that the C_1-H of the *cis* compound has 3—5 Hz of a J value but that of the *trans* 10—12 Hz. The fact that the signal[12] due to the C_1–H of these products (**12**) appears at δ 3.70 as a doublet having about 4 Hz of a J value allowed us to assign the configuration of them to be *cis*.

Refluxing these products (**12**) with chloral in $CHCl_3$ afforded 1,2,3,4-tetrahydro-1-naphthylformamides[11] (**13**) in 83.0% [**13a**: mp 182.5—185°] and 87.0% [**13b**: mp 161—162°] yields. Dehydrogenation of these formamides (**13**) with DDQ gave the fully aromatized formamides[11] (**14**) in 84.9% [**14a**: mp 217—219°] and 80.6% [**14b**: mp 211—215°] yields.

Bischler–Napieralski reaction of the trimethoxy-formamide (**14a**) with $POCl_3$ in xylene afforded red needles, mp 281—284° (lit.[5a] mp 275—276°) in 42.4% yield, which was identified with an authentic sample of sanguirubine[5] (**3**) chloride.

On the other hand, treatment of the pentamethoxy-formamide (**14b**) with $POCl_3$ in CH_3CN gave orange needles, mp 140—145° (dec.) (lit.[5a] mp 163—164°) in 60.8% yield, which was identified with an authentic sample of sanguilutine [5] (**4**) chloride. This material was also characterized as ϕ-cyanide (**15**), mp 228—232° (lit.[5a] mp 232—233°).

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Synthesis of Isoxazole Derivatives by Means of O-Acylation of Aliphatic Nitro Compounds in the Presence of Acetylenic Compounds[1]

O-Acylation of some aliphatic nitro compounds or their alkali metal salts with acid chlorides in N,N-dimethylacetamide in the presence of acetylenic compounds afforded isoxazole derivatives in fairly good yield. The reaction is shown to arise from 1,3-dipolar cycloaddition of acetylenic compounds to the nitrile oxide intermediates which would resulted from the fragmentation of the initially formed O-acylated product.

Keywords——isoxazole; aliphatic nitro compounds; nitrile oxide; acetylenic compounds; dipolar aprotic solvent; O-acylation; fragmentation; 1,3-dipolar cycloaddition

Several examples have been reported of the O-acylation of aliphatic nitro compounds in which stable nitronic carboxylic anhydrides (mixed anhydrides) are formed from secondary nitroalkanes with acylating agents, while in the case of primary nitroalkanes, the correspond-

1) The Synthetic Reactions of Aliphatic Nitro Compounds. Part XIII: Presented at the 37th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1978: Abstracts, II, p. 731: Part XII of this series: E. Kaji, H. Kohno, and S. Zen, *Bull. Chem. Soc. Jpn.*, **50**, 928 (1977).

ing mixed anhydrides have not been isolated and the rearrangement of initially formed mixed anhydrides to hydroxamic acid esters has been observed.[2,3]

Our current interest in alkylation of nitronate ambident anions in a dipolar aprotic solvent,[4] also directed towards acylation of aliphatic nitronate anions in such a solvent. We have found that the reaction of primary nitro compounds such as nitroethane, phenylnitromethane, and methyl nitroacetate with acetyl chloride in N,N-dimethylacetamide (DMA) at room temperature gave 3,4-disubstituted furoxanes (**3**: R^1=CH_3, C_6H_5, or $COOCH_3$)[5] characterized by physical and spectroscopic identification. The mechanism of formation of the furoxanes appears to involve dimerization of nitrile oxides as intermediates which would result from the fragmentation of initially formed mixed anhydrides (**1**) as shown in Chart 1.

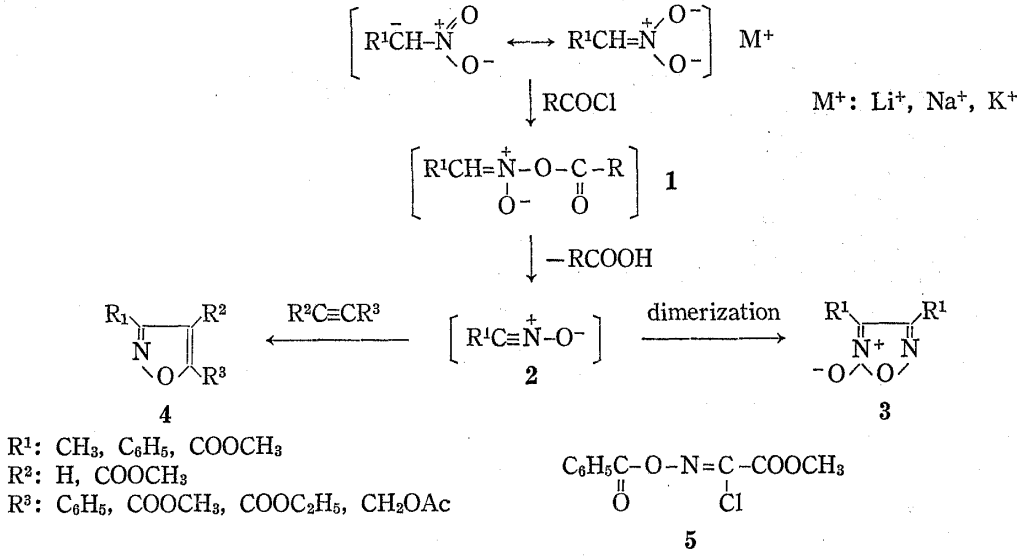

Chart 1

To support above suggestion and hoping this acylation to an isoxazole synthesis, we attempted to trap the nitrile oxides (**2**) with several acetylenic compounds as dipolarophiles.[6]

Typical experimental conditions are exemplified as follows (Method-A): to a stirred solution of 300 mg (4 mmol) of nitroethane in 15 ml of anhydrous DMA, was added 4 ml of 1 N sodium methoxide in methanol. The mixture was cooled to 5° in an ice-bath, 0.28 ml (4 mmol) of acetyl chloride and 0.49 ml (4 mmol) of dimethyl acetylenedicarboxylate were added. After the addition had been completed the mixture was stirred for about 16 hr at room temperature, then 60 ml of ice-water was added. The resulting mixture was extracted with benzene. The extract was concentrated, and the resultant syrup was chromatographed on silica gel with hexane–ethyl acetate (3: 1) as developer, giving 595 mg of 3-methyl-4,5-bis-(methoxycarbonyl)isoxazole (**4a**): mp 31—32° (methanol–water) in 75% yield. The infrared (IR), proton magnetic resonance (PMR) spectra, and elemental analysis of the product (**4a**)

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3) A. McKillop and R.J. Kobylecki, *Tetrahedron*, **30**, 1365 (1974).
4) E. Kaji, A. Igarashi, and S. Zen, *Bull. Chem. Soc. Jpn.*, **49**, 3181 (1976) and our preceding papers.
5) J.V.R. Kaufman and J.P. Picard, *Chem. Rev.*, **59**, 429 (1959).
6) A closely related work has been shown that reaction of primary nitroalkanes with isocyanate and a catalytic amount of triethylamine in the presence of acetylenic compounds gives isoxazoles, in which the intermediate is also believed to be nitrile oxide. (T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.* **82**, 5339 (1960); Some applications of the above reaction were reported: G.B. Bachman and L.E. Strom, *J. Org. Chem.*, **28**, 1150 (1963); J.E. McMurry, "Organic Syntheses," vol. 53, ed. by A. Brossi, John Wiley and Sons, Inc., New York, 1973, p. 59.)

Table I. Isoxazole Derivatives synthesized by Means of O-Acylation of Aliphatic Nitro Compounds with Acetyl Chloride

Compounds 4	R^1	R^2	R^3	mp (°C) bp (°C/Torr)	Yield (%) Method-A	Yield (%) Method-B
a	CH_3	CO_2CH_3	CO_2CH_3	31—32[a]	75	44
b	CH_3	H	CH_2OAc	65—73/2[b]	39	36
c	CH_3	H	$CO_2C_2H_5$	27—28[c]	54	45
d	CH_3	H	C_6H_5	65—66[d]	36	23
e	C_6H_5	CO_2CH_3	CO_2CH_3	63.5—64.5[e]	76	71
f	C_6H_5	H	CH_2OAc	37—38[f]	57	44
g	C_6H_5	H	$CO_2C_2H_5$	45—46[g]	63	53
h	C_6H_5	H	C_6H_5	141—143[h]	47	44
i	CO_2CH_3	CO_2CH_3	CO_2CH_3	101—102[i]	20	17

a) Reported bp 74—76° (0.05 Torr).[8]
b) *Anal.* Calcd. for $C_7H_9NO_3$: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.54; H, 5.49; N, 9.25. MS *m/e*: 155 (M^+). PMR ($CDCl_3$) δ: 2.21 (3H, singlet, $COCH_3$), 2.30 (3H, singlet, CH_3), 5.11 (2H, singlet, CH_2), 6.16 (1H, singlet, =CH).
c) Reported mp 27°.[7]
d) Reported mp 67°.[8]
e) Reported mp 62—63°.[9]
f) mp is not shown in Ref. 9.
g) Reported mp 47°.[10]
h) Reported mp 141°.[11]
i) *Anal.* Calcd. for $C_9H_9NO_7$: C, 44.45; H, 3.73; N, 5.76. Found: C, 44.42; H, 3.66; N, 5.60. MS *m/e*: 243 (M^+). PMR ($CDCl_3$) δ: 3.94 (3H, singlet, CO_2CH_3), 3.97 (6H, singlet, CO_2CH_3); Corresponding tris(ethoxycarbonyl)isoxazole has been reported in Ref. 12.

gave satisfactory results. Table I shows physical constants and analytical data of isoxazole derivatives synthesized by above manner. Another method employed sodium ethanenitronate (Method-B) also gave the isoxazole (**4a**) in relatively low yield (44%) as shown in Table I. Application of a phase transfer catalyst, *e.g.*, 18-crown-6 in benzene or triethylbenzylammonium chloride in benzene–water resulted in 31 and 14% yield respectively for **4a**.

When benzoyl chloride (one equivalent) was used as an acylating agent for methoxycarbonylmethanenitronate, methyl 2-chloro-2-benzoyloxyiminoacetate (**5**) was isolated as a by-product; mp 125.5—126.5° (methanol–water), 33% yield, IR ν_{max}^{KBr} cm^{-1}: 1770 (ester C=O), 1740 (C_6H_5C=O), 1608 (C=N), PMR ($CDCl_3$) δ: 4.00 (3H, singlet, ester CH_3), 7.50—8.22 (5H, multiplet, C_6H_5), *Anal.* Calcd. for $C_{10}H_8ClNO_4$: C, 49.69; H, 3.31; N, 5.80. Found: C, 49.28; H, 3.32; N, 5.74. This compound (**5**) would be formed by addition reaction of excess benzoyl chloride to the nitrile oxide.

It should be noted that this method of the synthesis of isoxazoles is relatively facile and mild comparing with already reported ones.[3,10] Furthermore, as using olefinic dipolarophiles such as dimethyl fumarate, methyl acrylate and ethyl β-nitrocinnamate, some isoxazoline derivatives could be obtained; further details of these cases are now in progress.

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