Studies in the Pyrolysis of N-Formylacetamides. The Imide–Isoimide Rearrangement

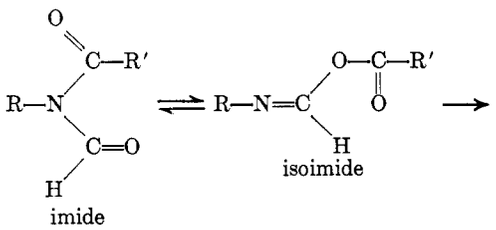
DANIEL J. HOY[1] AND EDWARD J. POZIOMEK

Physical Research Laboratory, Edgewood Arsenal, Maryland 21010

Received April 15, 1968

The purpose of this investigation is to obtain basic information on the reaction of substituted formamides giving isocyanides. Imide–isoimide equilibria were studied by an analysis of the thermal decomposition products of N-alkyl- (or -aryl-) N-formylacetamides. Relative yields in decarbonylation (arising from imide) *vs.* isocyanide formation (arising from isoimide) in the pyrolysis of N-phenyl-, N-*n*-butyl-, N-*sec*-butyl-, and N-cyclohexyl-N-formylacetamides were found to be >99:<1, 86:14, 57:43, and 51:49, respectively. Nitriles rather than isocyanides were isolated because of the isomerization which occurs at high temperatures. It is concluded that the quantities of amide and nitrile isolated may be the net result of a number of reactions: imide–isoimide reversible rearrangement, isoimide α elimination (possibly reversible), imide decarbonylation (irreversible), isocyanide–nitrile isomerization (irreversible), and imide regeneration from isocyanide and acid through formamide and acetic anhydride. Among the imides studied both an electronic and a steric effect appear to be operating.

It has been indicated that pyrolysis of N-alkyl- (or -aryl-) N-formylamides gives isocyanides because of the characteristic odor which accompanied the reaction.[2,3] Mumm detected an intensive odor of isocyanide in the decarbonylation of N-formylbenzanilide, but he did not report isolating the product. Similarly Wheeler[4] claimed that pyrolysis of N-formylstearanilide gave phenyl isocyanide and stearic acid, but he gave no supporting details. Isocyanide production in these reactions gives evidence of an imide–isoimide rearrangement (eq 1).[5]



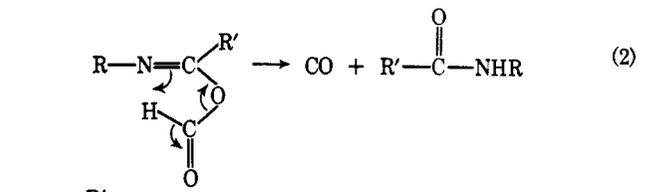
$$R{-}N{\equiv}C + R'COOH \quad (1)$$

The formation of isoimides as transient intermediates (which rearrange to the imide or which yield products logically derived from isoimide structures) is widely reported.[6-13] Isoimides have been isolated when the function is part of a five-membered ring which also contains a carbon–carbon double bond[14] or when the nitrogen bears a 2,4-dinitrophenyl group.[15] These isoimides rearrange *via* an oxygen to nitrogen acyl migration; when heated, however, the rearrangement observed for the cyclic case may depend on acid or base catalysis.[15]

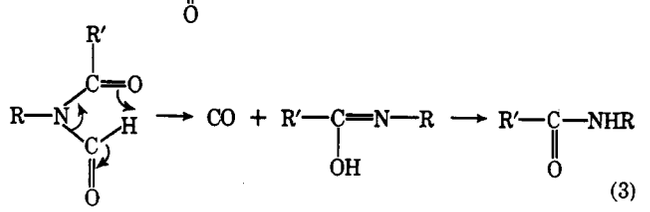
Mumm and coworkers,[2] postulated a reversible imide–isoimide rearrangement to explain three pyrolysis reactions. Expressing Mumm's specific examples in general terms the reactions are pyrolysis of acyclic imides to carboxylic acids and nitriles, pyrolysis of N-alkyl- (or -aryl-) N-formylamides to carboxylic acids and nitriles, pyrolysis of N-alkyl- (or -aryl-) N-formylamides to the N-alkyl- (or -aryl-) amides and carbon monoxide, and the pyrolysis of N-alkyl- (or -aryl-) N-formylamides to isocyanides and carboxylic acids.

For the pyrolysis of acyclic imides, Sheehan and Corey[9] have written a reversible imide–isoimide rearrangement as a part of the mechanism in agreement with Mumm's postulate. More extensive studies have recently been explained by postulating a concerted mechanism which omits a discrete isoimide intermediate, though the authors consider a path through an isoimide intermediate as a possible limiting case.[16]

In the pyrolysis of N-alkyl- (or -aryl-) N-formylamides to N-alkyl- (or -aryl-) amides, a decarbonylation mechanism for Mumm's postulated isoimide[2,3] can be written (eq 2). However, decarbonylation could also occur directly from the imide (eq 3).



(2)



(3)

For the pyrolysis of N-alkyl- (or -aryl-) N-formylamides to isocyanides, a mechanism is difficult to write unless prior rearrangement to an isoimide occurs. The isoimide can then undergo an α elimination (eq 1). The existence of this pyrolysis reaction gives the best evidence for a reversible imide–isoimide equilibrium

(1) Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16801.

(2) O. Mumm, H. Hesse, and H. Volquartz, *Ber.*, **48**, 379 (1915).

(3) O. Mumm, *ibid.*, **43**, 886 (1910).

(4) H. L. Wheeler, *Am. Chem. J.*, **18**, 695 (1896).

(5) Isocyanide formation by α elimination from an isoformimide is analogous to the mechanism postulated for isocyanide formation from nitrogen-substituted formamides by phosphorus and sulfur halides with tertiary amine. See I. Ugi and R. Meyr, *Chem. Ber.*, **93**, 239 (1960).

(6) F. Cramer and K. Baer, *ibid.*, **93**, 1231 (1960).

(7) C. L. Stevens and M. E. Munk, *J. Amer. Chem. Soc.*, **80**, 4065 (1958).

(8) H. H. Wasserman and M. B. Floyd, *Tetrahedron*, **22** (**S 7**), 441 (1966).

(9) J. C. Sheehan and E. J. Corey, *J. Amer. Chem. Soc.*, **74**, 4555 (1952).

(10) C. G. Overberger and E. Sarlo, *ibid.*, **85**, 2446 (1963).

(11) D. S. Kemp, *Tetrahedron*, **23**, 2001 (1967).

(12) A. Kornhauser and D. Keglevic, *ibid.*, **18**, 7 (1962).

(13) T. Shono, M. Kimura, Y. Ito, K. Nishida, and R. Oda, *Bull. Chem. Soc. Jap.*, **37**, 635 (1964), and L. R. Walters, E. G. Podrebarac, and W. E. McEwen, *J. Org. Chem.*, **26**, 1161 (1961), claim preparation of several isoimides based on the position of ir absorption bands. This may not be sufficiently conclusive evidence for the isoimide structure.

(14) W. R. Roderick and P. L. Bhatia, *ibid.*, **28**, 2018 (1963). E. Hedaya, R. L. Hinman, and S. Theodoropulos, *ibid.*, **31**, 1311 (1966); 1317 (1966).

(15) D. Y. Curtin and L. L. Miller, *Tetrahedron Lett.*, 1869 (1965); D. Y. Curtin and L. L. Miller, *J. Amer. Chem. Soc.*, **89**, 637 (1967).

(16) W. S. Durrell, J. A. Young, and R. D. Dresdner, *J. Org. Chem.*, **28**, 831 (1963).

at high temperatures. In order to investigate Mumm's postulated equilibrium,[2,3] to determine quantitatively the relative importance of decarbonylation *vs.* isocyanide formation as pyrolysis pathways, and to investigate the formation of isocyanides from substituted formamides, we studied the pyrolysis of N-phenyl-, N-*n*-butyl-, N-*sec*-butyl-, and N-cyclohexyl-N-formylacetamides.

Results and Discussion

Starting materials were synthesized by acetylating the appropriate formamide derivative with acetyl chloride. The N-formylacetamides were pyrolyzed by passing them through copper or glass tubes at 400°. Experimental results are summarized in Tables I and II.

TABLE I
PRODUCTS OBTAINED IN THE PYROLYSIS OF N-SUBSTITUTED N-FORMYLACETAMIDES

Nitrogen substituent	Acetamide, % yield	Nitrile, % yield	Acetic acid, % yield
Phenyl[a]	99	1	
n-Butyl[a]	75	12	13
n-Butyl[b]	74	10	16
sec-Butyl[a]	40	30	30
Cyclohexyl[a]	34	35	31

[a] Copper tube. [b] Glass tube.

TABLE II
RELATIVE REACTION PATHS IN THE PYROLYSIS OF N-SUBSTITUTED N-FORMYLACETAMIDES

Nitrogen substituent	Decarbonylation	Isocyanide–acid formation
Phenyl	99	1
n-Butyl	86	14
sec-Butyl	57	43
Cyclohexyl	51	49

Additional experiments were performed in conjunction with the N-(*n*-butyl)-N-formylacetamide pyrolysis reactions and included a variety of sealed-tube reactions (eq 4–8).

$$n\text{-}C_4H_9NHCHO \xrightarrow[30\text{ min}]{380^\circ} \text{no reaction} \quad (4)$$

$$n\text{-}C_4H_9N(COCH_3)CHO \xrightarrow[30\text{ min}]{365^\circ} n\text{-}C_4H_9NHCOCH_3 + \text{high pressure (CO)} \quad (5)$$
(100%)

$$n\text{-}C_4H_9NC + CH_3COOH \xrightarrow[30\text{ min}]{325^\circ} n\text{-}C_4H_9NHCOCH_3 + n\text{-}C_4H_9CN + n\text{-}C_4H_9NHCHO \quad (6)$$
(80%) (10%) (10%)

$$n\text{-}C_4H_9NC \xrightarrow[15\text{ min}]{310^\circ} n\text{-}C_4H_9CN \quad (7)$$
(100%)

$$n\text{-}C_4H_9NHCHO + (CH_3CO)_2O \xrightarrow[30\text{ min}]{350^\circ} n\text{-}C_4H_9NHCOCH_3 + CH_3COOH + \text{high pressure (CO)} \quad (8)$$
(50%) (50%)

If the reaction represented in eq 5 is not allowed to proceed to completion, then the odor of isocyanide is detectable upon opening the tube.

General Considerations.—The results are conveniently discussed in terms of Scheme I. Although the experimental information required to fulfill the necessary conditions for unimolecular reaction mechanisms[17] has not been determined, we postulate that the imide decarbonylation and the isoimide α elimination (isocyanide–acid formation) reactions are unimolecular. The agreement within experimental error of the results for pyrolysis of the *n*-butyl derivative in both the copper and glass tube supports the conclusion that the reactions whose rates determine the product ratios are homogeneous.

A mechanism for the formation of nitrile and carboxylic acid from the imide is difficult to conceive without the isoimide α elimination and the isocyanide isomerization. The four-centered cyclic transition state for the reversible imide–isoimide equilibrium (Scheme I) is that proposed by Curtin and Miller[15] for the isoimide–imide rearrangement.

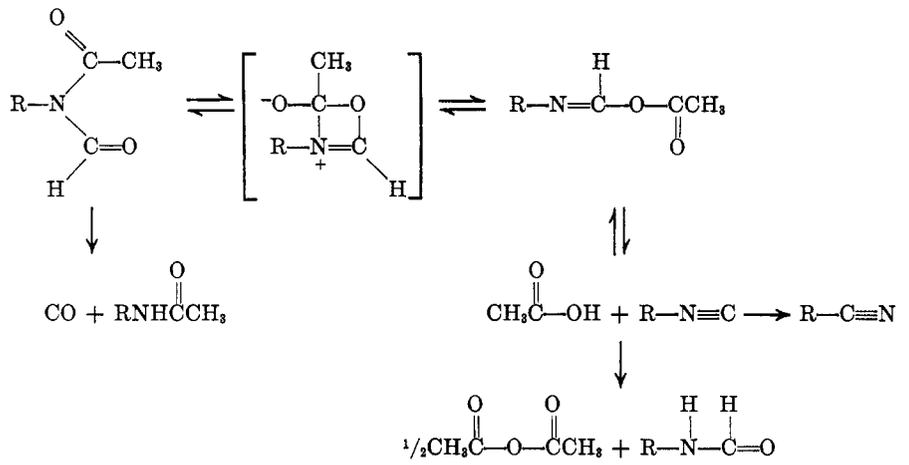
The quantities of amide and nitrile isolated may be the net result of a number of possible reactions: imide–isoimide reversible rearrangement, isoimide α elimination (possibly reversible), imide decarbonylation (irreversible), isocyanide–nitrile isomerization (irreversible), and imide regeneration from formamide and acetic anhydride (formed from isocyanide and acid). Though all these rates and their dependence upon the R group is not known, an explanation of the general features of the R-group influence upon reaction pathway can be proposed which seems logical in view of already determined isocyanide isomerization rates[18–20] and the electronic and steric effects of the R groups.

Isocyanide Isomerization.—The thermal unimolecular isomerization of isocyanides to nitriles explains the presence of the nitriles as the products of the pyrolysis.[18–20] Several of the isocyanides in this study were so completely isomerized under the exact conditions of imide pyrolysis that their odor was barely detectable in the nitrile product. Furthermore, isomerization rate constants can be estimated for the isocyanides by using the Arrhenius parameters for methyl isocyanide reported by Schneider and Rabinovitch[18] and the influence of the nitrogen substituent on the isomerization rate reported by Casanova, *et al.*[20] Thus an estimated lower limit is $k = 5\ \text{sec}^{-1}$, a number sufficiently large to explain the exclusive formation of nitrile.

Kohlmaier[19] and Rabinovitch determined the *p*-tolyl isocyanide gas phase isomerization rate to be $75 \times 10^{-5}\ \text{sec}^{-1}$ at 200°. Casanova, *et al.*,[20] showed phenyl isocyanide isomerization rates in diglyme to be only slightly dependent upon a *para* substituent, suggesting that the gas phase isomerization rate of phenyl isocyanide is probably very similar to that of *p*-tolyl isocyanide. They also determined the ethyl and *sec*-butyl isocyanide gas phase isomerization rates to be 10.4×10^{-5} and $3.45 \times 10^{-5}\ \text{sec}^{-1}$, respectively, at 200°. Thus comparison of gas phase isomerization constants gives this order: phenyl > *n*-alkyl > *sec*-alkyl. It is interesting to note that the rate of nitrile

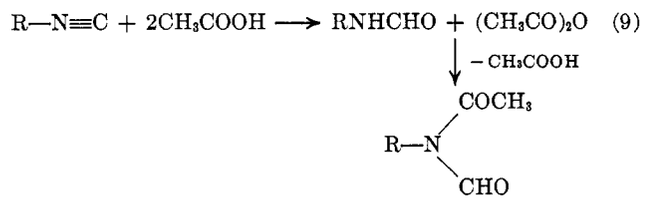
(17) A. Maccoll, *Advan. Phys. Org. Chem.*, **3**, 96 (1965).
(18) F. W. Schneider and B. S. Rabinovitch, *J. Amer. Chem. Soc.*, **84**, 4215 (1962).
(19) G. Kohlmaier and B. S. Rabinovitch, *J. Phys. Chem.*, **63**, 1793 (1959).
(20) J. Casanova, Jr., N. D. Werner, and R. E. Schuster, *J. Org. Chem.*, **31**, 3473 (1966).

SCHEME I
CONSEQUENCES OF THE IMIDE–ISOIMIDE REARRANGEMENT



formation relative to the rate of decarbonylation is *sec*-alkyl > *n*-alky > phenyl for imide pyrolysis, which is achieved *in spite of* the order of isocyanide isomerization rates. One might have expected a greater contribution from isocyanide chemical reactions in the case of the compounds which isomerize at lower rates.

Isocyanide Chemical Reactions.—Isomerization to nitrile may not be the only reaction of the isocyanide formed. Isocyanide and acid may revert into imide if the α elimination is a reversible reaction or if a second pathway through formamide and acetic anhydride[21] is operative (eq 9). Sealed-tube reactions (eq 6 and 8)

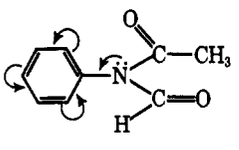


(9)

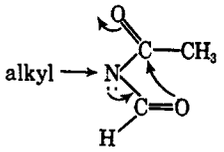
show that these reaction sequences are possible and conceivably could be present in the flow method pyrolysis. If imide originally decomposing to isocyanide and acid does re-form and decarbonylate, then the amount of nitrile isolated would be less than the case if the isocyanide reaction was exclusively isomerization.

Isocyanide isomerization may not compete favorably with the reaction of isocyanide and acid in the sealed-tube experiments. Thus, the higher pressures obtained by pyrolysis in a sealed tube may so enhance the re-formation of imide that decarbonylation is the only net reaction observed (note eq 5). Heating the imide to temperatures near its boiling point at atmospheric pressure gave a gas-evolving, isocyanide-smelling, rapidly darkening solution. Knowledge of the reactions possible for a solution of the parent imide, its corresponding amide and formamide, isocyanide, nitrile, acetic acid, and acetic anhydride between 100 and 200° discouraged further investigation.

Electronic Effects.—An electronic effect seems best able to explain the near absence of nitrile in the pyrolysis of the phenyl-substituted imide. The electron density of the nitrogen atom can affect the imide's ability to achieve the transition state shown in Scheme I. For the phenyl imide, the nitrogen electron density is significantly decreased by electron delocalization into the benzene ring (structure A). This is in comparison



A

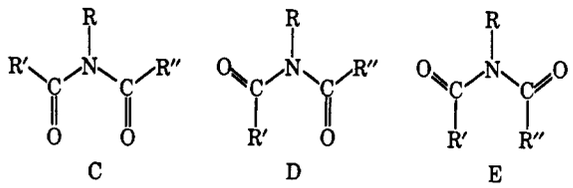


B

to the alkyl-substituted imides in which the nitrogen electron density (as well as the ability of the imide to achieve the transition state for isomerization to isoimide) is increased by an inductive effect (structure B). We suggest that these electronic effects are responsible for the higher amide/nitrile ratio for the phenyl imide compared with those for the alkyl imides.

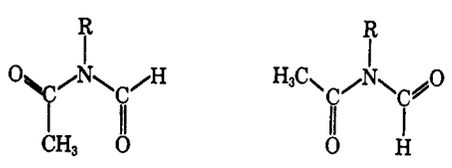
The same argument now based on the relative inductive effects of primary *vs.* secondary alkyl groups may contribute to the increase of nitrile yield in going from *n*-butyl to *sec*-butyl and cyclohexyl. However, steric considerations may also be important.

Steric Effects.—The rotational barrier of the amide bond[22] leads to three possible conformers for an imide.



C D E

Dipole moment data support assignment of conformation D to N-methyldiformamide, diacetamide, and N-methyldiacetamide.[23] Though not determined, it is likely that the D conformation (I or II) can also be assigned to the imides of this study. Monosubstituted



I II

(21) A. Gautier, *Ann. Chim. Phys.*, **17**, 224 (1869).

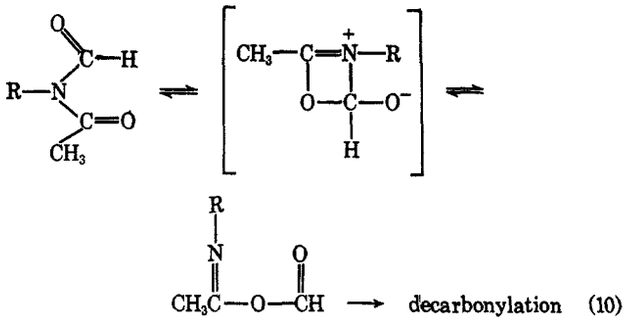
(22) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 366.

(23) C. M. Lee and W. D. Kumler, *J. Amer. Chem. Soc.*, **84**, 571 (1962).

formamides are predominantly *trans* and show a small trend toward the *cis* conformer with increasingly bulky substituents.[24] In unsymmetrical disubstituted formamides, the formyl hydrogen is *cis* to the bulkier substituent.[25]

Though the amide bond will no longer show *cis–trans* isomerism at the temperature of this pyrolysis,[26] the steric considerations can still be used to deduce the trend of conformation with the R group. Thus as one goes from a primary to secondary alkyl group, the trend will be toward a conformation I-D-like character even though rotation may occur. This is precisely the trend in conformation favorable for producing a trend toward rearrangement to an isoimide.

Isoacetimide Intermediates.—As mentioned previously, a unimolecular mechanism for decarbonylation can be written from either an isoimide (eq 2) or an imide (eq 3). As the trend in nitrile/amide ratio agrees with factors favoring isoformimide formation, rearrangement to isoformimide appears to be the rate-determining step for degradation to nitrile and acid. In view of this it is tempting to try to exclude the possibility of an isoacetimide in the decarbonylation mechanism (eq 10) by using an argument based on



inherent electronic or steric properties of a specific imide. For example, for the phenyl imide, the nitrile/amide ratio was much smaller than for alkyl imides because the lower electron density on nitrogen is unfavorable for rearrangement to the isoformimide. One would thus expect rearrangement to the isoacetimide. Because decarbonylation is rapid in comparison to nitrile formation, one is tempted also to exclude isoacetimide as a decarbonylation intermediate in favor of the alternative mechansim involving imide.

Experimental Section[27]

The pyrolysis apparatus was a gas chromatograph equipped with a 6 ft × 0.25 in. copper or glass tube in place of the usual column. Sufficient pyrolysis products were then obtained by multiple injection of reactant using a helium carrier gas flow rate of 60 ml/min and an oven temperature of 400°. The time of passage through the tube varied between 2 and 25 sec. The combined products were collected at ice–water temperature and separated by preparative glpc 20 ft × $^3/_8$ in. column, 30% SE-30 on $^{45}/_{60}$ Chromosorb W). The identity of each peak was determined by comparison of its retention time and ir spectrum with those of an authentic sample. Quantitative analyses were obtained with an estimated uncertainty of 3% by measuring peak areas using a Disc integrator.

The sealed-tube reactions were performed using 10-mm heavy-walled glass tubing. In a typical run, 0.10 ml of reactant was degassed and the tube was sealed under vacuum. After the appropriate length of time in the oven (see eq 4–8) the tube components were separated by preparative glpc. Product identification was based on glpc retention times and comparison of ir spectra with those of authentic samples.

N-Formylacetanilide.—Formanilide (24.2 g, 0.20 mol) was dissolved in 250 ml of methylene chloride and cooled in ice. Pyridine (31.7 g, 0.40 mol) and acetyl chloride (31.4 g, 0.40 mol) were added, and the mixture was stirred at room temperature for 1 hr. The mixture was then extracted twice with 100-ml and once with 50-ml portions of water. The methylene chloride solution was dried (Na_2SO_4) overnight, stripped with a rotary evaporator, and distilled with a spinning-band column giving 26.0 g (80%) of the imide: bp 81–82° (0.035 mm) [lit.[4] bp 157–158° (23 mm)]. The product was recrystallized from ether–ligroin: softens at 53°; mp 55° (lit.[4] mp 56°); ir ($CHCl_3$) 5.89 and 5.80 μ (C=O).

N-(*n*-Butyl)-N-formylacetamide.—N-Butylformamide (20.2 g, 0.20 mol) and acetyl chloride (62.7 g, 0.80 mol) were mixed and stirred at reflux for 5 hr, while protected from moisture. After the reaction solution stood at room temperature for 30 hr, the acetyl chloride was stripped off with a rotary evaporator. The residue was distilled through a spinning-band column giving 19.2 g (67%) of the imide: bp 74.5–75.5° (0.70–0.75 mm); $n^{23}D$ 1.4513; ir (neat) 1720 and 1670 cm^{-1} (C=O).

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.9; H, 9.3; N, 9.7.

Reduction of N-(*n*-Butyl)-N-formylacetamide.—To substantiate that reaction of acetyl chloride with N-monosubstituted formamide leads to imide rather than isoimide, N-(*n*-butyl)-N-formylacetamide was reduced with lithium aluminum hydride in THF to *n*-butyl-, ethyl-, or methylamine. The product was purified by vpc (39%) and then was alkylated with *n*-butyl iodide to give di(*n*-butyl)ethylmethylammonium iodide (77%): mp 178–179° (lit.[28] mp 176–178°) (recrystallized from EtOAc).

N-(*sec*-Butyl)-N-formylacetamide.—*sec*-Butylformamide (20.3 g, 0.20 mol) was dissolved in 200 ml of methylene chloride and pyridine (23.7 g, 0.30 mol). The solution warmed and turned yellow upon the start of acetyl chloride addition. The solution was then cooled in ice; a white salt formed when the acetyl chloride addition (17.3 g, 0.22 mol) was completed. The mixture was stirred at room temperature; an additional 10 ml of acetyl chloride and 5 ml of pyridine were added since glpc showed an incomplete reaction. The white salt was again filtered off, and the solution was concentrated. More white salt formed and was filtered off. The residue was vacuum distilled to give 22.2 g (77%) of imide: bp 53.5° (0.10 mm). The product was slightly impure by glpc and was purified by preparative glpc: $n^{23}D$ 1.4517; ir ($CHCl_3$) 5.98 and 5.80 μ sh (C=O).

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.5; H, 9.3; N, 9.9.

N-Cyclohexyl-N-formylacetamide.—Cyclohexylformamide (25.5 g, 0.20 mol) was dissolved in 250 ml of methylene chloride and pyridine (31.7 g, 0.40 mol). Acetyl chloride (31.4 g, 0.40 mol) was slowly added with ice cooling. A white salt formed immediately. The mixture turned light yellow and was allowed to stand for 1 hr. The mixture was poured into a separatory funnel and was washed three times each with 100 ml of water. The methylene chloride solution was dried (Na_2SO_4), concentrated, and distilled through a spinning-band column giving 23.2 g (68%) of imide: bp 74–75° (0.20 mm); $n^{23}D$ 1.4872; ir (neat) 1720 and 1672 cm^{-1} (C=O).

Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.8; H, 9.0; N, 8.3.

Pyrolysis of N-Formylacetanilide.—The imide was injected in 48-μl aliquots. White crystals, mp 109–113°, formed in the collector bottle without purification (acetanilide mp 113–115°). The collector bottle was washed with a small amount of $CHCl_3$. An ir spectrum of the $CHCl_3$ solution was identical with that of acetanilide except for a small peak at 4.48 μ, identical with that of benzonitrile. Glpc of the $CHCl_3$ solution gave a small peak with a retention time identical with that of benzonitrile, and a

(24) L. A. LaPlanche and M. T. Rogers, *J. Amer. Chem. Soc.*, **86**, 337 (1964)
(25) L. A. LaPlanche and M. T. Rogers, *ibid.*, **85**, 3728 (1963).
(26) R. C. Neuman, Jr., and L. B. Young, *J. Phys. Chem.*, **69**, 2570 (1965).
(27) Infrared spectra of N-(*n*-butyl)-N-formylacetamide and N-cyclohexyl-N-formylacetamide were obtained by Dr. R. A. Mackay, Edgewood Arsenal, from neat liquids between KRS-5 plates using a Perkin-Elmer Model 521 spectrophotometer. A study of the effect of metal ion complexation on the carbonyl stretching frequencies of these imides will be published later. Other ir data reported in the present paper were obtained using a Beckman IR-5A spectrophotometer. Boiling points are uncorrected.
(28) S. Wawzonek, J. Chua, E. L. Yeakey, and W. McKillip, *J. Org. Chem.*, **28**, 2376 (1963).

very large peak with a retention time identical with that of acetanilide.

Pyrolysis of N-(*n*-Butyl)-N-formylacetamide. Copper Tube.—The imide (228 mg, 1.59 mmol) was injected in 50-μl aliquots. The products (186 mg) were collected in ice and analyzed by glpc. Product weight corrected for carbon monoxide loss from 85% of the starting material was 224 mg.

Glass Tube.—The imide (228 mg, 1.59 mmol) was injected in 50-μl aliquots. The products (195.5 mg) were collected in ice and analyzed by glpc. Product weight corrected for carbon monoxide loss from 85% of the starting material was 234 mg.

Pyrolysis of N-(*sec*-Butyl)-N-formylacetamide.—The imide (461 mg, 3.22 mmol) was injected in 45-μl aliquots. The products (433 mg) were collected in ice and analyzed by glpc. The product weight corrected for carbon monoxide loss with 33% unreacted starting material and 57% of the reacted imide decarbonylating was 467 mg.

Pyrolysis of N-Cyclohexyl-N-formylacetamide.—The imide (980 mg, 5.80 mmol) was injected in 45-μl aliquots. The products (802 mg) were collected in ice and analyzed by glpc. The weight corrected for carbon monoxide loss with 8% unreacted starting material and 51% of the reacted imide decarbonylating was 880 mg.

Registry No.—N-(*n*-Butyl)-N-formylacetamide, 17604-86-3; N-(*sec*-butyl)-N-formylacetamide, 17604-87-4; N-cyclohexyl-N-formylacetamide, 17604-88-5.

Acknowledgment.—Elemental analyses were performed by the Analytical Chemistry Department, Chemical Research Laboratory, Edgewood Arsenal.

Synthetic Routes to Cyclopropyl-Substituted Azoalkanes. Some Reactions of Cyclopropylcarbinyl Cyanates, Isocyanates, Benzoates, and *p*-Nitrobenzoates

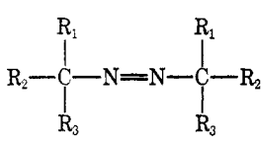
JACK W. TIMBERLAKE AND J. C. MARTIN

Department of Chemistry and Chemical Engineering, University of Illinois, Urbana, Illinois 61801

Received January 29, 1968

The syntheses of substituted azomethanes with one, two, and three cyclopropyl substituents on each methyl carbon (**1a–e**) have been approached *via* a variety of pathways starting from the appropriate cyclopropylcarbinols. We discuss complicating reactions which arise from the ready ionization of compounds such as tricyclopropylcarbinyl isocyanate and from ring-opening reactions of cyclopropyl carbonium ions. The most generally successful route to these azoalkanes involved ammonolyses of cyclopropylcarbinyl esters followed by oxidative coupling of the resulting amines by treatment with iodine pentafluoride. A second promising synthetic route converts a ketone into an azine to which chlorine is added to give an azo-α-chloroalkane. Replacement of the chlorine by an alkyl substituent occurs readily with alkylmagnesium bromides, under conditions which lead to regeneration of the azine on treatment with the corresponding alkylmagnesium iodide.

In connection with a kinetic study of the rates of formation of substituted cyclopropylcarbinyl radicals,[1] we have synthesized the following tertiary alkylazo compounds: 2,2′-dicyclopropyl-2,2′-azopropane (**1a**), 1,1,1′,1′-tetracyclopropyl-1,1′-azoethane (**1b**), 1,1,1′,1′-tetracyclopropyl-1,1′-azoisobutane (**1c**), and 1,1,1,1′,-1′,1′-hexacyclopropylazomethane (**1e**). This paper describes the synthesis of these compounds and the attempted synthesis of 1,1′-dicyclopropyl-1,1′-diisopropyl-1,1′-azoisobutane (**1d**).



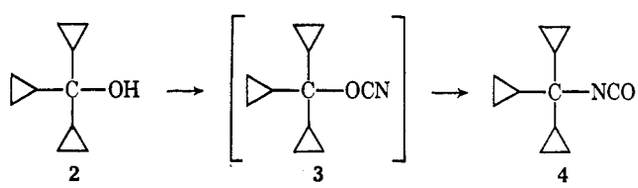
1a, $R_1 = R_2 = CH_3$; R_3 = cyclo-C_3H_5
b, $R_1 = CH_3$; $R_2 = R_3$ = cyclo-C_3H_5
c, $R_1 = i$-C_3H_7; $R_2 = R_3$ = cyclo-C_3H_5
d, $R_1 = R_2 = i$-C_3H_7; R_3 = cyclo-C_3H_5
e, $R_1 = R_2 = R_3$ = cyclo-C_3H_5
f, $R_1 = R_2 = R_3 = CH_3$
g, $R_1 = R_2 = CH_3$; $R_3 = C_6H_5$

Two possible synthetic approaches were considered likely to provide attractive routes to compounds such as **1**. The method of Esser, Rastadter, and Reuter[2] involves treatment of the appropriate isocyanate with excess hydrogen peroxide and leads directly to the azo compound. The method of Stevens[3] involves oxidative coupling of the appropriate amine with iodine pentafluoride. The latter method has been used to prepare the tertiary alkyl-substituted azo compounds 2,2′-azoisobutane[3,4] (**1f**) and azocumene[4] (**1g**).

Kauer and Henderson[5] have developed a method for preparation of isocyanates which involves treatment of an alcohol with sodium hydride followed by cyanogen chloride to give the aliphatic cyanates. The cyanates rearrange to the isocyanates on treatment with boron trifluoride etherate or, in some cases, simply on distillation.

$$ROH \xrightarrow{NaH} RO^-Na^+ \xrightarrow{ClCN} ROCN \xrightarrow{BF_3\cdot Et_2O} RNCO$$

Amine Syntheses.—Employing the method of Kauer and Henderson,[5] with only slight modification, we were able to prepare tricyclopropylcarbinyl isocyanate (**4**). The rapid rearrangement of **3** to **4** is suggested by our failure to detect any cyanate (**3**). Treatment of the isocyanate with hydrogen peroxide did not yield the desired azo compound. Instead, an almost quantitative yield of tricyclopropylcarbinol (**2**) was returned.



2 **3** **4**

It is possible that the isocyanate is hydrolyzed in the aqueous hydrogen peroxide solution even though attempts were made to remove all water. Hydroly-

(1) J. C. Martin, John E. Schultz, and Jack W. Timberlake, *Tetrahedron Lett.*, 4629 (1967).
(2) H. Esser, K. Rastadter, and G. Reuter, *Chem. Ber.*, **89**, 685 (1956).
(3) T. E. Stevens, *J. Org. Chem.*, **26**, 2531 (1961).
(4) S. F. Nelsen and P. D. Bartlett, *J. Amer. Chem. Soc.*, **88**, 137 (1966).
(5) J. C. Kauer and W. W. Henderson, *ibid.*, **86**, 4732 (1964).