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Studies on Ketene and Its Derivatives. XCV.[1] Reaction of Diketene with Acyl Azides

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Photolysis of acyl azides (**1**, **10**) in diketene was investigated. Irradiation of a mixture of benzoyl azide (**1a**) and diketene in dichloromethane gave 1-benzoyl-4-hydroxy-3-pyrrolin-2-one (**2a**) in 17% yield. Similarly, reaction of diketene with *p*-anisoyl azide (**1b**), *p*-toluoyl azide (**1c**), *p*-chlorobenzoyl azide (**1d**) and ethyl azidoformate (**10**) gave the corresponding pyrrolinones (**2b**, **2c**, **2d**, and **11**) in 7—22% yields.

Keywords——photoreaction; diketene; acyl azides; nitrene; tetramic acid; pyrrole derivatives; 4-benzamido-3-oxobutanoate

Most reactions of diketene fall into the category of addition reactions with concomitant opening of the β-lactone ring to give acetoacetyl derivatives or cyclic (mostly heterocyclic) compounds having a methyl or acetyl group.[3] On the other hand, little is known about reactions of the olefinic double bond which occur while the integrity of the β-lactone linkage is maintained. For instance, the homolytic addition of thiols to diketene gives γ-alkylthio-β-lactones.[4] Similarly, β-butyrolactone is obtained by catalytic reduction of diketene.[5]

During the course of our investigations on diketene, we have been focusing on the reactivity of the exo-methylene moiety of diketene, and we have found new addition reactions that occur keeping the β-lactone ring intact. Namely, carbenes add to the exo-methylene moiety giving spirocyclopropane derivatives.[6] On irradiation, some carbonyl compounds react with the methylene to afford spirooxetanone derivatives[7] and the olefinic double bonds of cyclohexenone derivatives add to the exo-methylene moiety to give cyclobutane derivatives.[8] These results prompted us to investigate the reaction of diketene with nitrenes, which is the subject of the present report.

Irradiation of a solution of benzoyl azide (**1a**)[9] and diketene in dichloromethane with a high-pressure mercury lamp gave 1-benzoyl-4-hydroxy-3-pyrrolin-2-one (**2a**) in 17% yield. Structural assignment was made on the basis of elemental analysis, spectral data and the following chemical reactions. Methylation of **2a** with diazomethane gave the methyl ether (**3**). Heating of **2a** in acetic anhydride gave the acetate (**4a**), which was hydrolyzed by potassium hydroxide in methanol, giving **2a**. Upon catalytic hydrogenation, the acetate (**4a**) was transformed to 1-benzoyl-2-pyrrolidone (**5**), which was identified by comparison with an authentic sample prepared according to the literature.[10]

1) *a*) Part XCIV: T. Kato, N. Katagiri, and R. Sato, *Chem. Pharm. Bull.* (Tokyo), **27**, 1176 (1979); *b*) A preliminary communication has appeared in *Chem. Lett.*, **1978**, 697.
2) Location: *Aobayama, Sendai 980, Japan.*
3) *e.g.*, T. Kato, *Acc. Chem. Res.*, **7**, 267 (1974).
4) *a*) C.W. Theobald, U.S. Patent 2675392 (1954) [*C. A.*, **49**, 4722*a* (1955)]; *b*) G.A. Hull, F.A. Daniher, and T.F. Conway, *J. Org. Chem.*, **37**, 1837 (1972).
5) J. Sixt, U.S. Patent 2763664 (1956) [*C. A.*, **51**, 5117*c* (1957)].
6) T. Kato and N. Katagiri, *Chem. Pharm. Bull.* (Tokyo), **21**, 729 (1973).
7) T. Kato, M. Sato, and Y. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **23**, 365 (1975).
8) T. Kato, M. Sato, and Y. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **26**, 632 (1978); *idem*, *J. Chem. Soc. Perkin Trans. I*, **1978**, 352.
9) E.W. Barret and C.W. Porter, *J. Am. Chem. Soc.*, **63**, 3434 (1941).
10) B.P. Munday, B.R. Larsen, L.F. McKenzie, and G. Braden, *J. Org. Chem.*, **37**, 1635 (1972).

It is of interest that hydrolysis and methanolysis of **2a** gave not the debenzoylated pyrrolinone (**8**)[11] but ring-opened benzamides (**6** and **7**), while alkaline hydrolysis afforded not ring-opened amides such as **6** and **7**, but debenzoylated pyrrolinone derivatives (**9**). For instance, refluxing of **2a** in water and in methanol gave benzamidoacetone[12] (**6**) and methyl 4-benzamidoacetoacetate (**7**) in 90 and 84% yield, respectively. Heating of **2a** with barium hydroxide gave a 50% yield of the pyrrolinylpyrrolinone derivative (**9**).

Photoreactions of diketene with some azides were also examined. On irradiation, *p*-toluoyl azide (**1b**),[9] *p*-chlorobenzoyl azide (**1c**)[9] and *p*-toluoyl azide (**1d**)[9] reacted with diketene giving the corresponding 1-aroyl-4-hydroxy-3-pyrrolin-2-ones (**2b**, **2c**, and **2d**). However, photoreaction of *p*-nitrobenzoyl azide[9] did not give the pyrrolinone.

The structures of compounds **2b**, **2c**, and **2d** were confirmed by elemental analyses and comparison of their spectral data with those of compound **2a**. Heating of compounds **2b**, **2c**, and **2d** in acetic anhydride afforded the acetates (**4b**, **4c**, and **4d**), which were hydrolyzed with potassium hydroxide in methanol to give **2b**, **2c**, and **2d**, respectively.

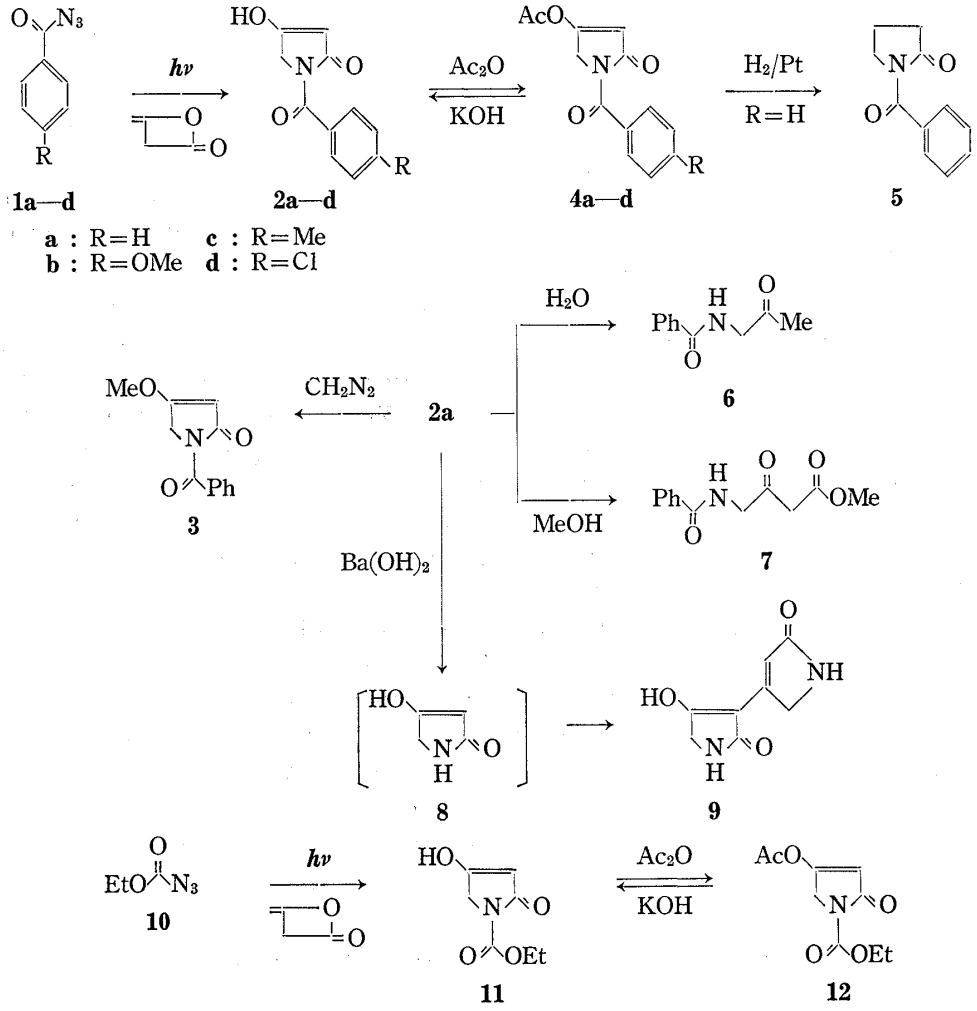

Chart 1

Photoreaction of ethyl azidoformate (**10**) with diketene also gave the pyrrolinone derivative (**11**), which was isolated as the acetate (**12**). Under mild conditions, the acetate was hydrolyzed to **11** in good yield. Without irradiation, reaction of diketene with benzoyl azide (**1a**) did not proceed, resulting in the recovery of the starting diketene.

11) G. Lowe and H.W. Yeung, *J. Chem. Soc. Perkin Trans. I*, **1973**, 2907.
12) S. Gabriel, *Ber.*, **43**, 1285 (1910).

Reaction of an aryl azide with an olefinic system such as an enol ether has been reported to give triazoline compounds,[13] but the reaction of phenyl azide with diketene failed to afford the corresponding triazoline derivative.

It is well-documented that the photochemical decomposition of acyl azides involves nitrene intermediates, which, in the presence of an olefin, can be transformed to aziridines.[13] As regards the formation of compounds **2** and **11**, the most likely pathway is as follows: that is, the nitrene intermediates produced on photolysis of acyl azides (**1**, **10**), add to the C=C double bond of diketene to give the spiro-compounds (**13**) as intermediates, and ring transformation of these would give the pyrrolinone derivatives (**2**, **11**). The low yields of the pyrrolinones (**2**) are presumably attributable to photo-Curtius rearrangement of the acyl azides (**1**) to the isocyanates.[14]

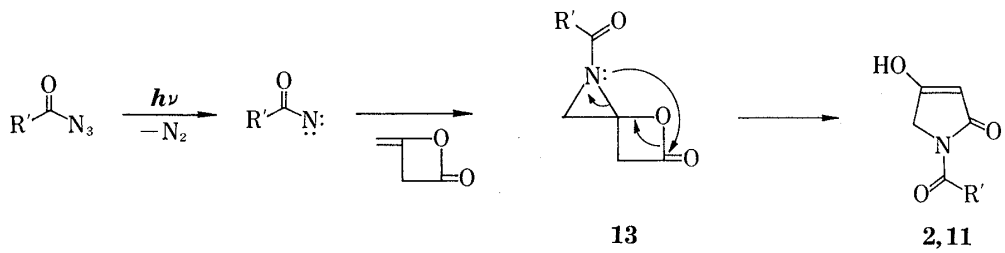

Chart 2

Experimental

Melting points are uncorrected. ^{1}H–Nuclear magnetic resonance (NMR) spectra were taken on a Hitachi R-20 spectrometer using tetramethylsilane as an internal standard. Infrared (IR) spectra were taken on a Nihonbunko IR-S unit, and mass spectra (MS) on a Hitachi RMU-7 machine. Alcohol-free dichloromethane was used for photoreactions.

1-Benzoyl-4-hydroxy-3-pyrrolin-2-one (**2a**)——A solution of benzoyl azide[9] (8.1 g) and diketene (42 g) in dichloromethane (200 ml) was irradiated[15] until the characteristic azide band at 2150 cm^{-1} had almost disappeared in the IR spectrum of the solution (6 hr). The solvent and excess diketene were evaporated off *in vacuo* at room temperature to give a crystalline residue, to which ethyl acetate was added, and crystals that separated were collected by filtration. Yellowish crystals (2.5 g) were recrystallized from methanol–ethyl acetate (1: 1) to give 2.05 g (17%) of yellowish prisms, mp 180° (dec.). *Anal.* Calcd. for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.06; H, 4.47; N, 6.64. IR (KBr) cm^{-1}: 3200—2560, 1670, 1580. NMR (DMSO-d_6): 4.39 (2H, s), 4.95 (1H, s), 7.46 (5H, s). MS *m/e*: 203 (M^+), 175, 105, 77.

1-Benzoyl-4-methoxy-3-pyrrolin-2-one (**3**)——To a suspension of **2a** (203 mg) in dioxane (10 ml), was added a solution of excess diazomethane in ether. The mixture was stirred at room temperature for 15 min. The solvent was evaporated off, and the residue was chromatographed on a silica gel (5 g) column using chloroform as an eluant. The crystalline material obtained was recrystallized from ether–hexane to afford 150 mg (70%) of needles, mp 130°. *Anal.* Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.21; H, 5.18; N, 6.49. IR ($CHCl_3$) cm^{-1}: 1730, 1660, 1630. NMR ($CDCl_3$) δ: 3.88 (3H, s), 4.47 (2H, s), 5.09 (1H, s), 7.32—7.74 (5H, m).

4-Acetoxy-1-benzoyl-3-pyrrolin-2-one (**4a**)——A mixture of **2a** (203 mg) and acetic anhydride (10 ml) was refluxed for 1 hr. The reaction mixture was evaporated to dryness *in vacuo* and the residue was crystallized from hexane. The crystals were filtered and recrystallized from cyclohexane to give 226 mg (92%) of needles, mp 133°. *Anal.* Calcd. for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.95; H, 4.73; N, 6.02. IR ($CHCl_3$) cm^{-1}: 1805, 1745, 1678, 1633. NMR ($CDCl_3$) δ: 2.29 (3H, s), 4.68 (2H, d, J=1 Hz), 6.02 (1H, t, J=1 Hz), 7.38—7.74 (5H, m).

Hydrolysis of Compound 4a——To a solution of **4a** (49 mg, 0.2 mmol) in methanol (10 ml), 0.2 N KOH–methanol (1 ml) was added with stirring. The mixture was stirred at room temperature for 20 min. A drop of 10% HCl was added, and the reaction mixture was rapidly evaporated down *in vacuo* at room temperature. Cold water (1 ml) was added to the residue, and the separated crystals were collected by suction. Yield 32 mg (80%). The IR spectrum was identical with that of **2a**.

13) G. L'abbe, *Chem. Rev.*, **64**, 345 (1968).
14) The reaction mixture of **1** and diketene showed strong absorption in the IR spectrum at 2260 cm^{-1}, which is assignable to –N=C=O of the corresponding isocyanate.
15) A 400 watt high-pressure mercury lamp with a Pyrex filter.

1-Benzoyl-2-pyrrolidone (5)——A mixture of **4a** (245 mg) and PtO_2 (50 mg) in AcOH (10 ml) was shaken in hydrogen at room temperature under atmospheric pressure for 1 hr, during which time 60 ml of hydrogen was absorbed. The catalyst was filtered off, and the filtrate was evaporated to dryness *in vacuo*. Recrystallization of the residue from ether–hexane gave 150 mg (79%) of needles, mp 89—90° (lit. mp 89—90°), undepressed on admixture with an authentic sample prepared according to the literature.[10]

Benzamidoacetone (6)——Compound **2a** (102 mg) was heated under reflux in water (10 ml) for 2.5 hr. The solution was evaporated to dryness *in vacuo*. Recrystallization of the residue from ether gave 80 mg (90%) of colorless leaves, mp 83°, undepressed on admixture with an authentic sample prepared according to the literature.[12]

Methyl 4-Benzamidoacetoacetate (7)——A solution of **2a** (102 mg) in methanol (10 ml) was refluxed for 5 hr. The solvent was evaporated off, and the residue was recrystallized from cyclohexane–chloroform to give 99 mg (84%) of colorless leaves, mp 88°. *Anal.* Calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.54; H, 5.68; N, 6.14. IR ($CHCl_3$) cm^{-1}: 3420, 1740, 1720, 1655. NMR ($CDCl_3$) δ: 3.52 (2H, s), 3.71 (3H, s), 4.40 (2H, d, J=4.7 Hz), 7.6 (1H, br), 7.20—7.90 (5H, m).

4-Hydroxy-3-[4-(2-oxo-3-pyrrolinyl)]-3-pyrrolin-2-one (9)——A mixture of **2a** (203 mg) and 0.2 N $Ba(OH)_2$ (10 ml) was warmed at 95° for 30 min. CO_2 gas was bubbled into the solution and precipitates were filtered off. The filtrate was condensed to 2 ml *in vacuo*, and acidified with dil. HCl. Crystals formed were collected and washed with cold water to give 90 mg (50%) of colorless crystals, mp>360°. *Anal.* Calcd. for $C_8H_8N_2O_3 \cdot 1/2\ H_2O$: C, 50.79; H, 4.80; N, 14.81. Found: C, 50.50; H, 4.73; N, 14.62. IR (Nujol) cm^{-1}; 3250, 2600, 1650, 1620. NMR (DMSO-d_6) δ: 3.90 (2H, s), 4.23 (2H, s), 6.27 (1H, s), 7.5 (1H, br), 7.9 (1H, br). MS *m/e*: 180 (M^+), 152, 123.

1-(*p*-Anisoyl)-4-hydroxy-3-pyrrolin-2-one (2b)——A solution of *p*-anisoyl azide[9] (10.6 g) and diketene (42 g) in dichloromethane (200 ml) was irradiated[14] and worked up as described above to give 3.5 g of crude crystals. Recrystallization from methanol–ethyl acetate (1:1) afforded 2.9 g (22%) of colorless leaves, mp 180° (dec.). An analytical sample was prepared by recrystallization from tetrahydrofuran. Prisms, mp 181° (dec.). *Anal.* Calcd. for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 62.04; H, 4.86; N, 5.64. IR (KBr) cm^{-1}: 3000—2400, 1680, 1640, 1620, 1560. NMR (DMSO-d_6) δ: 3.81 (3H, s), 4.38 (2H, s), 4.94 (1H, s), 6.80—7.65 (4H, m).

4-Acetoxy-1-(*p*-anisoyl)-3-pyrrolin-2-one (4b)——A mixture of recrystallized **2b** (233 mg) and Ac_2O (10 ml) was refluxed for 30 min. The mixture was evaporated to dryness *in vacuo*, and the residue was crystallized from hexane. Recrystallization from cyclohexane gave 248 mg (90%) of colorless needles, mp 125°. *Anal.* Calcd. for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.15; H, 4.78; N, 4.98. IR ($CHCl_3$) cm^{-1}: 1800, 1738, 1670, 1630. NMR ($CDCl_3$) δ: 2.31 (3H, s), 3.84 (3H, s), 4.59 (2H, d, J=1 Hz), 6.05 (1H, t, J=1 Hz), 6.80—7.85 (4H, m).

Using the method described for **2a**, **4b** (138 mg, 0.5 mmol) was treated with 0.2 N KOH–methanol (2.5 ml) in methanol (10 ml) to give 100 mg (85%) of colorless crystals, mp 181° (dec.), having an IR spectrum identical in every respect with that of **2b**.

4-Hydroxy-1-(*p*-toluoyl)-3-pyrrolin-2-one (2c) and 4-Acetoxy-1-(*p*-toluoyl)-3-pyrrolin-2-one (4c)——A solution of *p*-toluoyl azide[9] (1.61 g) and diketene (21 g) in dichloromethane (20 ml) was irradiated[16] for 10 hr. The reaction mixture was cooled in an ice bath. The precipitates were filtered and washed with benzene. The crude product (**2c**) was heated in Ac_2O (10 ml) at 100° for 30 min. The reaction mixture was evaporated to dryness *in vacuo*, and the residue was recrystallized from cyclohexane to give 223 mg (9%) of colorless needles (**4c**), mp 128°. *Anal.* Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.91; H, 5.01; N, 5.24. IR ($CHCl_3$) cm^{-1}: 1800, 1740, 1670, 1631. NMR (CCl_4) δ: 2.22 (3H, s), 2.39 (3H, s), 4.45 (2H, d, J=1 Hz), 5.88 (1H, t, J=1 Hz), 7.01—7.60 (4H, m).

Following the procedure given for the deacetylation of **4a**, the acetate (**4c**) (130 mg, 0.5 mmol) was treated with 0.2 N KOH–methanol (2.5 ml) to give 84 mg (77%) of crude **2c** as colorless crystals. Recrystallization from tetrahydrofuran gave prisms, mp 168.5° (dec.). *Anal.* Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.28; H, 5.14; N, 6.39. IR (KBr) cm^{-1}: 3000—2600, 1730 (sh), 1720 (sh), 1680, 1615, 1590. NMR (DMSO-d_6) δ: 2.35 (3H, s), 4.38 (2H, s), 4.96 (1H, s), 7.08—7.57 (4H, m).

1-(*p*-Chlorobenzoyl)-4-hydroxy-3-pyrrolin-2-one (2d) and 4-Acetoxy-1-(*p*-chlorobenzoyl)-3-pyrrolin-2-one (4d)——Following the procedure given for **2c**, *p*-chlorobenzoyl azide[9] (1.81 g) and diketene (21 g) were irradiated in dichloromethane (20 ml), and the crude product was acetylated to give 311 mg (11%) of needles (**4d**), mp 116° (from cyclohexane). *Anal.* Calcd. for $C_{13}H_{14}ClNO_4$: C, 55.83; H, 3.60; Cl, 12.68; N, 5.01. Found: C, 55.89; H, 3.72; Cl, 12.80; N, 4.96. IR ($CHCl_3$) cm^{-1}: 1795, 1735, 1675, 1630. NMR ($CDCl_3$) δ: 2.25 (3H, s), 4.47 (2H, d, J=1 Hz), 5.90 (1H, t, J=1 Hz), 7.32—7.65 (4H, m).

Compound **4d** (149 mg) was hydrolyzed to **2d** employing a procedure similar to that used for the deacetylation of **4a**. Yield, 84 mg (77%). Recrystallization from tetrahydrofuran gave needles, mp 175° (dec.). *Anal.* Calcd. for $C_{11}H_8ClNO_3$: C, 55.46; H, 3.39; Cl, 14.88; N, 5.88. Found: C, 55.78; H, 3.42; Cl, 14.88; N,

16) A 100 watt high-preseure mercury lamp with a Pyrex filter.

5.85. IR (KBr) cm^{-1}: 3000—2400, 1690, 1682, 1630, 1600, 1550. NMR (DMSO-d_6) δ: 4.39 (2H, s), 4.97 (1H, s), 7.51 (4H, s).

1-Ethoxycarbonyl-4-hydroxy-3-pyrrolin-2-one (11) and 4-Acetoxy-1-ethoxycarbonyl-3-pyrrolin-2-one (12) ——A solution of ethyl azidoformate[17] (8.5 g) and diketene (42 g) in dichloromethane (200 ml) was irradiated[14] until the characteristic azide bands at 2160 and 2200 cm^{-1} had disappeared in the IR spectrum of the solution (*ca.* 8 hr). The solvent and excess diketene were removed at room temperature under reduced pressure. The oily residue obtained was heated in Ac_2O (20 ml) under reflux for 30 min. Ac_2O was evaporated off *in vacuo*, and the oily residue was extracted with hot hexane (100 ml). Condensation of the hexane layer gave an oil, which crystallized in a refrigerator. Recrystallization from hexane–ether gave 1.5 g (7%) of colorless prisms (**12**), mp 60—61°. *Anal.* Calcd. for $C_9H_{11}NO_5$: C, 50.70; H, 5.20; N, 6.57. Found: C, 50.79; H, 5.00; N, 6.64. IR ($CHCl_3$) cm^{-1}: 1790, 1740, 1730. NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7 Hz), 2.32 (3H, s), 4.38 (2H, q, J=7 Hz), 4.45 (2H, d, J=1 Hz), 6.10 (1H, t, J=1 Hz).

To a stirred solution of the acetate (**12**) (426 mg) in methanol (5 ml) containing phenolphthalein as an indicator, KOH–methanol solution was added dropwise until the mixture became colored. After stirring for a further 5 min, the mixture was acidified (pH 3) with 10% HCl and evaporated down *in vacuo* at room temperature. Water (2 ml) was added to the residue, and insoluble material was collected, washed with cold water and dried to give 332 mg (91%) of colorless prisms (**11**), mp 102—105°. Recrystallization from benzene gave prisms, mp 105—108°. *Anal.* Calcd. for $C_7H_9NO_4 \cdot 1/2H_2O$: C, 46.67; H, 5.60; N, 7.78. Found: C, 47.05; H, 5.54; N, 7.78. IR (Nujol) cm^{-1}: 3500, 1760, 1670, 1600. NMR (DMSO-d_6) δ: 1.25 (3H, t, J=7 Hz), 4.19 (2H, q, J=7 Hz), 4.20 (2H, s), 4.95 (1H, s).

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17) W. Lwowski and T.W. Mattingly, Jr., *J. Am. Chem. Soc.*, **87**, 1947 (1965).