Notes

Reaction of Lithiated Oxazines with Esters and Nitriles

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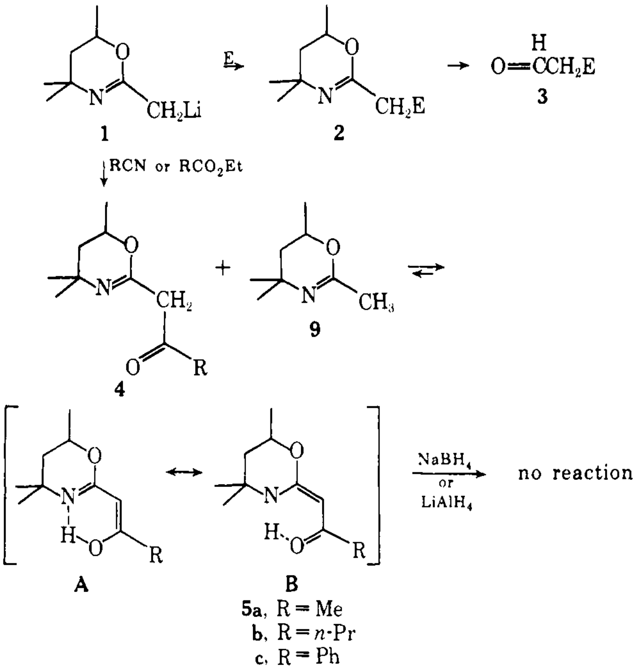
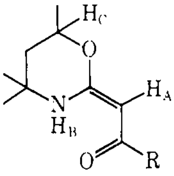
Among the various electrophiles, E (alkyl halides, carbonyl compounds, and epoxides), that react with the lithiooxazine 1[2] producing the elaborated oxazine 2, only those derived from esters and nitriles cannot be transformed into the homologated acetaldehydes 3. Although esters and nitriles acylated the lithio salt 1, the resulting β-keto oxazine 4 was inert to reduction by sodium borohydride and, therefore, could not be hydrolyzed (as its tetrahydro-1,3-oxazine) to β-keto aldehydes. The reason for this limitation in the oxazine-aldehyde synthesis is due mainly to the tautomeric behavior in 4 which was found to exist mainly as the delocalized species 5. The structures of 5a-c were deduced from their spectral properties (Table I).

Examination of the ultraviolet spectrum of the adducts 5 reveals long wavelength absorption (290-323 nm) with intense extinction coefficients (25,000-30,000) indicative of an extended conjugated chromophore. The infrared spectra for these derivatives were devoid of the typical C=N and C=O absorption bands at 1665 and 1710 cm^{-1}, respectively, while exhibiting delocalized absorption in the 1500-1610 cm^{-1} region. Further evidence that 5 and not 4 was the prevailing structure was gathered by the nmr spectrum which showed a one-proton vinyl signal as well as an NH proton that readily exchanged with deuterium oxide. This behavior is consistent with tautomerism observed in a variety of heterocyclic systems containing exocyclic β-carbonyl moieties.[3]



Recovery of the 2-methyl oxazine 9 was also noted in most cases when 1 was treated with the esters or nitriles. However, the amount of methyl oxazine recovered was always greater when acylation was performed with esters (% 9, Table I). For esters and nitriles possessing α protons, the appearance of 9 could be due to simple proton abstraction by 1 as a competitive reaction mode to addition. When benzonitrile or ethyl benzoate was used as the acylating agent, no α protons were present and yet 29% of 9 was still formed. Since the pK_a of the methyl group in acetonitrile and ethyl acetate have been estimated to be comparable (~25),[4] the greater recovery of 9 from ester

Table I
Reaction of 1 with Nitriles and Esters to Give 5 and 9

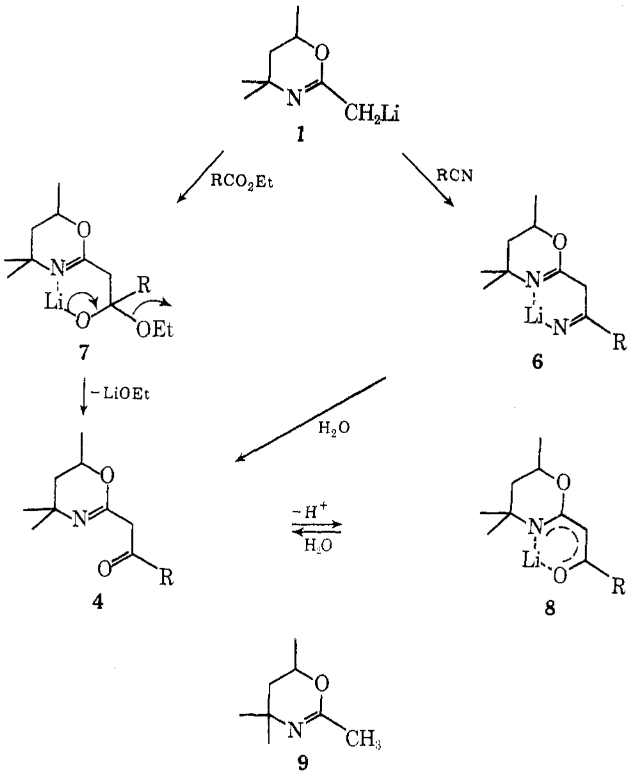


5

					5			Nmr (CCl$_4$)	
Nitrile[a] or ester		% **5**[b]	Mp,[c,d] °C	% **9**[b]	Uv (EtOH), nm (ε)	Ir (KBr), cm^{-1}	H$_A$	H$_B$	H$_C$
MeCN		70	64.5	30	293 (2.5 × 10^4)	1510	4.5	11.6	4.3
	5a					1550	(s, 1)	(b, 1)	(m, 1)
MeCO$_2$Et		50		50		1610			
n-PrCN		85	53	15	291 (2.4 × 10^4)	1500	4.5	11.8	4.3
	5b					1548	(s, 1)	(b, 1)	(m, 1)
n-PrCO$_2$Et		60		40		1610			
PhCN		100	85		323 (3.1 × 10^4)	1510	5.2	12.3	4.3
					231 (1.6 × 10^4)	1540	(s, 1)	(b, 1)	(m, 1)
	5c	71		29		1580			
PhCO$_2$Et						1600			

[a] Reactions run on a 0.02-mol scale. [b] Vpc ratios; isolated yields slightly lower. [c] Recrystallized from petroleum ether. [d] Elemental analysis: Calcd for $C_{10}H_{17}NO_2$ (**5a**): C, 65.54; H, 9.35; N, 7.64. Found: C, 65.28; H, 9.52; N, 7.60. Calcd for $C_{12}H_{21}NO_2$ (**5b**): C, 68.21; H, 10.02; N, 6.63. Found: C, 67.97; N, 9.94; N, 6.57. Calcd for $C_{15}H_{19}NO_2$ (**5c**): C, 73.44; H, 7.81; N, 5.71. Found: C, 73.63; H, 7.73; N, 5.74.

acylation must be due to proton abstraction from **4** generating the lithio salt **8**. Hence, **4** must be formed directly in the reaction medium. When acylation was performed using the nitrile, the initial intermediate is probably **6** which is much less acidic than **4** and the latter is not produced until the reaction is quenched. It is, therefore, concluded that acylations of oxazine carbanions are more efficiently performed using nitriles as the acylating agent.



Experimental Section[5]

α-Ketoalkyloxazines 5. General Acylation Procedure. A solution of **9** (0.02 mol) in 30 ml of tetrahydrofuran was cooled to −78° in Dry Ice-acetone and treated with 0.021 mol (1.6 *M*) of *n*-butyllithium (hexane). The system was under a nitrogen atmosphere throughout the addition. The anion **1** appeared within 1 hr as a yellow suspension and the ester or nitrile (0.21 mole) was added all at once. The reaction was allowed, while stirring, to warm to room temperature (8–15 hr) and then poured into water and acidified (1 *N* hydrochloric acid). The aqueous acid solution was extracted with ether-pentane (1:1) and the extracts were discarded. The aqueous solution was neutralized with 5% sodium bicarbonate and extracted with ether, dried (Na_2SO_4), and concentrated. The residue was recrystallized from petroleum ether to afford pure **5** (see Table I for physical constants).

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Registry No.—**1**, 50311-32-5; **5aA**, 50311-33-6; **5aB**, 50311-34-7; **5bA**, 50311-35-8; **5bB**, 50311-36-9; **5cA**, 50311-37-0; **5cB**, 50311-38-1; **9**, 26939-18-4; MeCN, 75-05-8; $MeCO_2Et$, 141-78-6; *n*-PrCN, 109-74-0; *n*-$PrCO_2Et$, 105-54-4; PhCN, 100-47-0; $PhCO_2Et$, 93-89-0.

References and Notes

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(2) A. I. Meyers, A. Nabeya, H. W. Adickes, I. R. Politzer, G. R. Malone, A. C. Kovelesky, R. L. Nolen, and R. C. Portnoy, *J. Org. Chem.*, **38**, 36 (1973).

(3) R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966).

(4) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, New York, N. Y., 1972, p 494.

(5) Melting points and boiling points are uncorrected. Analyses were performed by Midwest Microlabs, Indianapolis, Ind. Infrared, ultraviolet, and nmr spectra were recorded on Perkin-Elmer 257 and 202 and Varian T-60 instruments, respectively. Vapor phase chromatography was performed on a Hewlett-Packard 5750 using UCW-98 (80–100 mesh) columns.

Thermal Decomposition of β-Nitroalkyl Nitrates in Olefinic Solvents

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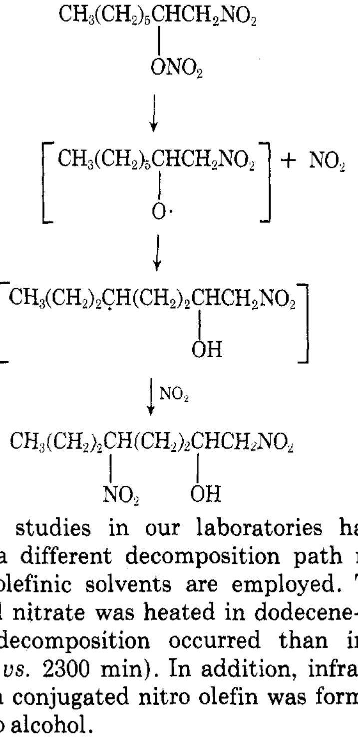
Kreuz and Larkin have shown that β-nitroalkyl nitrates decompose in paraffinic and aromatic solvents by a homolytic fission of the $O-NO_2$ bond, intramolecular rearrangement, and recombination to give dinitro alcohols.[1] Facile reaction requires somewhat higher temperatures for secondary (140–160°) than for tertiary (100–130°) nitrate structures.



$$CH_3(CH_2)_5\underset{ONO_2}{CH}CH_2NO_2 \rightarrow \left[CH_3(CH_2)_5\underset{O\cdot}{CH}CH_2NO_2\right] + NO_2 \rightarrow \left[CH_3(CH_2)_2\dot{C}H(CH_2)_2\underset{OH}{CH}CH_2NO_2\right] \xrightarrow{NO_2} CH_3(CH_2)_2\underset{NO_2}{CH}(CH_2)_2\underset{OH}{CH}CH_2NO_2$$

Subsequent studies in our laboratories have demonstrated that a different decomposition path may be followed when olefinic solvents are employed. Thus, when 1-nitro-2-octyl nitrate was heated in dodecene-1 at 138°, a more rapid decomposition occurred than in dodecane ($T_{1/2}$ 20 min *vs.* 2300 min). In addition, infrared analysis showed that a conjugated nitro olefin was forming instead of a 1,5-dinitro alcohol.

Product isolation was facilitated when the nitro nitrate, *e.g.*, 1-nitro-2-decyl nitrate, was heated in octene-1 at 123° for an extended period (8 hr). After removal of the solvent under reduced pressure, followed by chromatography of the residue on silica gel with hexane as eluent, 1-nitro-1-decene was isolated in 90% yield. Also isolated was a mixture of nitrogen-containing materials and evidently (from nmr analysis) solvent derived. In order to determine the importance of solvent nitration as a source of nitro olefin, 1-nitro-2-octyl nitrate was decomposed in 2,4,4-trimethylpentene-1. No nitro olefin derived from the solvent could be detected by nmr analysis of the product [lack of broadening of one of the doublet lines centered at δ 7.86 and absence of a methyl absorption near δ 8.22 [$-C(CH_3){=}CHNO_2$].

Table I gives the products formed and their yield as determined by isolation or nmr analysis for the decomposition of various β-nitroalkyl nitrates. One sees that secon-