A Novel Deamination. II. The Synthesis of Styrene and *trans*-Stilbene from 2-Phenylethylamine and N-1,2-Diphenylethylamine *via* the Utilization of Amide and Imide Anions as Leaving Groups[1]

RONALD J. BAUMGARTEN[2]

Department of Chemistry, University of Illinois at Chicago Circle, Chicago, Illinois 60680
and Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois 61801

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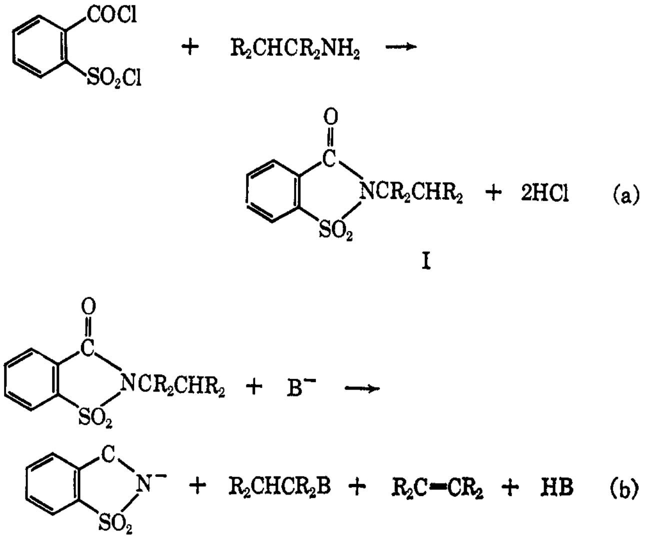
Whereas, SN1, SN2, E1, and E2 types of cleavage of alcohols and their ester derivatives are well-known reactions, most of the corresponding cleavages of amines and their amide derivatives are relatively unknown. The first examples of an apparent E2 type of deamination utilizing amide and imide anions as leaving groups are discussed here. In addition a few relatively obscure examples of apparent SN1 and E1 types of deaminations of certain amides and certain ammonium salts are reviewed.

Both the hydroxide ion and anions derived from amines are notoriously poor leaving groups in substitution or elimination reactions. But, whereas a variety of simple and practical procedures are available for the cleavage of carbon–oxygen bonds, most deamination techniques such as the nitrosoamide pyrolysis, nitrous acid, or the Hofmann elimination, are either relatively time-consuming processes or result in low yields of desired products. For example, one popular procedure for the breakage of carbon–oxygen bonds involves the initial formation of the tosyl ester derivative. The carbon–oxygen bond is probably cleaved with greater facility in such systems, because the weakly basic tosylate anion is thermodynamically a much better leaving group than the strongly basic hydroxide anion. In a recent review article on deaminations, the present author predicted that the analogous carbon–nitrogen cleavages should be feasible *via* similar derivatization of the amino functionality.[3] The major problem involves the proper choice of the derivative so that the system will have an isolable amount of the product(s) of deamination at the conclusion of the reaction.

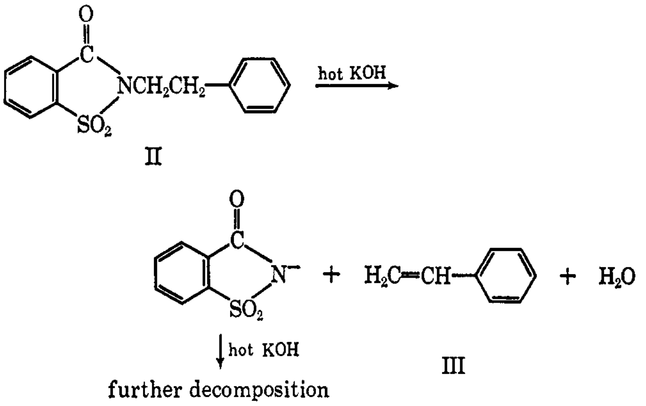
The logical analogy to tosylate anions would lead to the prediction that various sulfonamides might be good derivatives for subsequent substitution or elimination, but sulfonamide anions are still reasonably strong bases.[4] Sulfonimide anions [$(RSO_2)_2N^-$], on the other hand, are reasonably weak bases and, thus, would appear to be more promising potential leaving groups. Readily obtainable modifications of sulfonimides are saccharin derivatives (I).[5] Based on these considerations, the proposed new deamination sequence is summarized in Scheme I.

SCHEME I



The procedure (Scheme I, eq a) for the formation of the N-alkylsaccharin derivatives (I) has been described by Remsen and co-workers.[6,7] A successful example of the reaction described in Scheme I, eq b was reported in paper I of the series.[1] In particular, the indicated carbon–nitrogen bond cleavage was accomplished by heating the N-2-phenylethylsaccharin (II) with potassium hydroxide (Scheme II). Under these conditions styrene (III) was produced in 65% yield.

SCHEME II



Two questions arise concerning this type of deamination: (1) How general is the reaction in respect to the type activating group linked to the original amine, and (2) how general is the reaction in respect to the type R groups on the alkyl portion of the amine?

To answer question 1, it is profitable to return to the analogy of amines to alcohols. For example, alcohols may be dehydroxylated by simply protonating the hydroxyl group, wherein the leaving group becomes the weak base, water (Scheme III). On the other hand,

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[1] Paper I: R. J. Baumgarten and P. J. DeChristopher, *Tetrahedron Letters*, 3027 (1967).

[2] Please address all inquiries to the Chicago Circle campus.

[3] R. J. Baumgarten, *J. Chem. Educ.*, **43**, 398 (1966).

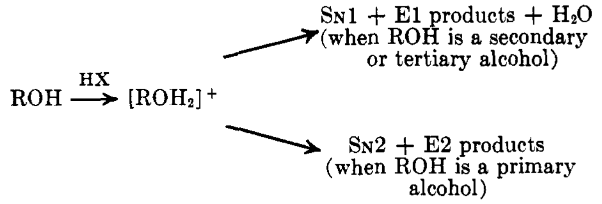
[4] Most sulfonamides have pK_a's of about 9–11: D. O. Jordan and H. F. W. Taylor, *J. Chem. Soc.*, 994 (1946); G. Dauphin and A. Kergomard, *Bull. Soc. Chim. France*, 486 (1961).

[5] The K_a for saccharin has been variously reported as 2.5×10^{-2} and 3.87×10^{-3}: K. Taufel and C. Wagner, *Ber.*, **58**, 910 (1925).

[6] I. Remsen, *Am. Chem. J.*, **30**, 247 (1903); I. Remsen and W. B. Holmes, *ibid.*, 273 (1903); I. Remsen and F. E. Clark, *ibid.*, 277 (1903).

[7] The N-alkylated saccharin derivatives were prepared here *via* the alkylation of the sodium salt of saccharin: H. L. Rice and G. R. Pettit, *J. Am. Chem. Soc.*, **76**, 302 (1954).

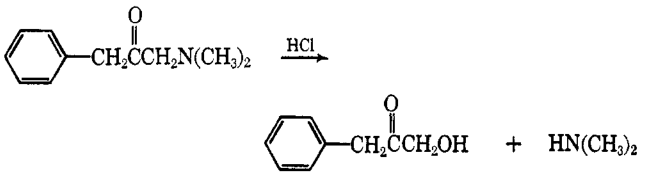
SCHEME III

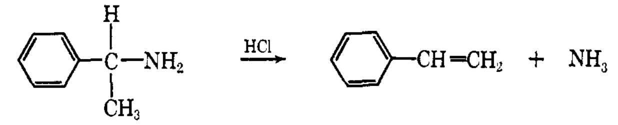


$$\mathrm{ROH} \xrightarrow{\mathrm{HX}} [\mathrm{ROH_2}]^+ \rightarrow \mathrm{S_N1} + \mathrm{E1}\ \text{products} + \mathrm{H_2O}\ \text{(when ROH is a secondary or tertiary alcohol)}$$

$$[\mathrm{ROH_2}]^+ \rightarrow \mathrm{S_N2} + \mathrm{E2}\ \text{products (when ROH is a primary alcohol)}$$

protonation of amines usually leads to stable ammonium salts. Nonetheless a few isolated cases of deamination have been reported wherein the leaving group is apparently ammonia or a secondary amine.[3,8,9,10a,10b]





More commonly, alcohols are first converted to ester derivatives as briefly described in the opening paragraph.[10c] When esters are treated with basic nucleophiles, the results given in Scheme IV may occur.

SCHEME IV

$\mathrm{R_2CHCH(R)OR'} \xrightarrow{\text{base}}$
1. nucleophilic substitution products
2. elimination products
3. ester hydrolysis or saponification products

where $\mathrm{R'} = \mathrm{RCO}$, $\mathrm{RSO_2}$, etc.

An analogous situation can be written for amides (Scheme V):

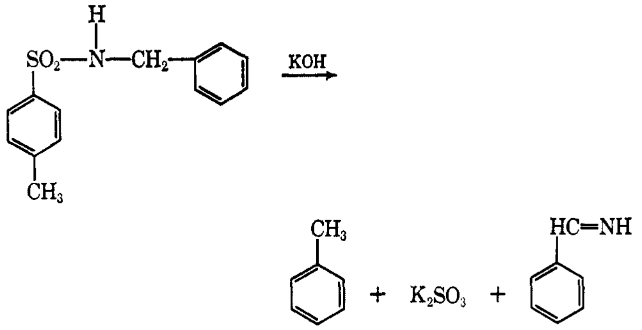
SCHEME V

$\mathrm{R_2CHCH(R)NH(R')} \xrightarrow{\text{base}}$
1. nucleophilic substitution products
2. elimination products
3. amide hydrolysis products

where $\mathrm{R'} = \mathrm{RCO}$, $\mathrm{RSO_2}$, etc.

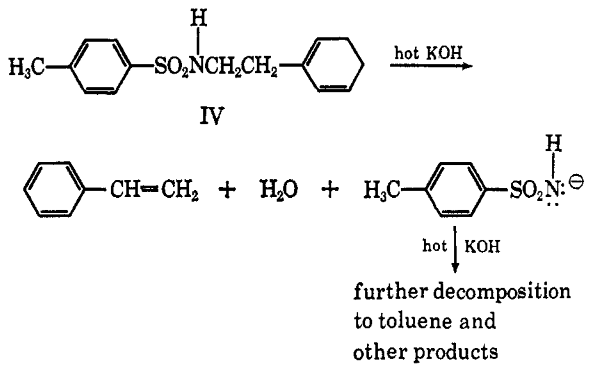
In the ester series the predominance of path 1, 2, or 3, will be dependent upon the nature of the alkyl and acyl moieties of the ester, the nature of the attacking nucleophile, and the other reaction conditions (*i.e.*, solvent, temperature, etc.). Thus, the favored pathway is saponification when carboxylic esters are treated with hydroxide ion.[11] On the other hand, when esters of strong acids such as sulfonic acids are treated with various bases or nucleophiles, products of substitution and elimination are preferentially formed. Displacement of the sulfonate anion presumably occurs more readily than the displacement of the carboxylate anion, because of the far weaker basicity of the sulfonate anion.[11b,12]

When virtually any amide is treated with strong base, only the products of saponification are observed. Certain sulfonamides, however, have been observed to give products resulting from initial attack at the carbon hydrogen α to the nitrogen[13] (eq 1). The



(1)

first example of carbon–nitrogen bond cleavage upon treatment of an amide or imide with hydroxide ion was the case where N-2-phenylethylsaccharin (II) gave styrene (Scheme II).[1] Since the saccharin anion is an anion of a reasonably strong acid,[5] it was of interest to determine whether the conjugate bases of amides and imides which are considerably weaker as acids, would also serve as effective leaving groups under the same conditions. N-2-phenylethyl-*p*-toluenesulfonamide (IV) (pK_a of parent acid = *ca.* 10),[4] N-2-phenylethylphthalimide (V) (pK_a of phthalimide = *ca.* 7),[14] and N-2-phenylethylbenzamide (VI) (pK_a of parent acid = *ca.* 16),[3] respectively, were heated with potassium hydroxide pellets. All three gave styrene, the yields from IV and V, being 50–71%. Since the 2-phenylethylamine derivatives II, IV, and V are easily obtained in good yield, this constitutes a simple and practical new procedure for the synthesis of styrene (and, presumably, substituted styrenes). The tosyl derivative IV was the easiest and cheapest to prepare and also gave the best yields (eq 2). The advantages of the



(2)

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(8) E. F. Jenny and A. Melzer, *Angew. Chem. Intern. Ed. Engl.*, **4**, 951 (1965).

(9) (a) M. Ishihara and R. Oda, *Kogyo Kagaku Zasshi*, **46**, 1268 (1943); *Chem. Abstr.*, **42**, 6333 (1948); M. Fileti and A. Piccini, *Ber.*, **12**, 1308 (1879); (b) C. Ainsworth and N. R. Easton, *J. Org. Chem.*, **27**, 4118 (1962).

(10) (a) P. Rabe and W. Schuler, *Ber.*, **81**, 139 (1948); R. B. Turner and R. B. Woodward in "The Alkaloids," Vol. 3, R. Manske and H. Holmes, Ed., Academic Press Inc., New York, N. Y., 1956, p 9. (b) Another analogous case in the amine series is the production of alkenes and alcohols upon the pyrolysis of quaternary ammonium hydroxides (Hofmann elimination). (c) Treatment of alcohols with phosphorus pentachloride or thionyl chloride also involves initial formation of labile esters before the cleavage of the carbon–oxygen bonds.

(11) (a) The elimination pathway is followed with 2-phenyl ethyl esters: C. R. Hauser, J. C. Shivers, and P. S. Skell, *J. Am. Chem. Soc.*, **67**, 409 (1945). References to the substitution pathway with other carboxylic esters are also given in this article. (b) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, pp 314–345.

(12) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 275–293.

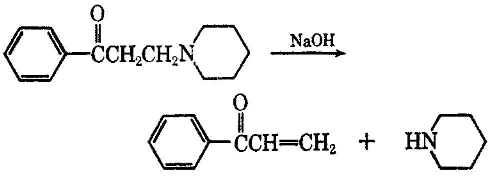
(13) E. L. Holmes and C. K. Ingold, *J. Chem. Soc.*, 1305 (1926).

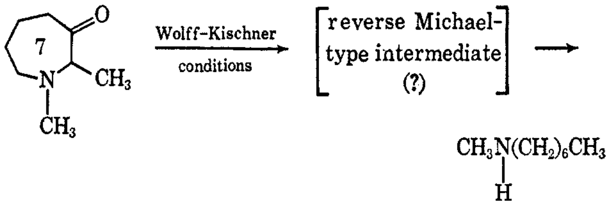
(14) J. K. Wood, *ibid.*, **89**, 1836 (1906).

present procedure over those already reported have been discussed in the earlier paper in this series.[1,15,16]

To answer the second question, which is concerned with the generality of the reaction in respect to the amine portion of the amide, several experiments were carried out wherein various N-alkylsaccharins derived from simple aliphatic amines (*e.g.*, N-hexylsaccharin) were heated with potassium hydroxide pellets and other nucleophiles. The results of these experiments indicate that carbon–nitrogen bond cleavage is not an important pathway for the simple aliphatic derivatives. Instead, the N-alkylsaccharins gave mainly products derived from attack at the carbonyl group (*i.e.*, sulfamic acid derivatives). These results are consistent with the earlier papers of Reid, Rice, and Grogan, wherein N-alkylsaccharins were reported to give N-alkylsulfamic acids when treated with alkali.[17]

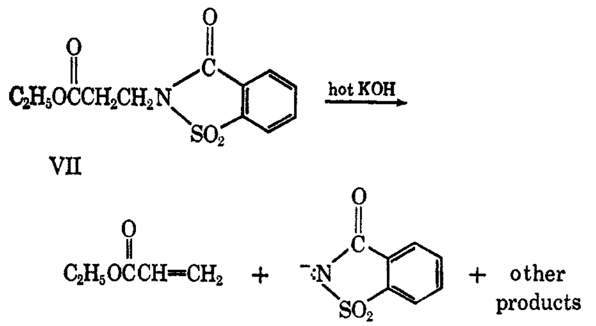
The nature of the R group appears to be the crucial factor in determining the ease of carbon–nitrogen bond breakage. Thus, reverse Michael additions and related reactions occasionally are observed with Mannich bases, wherein the amine (or its conjugate anion) serves as the leaving group.[18,19]



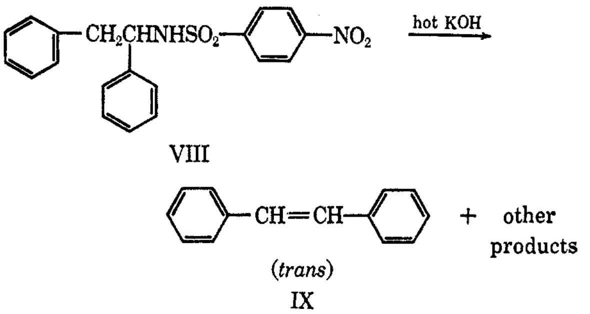


Horak and co-workers have observed that, in at least some cases, the elimination is unimolecular and probably involves a cyclic intermediate. Presumably the driving force for reverse Michael-type reactions is the formation of the conjugated alkene. Similarly in the reaction reported here, the driving force for the formation of styrene is probably the production of the conjugated system.

Two similar systems, N-2-carbethoxyethylsaccharin (VII) and N-1,2-diphenylethyl-*p*-nitrobenzenesulfonamide (VIII) were also pyrolyzed with potassium hydroxide. Small amounts of ethyl acrylate (*ca.* 5%) were detected from the basic pyrolysis of VII (eq 3) and fair amounts (29%) of *trans*-stilbene (IX) were formed upon the basic pyrolysis of VIII (eq 4). Since *trans*- rather than *cis*-stilbene was formed upon the pyrolysis, the elimination reaction is apparently of the *trans* type.

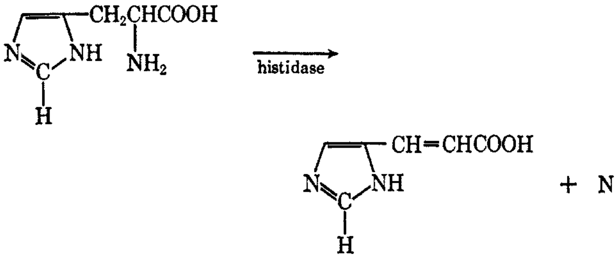


VII (3)



VIII IX (4)

At least one related biochemical example of a deamination of the types described here is known; namely histidine loses ammonia to give urocanic acid.[3,20]



In addition to the base-induced substitutions and eliminations of esters and amides, products resulting from carbon–oxygen bond cleavages often are observed during acid-catalyzed hydrolyses of esters derived from secondary and tertiary alcohols.[11,12,21] That carbon–nitrogen bond cleavages may take place during acid-catalyzed amide hydrolyses is not generally known, but various primary and secondary amides and benzenesulfonamides derived from tertiary carbinamines or benzylic amines have been observed to give SN1- and E1-type products.[22]

Experimental Section

N-2-Phenylethyl-*p*-toluenesulfonamide (IV) (mp 67–68°, lit.[23] mp 65–66°) was prepared in nearly quantitative yield essentially by the method of Carothers, Bickford, and Hurwitz.[24] **N-2-Phenylethylphthalimide (V)** (mp 131–132°, lit.[25] mp 131–132°) was prepared in excellent yield by the method of Ing and Manske.[25] N-2-Phenylethylbenzamide (VI) (mp 114–115°, lit.[26] mp 113–114°), was obtained by the method of Bischler and

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[15] W. S. Emerson, *Chem. Rev.*, **45**, 347 (1949).

[16] J. N. Hornibrook, *Chem. Ind.* (London), 872 (1962).

[17] L. M. Rice, C. H. Grogan, and E. E. Reid, *J. Am. Chem. Soc.*, **75**, 4304 (1953); **77**, 5628 (1955).

[18] P. Cársky, P. Zuman, and V. Horák, *Collection Czech. Chem. Commun.*, **29**, 3044 (1964); V. Horák, J. Michl, and P. Zuman, *Tetrahedron Letters*, 744 (1961).

[19] N. J. Leonard and S. Gelfand, *J. Am. Chem. Soc.*, **77**, 3269 (1955).

[20] A. H. Mehler, H. Tabor, and O. Hayaishi, *Biochem. Prep.*, **4**, 50 (1955).

[21] S. G. Cohen and A. Schenider, *J. Am. Chem. Soc.*, **63**, 3382 (1941).

[22] (a) K. Syhora and H. Bocková, *Tetrahedron Letters*, 2369 (1965); (b) J. W. Cook, G. T. Dickson, D. Ellis, and J. D. Loudon, *J. Chem. Soc.*, 1074 (1949); (c) P. A. Briscoe, F. Challenger, and P. S. Duckworth, *J. Chem. Soc.*, 1755 (1956).

[23] T. B. Johnson and H. H. Guest, *Am. Chem. J.*, **42**, 349 (1909).

[24] W. H. Carothers, C. F. Bickford, and G. J. Hurwitz, *J. Am. Chem. Soc.*, **49**, 2913 (1927).

[25] H. R. Ing and R. H. F. Manske, *J. Chem. Soc.*, 2350 (1926). Phthalimide V may also be obtained from the parent amine and phthalic anhydride: T. B. Johnson and H. H. Guest, *Am. Chem. J.*, **43**, 319 (1910).

[26] A. Bischler and B. Napieralski, *Ber.*, **26**, 1907 (1893).

Napieralski.[26] For the description of saccharin derivatives II and VII see paper I in this series.[1]

N-1,2-Diphenylethyl-*p*-nitrobenzenesulfonamide (VIII), mp 162–164°, was prepared by essentially the method described for sulfonamide IV.[24]

Anal. Calcd for $C_{20}H_{18}N_2SO_4$: C, 62.8; H, 4.71; N, 7.33. Found: C, 63.1; H, 4.78; N, 7.26.

Styrene (III).—A dry mixture of sulfonamide IV (3.2 g, 11.6 mmoles) and a fourfold molar excess of potassium hydroxide pellets was cautiously heated with a microburner for 10–15 min in a microdistillation apparatus kept at 50–100 mm. A mixture of styrene and water was distilled. The mixture was extracted with hexane, after which the hexane extract was dried over anhydrous sodium sulfate. Evaporation of the hexane left behind 850 mg (8.2 mmoles, 71%) of an almost colorless oil. The nmr and infrared spectra of the oil were almost identical with the corresponding spectra of authentic styrene. The only impurity detectable from the spectra was a small amount of toluene. Vacuum distillation of the oil gave 680 mg (5.9 mmoles, 51%) of a middle fraction of "water-white" styrene whose nmr and infrared spectra were identical with the corresponding spectra of authentic styrene. The saccharin II, phthalimide V, and benzamide VI, derivatives of 2-phenylethylamine, when treated under the same conditions, gave styrene in 65, 50, and 40% yields, respectively. No products resulting from the substitution pathway (*e.g.*, alcohols) were detected in any of these runs. No styrene was produced when amides II, V, and VI were heated in the absence of base 2-Phenethylamine gave no styrene, when heated with or without base.

***trans*-Stilbene (IX).**—The *p*-nitrobenzenesulfonamide, VIII (2.2 g, 5.8 mmoles), was very cautiously heated with a fourfold excess of potassium hydroxide pellets as described for *p*-toluenesulfonamide IV. If the reaction mixture is heated too rapidly, the reaction takes place so vigorously that severe foaming occurs. The volatile brown oil–water mixture was extracted with hexane after which the hexane was evaporated to give 300 mg (1.7 mmoles, 29%) of crude *trans*-stilbene (mp 100–123°, lit.[27] mp 124°). The nmr indicated peaks for *trans* but not for *cis*-stilbene. Recrystallization of the crude crystals from hexane gave crystals which melted at 122–124°, and whose nmr and infrared spectra were identical with those of authentic *trans*-stilbene.

Registry No.—III, 100-42-5; IX, 103-30-0; 2-phenyl ethylamine, 64-04-0; N-1,2-diphenylethylamine, 3082-58-14.

Acknowledgments.—Elemental analyses were performed by Mr. J. Nemeth and his group. The spectra were run by Mr. O. W. Norton and his group. Thanks are extended to these people.

(27) "The Merck Index," 6th ed, Merck and Co., Inc., Rahway, N. J., 1952, p 905.

Nitration of α-Olefins in Noncomplexing Solvents and Novel Reactions of the Products[1]

G. A. BONETTI, C. B. DESAVIGNY, C. MICHALSKI, AND R. ROSENTHAL

The Research and Development Department, ARCO Chemical Company, Division of Atlantic Richfield Company, Glenolden Pennsylvania 19036

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α-Olefins were nitrated with an equilibrium mixture of nitrogen dioxide–dinitrogen tetroxide in a noncomplexing solvent, *e.g.*, 2,2,4-trimethylpentane. Nitration at elevated temperatures, 50–100°, gave high yields of nitro nitrites and dinitro paraffins. Hydrolysis of these intermediates with water or alcohol gave products containing up to 52–53% nitro alcohol and 46–47% dinitro paraffins. At lower temperatures, 0–50°, in addition to formation of nitro nitrites and dinitro paraffins, increased amounts of nitro nitrates were obtained. Mechanisms for the formation of nitro nitrates at low temperatures are postulated. Several methods for the conversion of nitro nitrites, nitro alcohols, and dinitro paraffins to nitro olefins are described. Hydration of nitro olefins was accomplished readily with a basic salt as catalyst.

Nitration of α-Olefins.—The reaction of olefins and dinitrogen tetroxide has been investigated extensively and its chemistry and mechanism have been described in several reviews. Riebsomer[2] summarizes the work up to 1945 and describes the difficulties encountered in interpreting the data of the early literature. Shechter[3] has reviewed the more recent literature.

In the 1940's Levy, Scaife, and coworkers[4] investigated the reaction of pure nitrogen oxides with olefins under controlled conditions and found that dinitrogen tetroxide in the presence of oxygen adds smoothly to olefins when the reaction is carried out below 25° in an ether or ester type complexing solvent. Dinitro paraffins, nitro nitrites, and nitro nitrates were the principal reaction products along with up to 35% of other products such as nitro ketones, nitro nitroso compounds, and oximes. Since that time the reaction has been applied to unsaturated compounds besides simple olefins and its mechanism has been investigated.[5]

It must be noted, however, that in the work reported to date, Levy's procedure has been used throughout and assumed to be the only way to carry out a successful reaction between dinitrogen tetroxide and olefins.

We have now found that the reaction of olefins with dinitrogen tetroxide can be carried out in noncomplexing solvents. Optimum results are obtained by reacting alkenes with nitrogen dioxide in hydrocarbon diluents at temperatures of 50–100°.

Results

1-Hexadecene in 2,2,4-trimethylpentane solvent was nitrated with an excess of NO_2 in a continuous system at 70–75°. After hydrolysis with water the product analyzed 52.1% 1-nitro-2-hexadecanol and 46.5% 1,2-dinitrohexadecane. Nitration of 1-octene at 52° gave a product containing 48.8% 1-nitro-2-octanol and 50.5% 1,2-dinitrooctane.

The pure C_8 and C_{16} nitro compounds were isolated from nitration mixtures by liquid phase chromatog-

(1) Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965.

(2) J. L. Riebsomer, *Chem. Rev.*, **36**, 157 (1945).

(3) H. Shechter, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **25**, 55 (1964).

(4) N. Levy, C. W. Scaife, *et al.*, *J. Chem. Soc.*, 1093, 1096, 1100 (1946); 52 (1948); 2627 (1949).

(5) H. Shechter and F. Conrad, *J. Am. Chem. Soc.*, **75**, 5610 (1953).