Benzimidazole N-Oxides. V. Reactions of 1,2-Dimethylbenzimidazole 3-Oxide with Acetylenecarboxylates

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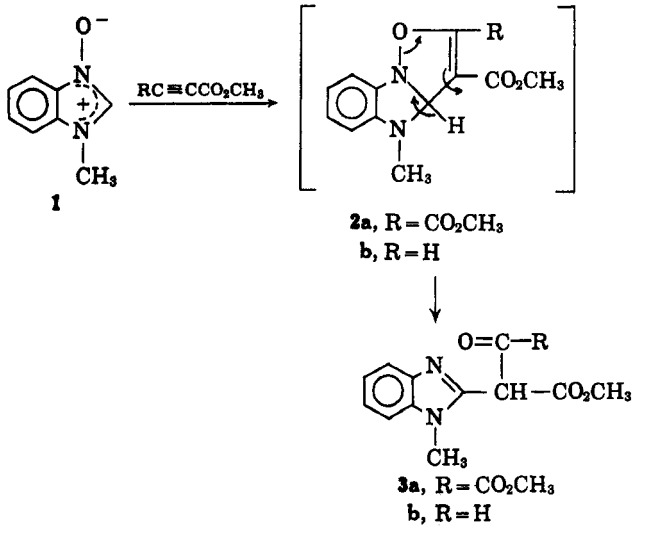
The reaction of 1,2-dimethylbenzimidazole 3-oxide (**4**) with dimethyl acetylenedicarboxylate or methyl propiolate afforded 1:1 adducts (**5** or **6**), respectively. The structures of these adducts were determined by spectra and chemical degradation and proved to be 1,2-dimethyl-3-(β-hydroxyvinyl)benzimidazolium betaine derivatives by independent synthesis. A mechanism for this reaction, which consists of an intermediate formation of cycloadducts, has been proposed tentatively.

In previous papers[1a,b] dealing with 1,3-dipolar cycloaddition reactions of 1-methylbenzimidazole 3-oxide (**1**), we have reported that the reaction of **1** with dimethyl acetylenedicarboxylate or methyl propiolate gives methyl methoxalyl- or methyl formyl(1-methyl-2-benzimidazolyl)acetate (**3a** or **3b**, respectively), and the formation of these products can be explained by the initial 1,3-dipolar cycloaddition followed by cleavage of the isoxazoline ring of the adducts (**2a** and **b**) (Chart I).

CHART I

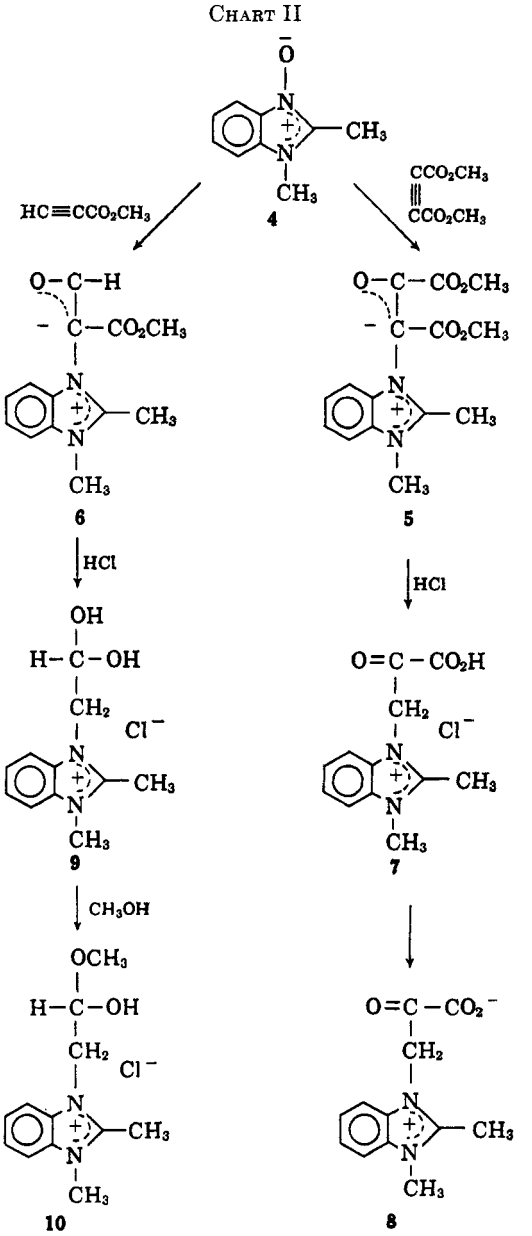


Continuing interest was fostered by these facts and our present investigation was undertaken to see if 1,2-dimethylbenzimidazole 3-oxide (**4**) would behave as a 1,3-dipole on reaction with the acetylenecarboxylates.

The N-oxide **4** reacted with dimethyl acetylenedicarboxylate or methyl propiolate in chloroform at room temperature to yield a 1:1 adduct (**5** or **6**, respectively) in excellent yield. Both of the adducts are very soluble in water and gave monohydrochlorides which in turn reproduced the free bases upon neutralization. The infrared spectra (in Nujol) of **5** and **6** in the carbonyl region showed very similar bands (1735, 1670, and 1550 cm.$^{-1}$ in **5**; 1660 and 1590 cm.$^{-1}$ in **6**) to those of **3a** and **3b**, respectively. The strong absorption bands near 1550 cm.$^{-1}$ assignable to enolate ion[2] together with the positive color reaction with ferric chloride suggest the presence of an enolate group in **5** and **6**. In the n.m.r. spectra (in $CDCl_3$), four methyl signals (τ 6.12, 6.21, 6.40, and 7.38) in **5** and three methyl signals (τ 6.26, 6.30, and 7.40) and an aldehyde proton signal (τ 0.55) in **6** were observed besides the signals of benzene ring protons.

In the light of these spectral data and the chemical evidence to be described below, the structures 3-(α,β-dimethoxycarbonyl-β-hydroxyvinyl)- and 3-(α-methoxycarbonyl-β-hydroxyvinyl)-1,2-dimethylbenzimidazolium betaines were assigned to **5** and **6**, respectively.

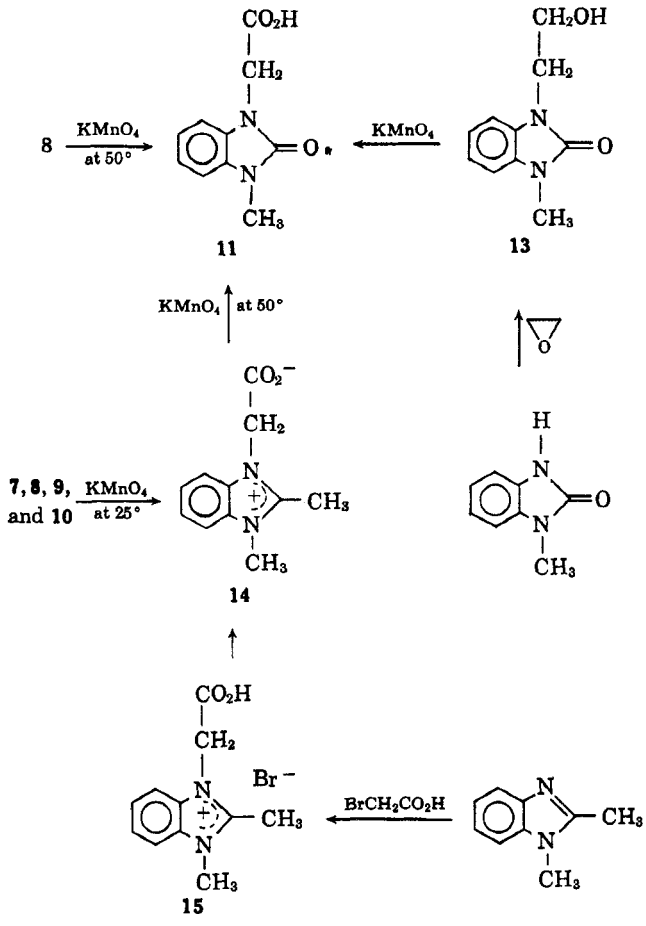
CHART II



(1) (a) S. Takahashi and H. Kanō, *Tetrahedron Letters*, **No. 25**, 1687 (1963); (b) *Chem. Pharm. Bull.* (Tokyo), **12**, 1290 (1964).

(2) R. Huisgen and H. Seidl, *Tetrahedron Letters*, **No. 29**, 2019 (1963).

CHART III



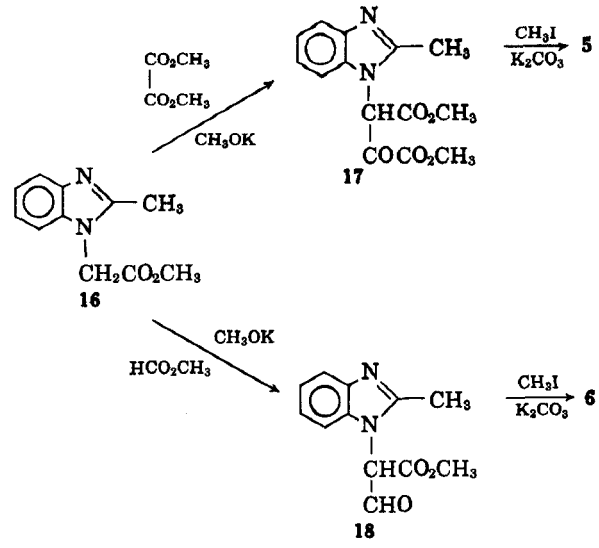
By presuming that the electron of the enolate ion of **6** is delocalized as depicted in the figure, this assignment would not be at variance with the appearance of an aldehyde proton signal in the n.m.r. spectrum (Chart II).

Hydrolysis of **5** with hydrochloric acid gave a hydrochloride (**7**), which was converted into its free base (**8**) by neutralization. Analytical figures for **7** suggested that the two ester groups of **5** were hydrolyzed and one of the resulting carboxyl groups was decarboxylated to yield **7**. The n.m.r. spectra (in CF_3COOH) of **7** and **8** also indicated that disappearance of two methyl groups of the esters and appearance of a $-CH_2-$ group (signal peaks at τ 4.41 and 4.00, respectively) had occurred upon hydrolysis. The infrared spectra (in Nujol) showed the presence of the -COCOOH group (2400–2800, 1743, and 1710 sh cm.$^{-1}$) in **7** and the $-COCOO^-$ group (1633, 1603, and 1412 cm.$^{-1}$) in **8**. On the basis of these studies it seemed most probable that the structures of **7** and **8** are represented by 1,2-dimethyl-3-hydroxalylmethylbenzimidazolium chloride and its free base, a betaine.

Similar hydrolysis with **6** gave a crystalline product (**9**), whose n.m.r. spectrum (in D_2O) showed a triplet at τ 4.51 and a doublet at 5.50 assignable to the protons of a $>CH-CH_2-$ group and indicated the disappearance of the methyl group of the ester **6**. The infrared spectrum lacked the absorption band in the carbonyl region.

From these spectral data together with elemental analysis, the structure of 1,2-dimethyl-3-(β,β-dihydroxyethyl)benzimidazolium chloride (as a hydrated aldehyde derivative) was assigned to **9**. Recrystallization of **9** from methanol–acetone gave the hemiacetal (**10**).

CHART IV



The compound **8** was oxidized with potassium permanganate at 50° to a carboxylic acid (**11**). Treatment of **11** with diazomethane gave its methyl ester (**12**), whose infrared spectrum (in Nujol) showed absorption bands at 1737 ($COOCH_3$) and 1706 cm.$^{-1}$ (C=O). The n.m.r. spectra (in $CDCl_3$) lacked the $C-CH_3$ signal peak observed before oxidation. By these data, the structures of **11** and **12** were deduced to be 3-carboxymethyl-1-methyl-2-benzimidazolinone and its methyl ester, respectively (Chart III).

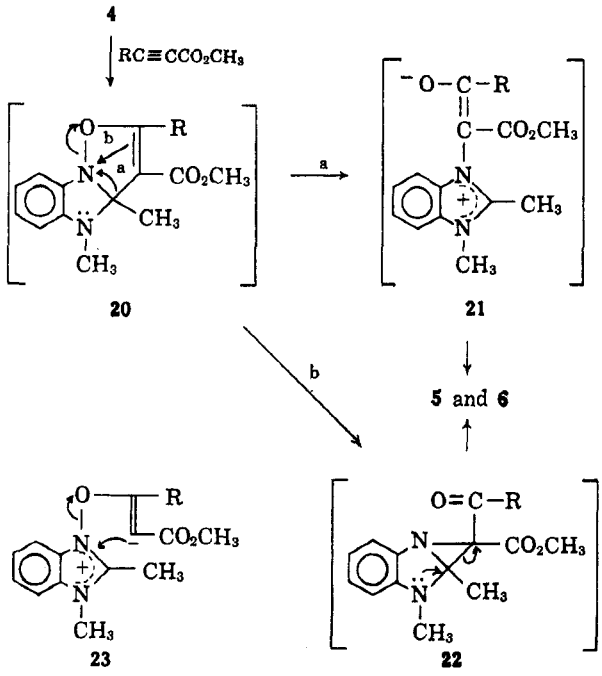
The structure assigned to **11** was confirmed by identification with a sample prepared independently from 3-(β-hydroxyethyl)-1-methyl-2-benzimidazolinone (**13**) which was obtained by treatment of 1-methyl-2(3H)-benzimidazolinone with ethylene oxide.

When the permanganate oxidation of **7**–**10** was carried out at 25°, an alternative product (**14**) was obtained. The n.m.r. spectrum (in D_2O) indicated a signal peak at τ 5.05 assignable to the $-CH_2-$ group in addition to those of the benzene ring protons, $N-CH_3$ and $C-CH_3$. The presence of a carboxylate group was suggested by its infrared absorption bands at 1660 (shoulder), 1620, and 1375 cm.$^{-1}$ (in Nujol). These results, in conjunction with the higher temperature oxidation of **14** which gave **11**, indicated that **14** is 3-carboxymethyl-1,2-dimethylbenzimidazolium betaine. This was confirmed by the following independent synthesis. Reaction of 1,2-dimethylbenzimidazole with bromoacetic acid gave the bromide (**15**), which gave the betaine **14** upon neutralization.

These transformation studies support the structures assigned to **5** and **6**. To prove the structure, these compounds were synthesized unambiguously as follows. Treatment of the silver salt of 2-methylbenzimidazole with methyl bromoacetate gave methyl (2-methyl-1-benzimidazolyl)acetate (**16**). Reaction of **16** with dimethyl oxalate or methyl formate in the presence of potassium methoxide gave methyl methoxalyl(2-methyl-1-benzimidazolyl)acetate (**17**) or methyl formyl(2-methyl-1-benzimidazolyl)acetate (**18**), respectively (Chart IV).

These esters **17** and **18** reacted with methyl iodide in the presence of potassium carbonate and produced the

CHART V



desired betaines **5** and **6**, respectively. The products were proven identical by infrared comparison and mixture melting point. In the absence of the carbonate, this reaction with **17** gave 1,2-dimethyl-3-methoxycarbonylmethylbenzimidazolium iodide (**19**). The same product **19** was obtained from **16** and methyl iodide.

On the basis of the analogy with the reaction **1** → **3**, the formation of **5** and **6** from **4** can be explained by a mechanism involving 1,3-dipolar cycloaddition intermediates (**20**), although the cycloadducts could not be isolated even when the reaction was carried out at −20°. In this case, in contrast to that of the intermediate **2** for the formation of **3** from **1**, the initial adducts **20** have no mobile proton at the 2-position of the imidazoline ring and no possibility to stabilize as in the transformation **2** → **3** (Chart V).

The rearrangement of the initial adducts to **5** and **6** may proceed *via* the following path. The N–O bond breaking of the unstable isoxazoline ring of **20** would cause the migration of the group bearing a methoxycarbonyl function from carbon to nitrogen through 1,2 shift of the σ bond (a) or through initial π-bond shift (b) followed C–C bond cleavage as illustrated in **21** and **22**, respectively.

An alternative mechanism involving the initial formation of a betaine (**23**) followed by the rearrangement to **21** through a four-membered transition state cannot be ruled out.

These new type compounds showed some interesting properties. The compounds **5** and **6** are very stable to boiling methanolic hydrochloric acid in contrast to **3a** and **b** which were readily hydrolyzed to methyl (1-methyl-2-benzimidazolyl)acetate (**24**). On standing overnight with hydroxylamine solution in methanol. **5** and **6** were recovered unchanged, while both **3a** and **3b** were converted to **24**.[1a,b] The aldehyde **6** resisted oxidation with hydrogen peroxide but was oxidized to 1,2-dimethylbenzimidazole with potassium permanganate and did not reduce Tollens reagent. Catalytic or sodium borohydride reduction of **6** did not proceed, and the material was recovered unchanged.

Some of these properties, especially the abnormal aldehyde character of **6**, may be due to the contribution of enolate ion structure, which is indicated by the spectral data mentioned above.

Experimental[3]

1,2-Dimethyl-3-(α,β-dimethoxycarbonyl-β-hydroxyvinyl)benzimidazolium Betaine (5).—Dimethyl acetylenedicarboxylate (2.20 g., 0.0155 mole) was added to a solution of 1,2-dimethylbenzimidazole 3-oxide (**4**) [colorless crystals, m.p. 178–180°, prepared from the dihydrate[4] (3.00 g., 0.0151 mole) by azeotropic dehydration with chloroform] in chloroform (15 ml.) with stirring and cooling in an ice–water bath. Then the resulting orange solution was allowed to stand for 0.5 hr. at room temperature. After evaporation, acetone was added to the residue to give nearly colorless crystals (4.20 g., 91%). Recrystallization from acetone gave colorless plates: m.p. 238–240° dec., λ_{max}^{EtOH} 263.5 mμ (log ε 4.31) and 277.2 (4.16).

Anal. Calcd. for $C_{15}H_{16}N_2O_5$: C, 59.20; H, 5.30; N, 9.21. Found: C, 59.29; H, 5.55; N, 9.04.

The same product was obtained when the dicarboxylic ester was added at −20° and the solution was allowed to stand at this temperature for 5 min., then evaporated under −20°.

This product was recrystallized from water to give the hydrate of **5** as white prisms, m.p. *ca.* 210–240°.

Anal. Calcd. for $C_{15}H_{16}N_2O_5 \cdot H_2O$: C, 55.89; H, 5.63; N, 8.69; H_2O, 5.59. Found: C, 55.78; H, 5.74; N, 8.69; H_2O, 5.18.

1,2-Dimethyl-3-(α-methoxycarbonyl-β-hydroxyvinyl)benzimidazolium Betaine (6).—This compound was obtained from **4** (dihydrate, 3.00 g., 0.0151 mole) and methyl propiolate (1.30 g., 0.0155 mole) by the same procedure as for the synthesis of **5**; yield 3.60 g. (96%). Recrystallization from dichloromethane–ether gave colorless prisms: m.p. 212° dec., λ_{max}^{EtOH} 256.7 mμ (log ε 4.42) and 277.0 (4.07).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.58; H, 6.02; N, 11.64.

Hydrolysis of 5.—A mixture of **5** (1.00 g.) in 6 *N* hydrochloric acid (10.0 ml.) was refluxed for 5 hr. The resulting colorless solution was evaporated and the crystalline residue was recrystallized from water–acetone to give 1,2-dimethyl-3-hydroxalylmethylbenzimidazolium chloride (**7**) as colorless prisms (0.90 g., 95%): m.p. 170° dec.; λ_{max}^{EtOH} 255.0 mμ (log ε 3.80), 263.5 (3.82), 270.5 (3.93), and 277.6 (3.96).

Anal. Calcd. for $C_{12}H_{13}ClN_2O_3 \cdot H_2O$: C, 50.26; H, 5.27; N, 9.77. Found: C, 50.29; H, 5.40; N, 9.56.

1,2-Dimethyl-3-hydroxalylmethylbenzimidazolium Betaine (8).—A solution of **7** in water was adjusted to pH 3–4 by aqueous sodium hydrogencarbonate solution, then evaporated. The residue was extracted with absolute ethanol and the ethanol was evaporated. Recrystallization from water–acetone gave colorless prisms, m.p. 170° dec.

Anal. Calcd. for $C_{12}H_{12}N_2O_3 \cdot H_2O$: C, 57.59; H, 5.64; N, 11.20; H_2O, 7.20. Found: C, 57.65; H, 5.96; N, 11.01; H_2O, 7 62.

Hydrolysis of 6.—A solution of **6** (1.20 g.) in 6 *N* hydrochloric acid (12 ml.) was refluxed for 7 hr., then evaporated. The colorless residue was recrystallized from water–acetone to give 1,2-dimethyl-3-(β,β-dihydroxyethyl)benzimidazolium chloride (**9**) as colorless prisms or plates (1.00 g., 85%): m.p. 210° dec. (turning brown above 150°); λ_{max}^{EtOH} 255.0 mμ (log ε 3.76), 263.5 (3.79), 270.3 (3.91), and 277.3 (3.95).

Anal. Calcd. for $C_{11}H_{15}ClN_2O_2$: C, 54.43; H, 6.23; N, 11.54. Found: C, 54.27; H, 6.49; N, 11.42.

(3) All melting points were taken on a Kofler hot stage and are uncorrected. Solvents were removed under reduced pressure. Each identification was made by comparison of the infrared spectrum, and, if the sample had a melting point, it was also compared by mixed fusion. Infrared spectra were recorded on a Kōken infrared spectrophotometer, Model IR-S. N.m.r. spectra were obtained on a Varian A-60 analytical n.m.r. spectrometer in $CDCl_3$ or CF_3COOH containing tetramethylsilane as an internal reference or in D_2O containing dioxane. Unless otherwise stated, each signal pattern is singlet.

(4) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **11**, 1375 (1963).

When the colorless residue was recrystallized from methanol–acetone, the methyl acetal **10** was obtained as colorless prisms, m.p. 180° dec.

Anal. Calcd. for $C_{12}H_{17}ClN_2O_3$: C, 56.14; H, 6.67; N, 10.91. Found: C, 55.93; H, 6.99; N, 10.85.

Oxidation of 8 to 11.—To a solution of **8** (0.40 g.) in water (20 ml.) was added finely ground potassium permanganate with stirring at 50° until the color of the oxidizing agent lasted for a time (*ca.* 0.9 g.). After removal of manganese dioxide by filtration, the filtrate was acidified with 6 *N* hydrochloric acid to give 3-carboxymethyl-1-methyl-2-benzimidazolinone (**11**) as colorless crystals (0.18 g., 55%). Recrystallization from water gave colorless prisms: m.p. 218–219°; λ_{max}^{EtOH} 230.4 mμ (log ε 3.90), 282.0 (3.95), and 287.0 (3.89 sh).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.58. Found: C, 58.27; H, 5.07; N, 13.60.

3-Methoxycarbonylmethyl-1-methyl-2-benzimidazolinone (12).—To a suspension of **11** (158 mg.) in chloroform (5.0 ml.) was added a solution of diazomethane in ether. The starting material dissolved rapidly into the solution as the reaction proceeded. Removal of the solvent left a colorless oil, which solidified on cooling. The product was purified by chromatography on alumina with chloroform, then recrystallized from carbon tetrachloride–petroleum ether (b.p. 60–70°) to give colorless plates (98 mg.), m.p. 121–123°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.29; H, 5.57; N, 12.51.

3-Carboxymethyl-1,2-dimethylbenzimidazolium Betaine (14).—To a solution of **7** (1.00 g.) in water (30 ml.) was added finely ground potassium permanganate with stirring at 25° until the color of the oxidizing agent lasted for a time (*ca.* 0.55 g.). After removal of manganese dioxide by filtration, the filtrate was evaporated and the residue was extracted with absolute ethanol. After the solvent was removed, recrystallization of the residue from ethanol–acetone gave colorless prisms (0.66 g., 82%): m.p. >230°; λ_{max}^{EtOH} 255.5 mμ (log ε 3.57), 264.0 (3.60), 271.0 (3.71), and 278.0 (3.74).

Anal. Calcd. for $C_{11}H_{12}N_2O_2 \cdot 1.5H_2O$: C, 57.13; H, 6.54; N, 12.12; H_2O, 11.70. Found: C, 57.14; H, 6.63; N, 12.07; H_2O, 12.15.

This compound was obtained by the oxidation of **8**, **9**, or **10** by the same procedure.

Oxidation of 14 to 11.—Oxidation of **14** (0.20 g.) by the same procedure as for **8** gave **11** (0.08 g.), which was identified with the sample obtained above.

3-(β-Hydroxyethyl)-1-methyl-2-benzimidazolinone (13).—To a solution of ethylene oxide (1.0 ml.) in water (5.0 ml.) were added 1-methyl-2(3H)-benzimidazolinone (0.50 g.) and aqueous sodium hydroxide solution (10%, 1 drop). After having been allowed to stand for 3 days with occasional shaking, the resulting solution was extracted with three 5-ml. portions of chloroform. Removal of the solvent gave a colorless oil (0.7 g.), chromatography of which on alumina with ethanol gave colorless crystals (0.30 g., 46%). Recrystallization from carbon tetrachloride gave colorless prisms, m.p. 108–109°.

Anal. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.61; H, 6.35; N, 14.40.

Oxidation of 13 to 11.—Oxidation of **13** (0.20 g.) by the same procedure as for **8** gave **11** (0.08 g.). This product and its methyl ester were identical with the samples obtained from **8**, respectively

3-Carboxymethyl-1,2-dimethylbenzimidazolium Bromide (15).—A solution of 1,2-dimethylbenzimidazole[5] (0.15 g.) and bromoacetic acid (0.15 g.) in ethanol (5.0 ml.) was heated at 120° in a sealed tube for 10 hr., then evaporated. The residue was recrystallized from ethanol–acetone to give colorless small needles (0.07 g., 23%), m.p. *ca.* 170°.

Anal. Calcd. for $C_{11}H_{13}BrN_2O_2 \cdot 0.5H_2O$: C, 44.89; H, 4.80; N, 9.53. Found: C, 44.84; H, 4.88; N, 9.41.

The bromide was dissolved in water and made alkaline with potassium carbonate. After evaporation, the residue was extracted with absolute ethanol. Acetone was added to the concentrated ethanolic solution to give colorless prisms, m.p. >230°. This compound was identical with above-obtained **14**.

Methyl (2-Methyl-1-benzimidazolyl)acetate (16).—To a solution of silver nitrate (8.50 g., 0.050 mole) in water (15 ml.) were added ethanol (50 ml.), then aqueous ammonia (30%) until the first precipitate dissolved (*ca.* 10 ml.). The resulting solution was added to a solution of 2-methylbenzimidazole (6.60 g., 0.050 mole) in ethanol (50 ml.) to give a white precipitate, which was collected by filtration (11.5 g.). To a suspension of the thus obtained silver salt of 2-methylbenzimidazole (9.55 g., 0.040 mole, finely ground) in toluene (75 ml.) was added methyl bromoacetate (6.30 g., 0.041 mole) dropwise with stirring and heating under reflux and, after the addition, stirring and heating were continued for 5 hr. The resulting solution was separated by decantation from the tarry residue and evaporated to give brown tar, which was chromatographed on alumina with chloroform to give a crystalline product (3.20 g., 37%). Recrystallization from benzene (plates), then isopropyl ether (needles) or carbon tetrachloride (prisms), gave colorless crystals: m.p. 117–119°, ν_{max}^{Nujol} 1735 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.73; H, 6.08; N, 13.93.

Methyl Methoxalyl(2-methyl-1-benzimidazolyl)acetate (17).—To a suspension of potassium methoxide in absolute ether, prepared by addition of methanol (0.50 ml.) to a suspension of powdered potassium (0.15 g., 0.00375 mole) in absolute ether (10 ml.), were added **16** (0.61 g., 0.0030 mole) and dimethyl oxalate (0.35 g., 0.0030 mole) with stirring at room temperature. After stirring for 3 hr., the mixture was allowed to stand overnight at room temperature. The resulting crystalline precipitate was collected by filtration, washed with ether, and dissolved in a small amount of water. The solution was acidified (pH 4) with 6 *N* hydrochloric acid to give colorless crystals (0.55 g., 63%). Recrystallization from methanol–acetone (or chloroform–benzene) gave colorless plates: m.p. 212° dec.; λ_{max}^{EtOH} 263.0 mμ (log ε 4.34), 266.8 (4.33 sh), and 275.6 (4.21); ν_{max}^{Nujol} 1733 and 1682 (C=O), and 1534 cm.$^{-1}$ (C=C—O$^-$); n.m.r. (in $CDCl_3$) τ 2.40–2.75 (benzene ring, complex pattern), 6.07 ($COOCH_3$), 6.34 ($COOCH_3$), and 7.62 (C–CH_3).

Anal. Calcd. for $C_{14}H_{14}N_2O_5$: C, 57.93; H, 4.86; N, 9.65. Found: C, 57.88; H, 5.06; N, 9.56.

Methyl Formyl(2-methyl-1-benzimidazolyl)acetate (18).—To a suspension of potassium methoxide in absolute ether, prepared by addition of methanol (1.00 ml.) to a suspension of powdered potassium (0.24 g., 0.0060 mole) in absolute ether (20 ml.), were added methyl formate (0.60 g., 0.0100 mole) then **16** (1.02 g., 0.0050 mole) with stirring at room temperature. After stirring for 3 hr., the mixture was allowed to stand overnight at room temperature. The resulting gummy product was washed with ether after separation from the solution by decantation, then dissolved in a small amount of water. The solution was acidified (pH 4) with 6 *N* hydrochloric acid and extracted with chloroform. Removal of the solvent gave a colorless oil (0.80 g., 69%), which solidified on standing. Recrystallization from methanol–acetone (or chloroform–benzene) gave colorless plates: m.p. 207° dec.; λ_{max}^{EtOH} 257.5 mμ (log ε 4.36), 267.2 (4.26 sh), and 275.7 (4.08); ν_{max}^{EtOH} 1677 (C=O) and 1564 cm.$^{-1}$ (C=C—O$^-$, broad); n.m.r. (in $CDCl_3$) τ 1.13 (CHO), 2.60–2.80 (benzene ring, complex pattern), 6.29 ($COOCH_3$), and 7.62 (C–CH_3).

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.02; H, 5.21; N, 12.06. Found: C, 61.80; H, 5.41; N, 12.12.

Synthesis of 5 from 17.—To a solution of **17** (145 mg., 0.50 mmole) in methanol (1.0 ml.) were added finely ground potassium carbonate (350 mg., large excess) and methyl iodide (0.10 ml. excess), and the mixture was heated in a sealed tube at 110° for 2 hr. After removal of insoluble materials by filtration, the filtrate was evaporated. The residue was extracted with chloroform, and removal of the solvent and addition of acetone then gave colorless crystals (105 mg., 69%), m.p. 238–240° dec., which were identical with **5** obtained from **4** and dimethyl acetylenedicarboxylate.

Synthesis of 6 from 18.—This experiment was carried out by the same procedure mentioned above. From **18** (232 mg., 1.0 mmole), potassium carbonate (350 mg.), methyl iodide (0.12 ml., 3.0 mmoles), and methanol (1.0 ml.), **6** (150 mg., 61%), m.p. 212° dec., was obtained. This compound was identical with **6** obtained from **4** and methyl propiolate.

1,2-Dimethyl-3-methoxycarbonylmethylbenzimidazolium Iodide (19). A. From 16.—To a solution of **16** (204 mg., 1.0 mmole) in methanol (2.0 ml.) was added methyl iodide (0.075 ml., 1.2 mmoles), and the solution was heated in a sealed tube at 120° for 5 hr. After evaporation of the resulting slightly brown solution, acetone was added to the residue to give colorless crystals (0.20 g.). Recrystallization from methanol–isopropyl ether gave colorless plates, m.p. 195–197° dec.

(5) O. Fischer, *Ber.*, **25**, 2838 (1892).

Anal. Calcd. for $C_{12}H_{15}IN_2O_2$: C, 41.64; H, 4.37; N, 8.09. Found: C, 41.96; H, 4.64; N, 8.09.

B. From 17.—A solution of **17** (145 mg., 0.50 mmole) and methyl iodide (0.20 ml., excess) in methanol (3.0 ml.) was heated in a sealed tube at 120° for 2.5 hr., then evaporated. Recrystallization of the residue from methanol–isopropyl ether gave colorless plates (0.12 g.), m.p. 195–197° dec.

This compound was identical with the above-obtained one.

1,2-Dimethyl-3-(α,β-dimethoxycarbonyl-β-hydroxyvinyl)benzimidazolium Chloride.—To a solution of **5** (0.40 g.) in water (5.0 ml.) was added 6 *N* hydrochloric acid (1.0 ml.), and the resulting solution was evaporated. The crystalline residue was recrystallized from methanol–isopropyl ether to give colorless plates (0.35 g.), m.p. 130° dec.

Anal. Calcd. for $C_{15}H_{17}ClN_2O_5 \cdot H_2O$: C, 50.21; H, 5.33; N, 7.81. Found: C, 50.35; H, 5.66; N, 8.09.

The aqueous solution of this compound was neutralized with aqueous sodium hydrogen carbonate solution then evaporated. The residue was extracted with chloroform, and the solvent was evaporated to give **5**, m.p. 238–240° dec., which was identical with above-obtained one.

1,2-Dimethyl-3-(α-methoxycarbonyl-β-hydroxyvinyl)benzimidazolium Chloride.—This compound was obtained from **6** by the same procedure as mentioned above. Recrystallization from methanol–isopropyl ether gave colorless plates, m.p. 188–190° dec.

Anal. Calcd. for $C_{13}H_{15}ClN_2O_3$: C, 55.23; H, 5.35; N, 9.91. Found: C, 55.14; H, 5.42; N, 10.03.

Neutralization of this compound by the same procedure as mentioned above reproduced **6**.

Treatment of 5 with Methanolic Hydrogen Chloride.—A solution of **5** (0.30 g.) in methanolic hydrogen chloride (10%, 3.0 ml.) was refluxed for 10 hr., then evaporated. After neutralization of the residue, the starting material (0.27 g.) was recovered.

Treatment of 6 with Methanolic Hydrogen Chloride.—This experiment was carried out by the same procedure as mentioned above. The same result, recovery of the starting material, was obtained by this treatment.

Treatment of 5 with Hydroxylamine.—To a solution of hydroxylamine hydrochloride (140 mg., 2.0 mmoles) and sodium acetate (200 mg., 2.4 mmoles) in water (1.0 ml.) and methanol (4.0 ml.) was added **5** (304 mg., 1.0 mmole). The resulting solution was allowed to stand at room temperature for 3 days. After evaporation, the starting material (280 mg.) was recovered.

Treatment of 6 with Hydroxylamine.—This experiment was carried out by the same procedure as mentioned above. The starting material was recovered unchanged by this treatment.

Attempted Oxidation of 6 with Hydrogen Peroxide.—To a solution of **6** (0.60 g.) in methanol (10.0 ml.) was added hydrogen peroxide (30%, 2.0 ml.) and the solution was refluxed for 2 hr. After evaporation, the starting material (0.50 g.) was recovered.

Oxidation of 6 with Potassium Permanganate.—To a solution of **6** (0.40 g.) in water (6.0 ml.) was added finely ground potassium permanganate with stirring at 25°, until the color of the oxidizing agent lasted for a time. Crystals separated as the reaction proceeded. At the end of the reaction, the mixture was heated to dissolve the crystalline product and filtered to remove manganese dioxide. After cooling, the product (0.20 g., m.p. 112–114°) was collected by filtration; it was identical with authentic 1,2-dimethylbenzimidazole.[5]

Attempted Reduction of 6 with Sodium Borohydride.—Sodium borohydride (50 mg.) was added to a solution of **6** (200 mg.) in water (5.0 ml.), and the solution was heated at 60° for 2 hr. The starting material (180 mg.) was recovered.

Attempted Reduction of 6 with Adams Catalyst.—A mixture of **6** (246 mg.) in methanol (20 ml.) containing platinum catalyst (prepared from Adams catalyst, 50 mg.) was treated with hydrogen at ordinary temperature and pressure. No hydrogen was absorbed during 6 hr. The starting material (240 mg.) was recovered.

Reaction of Methyl Methoxalyl(1-methyl-2-benzimidazolyl)-acetate (3a) with Methanolic Hydrogen Chloride.—To a solution of **3a** (0.40 g.) in methanol (3.0 ml.) was added methanolic hydrogen chloride (10%, 1.0 ml.) under cooling in a cold-water bath. After evaporation, acetone was added to the residue to give colorless crystals (0.30 g.). Recrystallization from methyl acetate gave methyl (1-methyl-2-benzimidazolyl)acetate hydrochloride as colorless prisms, m.p. 147–149°.

Anal. Calcd. for $C_{11}H_{12}N_2O_2 \cdot HCl$: C, 54.89; H, 5.45; N, 11.64. Found: C, 54.79; H, 5.70; N, 11.66.

Neutralization of this compound gave methyl (1-methyl-2-benzimidazolyl)acetate (**24**), m.p. 66–68°.[1a,b]

Reaction of Methyl Formyl(1-methyl-2-benzimidazolyl)acetate (3b) with Methanolic Hydrogen Chloride.—This experiment was carried out by the same procedure as mentioned above. By this treatment, **3b** also gave methyl (1-methyl-2-benzimidazolyl)-acetate hydrochloride, m.p. 147–149°, which was identical with the above obtained one.

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Decarboxylation of Oxamic and Oxanilic Acids in Aniline[1]

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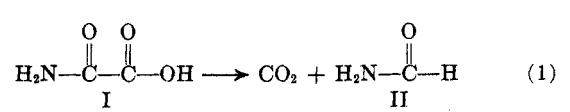
The decarboxylation of oxamic acid in aniline is complicated by a series of concurrent reactions and is not reversible as previously reported, but is accompanied by amidation and transamidation producing as final products oxanilide and formanilide.

As part of his extensive research on rates of decarboxylations in a variety of solvents, L. W. Clark has studied the decarboxylation of oxamic acid (I) in aniline,[3] *o*-toluidine,[3] quinoline,[4] dimethyl sulfoxide,[5] and triethyl phosphate.[5] In the paper on the decarboxylation of oxamic acid (eq. 1) in aniline and *o*-toluidine as



(1)

solvents,[3] there are several anomalous results including unusually high and positive ΔS^* values (Table I) and the formation of a white precipitate (A) in the condenser concurrent with resorption of the gaseous CO_2 produced during the decarboxylation. Clark attributed this to reversal of the decarboxylation with formation of oxamic acid in the condenser.[3] In a later paper,[4] it was

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(3) L. W. Clark, *J. Phys. Chem.*, **65**, 180 (1961).

(4) L. W. Clark, *ibid.*, **65**, 659 (1961).

(5) L. W. Clark, *ibid.*, **65**, 1651 (1961).