Silylation as a new strategy of the use of aliphatic nitro compounds in organic synthesis

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Silylation of aliphatic nitro compounds is considered as a versatile multistage process. Due to activation of the β- and γ-carbon atoms of the initial nitro substrates, these reactions give rise to a series of products untypical of the traditional chemistry of nitro compounds. A new redox process proposed in the present study involves controlled incomplete reduction of the nitro group with simultaneous oxidation of the carbon skeleton of the initial aliphatic nitro compound.

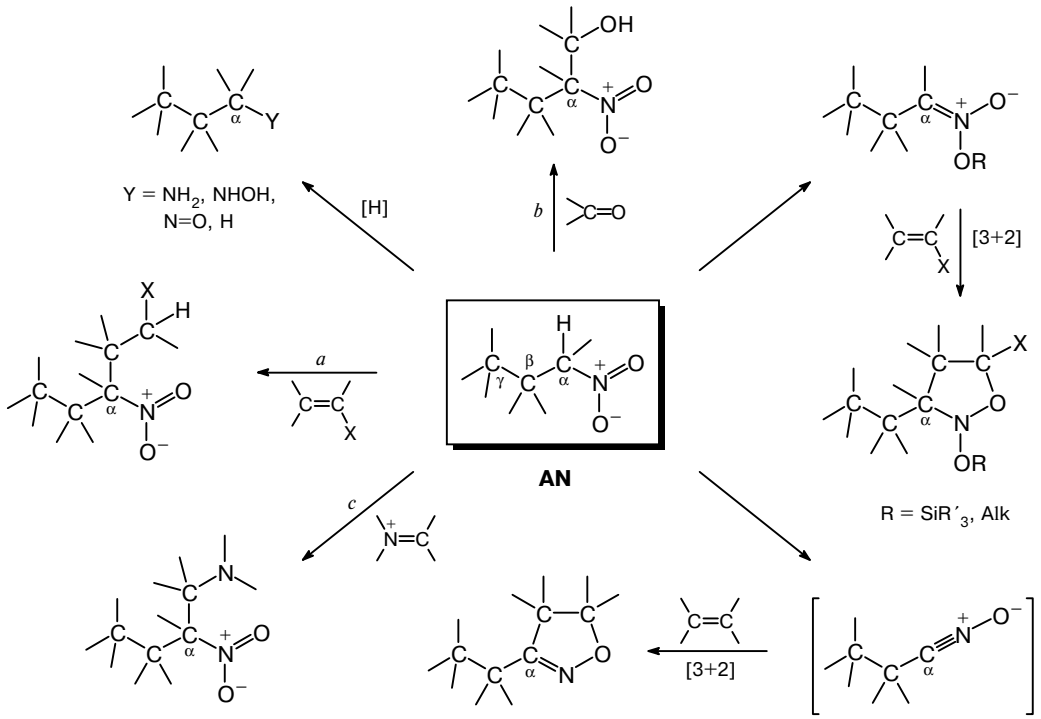
Key words: aliphatic nitro compounds, silylation, organic synthesis, elimination, cyclization, cross-coupling, cycloaddition, silyl nitronates, *N,N*-bis(silyloxy)enamines, conjugated nitrosoalkenes, oximes, ene oximes, ene nitriles.

Introduction

In the present-day organic chemistry, total syntheses of complicated compounds, the development of enantioselective processes, and metal complex catalysis take priority over studies of the chemical properties of the major functional groups. However, in our opinion, the chemistry of aliphatic nitro compounds (AN) remains an exception to this rule.

Due to diversified reactivities, AN attract the continuing interest as promising building blocks in the organic synthesis.[1—5] However, virtually all available synthetic procedures based on nitro compounds are limited to their application as α-nucleophilic

Scheme 1



a, Michael reaction; *b*, Henry reaction; *c*, Mannich reaction.

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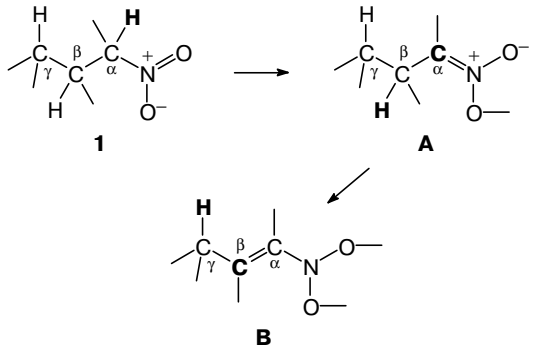
synthons (Scheme 1). Noteworthy also are reduction processes of the nitro group, which allow one to transform AN into amines, hydroxylamines, oximes, nitroso compounds, *etc.*, and radical processes resulting in the replacement of the nitro group by the hydrogen atom.

All the above-mentioned reactions are accompanied by changes exclusively at the C atom bound to the nitro group (the α carbon atom), whereas the β- and γ-carbon atoms of the AN skeleton remain intact. This fact is attributable to the much higher acidity of the protons bound to the α-carbon atom in AN compared to the remaining protons.

At the same time, chemical transformations of C atoms remote from the nitro group should substantially extend the possibilities of the use of AN in the organic synthesis.

In our recent investigations, we focused attention on the solution of this problem. The proposed approach can be stated as follows: the successive activation of the atoms of the carbon skeleton of the nitro substrate through its conversion into the aci derivative **A** followed by the transformation into the corresponding "enamine" **B** (Scheme 2; the "activated" carbon and hydrogen atoms are given in bold type).

Scheme 2



In the first stage of the process, the initial AN loses the α-proton to give the intermediate **A** containing the labile "heteraallyl" β-proton. The aci derivative **A** can eliminate the β-proton to give the corresponding "enamine" **B** in which the γ-hydrogen atom, being allylic, is activated.

This is a prerequisite for cascade processes resulting in a deep modification of the skeleton of the starting AN. The introduction of various electron-withdrawing groups at the β and γ positions of the carbon chain of a nitro compound can additionally activate the corresponding protons thus providing prerequisites for intramolecular interactions between the functional fragments and the reaction centers being generated.

In spite of the apparent simplicity, this approach has not conceptually been discussed in the literature. However, investigation into double metallation[6,7] of AN **1** have demonstrated that this is a fruitful idea (Scheme 3).

In the studies cited, the so-called "superenamines" **B′** were prepared. The latter reacted smoothly with a series of electrophiles to form products of C,C-cross-coupling at the β-carbon atom of the starting AN. Unfortunately, no investigations along this line have been carried out in succeeding years due, apparently, to the problems associated with instability of Li intermediates. Hence, activation of the carbon skeleton of AN remains a topical problem.

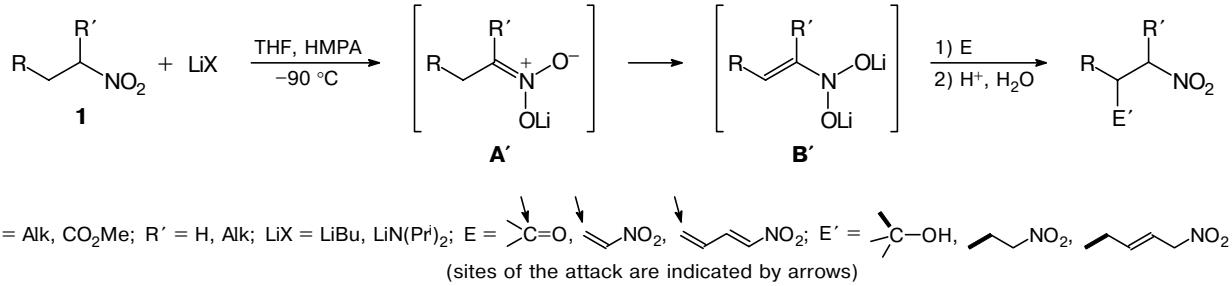
In the present study, we developed a new approach to this problem based on silylation of AN, *i.e.*, on the use of a mixture of R_3SiX/Et_3N (R_3 = Me_3 or Bu^tMe_2; X = Cl, Br, or OSO_2CF_3) for the generation of reaction centers of different types at the carbon atoms of the chain. The simplest aliphatic C_1—C_3 nitro derivatives were used as the key starting compounds. Most of other starting nitro substrates were prepared using conventional procedures applied in the chemistry of nitro compounds.

1. Silylation of aliphatic nitro compounds as a chemical process

Silylation of AN **1** is a very complicated process, which has no close analogy in organic chemistry (Scheme 4).

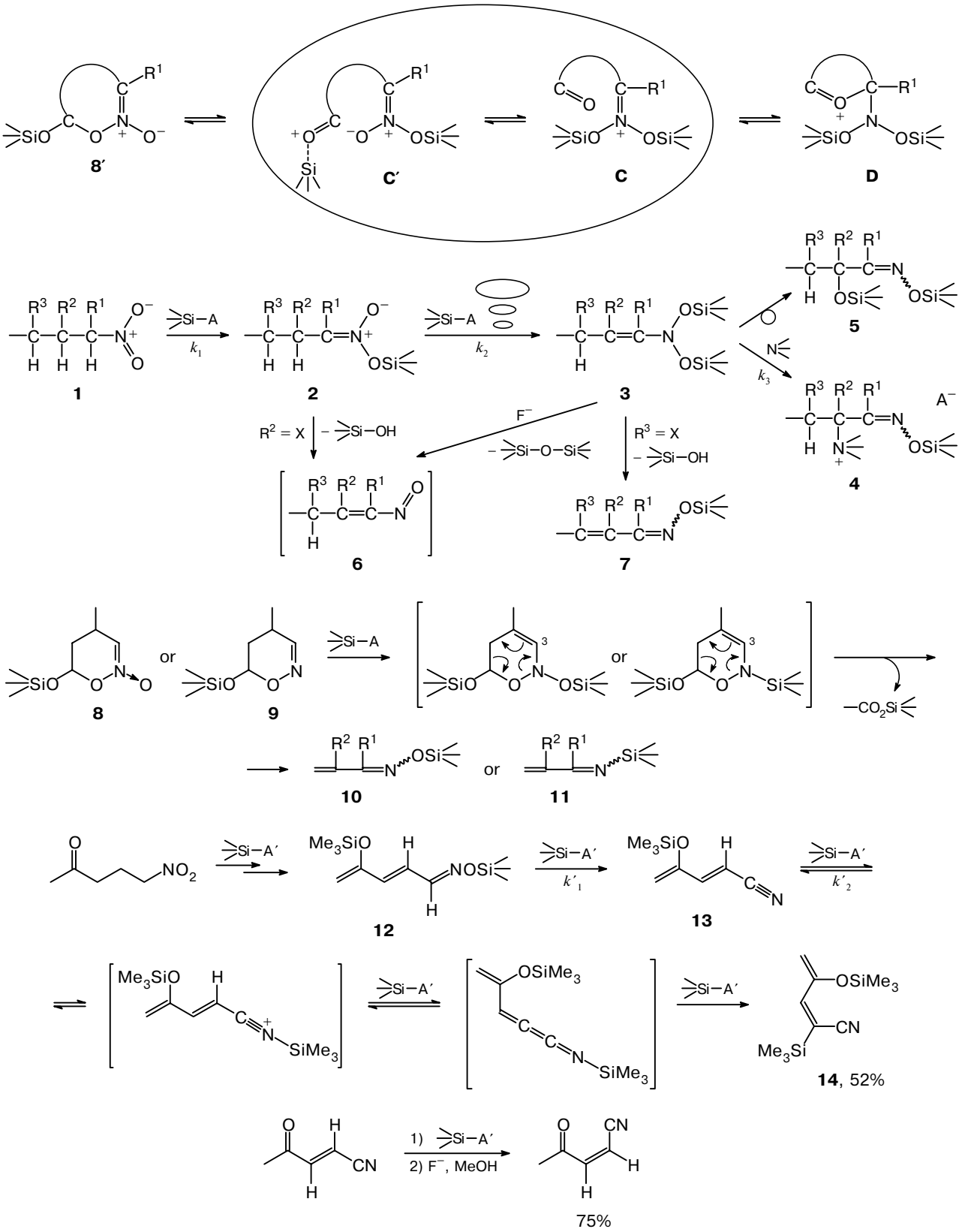
Within the framework of the proposed approach, the reactions presented in Scheme 4 can be divided into several groups, *viz.*, double silylation of AN, elimination, deep or exhaustive silylation of AN, and intramolecular cyclizations.

Scheme 3



(sites of the attack are indicated by arrows)

Scheme 4


8′
C′
C
D
1
2
3
4
5
6
7
8
9
10
11
12
13
14, 52%
75%
Si–A — silylating agent, Si–A′ = Me3SiOTf/Et3N

1.1. Double silylation of aliphatic nitro compounds

This process involves three stages (see Scheme 4, the transformations **1** → **4**), which can afford products of monosilylation of AN, *viz.*, silyl nitronates **2** (the stage with the rate constant k_1), products of double silylation of AN, *viz.*, *N,N*-bis(silyloxy)enamines (BENA) **3** (the constant k_2), or quaternary ammonium salts **4** (the constant k_3), depending on the nature of AN and the reaction conditions. Generally, the conversions **1** → **2** and **2** → **3** proceed chemo-, regio-, and stereoselectively.

Monosilylation of AN is governed by the rate of their deprotonation. The conditions, which make possible the preparation of silyl nitronates **2** in high yields, have been found previously (in our opinion, a procedure with the use of the DBU/Me_3SiCl pair[8] is most efficient).

We succeeded in searching for conditions for the chemoselective synthesis of products of double silylation of AN, *viz.*, BENA **3**, in high yields starting from virtually any AN (Table 1).

In the synthesis of BENA from silyl nitronates (the stage **2** → **3**), the transfer of the silyl fragment to the oxygen atom of silyl nitronate **2** is the governing factor. Hence, double silylation of AN required stronger silylating agents. Trimethylbromosilane made it possible to prepare BENA with the nonfunctionalized C=C bond. However, if BENA contained a functionalized double bond, the use of trimethylbromosilane caused acceleration of the reaction **3** → **4**. Consequently, more powerful trialkylsilyl triflates must be used in the latter case.

For stabilizing BENA, the resulting reaction mixtures must be treated with water. In most cases, we succeeded in isolating individual BENA. After treatment with water, BENA **3** are generally stable in solutions at room temperature, but some of these compounds can be detected only by NMR spectroscopy at below-zero temperatures. Probably, stable BENA cannot be prepared from β,β-dialkyl-susbtituted AN (see Table 1, entry 18).

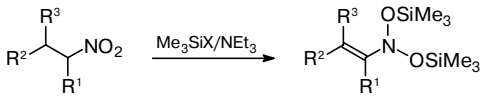
Double silylation is very sensitive to steric factors. In the presence of the methyl group bound to the α-carbon atom in the initial AN (R^1 = Me), the proton is generally eliminated from this group giving rise to terminal BENA **3**. Only the introduction of the electron-withdrawing COOR group at the β-carbon atom made it possible to change the direction of double silylation (see Table 1, *cf.* entries 5 and 15). *N,N*-Bis(silyloxy)enamines containing various trialkylsilyl groups can be synthesized with the use of different silylating agents in the stages **1** → **2** and **2** → **3** (k_1 and k_2, respectively) (see Scheme 4). It should be noted that the mechanisms of the major side reaction, *viz.*, of the rearrangement **3** → **5**, as well as of the transformation **3** → **4** remain unknown.

1.2. Elimination reactions

Due to the presence of acidic protons, intermediates **2** and **3** often enter into various N,C-elimination reactions to give trialkylsilanol molecules.

If aliphatic nitro compounds **1** contain an electron-withdrawing substituent in the β position (R^2 = X),

Table 1. Synthesis of *N,N*-bis(silyloxy)enamines **3** from aliphatic nitro compounds **1**



1 **3**

Run	R^1	R^2	R^3	X	*T*/°C	B.p./°C (*p*/Torr)	Yield (%)	Reference
1	H	H	H	Br	20	39—40 (0.4)	86	9
2	H	Me	H	Br	−30	24—25 (0.2)	80	9
3	Me	H	H	Br	20	29 (0.25)	82	9
4	—$(CH_2)_4$—		H	Br	−30	—	60	9
5	$CH_2CH_2CO_2Me$	H	H	Br	20	—	90	9
6	H	CH_2CO_2Me	H	Br	−30	—	71	9
7	H	$CH(Me)CO_2Me$	H	Br	−30	—	80	9
8	$Pr^iCH(OSiMe_3)$	H	H	Br	20	—	62	9
9	H	CO_2Me	H	OTf	−78	54—58 (0.05)	87	10
10	H	CO_2Me	Me	OTf	−78	60—65 (0.05)	87	10
11	H	$CH_2=C(OSiMe_3)$	H	OTf	−78	75—82 (0.05)	84	10
12	CO_2Me	H	H	OTf	−78	42—52 (0.08)	94	10
13	CO_2Me	Me	H	OTf	−50	43—49 (0.06)	92	10
14	H	$PhC(O)CH_2$	CO_2Me	OTf	−78	—	70	10
15	Me	CO_2Me	H	OTf	−30	52—55 (0.1)	85	10
16	Me	CO_2Et	H[a]	OTf	0	90—95 (0.1)	75	10
17	H	$CH_2=C(OSiMe_3)CH_2$	H[b]	OTf	−30	—	~90	11
18	H	Me	Me[b]	OTf	−30	—	—	—

[a] Me_2SiBu^t instead of Me_3Si.
[b] Identified by NMR spectroscopy (−30 °C).

silanol is spontaneously eliminated from silyl nitronates **2** to yield conjugated β-functionalized nitrosoalkenes **6**. This reaction may be of preparative interest[12] because nitrosoalkenes of this type remain poorly known and reliable procedures for their generation are lacking.[13]

Analogous elimination of silanol can occur in the case of *N,N*-bis(silyloxy)enamines **3** derived from AN **1** containing electron-withdrawing substituents X at the γ-carbon atom (R^3 = X, Scheme 4). The latter reactions afford silyl derivatives of the corresponding β-functionalized conjugated ene oximes **7** [14].*

A fresh example of elimination of silanol under the conditions of silylation of AN **1** is elimination of trimethylsilanol from silylated oximes of conjugated unsaturated aldehydes under the action of Me_3SiOTf/NEt_3 at 0 °C, the reaction proceeding with retention of the configuration of the C=C double bond (see Scheme 4, **12** → **13**).

All types of BENA can be involved in yet another elimination process giving rise to nitrosoalkenes after formal elimination of siloxane under the action of nucleophiles, which can selectively react at the silicon atom, (for example, the fluoride anion)[15] or electrophiles promoting heterolytic cleavage of the N—O bond[19] and, apparently, at high temperature.[20]

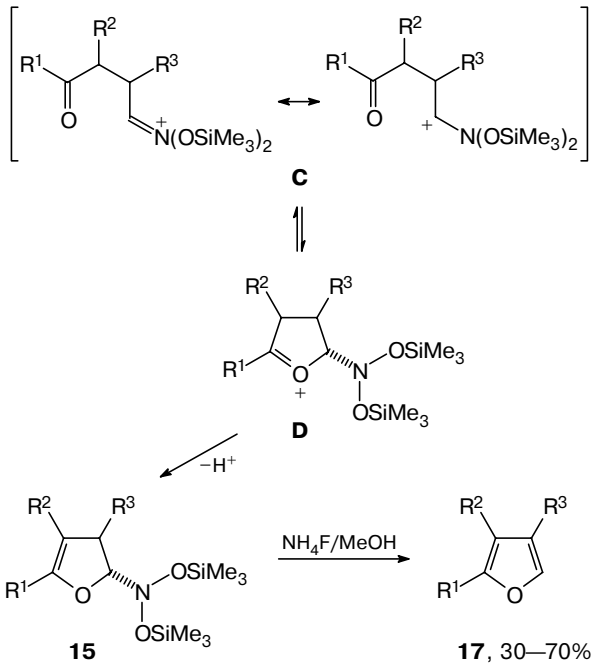
1.3. Deep silylation of aliphatic nitro compounds

Recently, we have also found the so-called "deep" silylation of AN **1** (see Scheme 4, the conversion **12** → **13** → **14**). The latter process was studied by NMR monitoring under the action of a large excess of a Me_3SiOTf/NEt_3 mixture on 5-nitropentan-2-one.[11] It appeared that this reaction proceeded successively *via* oxime **12** and the *trans* isomer of nitrile **13** to form finally the *E* isomer of nitrile **14** in 52% yield. It should be noted that the configuration of the C=C bond is changed in the last stage of the process. This gives promise that deep silylation might be used as a convenient procedure for the *trans-cis* isomerization of α,β-unsaturated nitriles.[11] This process remains to be developed; however, there is a good probablity that the reaction will have a general character and milder conditions would be expected to achieve.

1.4. Intramolecular cyclization

Let us consider the stage **2** → **3** in more detail (see Scheme 4). It can be assumed that this stage proceeds with the participation of stabilized carboimmonium intermediates **C**, which occur in equilibrium with silyl nitronates **C′**, as kinetically independent species. Intermediates **C** can act as α-C-electrophiles in intramolecular cyclization with nucleophilic fragments that are present in the starting AN **1** to give cyclic cations **D**. The cationic intermediates **C** or **D** are stabilized with elimination of an electrophilic species to give cyclic products containing the previously unknown fragment, *viz.*, the bis-trialkylsilyloxyamino group, bound to the sp^3-hybridized carbon atom (Schemes 5 and 6).

Scheme 5



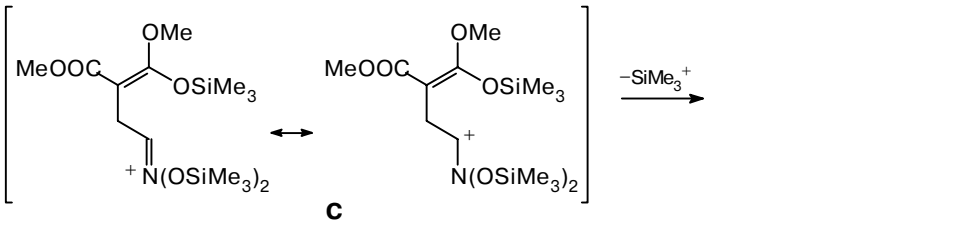
R^1	R^2	R^3	Yield of **15** (%)
Ph	H	Ph	88
Ph	H	4-ClC_6H_4	86
Ph	H	4-$MeOC_6H_4$	89
Ph	H	4-$NO_2C_6H_4$	72
cyclo-Pr	H	4-$MeOC_6H_4$	67
Pr^i	H	4-$MeOC_6H_4$	—
4-$MeOC_6H_4$	H	4-$MeOC_6H_4$	87
4-$NO_2C_6H_4$	H	4-$MeOC_6H_4$	—
Me	MeCO	Ph	78
Ph	Ph	Ph	50
Ph	H	Ph	95

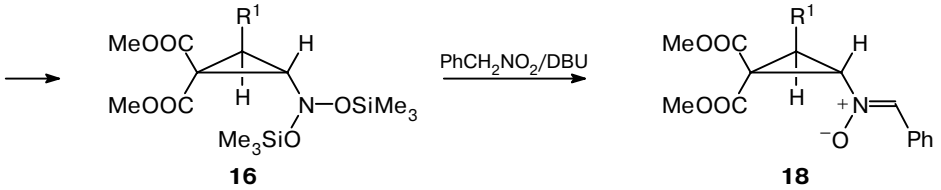
This procedure was used for the synthesis of substituted dihydrofurans **15** to generate a new C—O bond (proton abstraction after cyclization of the cation **C**)[21,22] and for the synthesis of cyclopropanes **16** to form a new C—C bond (elimination of the trimethylsilyl group after cyclization of the cation **C**).[21—23]

Both reactions are completely stereoselective and made it possible to obtain a series of reaction products containing the nitrogen atom characterized by a high inversion barrier of the lone electron pair.

* Noteworthy are two reactions of elimination of the silyl fragments from silyl nitronates, which we have described previously. These are 1,2-C,N-elimination of the Me_3SiOX fragment, where X = NO_2 [16] or H,[17] and 1,4-O,C-elimination of the Me_3SiX fragment (X = OAc or Br).[18] These reactions are not directly associated with a new strategy of the use of AN in the organic synthesis, although the latter so-called δ-elimination can be used for very gentle generation of conjugated nitroalkenes (primarily, of nitroethylene) *in situ* under the conditions of silylation.

Scheme 6



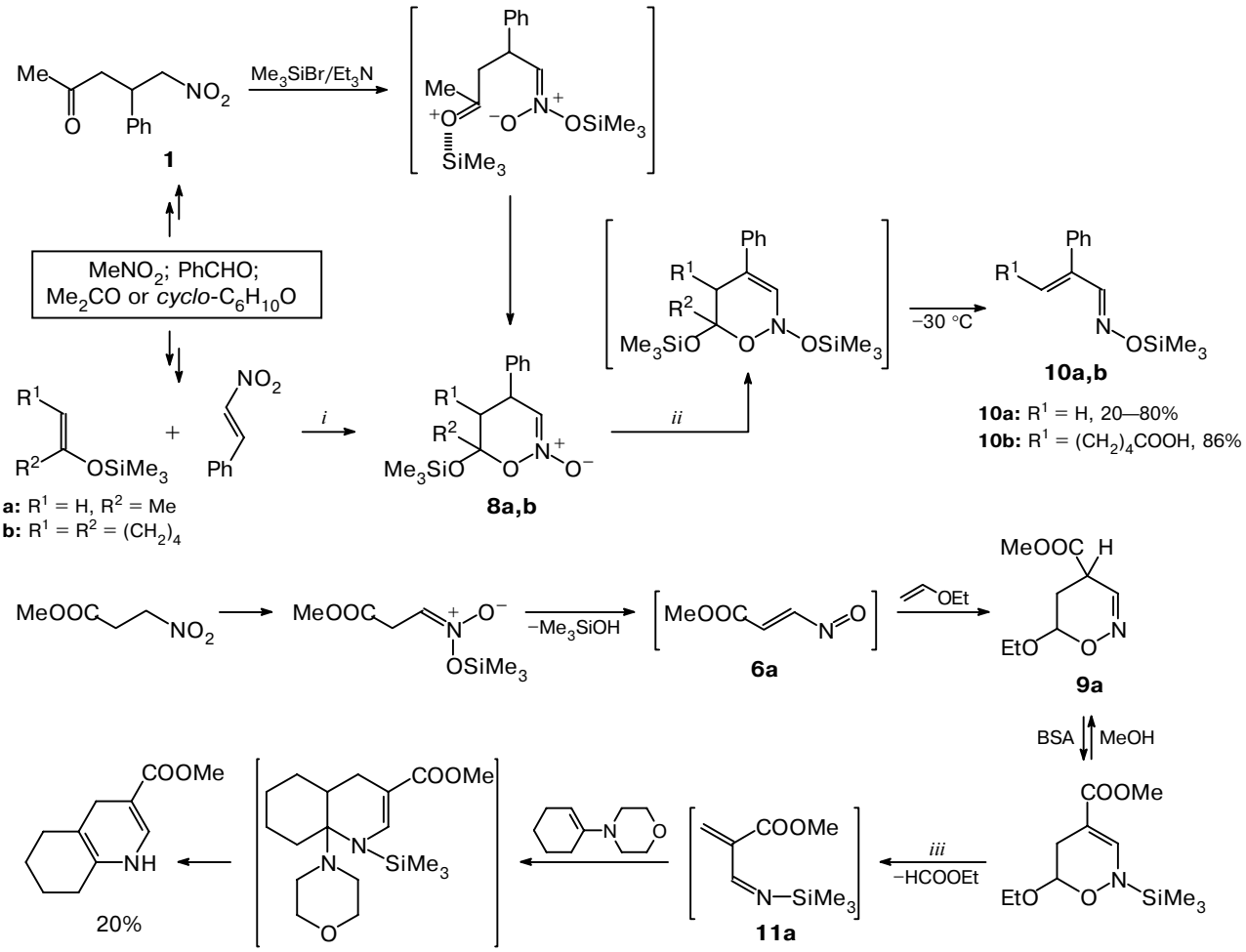


R^1	Yield of **16** (%)	R^1	Yield of **16** (%)
Ph	97	3-$NO_2C_6H_4$	90
4-MeC_6H_4	96	3-$MeOC_6H_4$	90
4-$MeOC_6H_4$	85	2-$MeOC_6H_4$	90
4-ClC_6H_4	80	Me	70
4-$NO_2C_6H_4$	95		

18

R^1 = Ph, 67%
R^1 = 4-$NO_2C_6H_4$, 44%

Scheme 7



Reagents and conditions: *i*. Lewis acid; *ii*. 1) Me_3SiX/Et_3N (X = Br or OTf), 2) $MeOH/F^-$; *iii*. 80 °C, 2 h.

The chemistry of cyclic substrates **15** and **16** remains to be developed. It should be noted that a new procedure was devised for the synthesis of 2,4-disubstituted furans **17** based on dihydrofurans **15**.[22] Cyclopropanes **16** are chemical equivalents of the corresponding nitrosocyclopropanes as evidenced by their reactions with the anion of phenylnitromethane according to a known scheme[24] to form nitrones **18**.[23]

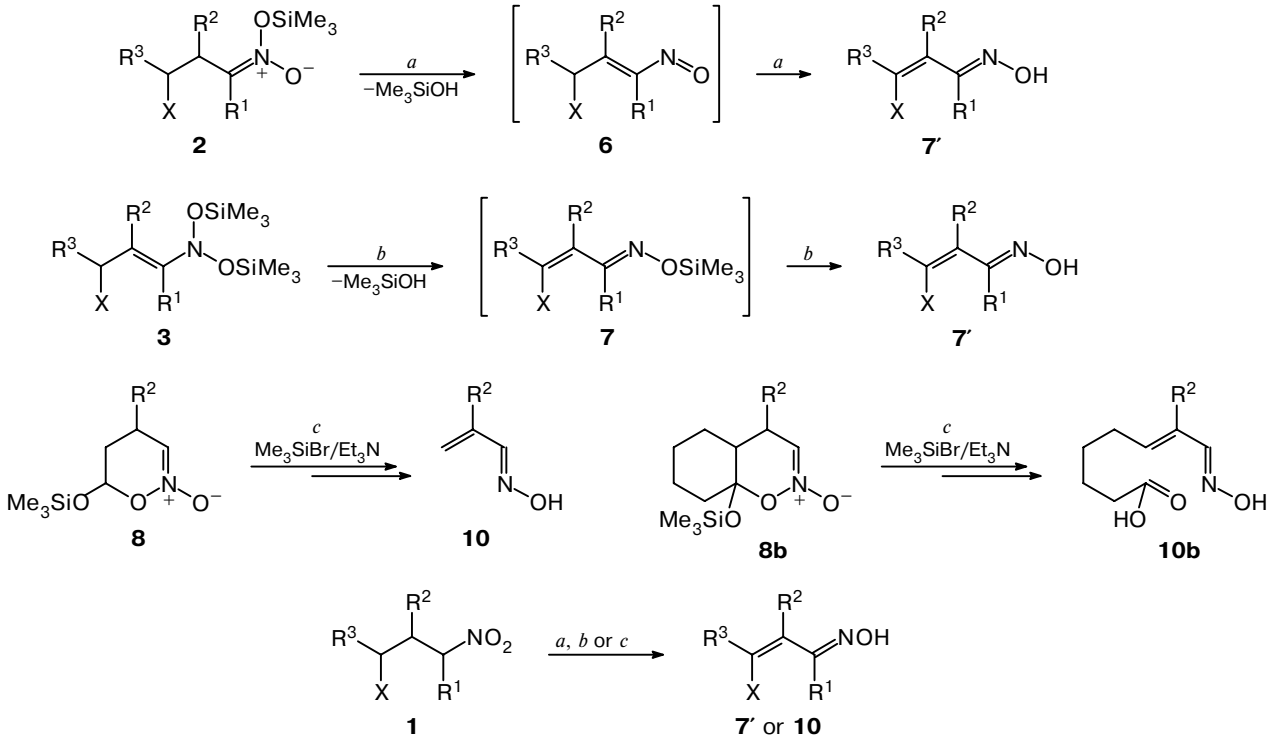
In the cyclizations **C′** → **8′** found recently (see Scheme 4), silyl nitronates **C′** apparently act as O-nucleophiles with respect to the carbon atom of the carbonyl group in the initial functionalized AN.[25] The subsequent migration of the trialkylsilyl group afforded cyclic nitronates **8** as intermediates (Schemes 4 and 7).

Nitronates of type **8** can be prepared in another way by the known [4+2]-cycloaddition reaction of silylenolates with α-nitroolefins in the presence of Me_3SiOTf (Scheme 7).[25]

Dihydrooxazine **9a** was prepared from intermediate **6a** generated after silylation of β-nitropropionate and elimination of trimethylsilanol.[12] β-Nitrosoacrylate **6a** was trapped by ethyl vinyl ether in the [4+2]-cycloaddition reaction (see Scheme 7).

Silylation of dihydrooxazines 8 and 9 is another very interesting aspect of the general process of AN silylation. This sequence involving the shift of the double bond followed by fragmentation of the oxazine ring affords either ene oximes **1** or unstable ene imines **11** (see Scheme 4; for more details, see Scheme 7).[13,25] The rate of fragmentation of oxazine derivatives is determined primarily by the environment about the nitrogen atom in the oxazine ring. The formation of ene oximes **10** is of most interest because it proceeds under mild conditions and allows the construction of various carboxylic acids containing the conjugated ene oxime fragment from very simple substrates. This is exemplified by silylation of bicyclic nitronate **8b** (Scheme 8).

Scheme 8



R^1	R^2	R^3	X	Path	Yield of **7′** or **10** (%)	R^1	R^2	R^3	X	Path	Yield of **7′** or **10** (%)
H	H	H	COOMe	*b*	75	CH_2CH_2COOMe	H	H	COOMe	*b*	92
H	H	H	CN	*b*	65	COOMe	H	H	CN	*b*	63
H	H	H	Ac	*b*	53	COOMe	H	H	COOMe	*b*	82
H	H	H	NO_2	*a*	78	Me	COOMe	H	COOMe	*a*	90
H	H	Me	COOEt	*b*	78	Ph	COOMe	H	COOMe	*a*	98
H	H	COOMe	COOMe	*b*	64	COOMe	COOMe	H	COOMe	*a*	73
H	Me	H	COOEt	*b*	54	H	COOMe	H	CN	*a*	71
H	Ph	H	COOMe	*b*	56	Me	COOMe	H	CN	*a*	90
H	COOMe	H	COOMe	*a*	82	H	Ph	H	H	*c*	53, 75*
H	COOMe	H	C(O)Ph	*a*	88	H	Ph	$(CH_2)_4COOH$	H	*c*	70*

* The yield upon silylation of N-oxides **8**.

Hence, AN **1** can be considered as a new convenient source of oximes **7** or **10** and nitrosoalkenes **6**. Three major procedures for the preparation of ene oximes starting from AN **1** are shown in Scheme 8.[13,25] The synthesis of ene oximes **7** and **10** is of interest from the preparative standpoint because ene oximes have attracted growing interest in recent years as starting compounds in the synthesis of potent biologically active molecules.[26—28]

The transformations of nitrosoalkenes **6**, which are generated by silylation of AN, studied by us are shown in Scheme 9. The direction of their chemical transformations depends on the structure and conditions of the generation of intermediates **6**.

Nitrosoalkenes **6**, which bear an electron-withdrawing substituent X at the β-carbon atom and are generated through 1,3-N,C-elimination of Me_3SiOH from β-functionalized silyl nitronates **2**, act as N-electrophiles with respect to their precursors and are stereoselectively converted into the corresponding divinylhydroxylamines **19**. Other nitrosoalkenes **6** devoid of the substituent X act as C-electrophiles in reactions with carbanions to give oximes **20** (these reactions are described in greater detail in Section 2). In some reactions involving nitrosoalkenes **6**, we observed the 1,5-C,O-shift of the proton accompanied by the rearrangement into the corresponding ene oximes **7**.

In cycloaddition reactions, only the behavior of nitrosoalkene **6a** (X = COOMe; R = H) was examined. Depending on the trapping agent used in the reaction, nitrosoalkene **6a** acts as either heterodiene (with respect to vinyl ethers) or heterodienophile (with respect to cyclic dienes) (see Scheme 9).[13,29] The reactions with dienes proceeded stereospecifically, the reaction with cyclopentadiene being noticeably reversible.[29] Hence, cycloadduct **21a** (n = 1) can be used as a crystalline "reservoir" of unstable nitrosoalkene **6a**.

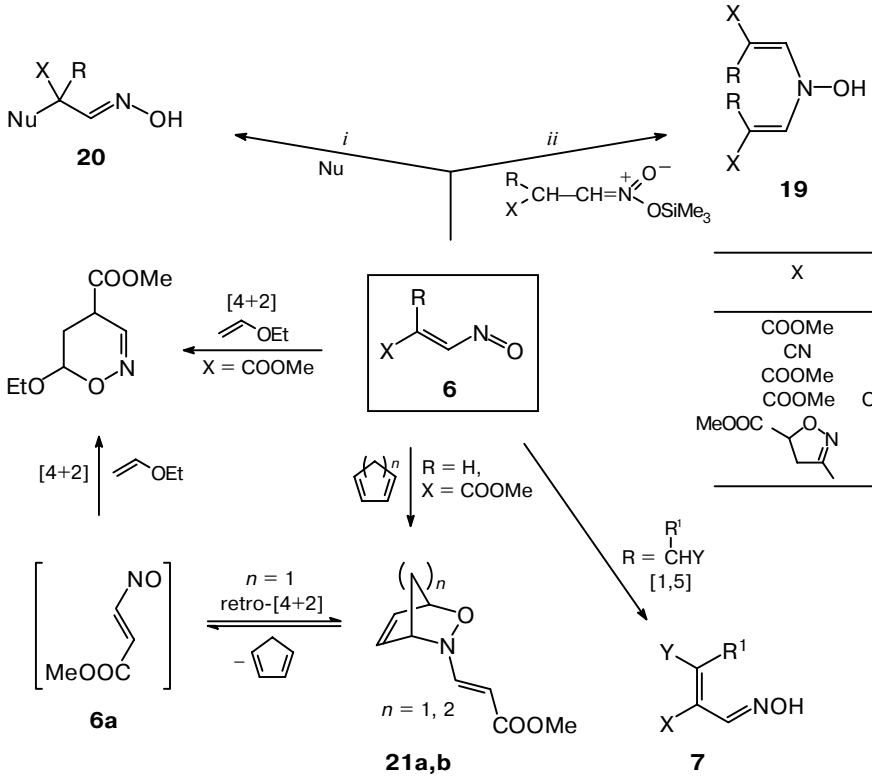
To summarize, it can be concluded that silylation of AN is not limited to the insertion of the protective group into the molecule of the initial substrate or to the modification of the already known reactions of nitro substrates. Actually, controlled incomplete reduction of the nitro group takes place with simultaneous oxidation of the carbon skeleton of AN, the process being promoted by a silylating agent.

2. Chemistry of *N,N*-bis(silyloxy)enamines

Since BENA **3** are readily accessible compounds and possess diversified reactivities, they can be considered as chemical reagents, which have promise comparable with that of the well-studied silyl nitronates **2**.

N,N-Bis(silyloxy)enamines act as "chemical chameleons". Depending on the second participant of the

Scheme 9

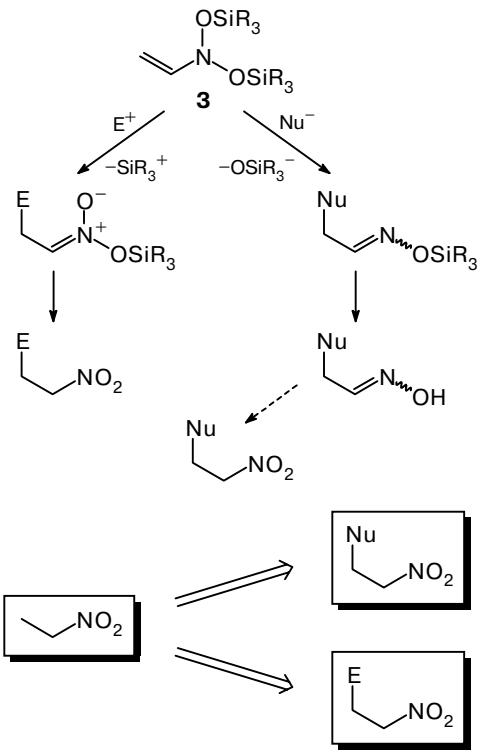


X	R	Yield of **19** (%)
COOMe	H	32
CN	H	29
COOMe	Me	47
COOMe	CH(Me)COOMe	72
	H	56

i. Nitrosoalkenes **6** act as N-electrophiles. *ii*. Nitrosoalkenes **6** act as C-electrophiles.

reaction, they can serve as either formal β-C-electrophiles or β-C-nucleophiles (Scheme 10).

Scheme 10



This allows one to modify the β-carbon atom of the initial AN **1** by various C,C- and N,C-cross-coupling reactions involving BENA.

In reactions with nucleophiles, conjugated nitrosoalkenes **6** serve, apparently, as actual active intermediates. For some reactions, this fact was proved.[15] Under the reaction conditions, the rearrangement of BENA into oximes **5** competed with the desired conversion (see Scheme 4). However, in most cases, this side process was reduced to minimum.[15]

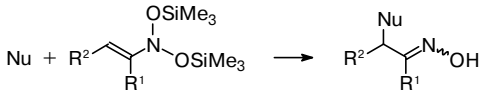
In the C,C-cross-coupling with BENA, carbanions[15] stabilized by nitro groups and other groups, the cyanide anion (Table 2), and silyl nitronates **2** [30,31] were also utilised as C-nucleophiles.*

In the N,C-cross-coupling with BENA, primary and secondary amines,[20,32] N-nitroamines,[19] derivatives of amino acids,[33] various azoles,[34] and the azide anion[33] were used as N-nucleophiles (Table 3).

In the C,C-cross-coupling with BENA, α-alkoxy-[35] or diarylmethyl cations[36] can be utilized as stabilized carbocations (Scheme 11).

* The C,C- or N,C-cross-coupling reactions of ambident nucleophiles with BENA are complicated because of their versatile reactivities (for more details, see Refs. 15 and 19).

Table 2. Reactions of *N,N*-bis(silyloxy)enamines with C-nucleophiles



Nu^-	R^1	R^2	Yield (%)	Procedure[a]
$CH_2NO_2^-$	Me	H	90	A
	$(CH_2)_2CO_2Me$	H	60	A
$EtCHNO_2^-$	Me	H	78	A
	$(CH_2)_2CO_2Me$	H	79	A[b]
$MeO_2CCHNO_2^-$	Me	H	64	A
	$(CH_2)_2CO_2Me$	H	78	A
$MeO_2CCH_2CHNO_2^-$	Me	H	94	A
	H	H	88	A
	$(CH_2)_2CO_2Me$	H	84	A[b]
$MeO_2C(CH_2)_2CHNO_2^-$	H	H	79	A
	Me	H	90	A
$Me_2CNO_2^-$	Me	H	72	B
	$(CH_2)_2CO_2Me$	H	50	B
$MeO_2C(CH_2)_2C(Me)NO_2^-$	H	H	62	B
	Me	H	71	B
	$(CH_2)_2CO_2Me$	H	70	B
α-Nitrocyclohexyl anion	H	H	47	B
	Me	H	54	B
$(MeO_2C)_2CH^-$	H	H	44	A
	H	H	55	B
	Me	H	81	A
	Me	H	77	B
	$(CH_2)_2CO_2Me$	H	70	A
	H	Me	59	A
	$-(CH_2)_4-$		47	A
$EtO_2CCH(COPh)^-$	H	Me	38	A
CN^-	Me	H	70[c]	[d]

[a] A: CH_2Cl_2, −78 °C, Bu_4NF; B: DBU, ether, 0 °C.
[b] −100 °C.
[c] The yield is given with respect to 5-amino-3-methyloxazole.
[d] Me_3SiCN was used without a solvent at 20 °C.

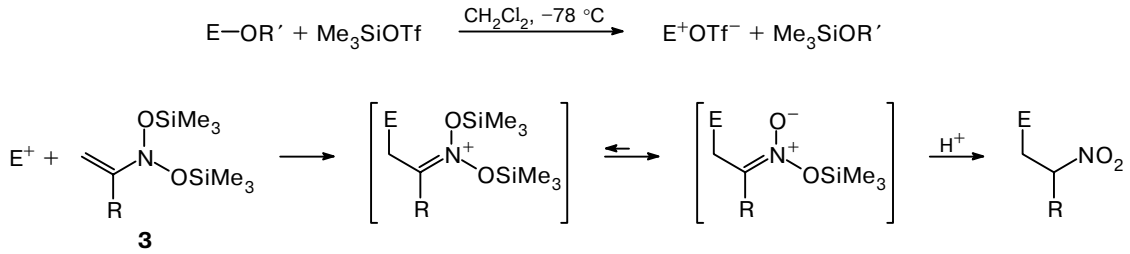
The scope of the reactions presented in Tables 2 and 3 and in Scheme 11 is not yet entirely known; in some cases, optimum conditions were not found. This is particularly true for the reactions of BENA with electrophiles, which are complex multistage processes. The nucleophilicity of the β-carbon atom in BENA, which was determined by kinetic methods, is nine orders of magnitude lower than those of standard *N,N*-dialkylenamines.[36]

In the reactions of BENA with C-electrophiles, one-pot functionalization of both methyl groups in 2-nitropropane can be carried out (Scheme 12).[35] Although the optimum reaction conditions remain to be found, this reaction would be expected to find wide use in syntheses based on AN taking into account that 2-nitropropane is a readily accessible compound.

Table 3. Reactions of *N,N*-bis(silyloxy)enamines with N-nucleophiles

Nucleophile	BENA	Product	Yield (%)
$Me—N(NO_2)SiMe_3$	$CH_2=C(Me)N(OSiMe_3)_2$	$MeN(NO_2)CH_2C(Me)=NOSiMe_3$	71
$Et—N(NO_2)SiMe_3$	$CH_2=C(Me)N(OSiMe_3)_2$	$EtN(NO_2)CH_2C(Me)=NOSiMe_3$	90
Piperidine	$MeCH=CHN(OSiMe_3)_2$	$C_5H_{10}N—CH(Me)CH=NOH$	90
N-Me-Piperazyl	$CH_2=C(Me)N(OSiMe_3)_2$	*N*-Me-Piperazine-$CH_2C(Me)=NOH$	65
n-$C_6H_{13}NH_2$ (excess)	$CH_2=C(Me)N(OSiMe_3)_2$	*n*-$C_6H_{13}NHCH_2C(Me)=NOH$	85
n-$C_6H_{13}NH_2$	$CH_2=C(Me)N(OSiMe_3)_2$	*n*-$C_6H_{13}NHCH_2C(Me)=NOH$	78
	$MeCH=CHN(OSiMe_3)_2$	*n*-$C_6H_{13}NHC(Me)=NOH$	57
	$CH_2=C(Me)N(OSiMe_3)_2$ and $MeCH=CHN(OSiMe_3)_2$	*n*-$C_6H_{13}N[CH_2C(Me)=NOH]CH(Me)CH=NOH$	67
$EtCH(Me)NH_2$	$MeCH=CHN(OSiMe_3)_2$	$EtCH(Me)NHCH(Me)CH=NOH$	~100
$PhCH(Me)NH_2$	$CH_2=C(Me)N(OSiMe_3)_2$	$PhCH(Me)NHCH_2CH=NOH$	76
	$MeCH=CHN(OSiMe_3)_2$	$PhCH(Me)NHCH(Me)CH=NOH$	~100
N-Me_3Si-Pyrazole	$CH_2=C(Me)N(OSiMe_3)_2$	Pyr-$CH_2C(Me)=NOSiMe_3$	95
	$MeCH=CHN(OSiMe_3)_2$	Pyr-$CH(Me)CH=NOSiMe_3$	78
	$CH_2=C[(CH_2)_2CO_2Me]—N(OSiMe_3)_2$	Pyr-$CH_2C[(CH_2)_2CO_2Me]=NOSiMe_3$	75
	$CH_2=C(CO_2Et)N(OSiMe_3)_2$	Pyr-$CH_2C(CO_2Et)=NOSiMe_3$	88
N-Me_3Si-Imidazole	$CH_2=C(Me)N(OSiMe_3)_2$	Im-$CH_2C(Me)=NOSiMe_3$	88
	$MeCH=CHN(OSiMe_3)_2$	Im-$CH(Me)CH=NOSiMe_3$	97
N-Me_3Si-1,2,4-Triazole	$CH_2=C(Me)N(OSiMe_3)_2$	1,2,4-Triazolyl-$CH_2C(Me)=NOSiMe_3$ (a 1 : 6 mixture of regioisomers)	~100
	$MeCH=CHN(OSiMe_3)_2$	1,2,4-Triazolyl-$CH(Me)CH=NOSiMe_3$ (a 1 : 3 mixture of regioisomers)	95
N-Me_3Si-1,2,3-Triazole	$CH_2=C(Me)N(OSiMe_3)_2$	1,2,3-Triazolyl-$CH_2C(Me)=NOSiMe_3$ (a 1 : 2 mixture of regioisomers)	97
	$MeCH=CHN(OSiMe_3)_2$	1,2,3-Triazolyl-$CH(Me)CH=NOSiMe_3$ (a 1.0 : 1.5 mixture of regioisomers)	95
N-Me_3Si-Benzotriazole	$CH_2=C(Me)N(OSiMe_3)_2$	Benzotriazolyl-*N*-$CH_2C(Me)=NOSiMe_3$ (a 1 : 4 mixture of regioisomers)	85
	$MeCH=CHN(OSiMe_3)_2$	Benzotriazolyl-*N*-$CH(Me)CH=NOSiMe_3$ (a 1 : 3 mixture of regioisomers)	92
3-(Me_3Si-Amino)-*N*-Me_3Si-1,2,4-triazole	$CH_2=C(Me)N(OSiMe_3)_2$	3-Amino-1,2,4-triazolyl-$CH_2C(Me)=NOH$ (a 1 : 3 mixture of regioisomers)	40
$EtO_2CCH_2NH_2$	$CH_2=C(Me)N(OSiMe_3)_2$	$EtO_2CCH_2N[CH_2C(Me)=NOH]_2$	82
	$MeCH=CHN(OSiMe_3)_2$	$EtO_2CCH_2NHCH(Me)CH=NOH$	81
$Me_3Si—N_3$	$CH_2=C(Me)N(OSiMe_3)_2$	$N_3—CH_2C(Me)=NOSiMe_3$	79

Scheme 11

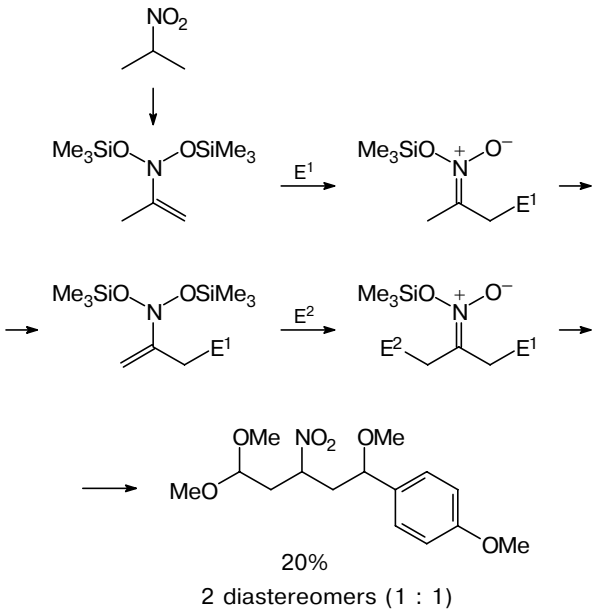


E—OR′	R	Yield (%)	E—OR′	R	Yield (%)
Ph-$CH(OMe)_2$	Me	77	$CH(OMe)_3$	Me	70
p-$ClC_6H_4CH(OMe)_2$	Me	74	$Me_2C(OMe)_2$	Me	26
p-$MeOC_6H_4CH(OMe)_2$	Me	67	Ph-$CH(OMe)_2$	$(CH_2)_2CO_2Me$	59
(E)-$MeCH=CHCH(OMe)_2$	Me	54	*p*-$ClC_6H_4CH(OMe)_2$	$(CH_2)_2CO_2Me$	56
$EtCH(OMe)_2$	Me	42	(E)-$MeCH=CHCH(OMe)_2$	$(CH_2)_2CO_2Me$	62
$EtCH(OMe)_2$	Me	40*	$CH(OMe)_3$	**	32
(*p*-$MeOC_6H_4)_2CHOSiMe_3$	Me	82	(*p*-$MeOC_6H_4)_2CHOSiMe_3$	$(CH_2)_2CO_2Me$	69

* Me_2Bu^tSi instead of Me_3Si in BENA.

** BENA from $MeO_2CCH(NO_2)Me$, the $(MeO)_2CHCH_2CH(NO_2)CO_2Me$ product.

Scheme 12



2 diastereomers (1 : 1)

E^1 = *p*-$MeOC_6H_4CH(OMe)^+$
E^2 = $(MeO)_2CH^+$

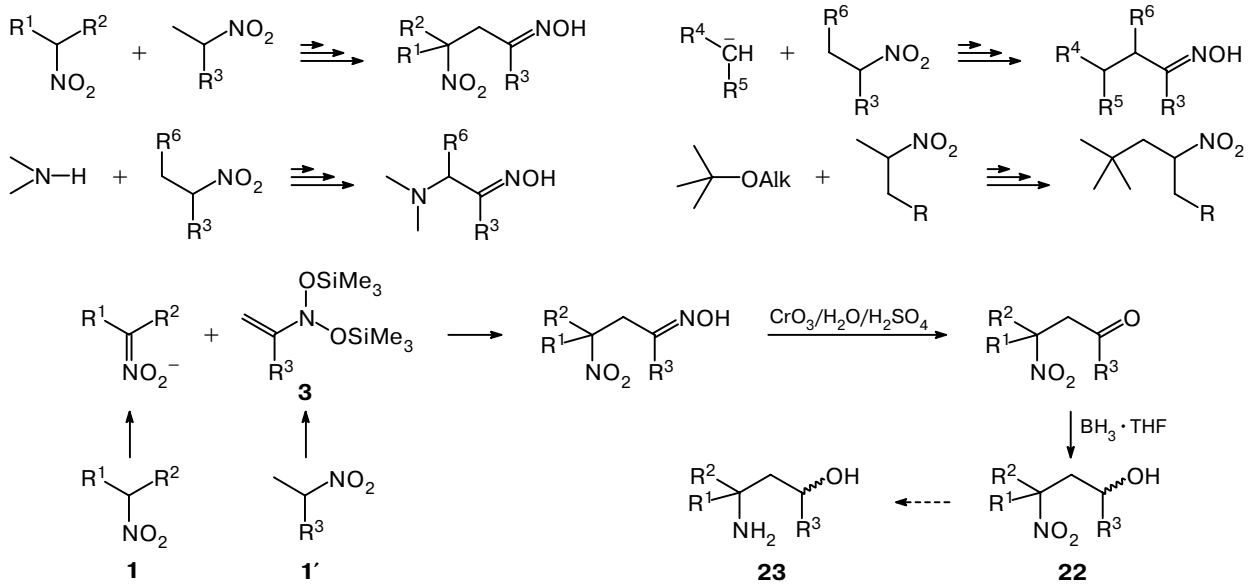
3. Activation of the carbon skeleton in aliphatic nitro compounds and the chemical design

The C,C- or N,C-cross-coupling reactions of BENA from available AN with other reagents can be applied to the synthesis of various functionalized oximes and nitro compounds (Scheme 13).

With a broad assortment of these products in hand, one can design "longer" sequences, which allow the construction of various polyfunctional compounds using simple and readily accessible AN **1**. These investigations are only in their infancy. However, prospects of this approach can be exemplified by the development of a general procedure for the synthesis of poorly studied γ-nitroalcohols **22**,[37] which are direct precursors of potent biologically active γ-aminoalcohols **23**.

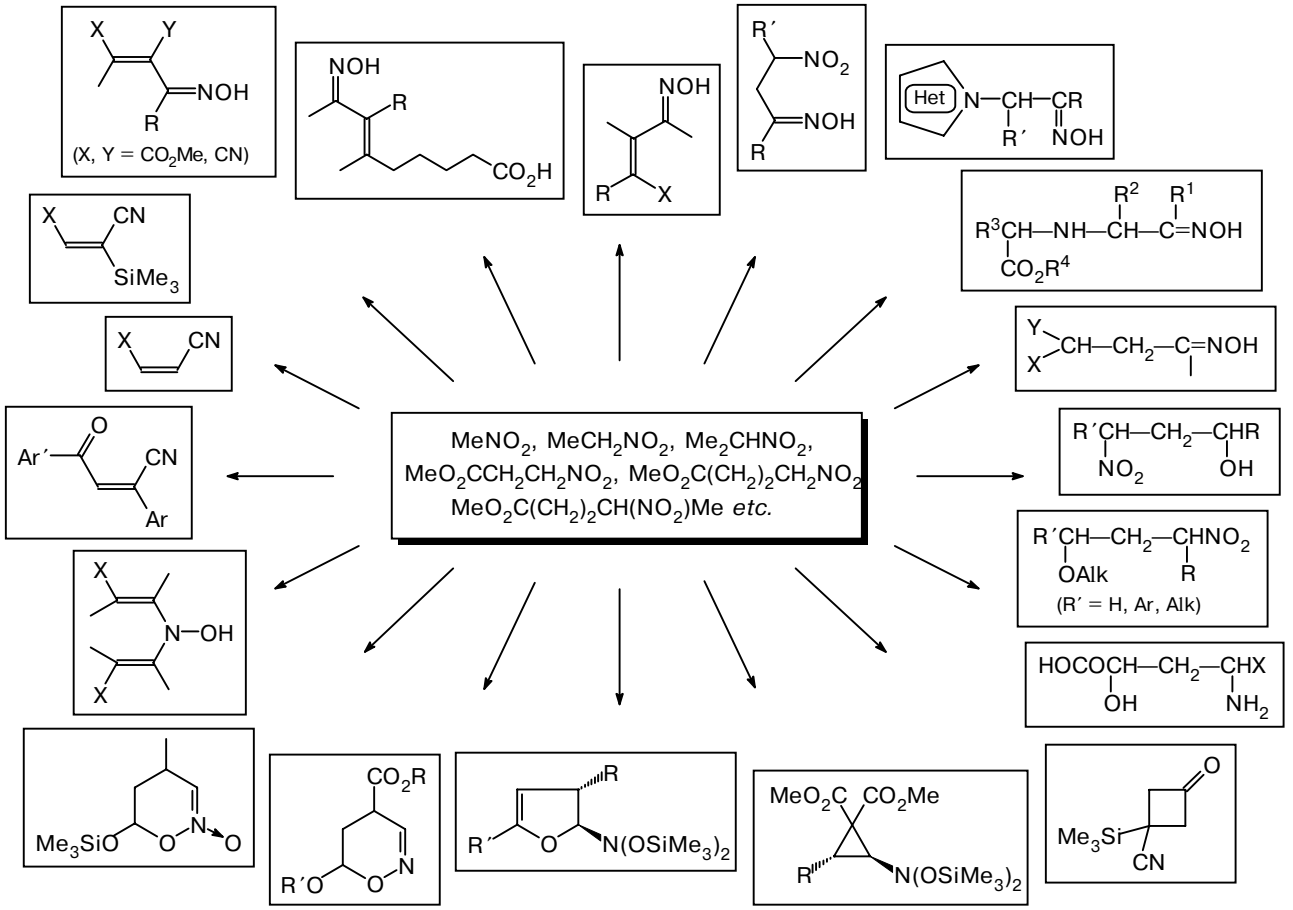
The three-step synthesis of these compounds starting from readily accessible nitro derivatives is shown in Scheme 13. Generally, the overall sequence of the reactions can be carried out without isolation of intermediates. The total yields of γ-nitroalcohols **22** are, as a rule, ~50% with respect to the starting AN. Functionalized alcohols **22** can also be prepared according to this scheme.

Scheme 13



1	**1′**	**22**	Yield (%)
Me_2CHNO_2	Me_2CHNO_2	$Me_2C(NO_2)CH_2CH(OH)Me$	43
$MeCH(NO_2)(CH_2)_2CO_2Me$	Me_2CHNO_2	$MeC[(CH_2)_2CO_2Me]NO_2CH_2CH(OH)Me$	47 (54, $NaBH_3CN$)
$EtCH_2NO_2$	Me_2CHNO_2	$EtCH(NO_2)CH_2CH(OH)Me$	48
$MeO_2C(CH_2)_3NO_2$	Me_2CHNO_2	$MeO_2C(CH_2)_2CHNO_2CH_2CH(OH)Me$	51
cyclo-$C_6H_{11}NO_2$	Me_2CHNO_2	1-NO_2-*cyclo*-C_6H_{10}-$CH_2CH(OH)Me$	45
$MeNO_2$	$MeCH(NO_2)(CH_2)_2CO_2Me$	$NO_2(CH_2)_2CH(OH)(CH_2)_2CO_2Me$	25
	Me_2CHNO_2	$NO_2(CH_2)_2CH(OH)Me$	45
$MeCH(NO_2)(CH_2)_2CO_2Me$	Me_2CHNO_2	$MeC(NO_2)[(CH_2)_3OH]CH_2CH(OH)Me$	48
$MeO_2C(CH_2)_3NO_2$	Me_2CHNO_2	$HO(CH_2)_3CH(NO_2)CH_2CH(OH)Me$	48

Scheme 14



Conclusion

To summarize, various classes of organic derivatives can be prepared starting from a limited number of inexpensive and readily accessible AN with the use of a general silylation process (Scheme 14).

Scheme 14 is not final and calls for further studies aimed at realizing new possibilities of the use of AN in the organic synthesis based on the proposed approach.

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