CHEMISTRY LETTERS, pp. 597-600, 1976. Published by the Chemical Society of Japan

REACTION OF PYRIDINIUM YLIDES WITH DIETHYL AZODICARBOXYLATE
—— A FACILE SYNTHESIS OF Δ^2-1,3,4-OXADIAZOLINES ——

Teruaki MUKAIYAMA*, Kunio ATSUMI**, and Takeshi TAKEDA**

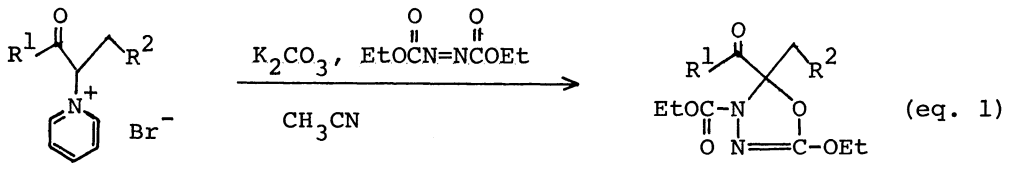
* Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

** Laboratory of Organic Chemistry, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152

The pyridinium ylides, derived from 1-(2-oxoalkyl)pyridinium salts, reacted with diethyl azodicarboxylate to give Δ^2-1,3,4-oxadiazolines, which isomerized to α-[N,N'-bis(ethoxycarbonyl)-hydrazino]-α,β-unsaturated carbonyl compounds on treatment with acid such as trifluoromethanesulfonic acid.

Several works have been reported on the synthesis of Δ^2-1,3,4-oxadiazolines by the reaction of diazo compounds with azodicarboxylic ester or dibenzoyldiimide.[1]

In the course of our study on the oxidation of pyridinium salts,[2] it was found that Δ^2-1,3,4-oxadiazolines (II) were obtained in good yields when the pyridinium ylides, easily produced from 1-(2-oxoalkyl)pyridinium bromides (I), were allowed to react with diethyl azodicarboxylate (eq. 1). The reaction may be carried out by the nucleophilic addition of the pyridinium ylide to diethyl azodicarboxylate followed by intramolecular displacement of pyridine similar to the reaction of 1,2-dibenzoylethylene with phenacylpyridinium ylide recently reported by Landberg and Lown.[3]



(I) (II) (eq. 1)

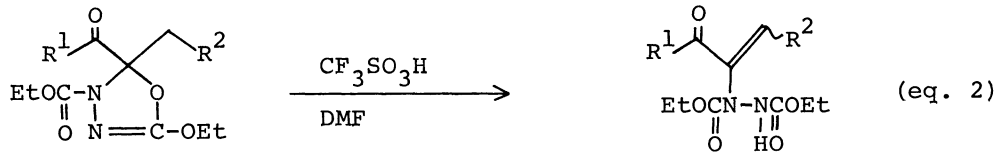
The typical reaction procedure is described for the reaction of 1-(1-ethylacetonyl)pyridinium bromide with diethyl azodicarboxylate; to a solution of 1-(1-ethylacetonyl)pyridinium bromide (0.500 mmol) and diethyl azodicarboxylate (0.525 mmol) in CH_3CN (5 ml) was added K_2CO_3 (0.525 mmol) at room temperature under an argon atmosphere and the mixture was stirred for 1 hr at 50-55°C. After cooling, the mixture was poured into a phosphate buffer solution (pH 7). An organic layer was extracted with ether and the extract was dried over anhydrous magnesium sulfate and condensed under reduced pressure. The residue was chromatographed on silica gel and 5-acetyl-2-ethoxy-4-ethoxycarbonyl-5-ethyl-Δ^2-1,3,4-oxadiazoline (IIa) was isolated in 91% yield.

In a similar manner, various Δ^2-1,3,4-oxadiazolines were prepared in good yields as shown in Table 1. However, Δ^2-1,3,4-oxadiazolines were too unstable to be isolated in the cases of 1-(α-alkylphenacyl)pyridinium bromides or 1-(1-methyl-2-oxoalkyl)pyridinium bromides.

Table 1. The synthesis of Δ^2-1,3,4-oxadiazolines (II)[4]

	R^1	R^2	Temp.(°C)	Time(hr)	Yield (%)
IIa	CH_3-	CH_3-	50-55	1	91
IIb	C_2H_5O-	H-	reflux	1	89
IIc	C_2H_5O-	$CH_3(CH_2)_8$	reflux	1	65
IId	C_2H_5O-	$C_2H_5OCCH_2$- (O)	reflux	1	61

It was also found that Δ^2-1,3,4-oxadiazolines (II) prepared according to the present procedure isomerized to α-[N,N'-bis(ethoxycarbonyl)hydrazino]-α,β-unsaturated carbonyl compounds (III) on treatment with trifluoromethanesulfonic acid in DMF (eq. 2).



(II) (III) (eq. 2)

The typical reaction procedure is as follows; 1-(1-ethylacetonyl)pyridinium bromide (0.500 mmol) was treated with diethyl azodicarboxylate (0.525 mmol) according to the above-mentioned procedure. The ethereal solution of 5-acetyl-2-ethoxy-4-ethoxycarbonyl-5-ethyl-Δ^2-1,3,4-oxadiazoline was condensed under reduced pressure and the resulting Δ^2-1,3,4-oxadiazoline was dissolved in DMF (5 ml). After trifluoromethanesulfonic acid (0.5 mmol) was added to the solution at 0°C, the reaction mixture was stirred overnight at room temperature. The mixture was poured into a phosphate buffer solution (pH 7), and an organic layer was extracted with ether. The extract was dried over anhydrous sodium sulfate and condensed under reduced pressure. The residue was chromatographed on silica gel and 3-[N,N'-bis(ethoxycarbonyl)hydrazino]-2-penten-4-one (IIIa) was isolated in 65% yield.

In a similar manner, various α-[N,N'-bis(ethoxycarbonyl)hydrazino]-α,β-unsaturated carbonyl compounds were obtained in fairly good yields (see Table 2).

Table 2. The synthesis of the α-[N,N'-bis(ethoxycarbonyl)hydrazino]-α,β-unsaturated carbonyl compounds (III) [4]

	R^1	R^2	The reaction conditions: The synthesis of the Δ^2-1,3,4-oxadiazolines Temp.(°C)	Time(hr)	The acid isomerization Temp.(°C)	Time(hr)	Yield (%)
IIIa	CH_3-	CH_3-	r.t.	overnight	r.t.	overnight	65
IIIb	C_2H_5O-	H-	r.t.	21	r.t.	overnight	77
IIIc	C_2H_5O-	$CH_3(CH_2)_8$			r.t.	25	66 a)
IIId	C_2H_5O-	$C_2H_5OCCH_2$- (O)			90-95	3	56 a),b)
IIIe	CH_3-	H-	r.t.	overnight	r.t.	overnight	47
IIIf	C_2H_5-	H-	45-50	overnight	r.t.	overnight	52
IIIg		H-	r.t.	2.5	r.t.	overnight	77
IIIh		CH_3-	r.t.	2.5	r.t.	overnight	85

a) Based on the isolated Δ^2-1,3,4-oxadiazoline.

b) Two molar equivalents of trifluoromethanesulfonic acid were used.

Further study on the reaction of Δ^2-1,3,4-oxadiazolines is now under investigation and will be reported soon.

References and Note

1) E. Müller, Ber., 47, 3001 (1914); H. Staudinger and A. Gaule, ibid., 49,1961 (1916); O. Diels and H. König, ibid., 71, 1179 (1938); L. Horner and E. Lingnan, Ann. Chem., 591, 21 (1955); E. Fahr, Angew. Chem., 73, 536 (1961); R. Breslow, C. Yaroslavsky, and S. Yaroslavsky, Chem. Ind. (London), 1961 (1961); E. Fahr, K. Döppert, and F. Scheckenbach, Angew. Chem., 75, 670 (1963).
2) T. Mukaiyama, K. Atsumi, and T. Takeda, Chem. Lett., 1033 (1975); T. Takeda and T. Mukaiyama, Chem. Lett., 347 (1976).
3) B. E. Landberg and J. W. Lown, J. Chem. Soc., Perkin Trans. I, 1326 (1975).
4) The structures of these compounds are supported by ir and nmr spectra and elemental analysis. (IIa): oil; ir 1742, 1700 , 1675 cm^{-1}; nmr ($CDCl_3$) δ1.00 (t, J=7 Hz, 3H), 1.31 (t, J=7 Hz, 3H), 1.43 (t, J=7 Hz, 3H), 2.00-2.60 (m, 2H), 2.26 (s, 3H), 4.30 (q, J=7 Hz, 2H), 4.45 (q, J=7 Hz, 2H). (IIb): mp 59.0-60.5°C (from n-hexane); ir 1758, 1705, 1677 cm^{-1}; nmr ($CDCl_3$) δ1.23 (t, J=7 Hz, 6H), 1.40 (t, J=7 Hz, 3H), 1.93 (s, 3H), 4.27 (q, J=7 Hz, 2H), 4.30 (q, J=7 Hz,2H), 4.41 (q, J=7 Hz, 2H); Anal. Calcd for $C_{11}H_{18}O_6N_2$: C, 48.17; H, 6.61; N,10.22%. Found: C, 48.46; H, 6.59; N, 10.35%. (IIc): oil; ir 1761, 1708, 1678 cm^{-1}; nmr ($CDCl_3$) δ0.72-1.67 (m, 28H), 2.10-2.60 (m, 2H), 4.06-4.60 (m, 6H). (IId): oil; ir 1760, 1740, 1710, 1680 cm^{-1}; nmr ($CDCl_3$) δ1.17-1.63 (m, 12H), 2.36-2.90 (m, 4H), 3.99-4.67 (m, 8H). (IIIa): oil; ir 1730, 1687, 1651 cm^{-1}; nmr ($CDCl_3$) δ1.27 (t, J=7 Hz, 6H), 2.11 (d, J=7 Hz, 3H), 2.37 (s, 3H), 4.20(q, J=7 Hz, 4H),6.79-7.26 (m, 2H); Anal. Calcd for $C_{11}H_{18}O_5N_2$: C, 51.15; H, 7.03; N, 10.85%. Found: C, 50.96; H, 6.98; N, 10.72%. (IIIb): oil; ir 1730, 1640 cm^{-1}; nmr ($CDCl_3$) δ1.28 (t, J=7 Hz, 3H), 1.32 (t, J=7 Hz, 3H), 1.26 (t, J=7 Hz, 3H), 4.25 (q, J=7 Hz, 4H), 4.32 (q, J=7 Hz, 2H), 6.01 (s, 1H), 6.23 (s, 1H), 7.55-7.78 (broad, 1H). (IIIc): oil; ir 1710-1760, 1650 cm^{-1}; nmr ($CDCl_3$) δ0.73-1.70 (m, 26H), 2.37-2.84 (m, 2H), 4.01-4.30 (m, 6H), 6.68 (t, J=7 Hz, 1H), 7.10-7.27 (broad, 1H). (IIId): oil; ir 1710-1770, 1668 cm^{-1}; nmr ($CDCl_3$) δ1.10-1.53 (m, 12H), 3.65 (d, J=7 Hz, 2H), 4.00-4.50 (m, 8H), 6.90-7.30 (m, 2H). (IIIe): oil; ir 1700-1760, 1623 cm^{-1}; nmr ($CDCl_3$) δ1.24 (t, J=7 Hz, 3H), 1.28 (t, J=7 Hz, 3H), 2.37 (s, 3H), 4.23 (q, J=7 Hz, 4H), 5.96 (s, 2H), 7.43-7.66 (broad, 1H). (IIIf): oil; ir 1700-1760, 1625 cm^{-1}; nmr ($CDCl_3$) δ0.97-1.53 (m, 9H), 3.76 (q, J=7 Hz, 2H), 4.21 (q, J=7 Hz, 2H), 4.24 (q, J=7 Hz, 2H), 5.92 (s, 2H), 7.47-7.72 (broad, 1H). (IIIg): mp 93.0-95.0°C (from cyclohexane-EtOH); ir 1730, 1675, 1625 cm^{-1}; nmr ($CDCl_3$) δ1.11 (t, J=7 Hz, 3H), 1.32 (t, J=7 Hz, 3H), 4.17 (q, J=7 Hz, 2H), 4.40 (q, J=7 Hz, 2H), 5.30-5.46 (m, 1H), 5.75-5.92 (m, 1H), 7.32-7.73 (m, 4H), 7.89-8.20 (m, 2H); Anal. Calcd for $C_{15}H_{18}O_5N_2$: C, 58.81; H, 5.91; N, 9.51%. Found: C, 58.52; H, 5.91; N, 9.34%. (IIIh): mp 80.0-81.5°C (from n-hexane-benzene); ir 1730, 1675 cm^{-1}; nmr ($CDCl_3$) δ1.06 (t, J=7 Hz, 3H), 1.29 (t, J=7 Hz, 3H), 1.61 (d, J=8 Hz, 3H), 4.07 (q, J=7 Hz, 2H), 4.25 (q, J=7 Hz, 2H), 6.31 (q, J=8 Hz, 1H), 7.27-7.70 (m, 4H), 7.93-8.12 (m, 2H).

(Received April 3, 1976)