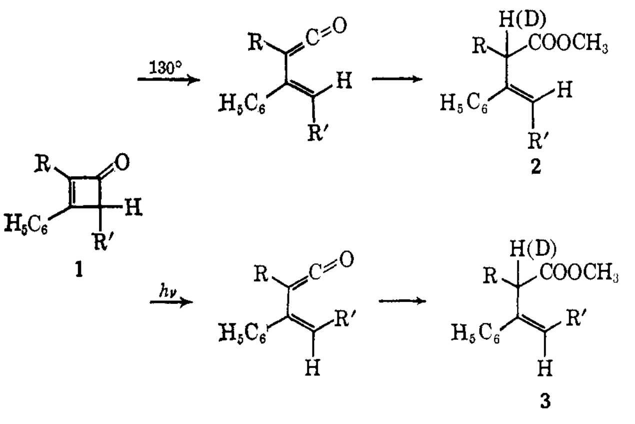
New Stereochemical Selectivities in Electrocyclic Reactions

Sir:

Those electrocyclic transformations[1] which may proceed in a conrotatory or disrotatory fashion are stereoselective,[1,2] giving one stereochemical mode of behavior thermally and the opposite photochemically. The fundamental determinants of these stereochemical selectivities are now well recognized.[1-5]

For the electrocyclic reactions of molecules like cyclobutene, the terms "conrotatory" and "disrotatory" remain meaningful, even though one could not discern experimentally the stereochemical course of these transformations without resorting to suitable deuterium-labeled analogs. But for other electrocyclic transformations, such as the conversions of cyclobutenones to the corresponding vinyl ketenes, the terms[1] "conrotatory" and "disrotatory" are meaningless. Neither current theory nor experimental precedent indicates the stereochemical characteristics of these electrocyclic reactions. We now report on three cases where they prove to be stereoselective, giving one isomer thermally and the other photochemically.

2,4-Dichloro-3-phenylcyclobutenone[6] (**1a**) at 130° in methanol gave the β,γ-unsaturated ester **2a** having hydrogen and phenyl disposed *trans* about the carbon–carbon double bond. In O-deuteriomethanol, the α-deuterio ester was obtained. Irradiation of **1a** with a Hanovia 450-w high-pressure mercury lamp gave the *cis* isomer **3a**. 2-Methyl-3-phenyl-4-chlorocyclobutenone[7] (**1b**) gave rise thermally to the *trans* product **2b** and photochemically to the *cis* product **3b**. Similarly, 2-chloro-3-phenyl-4-methylcyclobutenone[7] (**1c**) gave the *trans* and *cis* isomers **2c** and **3c** thermally and photochemically, respectively. In each case, *cis–trans* isomerization of the product under the reaction conditions was observed to be slow relative to the rate of conversion of cyclobutenone to ester.



a, R = Cl; R′ = Cl
b, R = CH₃; R′ = Cl
c, R = Cl; R′ = CH₃

Table I. Spectral Data for **1**, **2**, and **3**

Compd	Nmr absorptions[a] 1H singlets	Nmr absorptions[a] 1H quartet	3H	*J*, cps	Out-of-plane bending absorption,[b] cm⁻¹
1a	340				
2a (H)	402, 304				701
2a (D)	412[c]				
3a (H)	388, 352[d]				700
3a (D)	398[c]				
1b		330	126	1.5	
2b (D)	375		76[e]		699
3b (D)	371		78[e]		698.5
1c		229	82	7	
2c (D)		363	96	7	
3c (D)		354	114	7	

[a] In cycles per second downfield from internal tetramethylsilane at 60 Mc/sec in carbon tetrachloride. [b] Determined on carbon tetrachloride solutions with a Beckman IR7 instrument. [c] In O-deuteriomethanol. [d] In deuteriochloroform. [e] Broad absorption.

Assignments of stereochemistry of the three *cis–trans* pairs of olefins were based both on the observed regularities in the nmr chemical shift parameters for these compounds and on the relative energies of the out-of-plane bending absorptions in the infrared[8] (Table I); the criterion of stereoselectivity employed for the six reactions was nmr.

The observed stereoselectivities of these reactions may be a consequence of very different geometrical constraints operative in the transition states for the thermal and photochemical processes. The stereochemistries of the electrocyclic transformations of 6,6-disubstituted cyclohexadienones and other systems for which the conrotatory–disrotatory dichotomy is irrelevant are under continuing investigation.

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(7) This cyclobutenone was prepared through the addition of β-methylstyrene with 1,1-dichloro-2,2-difluoroethylene, dehydrochlorination, and hydrolysis of the *gem*-difluoro function with concentrated sulfuric acid.

(8) *Cf.* D. Y. Curtin and J. W. Hausser, *J. Am. Chem. Soc.*, **83**, 3474 (1961).

(9) Alfred P. Sloan Research Fellow.

(10) National Institute of General Medicine Sciences Fellow, 1966–1967.

A New and Convenient Alkylation and Acylation of Pyridine N-Oxides

Sir:

Nuclear proton abstraction from substituted pyridines has only found sporadic application, this usually involving the formation of pyridyne intermediates.[1] It was expected that base-catalyzed deprotonation of pyridine N-oxides should occur much more readily than in the pyridines themselves,[2] and that C_2–H would be the most acidic proton, and this prediction

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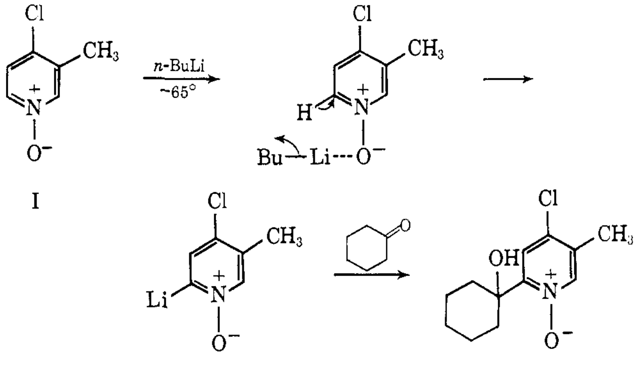
(1) (a) H. J. den Hertog and H. C. van der Plas, *Advan. Heterocyclic Chem.*, **4**, 121 (1965); (b) T. Kauffmann, *Angew. Chem. Intern. Ed. Engl.*, **4**, 543 (1965).

(2) J. A. Zoltewicz and C. L. Smith, *J. Am. Chem. Soc.*, **88**, 4766 (1966).

has been verified quantitatively.[3] For example, 3-bromopyridine 1-oxide undergoes H–D exchange readily with 0.1 *N* NaOD in D_2O, the order of reactivities being 2- > 6- > 4- >> 5-.[3] By making use of this principle we have now uncovered a facile alkylation and acylation of pyridine N-oxides in which the oxide group is retained. No simple direct introduction of such groups into this ring system has been available previously.

Treatment of 4-chloro-3-methylpyridine 1-oxide (I) with *n*-BuLi at −65° in ether gave the organolithium derivative II which, with cyclohexanone, gave 2-(1′-hydroxycyclohexyl)-4-chloro-5-methylpyridine 1-oxide (III) (38%), mp 164°. The nmr spectrum confirmed the structure and was as expected for pyridine N-oxides[4] [τ: 2.02 (1 H, singlet, C_6–H), 2.82 (1 H, singlet, C_3–H), 7.73 (3 H, singlet, CH_3–Ar)]. The infrared spectrum and microanalysis[5] were in agreement with structure III. No product resulting from the formation of the carbanion at C_2 was detected. Treatment of II with CO_2 gave 4-chloro-3-picoline-6-carboxylic acid 1-oxide (24%), mp 160°. The activating (−*I*) influence of the 4-chloro substituent was not required for proton abstraction as 3,4-lutidine 1-oxide gave a 6-lithio derivative which reacted with cyclohexanone to give 2-(1′-hydroxycyclohexyl)-4,5-dimethylpyridine 1-oxide (84%), mp 121–122°. Since the relative rates of deuterium–hydrogen exchange at C_2 and C_6 of 3-picoline methiodide with NaOD in D_2O are in the ratio $k_2:k_6 = 1.2$,[3] formation of the 2-lithio derivative in both the above N-oxides might have been expected to predominate slightly over the formation of the 6-lithio compound. That none of the former was detected indicates that steric hindrance by the 3-methyl group may be important in these metalations.[6] *The results described in this paper provide incontrovertible evidence for the proton-abstraction mechanism via a carbanion intermediate for the base-catalyzed H–D exchange in pyridine N-oxides.*[3]

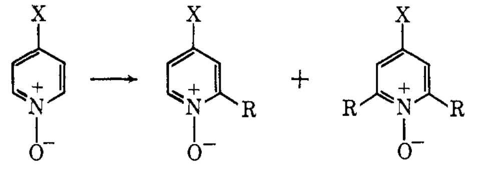


I

II

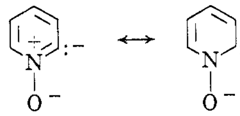
III

A number of 4-substituted pyridine N-oxides reacted in a similar manner. Tetrahydrofuran was a suitable solvent for those N-oxides which were too insoluble in ether. In the absence of a 3-substituent disubstitution at C_2 and C_6 also occurred to give VI as well as V. Thus, when X = OEt, V (R = 1′-hydroxycyclohexyl) (20%), mp 127–128°, and VI (R = 1′-hydroxycyclohexyl) (12%), mp 166–167°, were obtained. Similarly, when X = CH_3, V (R = 1′-hydroxycyclohexyl) (21%), mp 115°, and VI (R = 1′-hydroxycyclohexyl) (27%), mp 198–199°, were obtained. On the other hand, treatment of the lithium derivative of 4-chloropyridine 1-oxide with CO_2 only gave the known[8] 4-chloropicolinic acid 1-oxide (V, R = CO_2H) (49%), mp 135–136°. 4-Picoline 1-oxide yielded the 2,6-dicarboxylic acid, mp 160°. Pyridine N-oxide itself gave VI (R = 1′-hydroxycyclohexyl) (15%), mp 158°. Treatment of the intermediate organolithium derivatives with nitriles or amides gave interesting ketones whose structures and reactions will be discussed in a subsequent publication.



IV V VI

The action of other electrophilic reagents is now under study as are ring systems other than the pyridine N-oxides and pyridinium salts. It is anticipated that the reaction will prove to be a general one for suitable six-membered heteroaromatic compounds. The carbanions can be looked upon as being stabilized by resonance with the carbene structure (VII) which would be another example of the so-called nucleophilic carbenes.[3,9]



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(4) R. A. Abramovitch and J. B Davis, *J. Chem. Soc., Sect. B*, 1137 (1966).

(5) Satisfactory analyses and infrared and nmr spectra were obtained for all new compounds described in this paper.

(6) Steric hindrance may account for the fact that some 3,4- but no 2,3-pyridyne 1-oxide was detected in the reaction of 3-chloropyridine 1-oxide with piperidine in benzene.[7]

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Insertion of CCl_2 into the Silicon–Carbon Bond of Silacyclobutanes

Sir:

We wish to report a new reaction which is noteworthy for two reasons: it represents the first reported CCl_2 insertion into a silicon–carbon bond as well as the first