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(16) The pseudomixed anhydride **10** (Scheme III) was also detected by ^{1}H NMR spectroscopy.

(17) Ethyl 2-ethyl-3,3-dibromo-4-oxobutyrate was isolated in 7% yield (see Experimental Section) and was found to decompose upon standing at 10 °C for 72 h. Only a ^{1}H NMR spectrum was obtained. Ethyl 2-ethyl-3-bromo-4-oxobutyrate was probably present as a reaction intermediate but was not isolated.

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Alkyl Nitrite–Metal Halide Deamination Reactions. 5. In Situ Generation of Nitrosyl Halides. Effective Product Control from Nitrosyl Chloride Diazotization of Primary Aliphatic Amines in *N,N*-Dimethylformamide[1]

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Nitrosyl chloride and nitrosyl bromide are formed by an efficient halide/alkoxide exchange between titanium tetrahalides and alkyl nitrites. Complete replacement of halide by alkoxide occurs and results in the formation of titanium tetraalkoxides. Reactions of primary aliphatic amines with in situ generated nitrosyl halides in *N,N*-dimethylformamide effectively minimizes elimination, rearrangement, and oxidation processes normally encountered in alternate diazotization procedures and facilitates product recovery in high yield. Comparative results for the diazotization of benzylamine by nitrosyl chloride generated from selected metal halides and *tert*-butyl nitrite are reported; the generality of chloride/alkoxide exchange for the early transition metal halides is indicated. Diazotization of primary aliphatic amines by in situ generated nitrosyl chloride in dimethylformamide produces unrearranged alkyl chlorides, alcohols, and formate esters.

Methods for deaminaton of aliphatic amines by nitrosyl halides have received considerably less attention than corresponding processes that employ nitrous acid or dinitrogen tetroxide.[3] The gaseous nitrosyl halide reagents require special handling techniques and, as is characteristic in diazotization reactions of primary aliphatic amines, generally effect the production of complex reaction mixtures in moderate yields.[4–6] In chemical operations that employ nitrosyl halides in aprotic media, these reagents are generated externally and then passed into the reaction solution from a collection vessel employed to measure the volume of the nitrosyl halide. Methods for in situ generation of nitrosyl halides, based on known reactions of hydrogen halides with sodium nitrite,[7] dinitrogen tetroxide,[8] or alkyl nitrites,[9] have not been advanced for use in deaminaton or addition procedures due to their production of potentially interfering byproducts;[10] in addition, excess amounts of hydrogen halides are often used to facilitate nitrosyl halide formation or to avoid the normally complex stoichiometric measurement of the gaseous acid. In this paper we report general methods for in situ generation of nitrosyl chloride and nitrosyl bromide that avoid the complexities usually observed with the use of hydrogen halides.

In his recent thorough examinations of deamination reactions of aliphatic amines by nitrosyl chloride at low temperatures in aprotic media, Bakke[11] identified five principal reaction pathways of the intermediate alkyldiazonium chlorides: chloride substitution, elimination, rearrangement, displacement by solvent, and diazoalkane formation (eq 1–5).

$$\mathrm{RCH_2CH_2N_2{}^+Cl^- \rightarrow RCH_2CH_2Cl + N_2} \tag{1}$$

$$\mathrm{RCH_2CH_2N_2{}^+Cl^- \rightarrow RCH{=}CH_2 + HCl + N_2} \tag{2}$$

$$\mathrm{RCH_2CH_2N_2{}^+Cl^- \rightarrow RCHClCH_3 + N_2} \tag{3}$$

$$\mathrm{RCH_2CH_2N_2{}^+Cl^- + Sol{:} \rightarrow RCH_2CH_2\text{-}Sol^+Cl^- + N_2} \tag{4}$$

$$\mathrm{RCH_2CH_2N_2{}^+Cl^- \rightarrow RCH_2CH{=}N_2 + HCl} \tag{5}$$

Reactions were performed at −70 °C in ether solvents to minimize rearrangement and, under these conditions, the process represented by eq 1 was dominant (88% of products from eq 1–4).[11a] In hydrocarbon and chlorocarbon solvents, however, the production of both aldehydes and oximes, presumed formed from the corresponding nitrosoalkane, was dominant.[11c] These and prior reports of diazotization efficiency in reactions of aliphatic amines with nitrosyl chloride

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Table I. Product Yields from Reactions of Benzylamine with Titanium Tetrachloride-*tert*-Butyl Nitrite in Dimethylformamide[a]

	relative yield, %[b]				isolated
$[C_6H_5CH_2NH_2]/[TiCl_4]$	$C_6H_5CH_2Cl$	$C_6H_5CH_2OH$	$C_6H_5CH_2O_2CH$	C_6H_5CHO	yield, %[c]
10.0	41	59	0	0	37
4.00	72	25	1	2	88
3.33	73	24	1	2	90
3.33[d]	68	28	2	2	94
2.00	77	20	1	2	98
1.00	80	17	1	2	99

[a] Unless indicated otherwise, reactions were performed at 25 °C by adding 10 mmol of benzylamine to the combination of titanium tetrachloride and 10 mmol of *tert*-butyl nitrite in 50 mL of DMF. [b] Based on the isolated yield of these products as determined by GC and NMR analyses. From duplicate runs experimentally determined percentage yields were accurate to within ±2% of the reported values. [c] Combined actual yield of benzyl chloride, benzyl alcohol, benzyl formate, and benzaldehyde. [d] Reaction was performed at 25 °C by adding 10 mmol of *tert*-butyl nitrite to the combination of titanium tetrachloride and 10 mmol of benzylamine in 50 mL of DMF.

describe a multiplicity of reaction pathways that cast doubt on the general usefulness of this reagent in deamination procedures. However, diazotization reactions that employ nitrosyl halides in dipolar aprotic solvents (solvent media expected to moderate the reactivity of the nitrosyl halides and significantly modify the reaction pathways for deamination) have not been reported. Results from reactions between aliphatic amines and in situ generated nitrosyl halides in these solvents are described in this paper. The use of *N*,*N*-dimethylformamide as the reaction solvent effectively minimizes elimination, rearrangement, and oxidation processes in deamination reactions and facilitates product recovery in high yield.

Results and Discussion

In Situ Generation of Nitrosyl Halides. Halides of the early transition metal series exhibit a marked sensitivity toward moisture that reflects both the lability of the metal–halogen bond to solvolytic substitution and the tendency of these metals to form strong metal–oxygen bonds.[13] As Lewis acids[14] these metal halides form stable adducts with electron donor ligands such as nitriles, tertiary amines, and ethers that are also sensitive to nucleophilic substitution of halide.[13] These properties of the early transition metal halides (Lewis acidity, lability of metal–halogen bonds, and comparative strength of metal–oxygen bonds) are precisely those required for effective halide/oxide interchange. However, although numerous methods for the generation of nitrosyl chloride from dinitrogen tetroxide or alkyl nitrites and a variety of inorganic halides have been reported,[10,15] there is a surprising absence of similar information for the early transition metal halides.

We have found that titanium tetrachloride reacts rapidly with alkyl nitrites at or above 0 °C to form nitrosyl chloride. In contrast to comparable uncatalyzed reactions of titanium tetrachloride with alcohols in which only two of the four chloride substituents of titanium are effectively exchanged,[16] use of an equivalent amount of alkyl nitrite (based on chloride) results in quantitative chloride/alkoxide interchange.

$$\mathrm{TiCl_4 + 4RONO \rightarrow Ti(OR)_4 + 4NOCl} \qquad (6)$$

Both isopentyl nitrite and *tert*-butyl nitrite exhibit similar reactivities in reactions with titanium tetrachloride.

Nitrosyl chloride was identified by its characteristic nitrosyl infrared absorption.[17] Titanium tetra-*tert*-butoxide was formed in reactions between *tert*-butyl nitrite and 0.25 molar equiv of titanium tetrachloride and, even without elaborate precautions, the purified product could be isolated in yields that were comparable to those from the standard, but more complex, process involving the use of anhydrous ammonia.[18] Thus reactions of alkyl nitrites with titanium tetrachloride serve not only as a convenient preparative method for nitrosyl chloride but, also, as a superior process for the formation of the tetravalent alkoxides of titanium. Nitrosyl bromide is similarly produced from the combination of alkyl nitrites and titanium tetrabromide, but titanium tetrafluoride is unreactive toward alkyl nitrites and no evidence for nitrosyl fluoride formation could be obtained. The generality of halide/alkoxide or amide exchange for the in situ generation of a wide variety of reactive halide reagents from the early transition metal halides is currently under investigation.

Diazotization of Benzylamine. The utility of the titanium tetrachloride–alkyl nitrite generative method for the production of nitrosyl chloride was evaluated through investigations of amine diazotization reactions. Because of the complexity of products and the relatively low yields of substitution products in prior investigations of nitrosyl chloride diazotization reactions, we were surprised to find that benzylamine was converted to benzyl chloride and benzyl alcohol nearly quantitatively in reactions with nitrosyl chloride performed at 25 °C in dimethylformamide (Table I). Benzyl formate and benzaldehyde were also observed, but in a combined yield of less than 4%; neither benzyl *tert*-butyl ether nor dibenzyl ether were detected. The mole ratio of evolved gas to amine was 1.0 when at least 1 equiv of nitrosyl chloride was employed. These deamination reactions were characteristically exothermic; the reaction temperature was controlled by the slow addition of the amine to the solution containing nitrosyl chloride or by the slow addition of *tert*-butyl nitrite to the amine–titanium tetrachloride combination in solution. The mode of addition had no apparent effect on the yield of isolated products.

Results from a stoichiometric study (Table I) of the reaction between benzylamine and nitrosyl chloride (formed by the combination of *tert*-butyl nitrite and titanium tetrachloride) established the dependence of the benzyl chloride/benzyl alcohol product ratio on the relative molar amount of titanium tetrachloride employed. These results suggest that the water produced in the diazotization reaction was partially trapped by a chlorotitanium compound and, consequently, inhibited from reaction with the benzyldiazonium ion. The use of phosphorus pentoxide to effect a similar result in nitrosyl halide deamination reactions has recently been described.[19] Alternatively, hydrogen chloride produced by hydration of titanium tetrachloride may have been responsible for the higher benzyl chloride/benzyl alcohol product ratio at the lower benzylamine/titanium tetrachloride ratios. Control experiments established that benzyl chloride was not formed in reactions between benzyl alcohol and titanium tetrachloride under the same conditions.[20]

The dramatic effect of solvent on the products from deamination of benzylamine by nitrosyl chloride is evidenced

Table II. Product Yields from Reactions of Benzylamine with Titanium Tetrachlorine–*tert*-Butyl Nitrite in Aprotic Solvents[a]

solvent	relative yield, %[b]			isolated yield, %[c]
	$C_6H_5CH_2Cl$	$C_6H_5CH_2OH$	C_6H_5CHO	
$(CH_3)_2NCHO$	81	17	2	98[d]
$[(CH_3)_2N]_3PO$	76	22	2	74
CH_3CN	80	18	2	83[e]
$(CH_3CH_2)_2O$	78	17	5	64
C_6H_6	66	22	12	65[f]
CH_2Cl_2	69	14	17	78

[a] Reactions were performed at 25 °C by adding 10 mmol of benzylamine to the combination of titanium tetrachloride (10 mmol) and *tert*-butyl nitrite (10 mmol) in 50 mL of the aprotic solvent. [b] Based on the isolated yields of these products as determined by GC and NMR analyses. [c] Combined actual yield of benzyl chloride, benzyl alcohol, and benzaldehyde. [d] Benzyl formate was formed in 1% yield. [e] *N*-Benzylacetamide was produced in 3% yield. [f] Diphenylmethane was formed in 6% yield.

by the data presented in Table II. The most significant differences are found in isolated product yields and in the percentage yield of benzaldehyde. Higher yields of substituted products, benzyl chloride and benzyl alcohol, are formed from reactions performed in dipolar aprotic solvents. Solvents such as benzene and methylene chloride that are less capable of stabilizing the reaction intermediates formed by diazotization of benzylamine promote oxidation. Both nitrous oxide and nitric oxide are produced during the deamination of benzylamine in methylene chloride. The formation of these gaseous products suggests that benzaldehyde is formed by direct oxidation of benzylamine.[21]

$$C_6H_5CH_2NH_2 + NOCl \rightarrow C_6H_5CH{=}NH_2^+\,Cl^- + HNO \qquad (7)$$

Disproportionation of nitrosyl hydride to nitrous oxide and water[22] or subsequent reaction of nitrosyl hydride with nitrosyl chloride to form nitric oxide[23] accounts for the observed gaseous products.

Products from solvent interception of the benzyl cation were evident, although as minor constituents of the reaction mixtures, in reactions performed in dimethylformamide, acetronitrile, and benzene (Table II). The production of benzyl formate is consistent with the process outlined in eq 8.

$$C_6H_5CH_2N_2^+ + HCON(CH_3)_2 \xrightarrow{(-N_2)} C_6H_5CH_2OCH{=}N^+(CH_3)_2 \xrightarrow{H_2O} C_6H_5CH_2OCHO \qquad (8)$$

Although alkyl ethyl ethers have been detected in low-temperature nitrosyl chloride deaminations of aliphatic amines in ethyl ether,[11a,24] benzyl ethyl ether was not observed as a product from reactions performed at 25 °C in this study. Corresponding solvent-intercepted products from reactions in hexamethylphosphoramide were not isolated.

The generation of nitrosyl chloride from dinitrogen tetroxide or alkyl nitrites by reactions with a wide variety of metal halides, including aluminum chloride and stannic chloride,[10c] has been reported. However, the comparative facility of these conversions has not been determined. In addition, metal halides of the early transition metal series such as tantalum pentachloride form stable complexes with nitrosyl chloride[25] that may be expected to significantly modify the reactions and reactivities of nitrosyl chloride. To compare the utility of these methods for nitrosyl chloride production with the titanium tetrachloride–alkyl nitrite generative method, the deamination of benzylamine in dimethylformamide has been investigated. The results from this study are presented in Table III. Data for the hydrogen chlorde–*tert*-butyl nitrite deamination process are provided for comparison.

The combination of aluminum chloride, ferric chloride, or stannic chloride and *tert*-butyl nitrite in dimethylformamide at 25 °C did not result in the formation of nitrosyl chloride in observable amounts. Product yields from benzylamine deaminations were characteristically low, and relatively high yields of benzaldehyde were obtained. In contrast, hydrogen chloride and representative metal halides of the early transition series uniformly produced nitrosyl chloride. Addition of benzylamine to these reaction media effected a rapid and quantitative evolution of gas and resulted in the production of high yields of substitution products. The ratios of benzyl chloride to benzyl alcohol for deamination reactions employing comparable amounts of titanium tetrachloride and molybedenum pentachloride were nearly identical at the low molar ratios of benzylamine to MX_n. Hydrogen chloride and tantalum pentachloride exhibited similar capabilities in forming benzyl chloride at the expense of benzyl alcohol, presumably by substitutive conversion of benzyl alcohol to benzyl chloride.[26] Complete chloride/alkoxide exchange is observed from the combination of either molybdenum pentachloride or tantalum pentachloride with 5.0 molar equiv of *tert*-butyl nitrite in diazotization reactions with benzylamine; in contrast, only three of the six chlorides of tungsten hexachloride are effectively utilized, and results similar to those from the stannic chloride promoted diazotization are obtained when the molar ratio of benzylamine to WCl_6 is 6.0.

The addition of benzylamine to nitrosyl bromide generated from *tert*-butyl nitrite and 0.25 molar equiv of titanium tetrabromide in dimethylformamide at 0 °C results in low product recovery (55% isolated yield) and the dominant production of benzaldehyde (51% relative yield). The low product recovery is predictably due to the utilization of 2 molar equiv of the nitrosyl compound for oxidative formation of benzaldehyde. Although alteration of the mode of addition through treatment of the combination of benzylamine and 0.25 molar equiv of titanium tetrabromide at 0 °C with *tert*-butyl nitrite results in a decreased yield of benzladehyde (20% relative yield, 65% isolated yield of products), only when an equivalent amount of titanium tetrabromide is employed do the product yields resemble those from nitrosyl chloride diazotization of benzylamine: 70% benzyl bromide, 22% benzyl alcohol, 2% benzyl formate, and 6% benzaldehyde (94% isolated yield). Nitrosyl bromide is apparently a more active oxidant than is nitrosyl chloride. However, complexation of the amine with titanium tetrabromide is effective in minimizing hydrogen abstraction from the α position of the amine.

Diazotization of Primary Aliphatic Amines. The superior capability of nitrosyl chloride in dimethylformamide to effect deamination of aliphatic primary amines is evident from the results presented in Table IV. Comparative data are given for reactions in which nitrosyl chloride is generated from the combination of *tert*-butyl nitrite with tantanium tetrachloride, tantalum pentachloride, and hydrogen chloride. Reactions that employ the *tert*-butyl nitrite–titanium tetrachloride combination do not exhibit capabilities for substitutive conversions of alcohols to alkyl halides that are evident in reactions that utilize tantalum pentachloride or hydrogen chloride. Product accountability is high in these deaminative conversions, the yields of aldehyde products are low (<2%), elimination is a minor competitive process (<4%), and there is a notable absence of rearranged products (<1%). However, in contrast to deamination reactions of benzylamine, the for-

Table III. Product Yields from Reactions of Benzylamine with *tert*-Butyl Nitrite and Selected Metal Halides in Dimethylformamide[a]

MCl_n	$[C_6H_5CN_2NH_2]/[MCl_n]$	relative yield, %[b]				isolated yield, %[c]
		$C_6H_5CH_2Cl$	$C_6H_5CH_2OH$	$C_6H_5CH_2O_2CH$	C_6H_5CHO	
HCl	*d*	84	12	3	1	88
$AlCl_3$[e,f]	1.0	75	15	1	9	35
$TiCl_4$	1.0	80	17	1	2	99
$FeCl_3$[f]	1.0	28	57	7	8	61
$MoCl_5$	1.7	81	15	1	3	78
$SnCl_4$	1.0	10	8	3	80	40
$TaCl_5$	1.0	88	3	2	7	85
WCl_6	1.5	81	13	4	2	90

[a] Unless indicated otherwise, reactions were performed at 25 °C by adding 10 mmol of benzylamine to the combination of the metal halide and 10 mmol of *tert*-butyl nitrite in 50 mL of DMF. [b] Based on the isolated yield of these products as determined by GC and NMR analyses. From duplicate runs, experimentally determined percentage yields were accurate to within ±3% of the reported values. [c] Combined actual yield of benzyl chloride, benzyl alcohol, and benzaldehyde. [d] Reaction performed at 0 °C after passing gaseous hydrogen chloride through the reaction solution (100 mL) for 5 min (30 mL/min) prior to the addition of benzylamine. [e] Identical results were obtained when *tert*-butyl nitrite was added to the combination of aluminum and benzylamine. [f] Slow evolution of gas after addition of amine. Reaction solution was heated to 65 °C after complete gas evolution was observed at 25 °C.

Table IV. Product Yields from Reactions of Primary Amines with *tert*-Butyl Nitrite and Selected Metal Halides in Dimethylformamide[a]

amine	registry no.	MCl_n	$[RNH_2]/[MCl_n]$	relative yield, %[b]						isolated yield, %[c]
				RCH_2Cl	registry no.	RCH_2-OH	registry no.	RCH_2O_2-CH	registry no.	
$C_6H_5CH_2CH_2NH_2$	64-04-0	$TiCl_4$	4.0[d]	76	622-24-2	10	104-62-1	14	4830-93-7	82
		$TaCl_5$	2.5	80		8		12		59
		HCl	*e*	79		5		16		54
$C_6H_5(CH_2)_3CH_2NH_2$	13214-66-9	$TiCl_4$	4.0	59	4830-93-7	19	3360-41-6	22	67421-63-0	80[f]
$CH_3(CH_2)_6CH_2NH_2$	111-86-4	$TiCl_4$	3.3	53	111-85-3	22	111-87-5	25	112-32-3	72
		$TaCl_5$	2.5	48		28		24		71
		HCl	*e*	64		13		23		79
$CH_3(CH_2)_8CH_2NH_2$	2016-57-1	$TiCl_4$	3.3	52	1002-69-3	21	112-30-1	27	5451-52-5	77
		$TaCl_5$	2.5	58		9		33		66
		HCl	*e*	62		7		31		84

[a] Unless indicated otherwise, reactions were performed at 25 °C by adding 10 mmol of the amine to the combination of metal halide and 10 mmol of *tert*-butyl nitrite in 50 mL of DMF. [b] Based on the isolated yield of these products as determined by GC analyses. From duplicate runs, experimentally determined percentage yields were within ±2% of the reported values for reactions with $TiCl_4$ and $TaCl_5$ and within ±4% of the reported values for RCH_2Cl and RCH_2OH for reactions with hydrogen chloride. [c] Combined actual yield of reported products. The yields of secondary alkyl chloride and secondary alcohol were less than 0.5% for reactions with $TiCl_4$ and were 1–3% for reactions with hydrogen chloride and $TaCl_5$. Yields of styrene from reactions of 2-amino-1-phenylethane were less than 2%; olefin yields (>95% terminal alkene) from reactions of 1-aminodecane, 1-aminooctane, and 1-amino-4-phenylbutane were 2–4%. [d] Nearly identical results were obtained with $[RNH_2]/[TiCl_4] = 3.3$ (isolated yield = 75%). [e] Reaction performed at 0°C after passing gaseous hydrogen chloride through the reaction solution (100 mL) for 5 min (30 mL/min) prior to the addition of amine. [f] Tetralin was not produced under these reaction conditions.

mation of formate esters is an important product-forming process. The production of formate esters in remarkably consistent yields, despite the variation in reaction conditions,[28] indicates that interception of the intermediate diazonium ion by dimethylformamide (eq 9) is not a reversible process.[29]

$$RCH_2N_2^+ + HCON(CH_3)_2 \rightarrow RCH_2OCH{=}N^+(CH_3)_2 + N_2 \quad (9)$$

Variation of the reaction temperature from −15 °C does not appreciably affect the relative yield of formate ester formed by nitrosation of 1-amino-2-phenylethane in dimethylformamide.[30]

Reactions of titanium tetrachloride/*tert*-butyl nitrite generated nitrosyl chloride with 1-amino-2-phenylethane and with 1-aminodecane in acetonitrile or in benzene result in a considerably greater yield of rearranged products than those observed from comparable reactions in dimethylformamide. In acetonitrile at 25 °C, 7–13% of the alkyl chloride (60% yield) and 40–60% of the alcohol (10% yield) products result from 1,2-hydrogen transfer. In benzene at 25 °C, 7–10% of the alkyl chloride (58% yield) and 55–65% of the alcohol (8% yield) products result from 1,2-hydrogen transfer. In addition, both rearranged and unrearranged acetamide products (6:8, 14% yield) are produced from reactions of nitrosyl chloride with 1-aminodecane in acetronitrile. Thus, the use of dimethylformamide as the reaction solvent for nitrosyl chloride diazotizations of primary aliphatic amines minimizes structural rearrangement and elimination as well as oxidation. However, a multiplicity of product-forming pathways remain. Methods for the effective control of this product distribution through selective capture of diazotization reaction intermediates are currently under investigation.

Experimental Section

General. Instrumentation has been previously described.[31] Analytical gas chromatographic analyses were performed on a Varian Aerograph Model 2720 gas chromatograph with thermal conductivity detectors; a Varian Model 485 digital integrator was used to determine peak areas. Use was made of 5–7-ft columns of 10% DEGS, 20% SE-30, and 20% Carbowax 20M, all on Chromosorb P. *tert*-Butyl nitrite was prepared from *tert*-butyl alcohol according to the procedure of Noyes;[32] isopentyl nitrite was obtained commercially. The amines that were employed in this study were commerically available and were used without prior purification. Titanium tetrafluoride, tetrachloride, and tetrabromide, tantalum pentachloride, molybdenum pentachloride, and tungsten hexachloride were obtained commercially from Alfa and were stored in a desiccator. Reagent grade *N*,*N*-dimethylformamide, acetronitrile, hexamethylphosphoramide, and benzene were distilled from calcium hydride prior to their use as reaction solvents. Ethyl ether was distilled from lithium aluminum hydride.

Nitrosyl Chloride. To 4.74 g of titanium tetrachloride (0.025 mol) in 25 mL of benzene contained in a three-necked flask fitted with a gas bubbler, a reflux condenser joined to a gas trap cooled to −78 °C, and a rubber septum was added 10.3 g of *tert*-butyl nitrite (0.100 mol) over a 20-min period. Dry nitrogen was slowly bubbled through the reaction solution during the addition and continued until the dark orange-red solution color disappeared. The reaction temperature was maintained at 25 °C. The volume of nitrosyl chloride collected in the cold trap was 3.8 mL which corresponded to an 82% isolated yield of product. IR analysis of the collected gas showed exact correspondance with published spectra of nitrosyl chloride.[17]

In separate experiments the combination of titanium tetrachloride and 4 molar equiv of *tert*-butyl nitrite in carbon tetrachloride, acetonitrile, and dimethylformamide was analyzed by IR spectroscopy. Although nitrosyl chloride formation was rapid at temperatures above 0 °C, the reaction was substantially slower at −10 °C. The conversion of titanium tetrachloride and *tert*-butyl nitrite to nitrosyl chloride was estimated to be only 25% complete after 1 h at −10 °C.

Titanium Tetra-*tert*-butoxide. *tert*-Butyl nitrite (10.3 g, 0.100 mol) was added to 2.75 mL of titanium tetrachloride (4.75 g, 0.025 mol) in 30 mL of carbon tetrachloride at room temperature over a 15-min period. After addition was complete, nitrosyl chloride and carbon tetrachloride were removed under reduced pressure and the resulting solution was vacuum distilled through a 12.5-cm Vigreux column. The fraction boiling at 74 °C (0.50 Torr) was collected, and this colorless transparent liquid was identified as titanium tetra-*tert*-butoxide by comparison of its physical and spectral properties with those reported in the literature[18,33] (4.63 g, 55% yield).

In separate experiments titanium *tert*-butoxide and titanium isopentoxide were identified from reactions between the corresponding alkyl nitries and titanium tetrachloride and tetrabromide in dimethylformamide by ^{1}H NMR spectroscopy. The shift in the -CH_2O- proton absorption from δ 4.28 (CH_2ONO) to 4.75 was immediate following addition of isopentyl nitrite to the titanium tetrahalide in dimethylformamide at 37 °C.

Diazotization of Primary Aliphatic Amines. General Procedure. Reaction solutions of titanium tetrachloride in dimethylformamide were prepared by three methods: (a) direct addition of the desired weight of the moisture-sensitive liquid reagent to dimethylformamide, (b) use of a separately prepared saturated solution of the yellow $TiCl_4 \cdot 2DMF$ adduct [13b] which by silver nitrate gravimetric titration was determined to be 0.60 ± 0.05 M in titanium tetrachloride at 25 °C, or (c) direct employment of the solid $TiCl_4 \cdot 2DMF$ adduct.[24] Results obtained for diazotination of benzylamine in dimethylformamide were independent of the method of reaction solution preparation. For the preparation of reaction solutions of titanium tetrachloride in solvents other than dimethylformamide, direct addition by syringe was employed. The solid reagents titanium tetrabromide, tantalum pentachloride, molybdenum pentachloride, tungsten hexachloride, aluminum chloride, and ferric chloride were rapidly weighed in the reaction flask prior to addition of dimethylformamide. All glassware was oven dried prior to use with these moisture-sensitive reagents.

To a rapidly stirred solution of the metal halide in 40 mL of the appropriate solvent maintained at 25 °C in a three-necked flask fitted with a reflux condenser, gas outlet tube, and rubber septum was added the appropriate amount of the alkyl nitrite in 5 mL of the reaction solvent. An immediate color change to orange-red was observed. The primary aliphatic amine in 5 mL of the reaction solvent was then added to this reaction solution over a 20-min period. In dimethylformamide a color change from orange-red to yellow was observed during the addition of the amine.[35] Gas evolution was immediate, continued throughout the addition, and was complete within 5 min following complete addition of the amine. Total gas evolution was measured on the closed system by water displacement from a calibrated gas buret. For reactions in dimethylformamide the yield of gaseous products was 220 ± 20 mL (based upon 10.0 mmol of the limiting reagent). After complete gas evolution, the reaction solution was poured into 200 mL of 20% aqueous hydrochloric acid and extracted with two 100-mL portions of ether. The organic layer was washed once with 100 mL of aqueous hydrochloric acid, the resulting ether solution was dried over anhydrous magnesium sulfate, and the ether was removed under reduced pressure. Ether solutions containing volatile products were distilled at atmospheric pressure through a 12.5 cm Vigreux column.

For reactions performed with hydrogen chloride, the dry gaseous acid was bubbled through a gas trap containing mineral oil and into a transparent solution of *tert*-butyl nitrite (10.0 mmol) in 100 mL of dimethylformamide at −10 °C for 5 min at 30 mL/min. A color change from yellow to orange was observed as the solution became saturated with hydrogen chloride. Addition of the amine in 20 mL of dimethylformamide to the reaction solution from an addition funnel produced an initial rise in the reaction temperature to 0 °C that was maintained at that temperature by slow addition of the amine over a 20-min period. The addition of gaseous hydrogen chloride was continued until amine addition was complete. As in the previously described reactions, a color change from orange to yellow was observed during the addition of the amine. After complete addition of the amine, the reaction mixture was allowed to warm up to room temperature and was then subjected to the previously described product isolation procedures.

Product Analyses. Structural assignments for the products produced in diazotization reactions were made following extraction by ^{1}H NMR spectral comparisons and GC retention time and peak enhancement with authentic samples. To ensure accurate determination of the extent of rearrangement in diazotization reactions of 1-amino-2-phenylethane in dimethylformamide, the reaction mixture was fractionally distilled and analyzed by 1H NMR spectroscopy; within detection limits no 1-phenylethyl product was detected. Symmetrical ethers, nitrite esters, nitriles, and geminal dihalides were not observed as reaction products from amine diazotization reactions. Formate esters were identified by NMR and IR spectroscopy following isolation of these products from their reaction solutions by GC separation. The gaseous products from nitrosation of benzylamine in methylene chloride were identified by infrared spectral analysis.

Product yields were determined by GC analyses for the reactions reported in this study. Prior to workup a weighed amount of dibenzyl ether or diphenylmethane was added to the reaction mixture as an internal standard. The average integrated area ratio from at least two GC traces was employed in each yield determination. Absolute yields were calculated with the use of experimentally determined thermal conductivities for each of the alkyl halides, alcohols, formate esters, and aldehydes examined by this method. Thermal conductivity ratios were determined immediately prior to product analyses to ensure accuracy in these calculations. Olefin yields were determined by ^{1}H NMR spectral analyses.

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Registry No.—Benzaldehyde, 100-52-7; benzylamine, 100-46-9; dimethylformamide, 68-12-2; *tert*-butyl nitrite, 540-80-7; benzyl chloride, 100-44-7; benzyl alcohol, 100-51-6; nitrosyl chloride, 2696-92-6; titanium tetrachloride, 7550-45-0; titanium tetra-*tert*-butoxide, 3087-39-6.

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(26) By continuing the flow of hydrogen chloride through the reaction solution during the addition of benzylamine, benzyl chloride was produced with the total exclusion of benzyl alcohol.

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(28) No apparent variation in the percentage yield of formate esters was observed in separate experiments in which 1 equiv of water (relative to amine) was added to the NOCl/DMF reaction solution prior to introduction of the amine.

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(30) Observed percentage yields were within ±2% of the results reported for $TiCl_4$-generated nitrosyl chloride in Table IV. However, significant variation in the relative yields of alcohol product was observed: % RO_2CH/% ROH (temp, C°) = 4.3 (−15), 2.0 (0), 1.4 (25), 1.0 (50).

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Azoloquinoxaline *N*-Oxides

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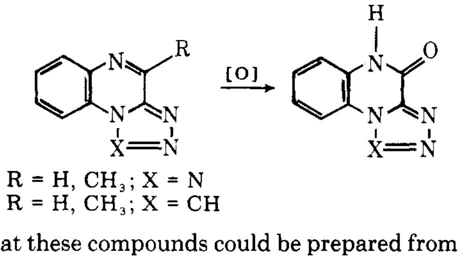
The previously inaccessible *v*-triazolo[1,5-*a*]quinoxaline 5-oxide (**3**), *s*-triazolo[4,3-*c*]quinoxaline 5-oxide (**6**), and tetrazolo[1,5-*a*]quinoxaline 5-oxide (**7**) ring systems have been prepared from *N*-oxide precursors. Previous attempts by others to prepare these compounds by N-oxidation of the appropriate azoloquinoxalines led to C-4 oxidation instead of N-oxidation. This study shows that by introducing the *N*-oxide function at an early stage in the synthetic sequence, the problem of ring carbon oxidation at C-4 is avoided.

Although the chemistry of *s*-triazolo[4,3-*c*]quinoxalines has been extensively studied[1–10] and there is one report[11] concerning the preparation of the *v*-triazolo[1,5-*a*]quinoxaline ring system, the corresponding *N*-oxides in either system have not been prepared. Similarly, tetrazolo[1,5-*a*]quinoxalines are known,[12,13] but the *N*-oxides are not. Attempts by others to prepare these *N*-oxides by oxidation of the known azoloquinoxalines with hydrogen peroxide in acetic acid, alkaline potassium permanganate, or acidic chromic anhydride resulted in oxidation at C-4 instead of N-oxidation (eq 1).[1] We reasoned that these compounds could be prepared from *N*-oxide precursors, thereby avoiding the necessity for N-oxidation at a late stage in the synthesis. Until recently, there were few methods available for the selective synthesis of suitable 3-substituted quinoxaline 1-oxide (**1**) precursors, but it has been demonstrated in these laboratories that certain quinoxaline 1,4-dioxides bearing an electron-withdrawing group in the 2 position can be selectively monodeoxygenated to afford good yields of the desired starting materials.[14] Following this concept, we have developed general procedures for the synthesis of *v*-triazolo[1,5-*a*]quinoxaline 5-oxides (**3**), *s*-triazolo[4,3-*c*]quinoxaline 5-oxides (**6**), and tetrazolo[1,5-*a*]quinoxaline 5-oxides (**7**).



R = H, CH_3; X = N
R = H, CH_3; X = CH

None of the known methods for preparing *v*-triazolopyridine and *v*-triazoloquinoline derivatives[15–17] proved to be satisfactory for the preparation of the corresponding quinoxaline analogues. Eventually, we succeeded in obtaining *v*-triazolo[1,5-*a*]quinoxaline 5-oxides (**3**) by modifying a procedure for preparing α-pyridyldiazomethane *N*-oxides.[18,19] The requisite 3-substituted quinoxaline 1-oxides (**1**) were available from the corresponding quinoxaline 1,4-dioxides by selective monodeoxygenation.[14] Treatment of **1** with *p*-toluenesulfonylhydrazine in methanol gave the tosylhydrazones

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