indicated that 2,5-dimethylene-2,5-dihydrofuran intermediate (12, X = O)[9] was generated and existed in the mixture under the reaction conditions. When the mixture of 5 and tetrabutylammonium fluoride was heated at 110 °C for 4 h in a sealed tube, cyclodimerization of 12 (X = O) initially formed took place to give a 73% yield of [2.2](2.5)furanophane (7), whose structure was confirmed by comparison of NMR and IR spectra with those reported.[1a]

5, X = O
6, X = S

12

7, X = O
8, X = S

13, X = S
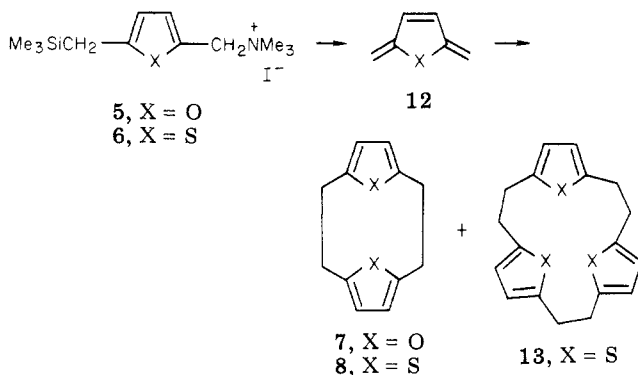
In the reaction of 6 with tetrabutylammonium fluoride[10] in acetonitrile at reflux, a mixture of [2.2](2.5)thiophenophane (8, 37%) and cyclic trimer (13,[12] 14%) of 2,5-dimethylene-2,5-dihydrothiophene (12, X = S) was produced, which was separable by preparative TLC. The former was identified by comparison of its spectral data with those reported[1a] and by its mass spectrum.[11] The latter was assigned by its NMR and mass spectra.[12]

Further work to prepare a variety of cyclophane derivatives by the present methodology is in progress.

(9) Trahanovsky, W. S.; Park, M. G. J. Org. Chem. 1974, 39, 1448.
(10) Use of CsF in place of tetrabutylammonium fluoride in the reaction with 6 gave 8 and 13 in 43% and 17% yields, respectively.
(11) 8: white needles; TLC (silica gel, 3:1 hexane–CHCl₃) R_f 0.44; mp 194–197 °C (lit.[1a] mp 194.5–196 °C); NMR (CDCl₃, Me₄Si) δ 3.04 (AA'BB' m, 8 H), 6.75 (s, 4 H); UV (C₂H₅OH) λ_{max} 245 nm (ε 6.7 × 10³), 274 (5.0 × 10³); mass spectrum, m/e (relative intensity) 220 (24), 110 (100).
(12) 13: yellow solid; TLC (silica gel, 3:1 hexane–CHCl₃) R_f 0.32; mp 126.5–127 °C; NMR (CDCl₃, Me₄Si) δ 3.01 (s, 12 H), 6.60 (s, 6 H); UV (C₂H₅OH) λ_{max} 240 nm (ε 19.8 × 10³); mass spectrum, m/e (relative intensity) 330 (100), 220 (36), 110 (61).

Yoshihiko Ito, Satoru Miyata
**Masashi Nakatsuka, Takeo Saegusa***

Department of Synthetic Chemistry
Faculty of Engineering
Kyoto University
Yoshida, Kyoto 606, Japan
Received September 22, 1980

Rearrangement of an Exchangeable Hydrogen during the Reduction of Maleimide with Lithium Aluminum Hydride

Summary: Reduction of maleimide with LiAlD₄ yields pyrrolidine containing five C–D bonds rather than the expected six. N-Deuterated maleimide results in pyrrolidine-3-d. These results are consistent with the migration of hydrogen from nitrogen to carbon. This is an example

Scheme I
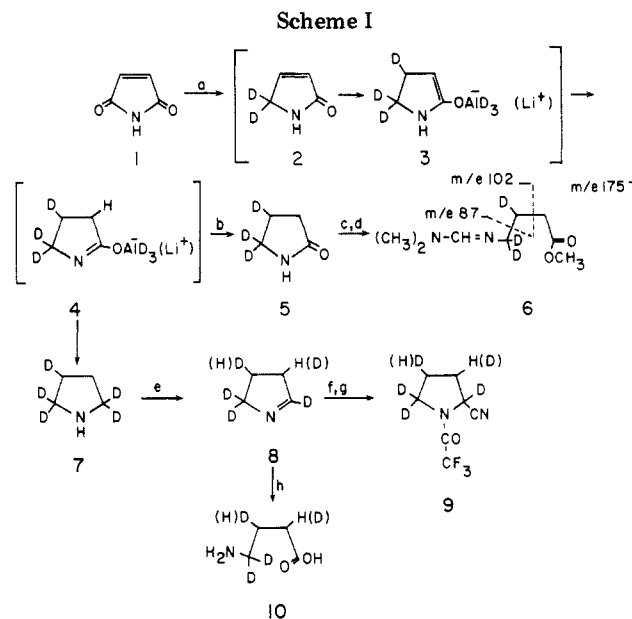
a (a) LiAlD₄; (b) H₂O; (c) 5 N HCl; (d) dimethylformamide dimethyl acetal; (e) Na₂S₂O₈, NaOH; (f) HCN; (g) (CF₃CO)₂O; (h) rabbit liver homogenate.

where reduction is favored over abstraction of an active hydrogen.

Sir: Attempted preparation of pyrrolidine-2,2,3,4,5,5-d₆ by the reduction of maleimide with lithium aluminum deuteride surprisingly resulted in pyrrolidine containing only 5 C–D bonds. Although it is generally accepted that the first step in the reaction of compounds containing active hydrogen atoms with metal hydrides is the liberation of H₂,[1] our findings indicate that the reduction of maleimide with LiAlH₄ does not take this course. The results are consistent with a hydrogen rearrangement from nitrogen to carbon and thus provide an example where reduction is favored over active proton abstraction.

Reduction was carried out in refluxing tetrahydrofuran with excess LiAlD₄ for 16 h. Quenching the reaction with either H₂O or D₂O resulted in the same product. GC–MS analysis of the N-trifluoroacetyl derivative of the pyrrolidine formed indicated that it contained 95% d₅ and 5% d₆ and the loss of deuterium from M⁺. No significant (M − H)⁺ could be observed, indicating the presence of four deuterium atoms in the α positions of 7.

Additional evidence that the positions α to the nitrogen were completely labeled was gained by the analysis of oxidation products. Thus, 1-pyrroline (8), prepared by the sodium persulfate oxidation[2,3] of the product, on treatment with cyanide[4] followed by trifluoroacetic anhydride yielded 9 which, by GC–MS analysis, showed the presence of four deuterium atoms. Further oxidation of 8 by a rabbit liver homogenate[3] resulted in the formation of labeled 4-aminobutanoic acid (10) containing three deuterium atoms. Analysis following derivatization with dimethylformamide dimethyl acetal to form labeled methyl 4-(N,N-dimethyl-N′-formamidino)butanoate[5] showed that 4 con-

(1) Brown, W. G. Org. React. 1951, 6, 469–509.
(2) Nomura, Y.; Ogawa, K.; Takenchi, Y.; Tomoda, S. Chem. Lett. 1977, 693–696.
(3) Callery, P. S.; Nayar, M. S. B.; Geelhaar, L. A.; Stogniew, M.; Jakubowski, E. M. Biomed. Mass Spectrom., in press.
(4) Bonnett, R.; Clark, V. M.; Giddey, A.; Todd, A. J. Chem. Soc. 1959, 2087–2093.
(5) Callery, P. S.; Stogniew, M.; Geelhaar, L. A. Biomed. Mass Spectrom. 1979, 6, 23–26.

sisted of an equimolar mixture of **10**-*2,4,4-d₃* and **10**-*3,4,4-d₃*.

These results are consistent with the migration of the imide hydrogen of maleimide to a β-carbon during the reduction. Analysis of 2-pyrrolidinone (**5**) isolated from the reaction mixture suggests that this migration precedes the reduction of at least one of the carbonyl groups (Scheme I). GC–MS of the trifluoroacetyl derivative showed that three deuterium atoms have been incorporated. The mass spectrum of a derivative of its hydrolysis product (**6**) indicated that **5** was 2-pyrrolidinone-*3,4,4-d₃*.

A mechanism consistent with these results is presented in Scheme I. The first step of the reaction involves attack at the most electropositive carbon[6] which results in the reduction of one of the carbonyl groups by 1,2-addition.[7] Δ³-Pyrrolin-2-one (**2**) thus formed could then undergo 1,4-reduction to yield the intermediate **3**. The enamine **3** rearranges to the more stable imine[9] **4** with the migration of a hydrogen atom from N to C-3. Further reduction of the lactim salt **4** leads to pyrrolidine (**7**).

Regardless of the mechanism, it is obvious that the reaction has involved a transfer of hydrogen from nitrogen to carbon, since the reduction of N-deuterated maleimide (prepared by recrystallization from D_2O) with $LiAlH_4$ gave exclusively pyrrolidine-*3-d*.[10]

(6) Matsuo, T. *Bull. Chem. Soc. Jpn.* **1968**, *38*, 557–562.

(7) This is analogous to the addition of Grignard reagents to N-substituted maleimide. Equimolar amounts of the reactants results in 5-substituted-5-hydroxy-2-pyrrolinones.[8]

(8) Queen, A.; Reipas, A. *J. Chem. Soc. C* **1967**, 245–246.

(9) Alt, G. H. "Enamines"; Cook, G. A., Ed.; Marcel Dekker, Inc.: New York, 1969; pp 115–168.

(10) The mass spectrum of the N-trifluoroacetyl derivative showed the presence of one deuterium. No $(M - D)^+$ could be detected, indicating the label was not on C-2.

M. S. Balachandran Nayar, Patrick S. Callery*

*Department of Medicinal
Chemistry/Pharmacognosy
University of Maryland
Baltimore, Maryland 21201*

Isocyanoamines, R–NH–NC[1]

Summary: Secondary isocyanoamines, R–NH–NC, are obtained by flash vacuum pyrolysis of 3-methyl-4-(arylhydrazono)isoxazol-5(4H)-ones.

Sir: Isocyanoamines are little known compounds. "Isodiazomethane", H_2NNC,[2] and a few *N,N*-dialkyl derivatives, R_2NNC,[3] and *N*-isocyanoimines, $R_2C=N—NC$,[4] are

(1) This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Mr. L. A. J. Köhler for construction of the pyrolysis apparatus.

(2) Müller, E.; Kästner, P.; Beutler, R.; Rundel, W.; Suhr, H.; Zeeh, B. *Justus Liebigs Ann. Chem.* **1968**, *713*, 87–95. Müller, E.; Beutler, R.; Zeeh, B. *Ibid.* **1968**, *719*, 72–79.

(3) Bredereck, H.; Föhlisch, B.; Walz, K. *Justus Liebigs Ann. Chem.* **1965**, *686*, 92–101.

(4) Hagedorn, I.; Eholzer, U. *Angew. Chem.* **1962**, *74*, 499; *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 514. Jakobsen, P. *Acta Chem. Scand., Ser. B* **1976**, *30*, 995–996. See also: Anselme, J.-P. *J. Chem. Educ.* **1977**, *54*, 296–298.
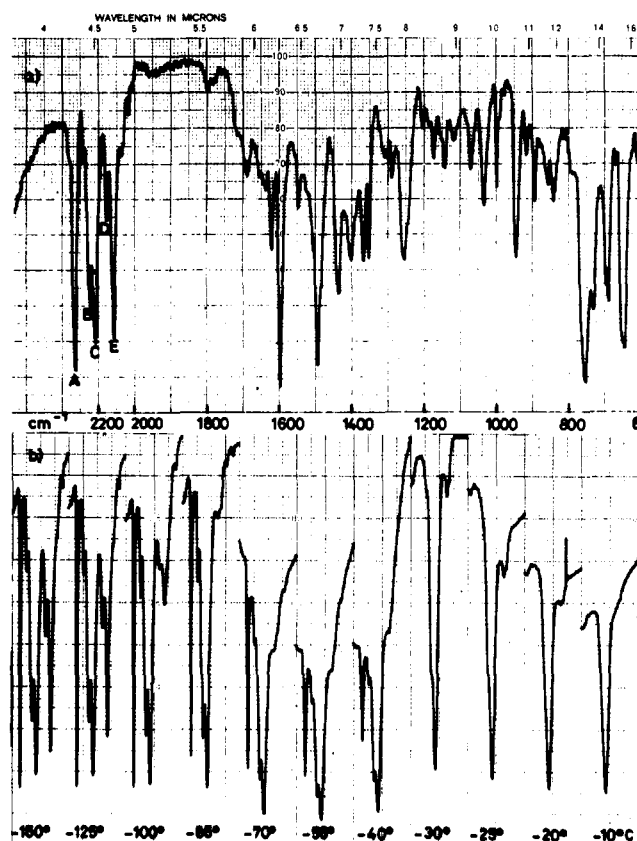

Figure 1. (a) Infrared spectrum (–196 °C) of the pyrolyzate formed from **1a** at 600 °C (10⁻⁴ torr). The marked peaks are as follows; A, CO_2; B, CH_3CN; C, phenylcyanamide (**3a**); D and E, phenylisocyanoamine (**2a**). (b) Repetitive scanning of the 2400-2000-cm⁻¹ region during warm-up.

known. However, no aromatic isocyanoamines have been prepared, and the entire class of secondary amine derivatives, R–NH–NC, is unknown. We now report direct spectroscopic evidence for the formation of these extremely unstable compounds by pyrolysis of 4-hydrazonoisoxazol-5(4H)-one derivatives.[5]

Flash vacuum pyrolyses were carried out at ca. 10⁻⁴ torr, and the products were collected directly on a turnable KBr disk attached to a liquid nitrogen cryostat and mounted in a vacuum shroud equipped with KBr windows for infrared spectroscopy. The pyrolysis of **1a** at 600 °C gave a product showing intense isocyanide absorptions at 2120 and 2155 cm⁻¹, together with phenylcyanamide (**3a**) (2220 cm⁻¹) and CO_2 (2330 cm⁻¹) (Figure 1a). Acetonitrile, a byproduct of the reaction shown in eq 1, lies partly under
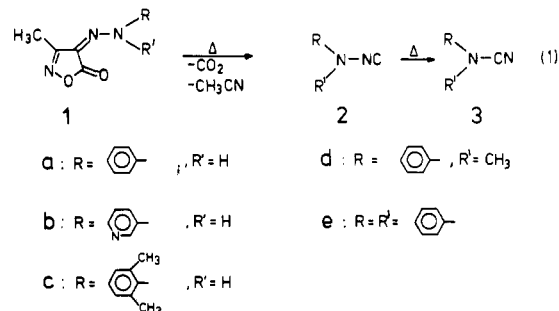
the phenylcyanamide peak but is a weaker absorber. The 2250-cm⁻¹ absorption is clearly visible in Figure 1a. This peak is seen to decrease on warming (Figure 1b) due to the

(5) Reichen, W.; Wentrup, C. *Helv. Chim. Acta* **1976**, *59*, 2618–2620.