum of this compound establishes it to be pyrrolizidinone derivative **7** rather than the desired (and expected) dehydration product, **6**. Clearly, **7** arises by deprotonation of a benzylic carbon followed by internal aldolization. It will be seen that this deprotonation produces an extensively delocalized anion, one resonance form of which is drawn as **4a**.

In an effort to influence the course of cyclodehydration in the direction of compound **6**, lactam **4** was treated with magnesium methyl carbonate (MMC) in methanol.[7-9] The high tendency of MMC to effect specific carboxylation of the methyl group of methyl alkyl ketones is well known.[10] The hope was that such a carboxylation would increase the likelihood of Knoevenagel-type attack toward the carbonyl group of the lactam function.

We were thus surprised to find that reaction of **4** with MMC in methanol turned out to be the best way we have yet devised (65–75%) to effect its transformation to **7**. Initially it was assumed that carboxylation would occur at the

methyl group. In an effort to produce compound **6** the product of the MMC reaction was heated with potassium *tert*-butoxide. Instead compound **7** was obtained in 67% yield. Subsequently it was shown that the base treatment is not necessary, i.e. that compound **7** was produced by the MMC treatment alone.

That this reaction is not due to a special catalytic effect of magnesium methoxide was shown by treatment of **4** with methanolic magnesium methoxide under reflux. These conditions gave largely (75%) recovered **4** and some retro-Michael product, **1**.

The simplest interpretation of the remarkable effect of the MMC is that carboxylation occurs at the benzylic position, thus facilitating formation of deprotonated system **4b**. This is followed by aldolization, decarboxylation, and dehydration.

A crucial element in this formulation is the feasibility of carboxylation at the benzylic center α to the lactam nitrogen. A test of this proposal involved attempted carboxylation of the *N*-methyl lactam, **9**. This compound, mp 260–262°, was obtained by bromination (NBS–CCl_4) of 2-carbomethoxy-3-methylquinoline (**8**)[3] followed by reaction of the intermediate 3-bromomethyl compound with methanolic methylamine.

Compound **9** was subjected to the action of MMC in methanol under reflux for 48 hr. Upon acidification, it was recovered to the extent of 98%. While we cannot rule out the possibility of carboxylation to a very slight extent, or the occurrence of decarboxylation under our conditions of work-up, no positive evidence favoring carboxylation of the pyrrolo system under the influence of MMC could be obtained. Accordingly, the mechanism for the MMC-induced transformation of **2** → **3** is, at this time, not understood. Nevertheless, this work suggests that MMC may be useful in catalyzing a greater variety of processes than has been supposed.

Experimental Section[11]

Acetoacetylation of Lactam 1. Formation of Imide 2. To a suspension of quinoline lactam **1** (1.302 g, 7.1 mmol) in 50 ml of dry monoglyme was added *n*-butyllithium (8 mmol) in hexane under nitrogen. After 30 min, a solution of diketene (0.660 g, 7.9 mmol) in 20 ml of dry monoglyme was added dropwise. The reaction mixture was heated under reflux for 10 hr.[12] The solution was made weakly acidic with dilute HCl and reduced in volume to 10 ml. A solid which separated was filtered and recrystallized from chloroform to give imide **2**, mp 242–245°.

Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 66.95; H, 4.55; N, 10.35.

λ_{max} (Nujol) 5.73, 5.82, and 5.90 μ; δ (CF_3CO_2H) 2.57 (s, 3), 4.56 (s, 2), 5.46 (s, 2), 8–9 (m, 4); 9.84 (s, 1); MS *m/e* 268 (parent), 184 (base peak).

Alkylation of Lactam 1 with 1,3-Dichloro-2-butene. Formation of 5. Lactam **1** (2.25 g, 0.012 mol) was suspended in 100 ml of dry DMF. Sodium hydride (0.61 g of 57% oil suspension, or 0.015 mol) was added and the mixture was heated at 35° for 23 hr. After cooling to room temperature, freshly distilled 1,3-dichloro-2-butene (4.10 g, 0.032 mol) was added, dropwise, over a 15-min period. The mixture was heated at 50–60° for 4 hr. Water (50 ml) was added, the solution was extracted with methylene chloride, and the organic phase was dried over $MgSO_4$. The volatiles were evaporated at the water pump and the residue was recrystallized from THF to afford 1.89 g (57%) of **5**, mp 202–203°.

Anal. Calcd for $C_{15}H_{13}N_2OCl$: C, 66.06; H, 4.80; N, 10.27. Found: C, 66.26; H, 4.66; N, 10.35.

λ_{max} (Nujol) 5.93, 6.00 μ; δ ($CDCl_3$) 2.16 (s, 3), 4.3–4.7 (m, 4), 5.6–5.8 (m, 1), 7.3–8.5 (m, 5); MS *m/e* 272 (parent), 184 (base peak).

Hydrolysis of 5. Formation of Acetoethylated Lactam 4. A solution of compound **5** (2.48 g, 9.1 mmol) in 20 ml of concentrated H_2SO_4 was kept at 0° for 3.5 hr. After dilution with 10 ml of water the system was cautiously neutralized with aqueous sodium hydroxide and extracted with methylene chloride. The organic layer was dried over $MgSO_4$ and the volatiles were evaporated at the water pump. The solid residue was recrystallized from THF to give 1.96 g (86%) of **4**, mp 184–185°.

Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 71.02; H, 5.64; N, 10.91.

λ_{max} ($CHCl_3$) 5.88 μ; λ_{max} (EtOH) 305 mμ (ϵ 9600), 317 sh, 328 sh; δ ($CDCl_3$) 2.2–3.0 (m, containing s at 2.17, 5), 3.9 (t, 2), 4.6 (s, 2), 7.3–8.6 (m, 5).

Cyclization of Keto Lactam 4 with Magnesium Methyl Carbonate. Formation of 7. A. With Added Base. A solution of keto lactam **4** (1.18 g, 4.7 mmol) was treated with a 16-fold excess of methanolic MMC[13] (based on 0.75 mol of magnesium). After 65 hr, 12 ml of a solution of potassium *tert*-butoxide–*tert*-butyl alcohol (0.4 *M*) was added. Refluxing was continued for an additional 54 hr. The reaction mixture was poured into 100 ml of 15% HCl and stirred for 30 min. The aqueous solution was made weakly basic with aqueous sodium bicarbonate and extracted with methylene chloride. Evaporation of the volatiles at the water pump left a residue which upon recrystallization from chloroform gave 73.4 mg (71%) of **7**, mp 280–284°.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.11; H, 5.11; N, 11.63.

λ_{max} (Nujol) 5.82, 5.92, and 5.95 μ; δ (CF_3CO_2H) 2.57 (s, 3), 3.5 (s, 2), 4.35 (s, 2), 8–10 (m, 5, containing s at 9.6); MS *m/e* 236 (parent).

B. Without Added Base. The keto lactam (200 mg, 0.78 mmol) was added to 11.2 mmol of MMC[13] in 25 ml of methanol. The solution was heated under reflux for 48 hr. An aliquot[14] of 10 ml was withdrawn and added to 5 ml of saturated methanolic HCl. This was added to 25 ml of water and extracted with 50 ml of methylene chloride. Evaporation of the volatiles left a residue of 71 mg of a yellow solid (crude compound **7**). Another aliquot[15] of 8 ml was withdrawn and added to 5 ml of aqueous HCl. Extraction with methylene chloride and evaporation left 61 mg of a yellow solid (crude compound **7**). Recrystallization of the combined solids gave compound **7**, mp 278–282°, in 71% yield.

Preparation of 2-Methyl-3-oxopyrrolo[3,4-*b*]quinoline. To a solution of 2-carbomethoxy-3-methylquinoline (0.69 g, 3.4 mmol) in 20 ml of CCl_4 was added *N*-bromosuccinimide (0.68 g, 3.8 mmol) and dibenzoyl peroxide (5 mg, 0.02 mmol). The mixture was heated under reflux for 24 hr. The reaction mixture was cooled and filtered. The filtrate was concentrated at the water pump, leaving an oily residue (2-carbomethoxy-3-bromomethylquinoline) which was dissolved in 50 ml of anhydrous methanol. A stream of methylamine was passed through the solution, which was heated under reflux for 2 hr. After the reaction mixture was cooled to room temperature, a white solid compound, **9** (332 mg), was obtained by crystallization. A second crop (200 mg) was obtained by concentration of the filtrate. The combined solid (77%) was recrystallized from methylene chloride–ether to give an analytical sample of **9**, mp 260–262°.

Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.72; H, 5.05; N, 14.14. Found: C, 72.54; H, 5.15; N, 13.96.

λ_{max} ($CHCl_3$) 5.87 μ; δ ($CDCl_3$–CF_3CO_2H) 3.47 (s, 3), 5.00 (s, 2), 8.0–8.3 (m, 4), 9.98 (s, 1); MS *m/e* 198 (parent).

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Registry No.—**1**, 34535-42-7; **2**, 53544-18-6; **4**, 54934-00-8; **5**, 54934-01-9; **7**, 54934-02-0; **8**, 53821-46-8; **9**, 54934-03-1; glyme, 110-71-4; 1,3-dichloro-2-butene, 926-57-8; magnesium methyl carbonate 142-72-3; *N*-bromosuccimide, 128-08-5; 2-carbomethoxy-3-bromomethylquinoline, 54934-04-2.

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(11) Melting points are uncorrected. NMR spectra were measured at 60 MHz

on Varian Associates A-60, A-60D, and T-60 spectrometers with tetramethylsilane as internal standard. Data are reported in parts per million (δ) from Me_4Si. Infrared spectra were obtained from Perkin-Elmer 137 or 247 spectrophotometers. Mass spectra were measured on an LKB 9 combined GLC–mass spectrometer by direct insertion. Analyses were conducted by Galbraith Laboratories, Inc., Knoxville, Tenn.

(12) This heating was not necessary for the formation of **2**, but was done in an effort to achieve cyclodehydration.
(13) M. Stiles, *J. Am. Chem. Soc.*, **81**, 2598 (1959).
(14) This was done in an effort to isolate a methyl ester of carboxylated material.
(15) This was done in an effort to isolate intermediate acid.

Isolation of a Cyclopropene from Dehydrochlorination of a *gem*-Dichlorocyclopropane

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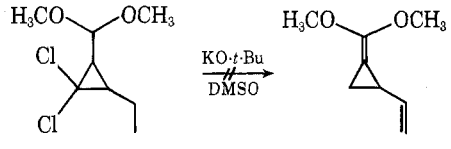
Although the direct observation of cyclopropenes from dehydrochlorination of chlorocyclopropanes has been reported,[2] usually isomerization products[3] or adducts with nucleophiles[4] are obtained. We report here an unusual example of cyclopropene formation from dehydrochlorination which we observed while attempting to prepare **1**, a potentially interesting receptor of singlet oxygen.[5]

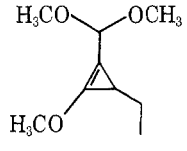
Thus addition of KO-*t*-Bu (2.36 equiv) in dimethyl sulfoxide (DMSO) to a solution of **2** (eq 1) in DMSO did not



(1)

2 **1**

give the expected **1**; however, the reaction was reproducible and gave a single major product (decomposition occurred on GLC columns) whose NMR, ir, and mass spectrum allowed assignment of structure **3**. The mass spectrum re-

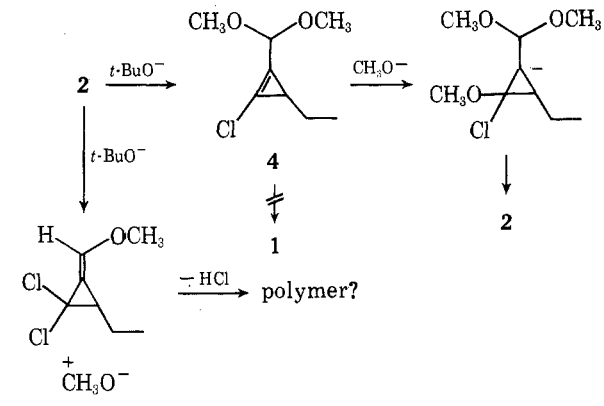


3

vealed the absence of chlorine and showed a parent ion at *m/e* 172. The NMR spectrum showed methoxyl signals at δ 3.27, 3.37, and 3.92. The dimethyl acetal proton appeared as a singlet at δ 5.1, in good agreement with the one at δ 5.0 in *cis*-2-pentenal dimethyl acetal. A triplet at δ 0.9 (3 H) and a multiplet at δ 1.4 (2 H) showed that the ethyl group was undisturbed. A strong, broad ir band at 1880 cm^{-1} was so unusual that it was relatively simple to assign it to the C=C stretch of a disubstituted cyclopropene.[6] These data and the absence of olefinic protons in the NMR spectrum showed that the ethyl, dimethyl acetal, and methoxyl were bound to different cyclopropene carbons. The collapse of the triplet at δ 2.25 upon irradiation of the methylene group identified the methine carbon of the cyclopropene.

A plausible mechanism for the formation of **3** is shown in Scheme I. The failure of product **3** (or **4**) to undergo double-bond isomerization[3] to the exocyclic position is unprecedented; we conclude, on the basis of a study by Davis and Brown,[7] that the cause was steric hindrance of the approach of *t*-BuO^- to the acetal methine proton.

Scheme I



Experimental Section

Infrared spectra were run on a Beckman IR-8 instrument and NMR spectra were recorded on a Varian A-56/60 spectrometer. The mass specta were recorded on a CEC 21-110B instrument. All reactions were conducted in a nitrogen atmosphere.

***cis*-2-Pentenal Dimethyl Acetal (5).** Ethylmagnesium bromide (2 mol) in THF was prepared by the method of Skattebøl, Jones, and Whiting.[8] The flask was then equipped with a Dry Ice–acetone condenser and 1-butyne (Farchan Research Laboratories, 100 g, 1.85 mol) was added dropwise over a 7-hr period at 25° with evolution of ethane. The solution was allowed to stand for 15 hr and trimethyl orthoformate (244 g, 2.3 mol) was added. The resulting brown transparent solution was heated with stirring to about 50° for 5 days and then 1 l. of THF was removed by distillation. CuCl (1%) was then added and the reaction mixture was refluxed for 11 hr. The remaining THF was distilled until the stillhead temperature reached 95°. The black reaction mixture was cooled and diluted with 500 ml of ether and the magnesium salts were filtered and washed with an additional 50 ml of ether. A 38% solution of NH_4Cl was used to destroy any remaining Grignard. The ethereal solution was decanted, dried through a cone of $MgSO_4$, and stored over Na_2SO_4. Distillation provided 122.4 g (50%) of alkyne, bp 77–78° (47 mm).

Reduction to the olefin was carried out as follows. The alkyne (40 g, 0.312 mols), quinoline (800 mg, 2% by wt), 5% $Pd/CaCO_3$ (800 mg, 2% by wt), and 200 ml of pentane were shaken in a Parr apparatus under H_2 (5 lb) until 1 equiv was absorbed. The product was then filtered through Celite and the pentane removed in vacuo. The light-yellow product, containing the quinoline, weighed 40.8 g (99% yield). GLC on a 10 ft × 0.25 in. 10% Apiezon J on 80–100 mesh Chromosorb W (acid washed) column at 100° showed only a single peak. Spectra: NMR δ 9.0 (t, J = 7 Hz, 3 H), 2.15 (quintet, J = 7 Hz, 2 H), 3.2 (s, 6 H), 5.0 (d, J = 5 Hz, 1 H), 5.15–5.9 (m, 2 H); ir 3040, 2830, 1665, 1190, 1112, and 1050 cm^{-1}. Spectral properties match reported values.[9]

***cis*-2,2-Dichloro-3-ethylcyclopropanecarboxaldehyde Dimethyl Acetal (2).** The olefin **5** (40.8 g, 0.314 mol, 1 equiv) and ethanol-free $CHCl_3$ (94 g, 0.785 mol, 0.015 equiv) were stirred rapidly in a 1-l. Morton flask, after which 50% aqueous NaOH was added. The reaction mixture quickly warmed to 60° and turned black. More NaOH was added when the reaction mixture had cooled to 50° until a total of 110 g (1.37 mol, 4.38 equiv) was added. When the reaction mixture had cooled to 45°, about 2 hr, it was poured into a separatory funnel and extracted with ether, and the ethereal solution was washed three times with water. The ethereal solution was then washed with saturated sodium chloride solution and dried over sodium sulfate. After removal of pentane in vacuo, distillation afforded first a reaction weighing 10.5 g, bp 50° (40 mm), followed by **2**, bp 60° (4 mm) (12.9 g, 19.3%). The product gave a single GC peak on the Apiezon J column described above. Spectra: NMR δ 1.09 (t, J = 5 Hz, 3 H), 1.3–1.9 (m, 4 H), 3.27 (s, 3 H), 3.37 (s, 3 H), 4.18 (d, J = 7 Hz, 1 H); ir 2980, 1450, 1195, 1142, 1110, 1065, and 810 cm^{-1}. The mass spectrum had no parent ion but showed peaks at *m/e* 211 (M − 1) and 181 (M − OCH_3); exact *m/e* calcd for $C_7H_{11}OCl_2$ (M − OCH_3), 181.0186; found, 181.0188.

2-Methoxy-3-ethylcycloprop-1-enecarboxaldehyde Dimethyl Acetal (3). The cyclopropane **2** (1 g, 4.96 mmol, 1 equiv) and DMSO (7 ml) were placed in a 50-ml flask equipped with a magnetic stirring bar and pressure-equalizing addition funnel.