THE TRIAZENE METHOD FOR THE DEAMINATION OF ALIPHATIC AMINES Emil H. White and Hanspeter Scherrer Department of Chemistry The Johns Hopkins University Baltimore 18, Maryland (Received 2 November 1961)

TWO general methods for the deamination of primary aliphatic amines, the nitrous acid-amine reaction¹ and the nitrosoamide decomposition,² have been reported in the chemical literature. We would like to call attention to a third method which we have found to be useful for the conversion of primary amines into esters, alkyl halides, ethers, and related derivatives. This method, suggested by work on the reaction of nitrosyl chloride with aliphatic amines,³ involves triazene intermediates as outlined in equation (1).



¹ C.R. Noller, <u>Chemistry of Organic Compounds</u> (2nd Ed.) p. 238. W.B. Saunders Philadelphia (1957); A. Streitweiser, Jr., <u>J.Org.Chem.</u> <u>22</u>, 861 (1957).

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² Emil H. White, <u>J.Amer.Chem.Soc.</u> <u>77</u>, 6011 (1955); R. Huisgen and C. Rüchardt, <u>Leibigs Ann.</u> <u>601</u>, 21 (1956).

⁹ Unpublished work by Dr. Bernard E. Weller. Isolated examples of steps a and b (equation 1) have been reported before (footnotes 4 and 5), but the sequence has not been examined previously as a method for the deamination of amines.

The yields for step a^4 in dimethylformamide as the solvent are essentially quantitative and the triazenes formed may be used directly in step b^5 (alternatively, the triazenes may be isolated and purified for use in the nitrogen elimination step). The overall yields for the deamination (Table 1) are superior to those reported for the nitrous acid deamination of amines and about equal to those reported for the nitrosoamide decomposi-

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Yields for the Triazene Method of Deamination^a RNH₂ RNHN = NC₆H₄R' \rightarrow RX + N₂ + R'C₆H₄NH₂^b

Run	R	Acid HX	Solvent (step b)	% RX	% Olefin	% R'C6H4NH2
ıc	Methyl	3,5DNB ^d	Ether	95	-	-
2	n-Butyl	3,5DNB ^d or HBr	Ether	63	-	-
3	Isobutyl	3,5DNB ^d	Ether	56	-	86
4	Cyclohexyl	Acetic	сн ₂ с1 ₂	38	30	65 ^e
5	l-Phenyl- ethyl	Acetic	Hexane	44	28	48 ^e
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^a Ave Yields for the two steps, determined for recrystallized or distilled products, and based on the amine (except Run 1 based on triazene).

- ^b R' = <u>p</u>-Cl for Run 2 and <u>p</u>-CH₃ for the others.
- ^c We thank Mr. Anthony Baum for carrying out this run.
- ^d 3,5-Dinitrobenzoic acid.
- ^e Secondary amines (RNHC₆ H_4 R[•]) were isolated from these runs, 16% in run 4 and 25% in run 5.
- f Little acetate was formed; the value in this case pertains to the solvolysis product ROCH₃ (formed with predominant inversion of configuration).

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tion.^{1,2} Negligible skeletal isomerization occurs in non-polar solvents; in run 2 no detectable s-butyl ester was formed, and in run 3, less than 2% of the iso- and t-butyl isomers was formed. The principle side reactions lead to olefins (equation 1) and to secondary amines. The latter compounds are formed, however, only in the deamination of secondary carbinamines; in run 4, 16% of N-cyclohexyl-p-toluidine was formed, and in run 5, 25% of N-(1-phenylethyl)-toluidine (optically active). These byproducts are in general easily removed from the main product.

The triazene method of deamination leads to considerable apparent racemization; the reaction of 1-(1-phenylethyl)-3-(4 methylphenyl)-triazene with acetic acid gave 1-phenylethyl acetate containing 54% of the enantiomer corresponding to retention of configuration in hexane (run 5), 55% of that form in ether, and 57% in acetic acid. These results and the reaction characteristics cited above can be accounted for by a mechanism related to that proposed for the nitroscamide decomposition.⁶



In addition to their role as intermediates in the deamination reaction, the triazenes show considerable promise as alkylating agents. Methyl esters

⁴ The method of Goldschmidt [<u>Ber.Dtsch.Chem.Ges. 21</u>, 1016 (1888)] and Dimroth [<u>Ber.Dtsch.Chem.Ges. 28</u>, 670 (1905)], namely the reaction of amines with aqueous solutions of diazonium salts, leads to reasonable triazene yields only if simple, water soluble amines are employed. In Dimroth's later work and in recent work reported in the literature, the alkaryl:riazenes used were prepared by the reaction of an aryl azide with an alkyl Grignard reagent.

² Goldschmidt⁴ was the first to report the acid decomposition of alkaryltriazenes. Dimroth subsequently isolated esters from the reaction of 1-methyl-3-phenyltriazene with a number of acids, and recent Russian work⁷b has extended this to a study of the reaction of benzoic acid with a number of n-alkylnaphthyltriazenes (synthesized from naphthyl azide).

of carboxylic acids can be prepared in high yield with N-methyltriazenes (run 1), and the ease of handling these stable, crystalline compounds (e.g. \underline{p} -CH₃C₆H₆N=NNHCH₃, m.p. 82^o) recommends them for use as substitutes for diazomethane and for the higher diazoalkanes. The triazenes have also been used (with aluminium alcoholate catalysts) to alkylate certain alcohols, phenols, and mercaptans.⁷

Experimental

A solution of <u>p</u>-chlorobenzenediazonium hexafluorophosphate⁸ (recrystallized from acetone-methanol) (2.87 g, 10.1 mmoles) in dimethylformamide (dimethylamine-free) was added slowly to a stirred mixture of n-butylamine (0.73 g, 10.0 mmoles), powdered sodium carbonate (15 g), and dimethylformamide (30 ml) stirred and maintained at -5° . The diazonium salt solution may be used at room temperature; however, a purer product is usually obtained if the diazonium salt solution is prepared in and delivered from a cooled separatory funnel maintained at ca. -50° . The mixture was warmed to 0° and stirred until a negative test was obtained with 2-naphthol (only a few minutes are usually required). Ether was added, the mixture was filtered, and the filtrate was washed thoroughly with water, then dried. (The triazene may be isolated at this point and recrystallized from pentane at low temperatures.⁹ The triazene in run 2 melted at 40° , that in run 3 at 19° , and that in run 5 at 39° .)

- ⁶ Emil H. White and Carl Aufdermarsh, Jr., <u>J.Amer.Chem.Soc.</u> <u>83</u>, 1179 (1961).
- 7^a V.Y. Pochinok and L.P. Limarenko, <u>Ukrain.Khim.Zh. 21</u>, 496,628 (1955); <u>b</u> V.Y. Pochinok and V.A. Portayagina, <u>Ibid. 18</u>, 631 (1952).
- ⁸ Ozark-Mahoning Co., 310 W. 6th St., Tulsa 19, Oklahoma.

Small amounts of 1,1-dimethy1-3-aryltriazene, 1,3-diaryltriazene, and 3-alky1-1,5-diarylpentazdiene represent the principle impurities in the crude triazene.

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A solution (or less satisfactorily a suspension) of 3,5-dinitrobenzoic acid (4.24 g, 20.0 nmoles) in ether was added to the crude triazene and the solution was kept at 25° until nitrogen evolution had ceased (ca. 1-2 hr). (The nitrogen evolution is instantaneous with HBr whereas the reaction with acetic acid requires ca. 12 hr for completion; the reaction is considerably faster in hydrocarbon solvents.) The solution was washed with dilute acid and dilute base, dried, and then evaporated to yield butyl 3,5-dinitrobenzoate, m.p. $61-62^{\circ}$ (1.96 g, 73%) tinted with a small amount of a colored impurity. The infra-red spectrum in CCl₄ was superimposable on that of pure n-butyl 3,5-dinitrobenzoate. Recrystallization from hexane yielded in the first crop, 1.69 g (63% yield) of the ester, m.p. $63-64^{\circ}$ (lit.¹⁰ 64-64.5°).

Similar results were obtained with <u>p</u>-tolydiazonium fluoborate as the coupling agent, but the products (RX) were less pure.

Methyl triazenes (for alkylations) can be readily prepared by the addition of aqueous solutions of diazonium salts raised to a pH of 7 (Na_2CO_3) to an excess of methylamine at 0° . The product is sublimed and recrystal-lized.

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¹⁰ Emil H. White, <u>J.Amer.Chem.Soc.</u> <u>77</u>, 6081 (1955).