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LITHIUM ION CATALYZED REACTIONS AND SALT-FREE PYROLYSIS OF AN α-IMINOOXETANE

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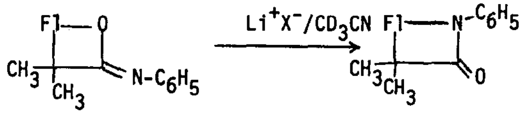
During a previous study of the photocycloaddition of fluorenone to ketenimines (2), we noted an interesting rearrangement of α-iminooxetanes to β-lactams during chromatography on Florisil (magnesium-silica gel support). Subsequent work shows that this rearrangement with iminooxetane **1** can be duplicated and manipulated in acetonitrile with lithium salts at moderate temperatures. Interestingly, with the perchlorate salt, a product resulting from incorporation of acetonitrile is formed in a Ritter-type reaction.



$Fl{=}C(CH_3)_2$ $Fl(OH)C(CH_3)_2CONHC_6H_5$

1, Fl=Fluorenyl **2** **3** **4**

The rearrangement of **1** (2) to **2** (2) is followed conveniently by proton nmr spectroscopy (**1**, *gem*-CH_3 δ1.4; **2**, *gem*-CH_3 δ1.3) in acetonitrile-d_3. The first-order rate constants, k_{obs}, were determined by conventional graphical analysis of the nmr data using the trace acetonitrile-d_2 multiplet at δ1.9 as an internal standard.

Reactions of **1** at 70° C in the presence of variable amounts of lithium bromide (dried by heating at 270° C/1 mm for several days) in degassed and sealed nmr tubes led to **2** (91%) and cleavage (9%) (2) to isopropylidenefluorene (*gem*-CH_3 δ2.5) and phenyl isocyanate. The k_{obs}'s and product yields are given in Table 1. From the good linear plot of k_{obs} vs salt conc., the second order rate constant for disappearance of **1** is determined to be $k_{LiBr} = (8.40 \pm 0.38) \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$ indicating a clear dependence on salt conc. Further, the salt-free reaction of **1** in acetonitrile-d_3 at 70° C proceeds with $k_{obs} = 2.6 \times 10^{-6}\ sec^{-1}$ and leads to 93% cleavage and only 7% **2**.

Under similar conditions with lithium perchlorate (dried at 270° C/1 mm for several days), **2**,**3**,**4** (3) and **5** were formed. Compound **5** is observed as a singlet at δ1.05 and will be discussed further below. Although, in individual runs where the water content was low (4), pseudo

Table 1. Kinetic data for the lithium bromide catalyzed reaction of **1** in acetonitrile-$\underline{d}_3$.[a]

[LiBr], $\underline{M}$	$k_{obs} \times 10^5$, sec^{-1} [b]		Products[c], mole fraction **2**	**3**
0.029	2.80 ± 0.24		0.89	0.11
0.036	3.93 ± 0.25		0.90	0.10
0.098	7.09 ± 0.28		0.92	0.08
0.218	17.4 ± 1.55		0.93	0.07
0.275	23.5 ± 0.97		0.92	0.08
		Ave.	0.91 ± 0.01	0.09 ± 0.01
0.000	0.26 ± 0.11		0.07	0.93

[a] At 70.3 ± 0.3° C in degassed and sealed nmr tubes. Followed by nmr spectroscopy with CD_2HCN as internal standard.

[b] Each entry is an average of at least two runs.

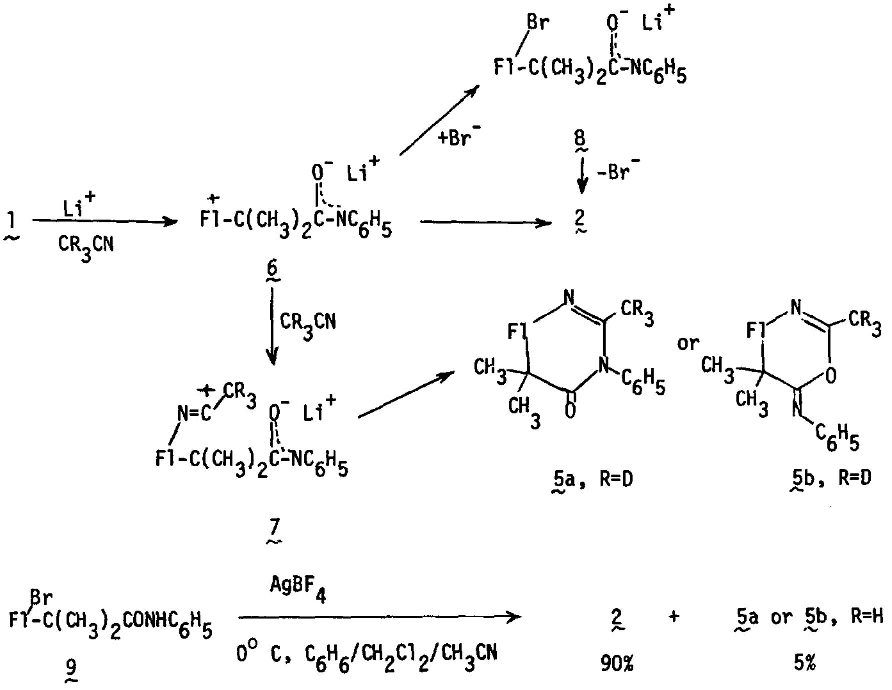
[c] Both **2** and **3** are stable to the reaction conditions. The yield of **2** and **3** accounted for >95% of starting **1**.

first order kinetics at rates comparable to the lithium bromide runs were noted out as far as 85% reaction, reproducible rate data could not be obtained. Under our "driest" conditions (<0.02% water), the major products were **2** and **5** (>90% formed 1:1) and **4** (<10%).

Compound **5**, tentatively, has been identified as a Ritter-type product resulting from incorporation of acetonitrile into **6** leading to nitrilium ion **7**, and then closure to **5a** or **5b**. This same product is formed (~5%) upon treatment of bromoamide **9** with silver tetrafluoroborate at 0° C in the presence of excess acetonitrile. (5) Compound **5** shows ir and nmr data consistent with **5a** or **5b**, with the latter data including singlets at δ1.05 and δ2.10 in a 2:1 ratio. Mass spectral analysis indicates a nominal MW = 366 (**5**, $C_{25}H_{22}N_2O$), a base peak at m/e 145 $[(CH_3)_2C{=}C{=}NC_6H_5]^{\dot{+}}$, and a well-defined metastable peak at m/e 57.4 corresponding to m/e 366 ⟶ m/e 145. The m/e 145 fragment supports structure **5b**.

The accelerated rates of disappearance of **1** in the presence of the lithium salts strongly suggest cation assisted ring-opening to an intermediate such as **6**. We propose that with lithium bromide, **6** is efficiently intercepted by Br^- to form **8**. The latter ring closes with high efficiency to **2** since the Ritter-type pathway is blocked. (6)

In the absence of added salt, cleavage dominates over isomerization and the product compositions and rate constants for disappearance of **1** are only slightly affected by solvent polarity (E_T) (7), Table 2. For comparision, second-order rate constants for the addition of piperidine to methyl propiolate, an ionic process, show a spread of 10^3 over a similar polarity range (8), while those for the dimerization of dimethylketene differ by a factor of only 30. (9)



This striking difference was taken as evidence that the transition state for the dimerization has little charge separation. (9) We reach the same conclusion for the salt-free pyrolysis of 1 which precludes the formation of a zwitterionic intermediate as is proposed for the lithium catalyzed rearrangement of 1.

Mechanisms consistent with little or no charge separation in the transition state are i) a concerted cleavage and ii) a diradical process. The first possibility falls into the category of a retrograde $[{}_{\sigma}2_s + {}_{\sigma}2_a]$ cycloaddition which is thermally allowed according to a modification of the Woodward-Hoffman rules for electrocyclic reactions. (10) This mechanism is believed to operate in the pyrolysis of β-lactams. (10) A short-lived diradical intermediate also is consistent with our available data for the uncatalyzed pyrolysis of 1. While the formation of 2 as a minor product in these pyrolyses is understandable *via* the diradical mechanism, the possibility of competing major (concerted) and minor (diradical) pathways cannot be excluded at this time.

Table 2. Rate constants and product compositions for pyrolysis of 1 in various solvents.[a]

Solvent	E_T[b]	$k_{obs} \times 10^4$, sec^{-1} [c]	Products[d], mole fraction	
			2	3
CD_3CN	46.0	4.23 ± 0.21	.04	.96
C_6H_5CN	42.0	4.87 ± 0.38	.05	.95
$CHCl_3$	39.1	2.59 ± 0.05	.11	.89
C_6H_6	34.0	0.81 ± 0.03	.11	.89
CCl_4	32.5	0.57 ± 0.02	.10	.90

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[a] Measured at 125.1 ± 0.3° C in degassed and sealed nmr tubes. Followed by nmr spectroscopy with hexamethyldisiloxane or acetonitrile-d_2 as internal standard.

[b] From reference 7.

[c] All entries are the average of at least two runs.

[d] Both 2 and 3 are stable to the reaction conditions. No other products were detected by nmr analysis although the formation of phenyl isocyanate was readily noted by ir analysis.

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(3) 4 was independently synthesized by a modified Reformatsky reaction between α-bromoisobutyranilide and fluorenone. Nmr: gem-CH_3, δ1.18 (CD_3CN).

(4) Water detected at > 0.02% via a resonance between δ2.3 and δ3.2. We suspect that 0.02% water (0.009 M) has a dramatic effect on the catalytic reactivity of lithium ion in aprotic media.

(5) The major product from this reaction is 2. 5 is isolated by alumina chromatography contaminated with 5-10% of 2. See R. Madroñero, G. Garcia-Munoz and H. Leippard, *Chem. Ber.*, **97**, 2234 (1964) for a similar reaction of a chloroketone with stannic chloride/acetonitrile. Bromoamide 9 yields 2 in 85% isolated yield by simply refluxing in chlorobenzene for 15 hrs.

(6) See B. Rickborn and R. M. Gerkin, *J. Amer. Chem. Soc.*, **93**, 1963 (1971) for similar observed differences between lithium bromide and perchlorate salts on the catalyzed rearrangement of 1-methylcyclohexane oxide.

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