CHEMISTRY OF N-NITROSOIMINES

Kin-ya Akiba and Naoki Inamoto

Department of Chemistry, Faculty of Science,

The University of Tokyo, Hongo, Tokyo 113, Japan

N-Nitrosoimines of general formula, $R^1R^2C{=}N{-}N{=}O$, are thermally unstable and apt to decompose to the corresponding carbonyl compounds and nitrogen. When the nitrosoimines are contained in heterocycles such as thiazoline, thiadiazoline, pyrrolidine, and etc., they are stable for isolation and show mesoionic character. This article gives a first survey of the chemistry of nitrosoimines.

1. Preparation and Spectral Character
2. Thermal and Photochemical Decomposition
3. Reduction with Lithium Aluminum Hydride
4. Reactions with Grignard Reagents and Organolithiums
5. Miscellaneous Reactions

Introduction N-Nitrosoimines of general formula, 1, are not well known in spite of the expected interesting character

related to diazo oxide (1') and diazoniumimino (azidinium) compounds (2). By inspection of the structure (1), one can expect 1 to be a potent reagent as a 1,4-dipole, a trans-nitrosating reagent, and a starting material for preparation of the diazo compound by deoxygenation.

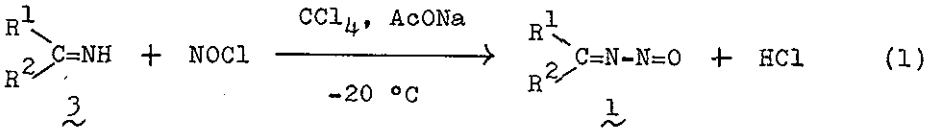
During the course of the investigation on the reaction of alkylidenetriphenylphosphoranes with nitric oxide, we postulated the intermediacy of the nitrosoaldimine and diazoniumaldimine as precursors for the production of the corresponding aldehydes and nitriles.[1] At that time (1966-1968), azidinium salts attached to heterocycles have been prepared and some of their reactions were reported by Balli and Huenig's groups,[2] however, there was no definite description on typical nitrosoimines at all.

1 1' 2 2'

Therefore, we started to prepare this new class of compounds, i.e., nitrosoimines, which turned out to be thermally unstable and apt to decompose to the corresponding carbonyl compounds and nitrogen.

Preparation and Spectral Character Nitrosoimines (1) are generally prepared by nitrosation of the corresponding imines (3) with nitrosyl chloride in dry carbon tetrachloride at low temperature (-10--20 °C) in the presence of sodium

acetate or triethylamine. Yields of isolated products depend mainly on thermal stability of the nitrosoimines.

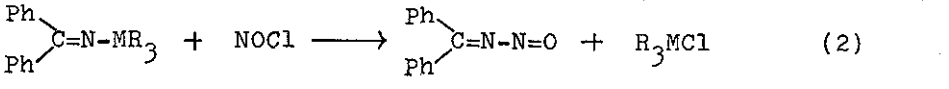


(1)

Sterically hindered nitrosoimines were prepared by this method, but it is usually difficult to obtain analytically pure products: 1) R^1, R^2, mp (°C); 1a) R^1=2-MeC_6H_4, R^2=i-Pr, oil[3]; 1b) R^1=t-Bu, R^2=2-MeC_6H_4, oil[3]; 1c) R^1=R^2=Ph, 50-53[3]; 1d) R^1=R^2=4-ClC_6H_4, 61-63[3]; 1e) R^1=4-MeC_6H_4, R^2=2-MeC_6H_4, 43[3]; 1f) R^1=2-ClC_6H_4, R^2=4-ClC_6H_4, 69-71[3]; 1g) R^1=R^2=2,4,6-$Me_3C_6H_2$, oil[4]; 1h) R^1=R^2=2,6-Me_2-4-$MeOC_6H_2$, oil[4].

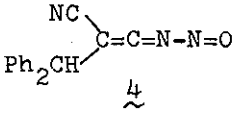
Also, resonance-stabilized nitrosoimines were prepared and their UV spectra were reported, but only 5d was obtained in analytically pure state[5]: 5a) R^1=R^2=Et_2N; 5b) R^1=R^2= ; 5c) R^1=R^2=PhMeN; 5d) R^1=R^2=Ph_2N; 5e) R^1=$PhCH_2S$, R^2=EtPhN.

Group IV organometallic ketimines were cleaved with nitrosyl chloride to give the corresponding nitrosoimines.[6]



(2)

M,R: Si, Ph; Sn, Me; Sn, Ph; Pb, Et

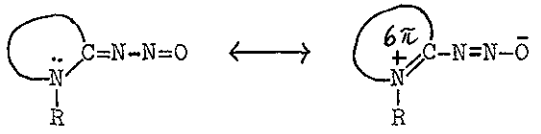


Conjugated nitrosoimine (4) was prepared by this method.[6]

When imines contained in heterocycles are nitrosated, aqueous solution of sodium nitrite is added to the solution of the imines in acetic acid to give thermally stable nitrosoimines.

UV spectra of nitrosoimines and related compounds are shown in Table 1. There are two n-π^* bands for 1d-1f, and they may be assigned as N(C=N) n-π^* and N(N=O) n-π^* bands. When the nitrosoimino group is conjugated with at least one nitrogen atom, those bands are not observed separately. Visible absorptions of 6a[7] and 5b[5] shift toward the shorter wave length (blue shift) by changing solvents from non-polar to polar ones and from aprotic to protic ones and are assigned to n-π^* band, while the most intense absorptions are not affected by the polarity of the solvent and are assigned to π-π^* band.

When the nitrosoimino group is contained in five-membered heterocycles as 6 and 7 in Table 1, the compounds are thermally stable probably due to the large contribution of polar structure as shown below.



To evaluate such charge distribution, core electron binding energies of 3-substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles (6a and 6b) and related compounds were measured by ESCA and the results are shown in Table 2.[10] Observed

Table 1 UV Spectra of Nitrosoimines and Related Compounds

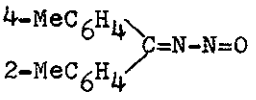
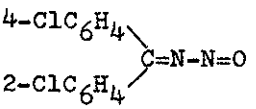
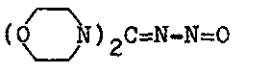
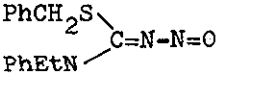
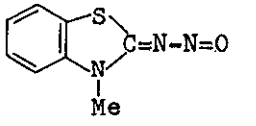
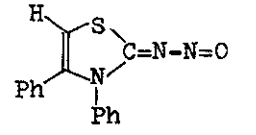
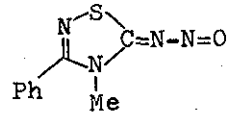
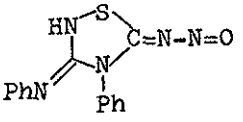
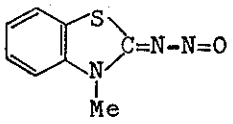
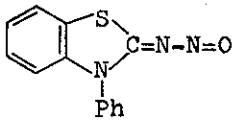
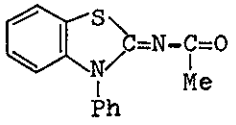
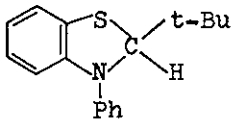
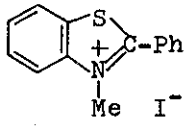
Nitrosoimines and Related Compounds	Solvent	λ_{max} (logϵ or ϵ*) $\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	Ref.
1d $(4\text{-}ClC_6H_4)_2C{=}N{-}N{=}O$	CCl_4	306 (3.943)	522 (2.033) 596 (2.033)	3
1e 	EtOH	312 (3.925)	492 (1.380) 520 (1.518)	3
1f 	EtOH	310 (3.721)	523 (2.079) 585 (2.033)	3
5a $(Et_2N)_2C{=}N{-}N{=}O$	CH_2Cl_2	277	458	5
5b 	CH_2Cl_2	276	473	5
5c $(PhMeN)_2C{=}N{-}N{=}O$	$CHCl_3$	289	488	5
5d $(Ph_2N)_2C{=}N{-}N{=}O$	$CHCl_3$	330 (9,550)*	519 (183)*	5
5f 	CH_2Cl_2	330	504	5
6a 	$CHCl_3$	350 (14,500)*	496 (68)*	7
7a 	MeCN	350 (10,800)*	454 (111)*	7

Table 1 (Continued)

Nitrosoimines and Related Compounds	Solvent	λ_{max} (ϵ) $\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	Ref.
7b 	PhH	317.5 (9,080)	429 (100)	8
7c 	PhH	359 (4,000)	433 (200)	8
Ph-N=N-Ph (trans)	EtOH	320 (21,300)	443 (510)	9
$(Et_2N)_2C=NH$	EtOH	225 (9,500)		5
$Ph_2C=NH$	$CHCl_3$		340 (125)	9
t-Bu-N=O	Et_2O		300 (100) 665 (20)	9
$Me_2N-N=O$	C_5H_{12}	232 (5,900)	361 (125)	9
t-Bu-O-N=O	C_5H_{12}	222 (1,700)	356 (87)	9
$Ph-NO_2$	C_6H_{14}	280 (1,000)	330 (125)	9

Absorptions due to the nitrosoimino group are shown and those due to aryl groups and ring systems are omitted. Compounds without molar extinction coefficients are labile during measurement.

Table 2 Core Electron Binding Energies (eV) of Nitrosoimines and Related Compounds[10]

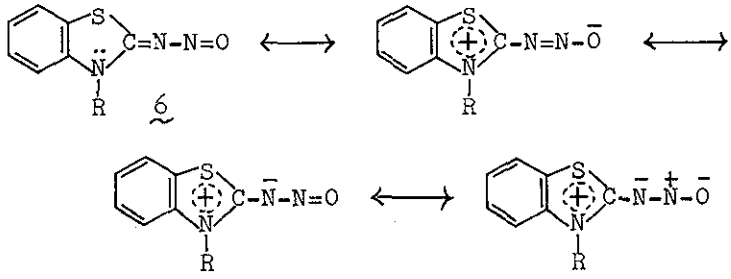
Compounds	N 1s	O 1s	C 1s
6a 	398.9 400.8 (1:2)	531.4	284.4
6b 	398.8 400.8 (1:2)	531.2	284.6
8 	398.6 400.6 (1:1)	531.3	285.3
9 	399.4		284.7
10 	401.7		285.2

The Al-K$\alpha_{1,2}$ line (1486.6 eV) was used for activation and Au-4$f_{7/2}$ line was adjusted to fall at 84.0 eV (accuracy: ± 0.2 eV).

binding energies of 8 show the presence of two kinds of nitrogen atoms: i.e., nitrogen with lower binding energy (398.6 eV) and that with higher binding energy (400.6 eV). The former nitrogen (corresponding to the imino nitrogen) should be negatively charged and the latter (corresponding to the thiazoline nitrogen) should be positively charged, because the neutral nitrogen (9) has the binding energy between both nitrogens as above and the thiazolium nitrogen (10) has higher binding energy than the two.

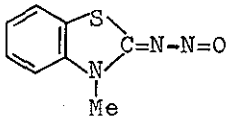
It is therefore concluded for the nitrosoimines (6a and 6b) that the imino nitrogen [398.9 eV (6a) and 398.8 ev (6b)] should be negatively charged and the thiazoline and the nitroso nitrogens [400.8 eV] should be positively charged. The difference of 2.0 eV for the binding energies of two kinds of nitrogens can be estimated to correspond to a charge difference of 0.40 charge unit and the oxygen atom of 6a and 6b is considerably negatively charged (ca 0.2-0.3 charge unit).

This result shows large contribution of polar structures shown below.

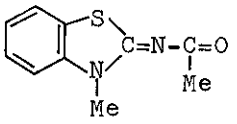


This conclusion is supported by observed proton chemical shifts (NMR: δ from TMS in $CDCl_3$) of 3-methyl group of benzo-

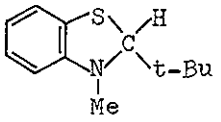
thiazolines as shown below.



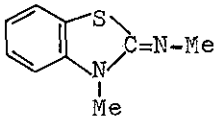
6a 3.90



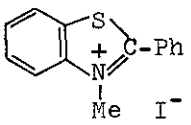
8 3.85



9 2.99



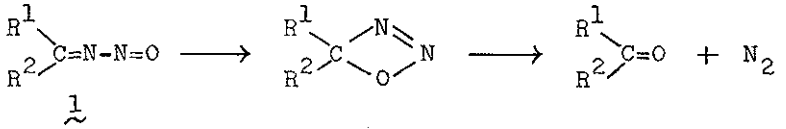
3.41



10 4.30 (in DMSO-d_6)

IR spectra of 1-substituted 2-nitrosoiminopyrrolidines were measured in chloroform and absorption at 1563-1592 cm^{-1} was assigned to $\nu C{=}N$ and that at 1418-1438 cm^{-1} to $\nu N{=}O$.[11] IR spectra of 1d-1f in Table 1 were also recorded without assignment.[3]

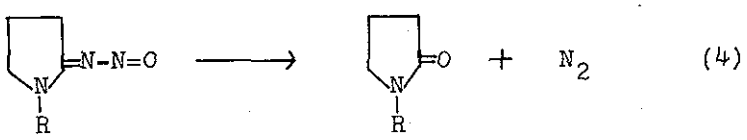
Thermal Decomposition Open-chain nitrosoimines are usually unstable thermally and readily decompose to the corresponding carbonyl compounds and nitrogen under anhydrous conditions. The rate of decomposition follows first-order kinetics as measured by the amount of evolved nitrogen,[3] IR,[11] and UV spectroscopy.[5]



(3)

Steric hindrance around the methylene carbon is primarily important to stabilize the nitrosoimines and electron-donating substituents seem to stabilize the nitrosoimines better than

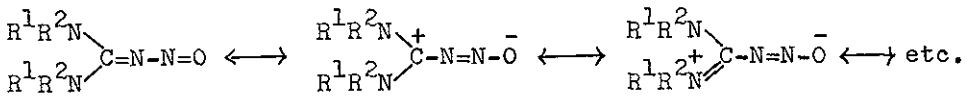
electron-withdrawing ones. Nitrosoimines are much more reluctant for hydrolysis than the parent imines. Rates of decomposition of 1-substituted 2-nitrosoiminopyrrolidines were measured in chloroform by monitoring the decrease of the absorption of nitroso group and the increase of carbonyl group by IR and the following order of stability was obtained,[11] which is consistent to the above statement:



(4)

Order of thermal stability: R; cyclohexyl > 2,6-$Me_2C_6H_3$ > 2,6-$Cl_2C_6H_3$ > 2-$NO_2C_6H_4$ ≈ 2-MeC_6H_4 > 2-ClC_6H_4 > 2-BrC_6H_4 ≈ 3-NO_2-C_6H_4 > Ph ≈ 3,5-$Me_2C_6H_3$ > 3-MeC_6H_4 ≈ 4-MeC_6H_4 > 4-BrC_6H_4 > 3-BrC_6H_4 ≫ 4-$NO_2C_6H_4$

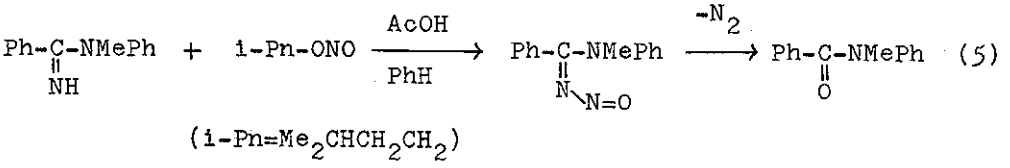
Preparations of 1,1,3,3-tetrasubstituted 2-nitrosoguanidines were attempted to see the effect of resonance stabilization of the nitrosoimino group by two nitrogens and it was found that this effect is not so effective as steric hindrance because only 1,1,3,3-tetraphenylguanidine gave stable nitrosated product (5d).[5]

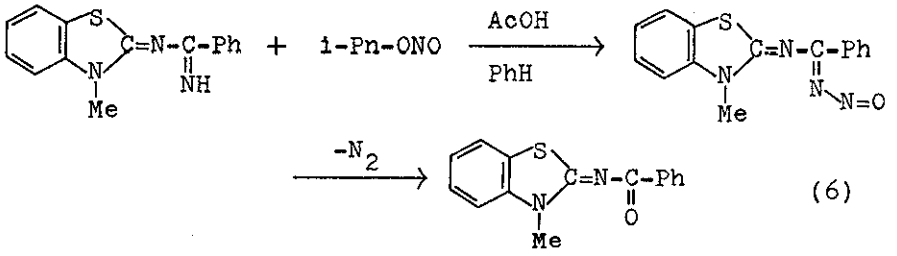


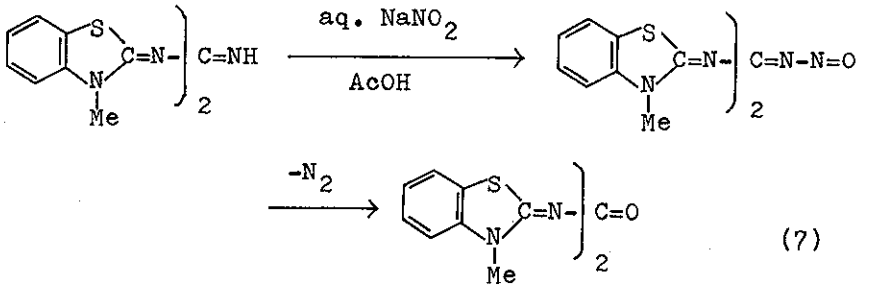
Rates of decomposition of bis(morpholino)-N-nitrosomethyleneimine (5b) were measured in four solvents and it is

apparent that the nitrosoimine is greatly stabilized by protonation: k (sec^{-1} at 13.5 °C); $3.5x10^{-3}$ (CH_2Cl_2); $2.8x10^{-4}$ (EtOH); $4.0x10^{-4}$ (MeOH); and $1.5x10^{-5}$ (H_2O).

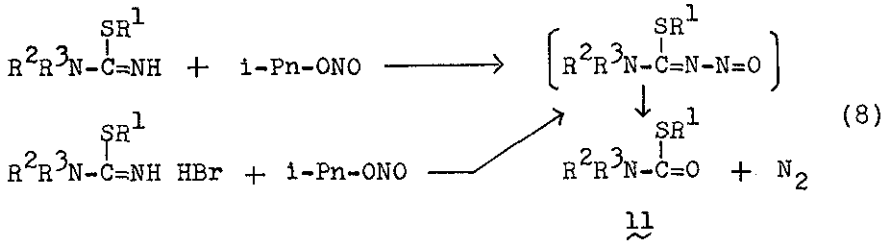
From these facts, it is expected that some types of imines which cannot be hydrolyzed easily can be converted to the corresponding carbonyl compounds under anhydrous and mild conditions. This was exemplified by the following reactions and quantitative amount of nitrogen was evolved during the reactions. Conjugated nitrosoimines could nct be obtained in reactions (6) and (7).[12]





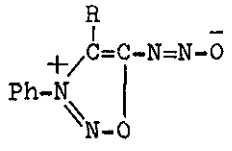


This type of novel conversion of the imino group into the carbonyl group via nitrosoimines has some synthetic utility as shown for the preparation of S-alkyl thiocarbamates (11) from S-alkylisothioureas. The reaction proceeds in benzene at 50 °C for 2 hr.[13]



(8)

Yields of S-alkyl thiocarbamates (11) are shown: R^1, R^2, R^3, %: $PhCH_2$, Me, Ph, 61; $PhCH_2$, Et, Ph, 86; $PhCH_2$, Ph, Ph, 85; Et, Me, Ph, 66; Et, Et, Ph, 61; Et, Ph, Ph, 62.

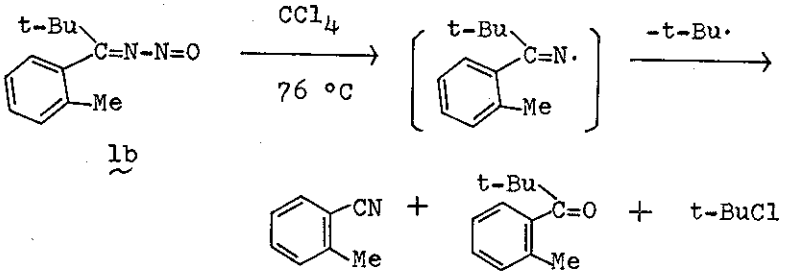


12: R=H, Me, Ph

When the nitrosoimino group is contained in heterocycles, compounds are usually thermally stable, probably due to large contribution of charge-separated structures. In connection with this, sydnone imines were nitrosated with sodium nitrite to give mesoionic nitrosoimines (12).[14] All these compounds are decomposed by reflux in anhydrous toluene or xylene to the corresponding carbonyl compounds and this can be a unique method to convert many heterocyclic imines to the corresponding carbonyl compounds under anhydrous conditions.

There is one example in which radical mechanism has been proposed to take part in the decomposition of a sterically

hindered nitrosoimines.[6]

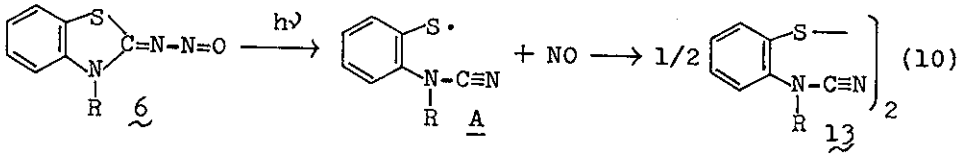


1b

(9)

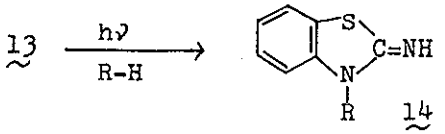
Photolysis Photolysis of 3-substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles was investigated in some detail.[7,15]

The photo-product was bis(o-(N-substituted cyanamino) phenyl) disulfide (13) and photolysis of 13 was also observed on prolonged irradiation to give the corresponding 2-iminothiazoline (14). The yields of 13 and 14 were as follows: 13 (%), 14 (%): a) R=Me, 48, 17; b) R=Ph, 74, -; c) R=Et, 45, 5.



(10)

a) R=Me, b) R=Ph, c) R=Et



(11)

UV absorptions of π-π^* and n-π^* excitations of 6 are very well separated each other as shown in Table 1. Compounds 6 were irradiated at each absorption by using filter solutions and it was found that irradiation of the π-π^* absorption at

365 nm showed the same relative photolysis rates as those by a pyrex filter and that irradiation of the n-π^* absorption at 546 nm did not initiate photo-reaction at all as shown in Table 3.

Table 3. Relative Rates of Photolysis of 6b with Filters

Solvent	Filter		
	Pyrex	365 nm[a)]	546 nm[b)]
C_6H_6	2.3	2.3	—
CH_2Cl_2	1.0	1.0	—
CH_3CN	1.0	1.0	—

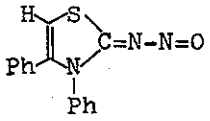
a) Aqueous solution of cobaltous sulfate and cupric sulfate

b) Aqueous solution of calcium chloride and cupric chloride

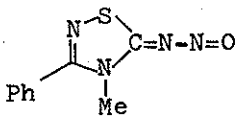
Quantum yield of photolysis of 6b was 0.38 in acetonitrile by irradiation with 365 nm light. From these results, it was proposed that photolysis of 6 proceeds through simultaneous C-S and N-N bonds fission to produce directly the thiyl radical (A) and nitric oxide.

This result is in significant contrast to photo-reactions of nitrites[16] or nitrosoalkanes[17] which lead to the cleavage of RO-NO or C-NO bond with high quantum yield even by the irradiation of their n-π^* bands to give alkoxy or alkyl radical together with nitric oxide, respectively. The different behavior of nitrosoimine (6) is ascribable to the fact that its N-N bond has a strong double bond character with a larger bond energy than O-N and C-N bond of nitrites and nitrosoal-

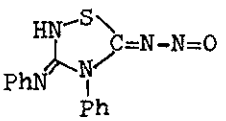
kanes. A similar result to 6 was reported for the photolysis of 7a and more complex results were obtained for 7b and 7c, because secondary reactions took place during photolysis.[18]



7a



7b



7c

Reduction with Lithium Aluminum Hydride Zimmerman and Paskovich prepared sterically hindered diazo compounds by deoxygenation of the corresponding nitrosoimine with lithium aluminum hydride (LAH).[4]

$$(4\text{-X-2,6-Me}_2\text{C}_6\text{H}_2)_2\text{C=NH} \xrightarrow{N_2O_4} (4\text{-X-2,6-Me}_2\text{C}_6\text{H}_2)_2\text{C=N-N=O}$$

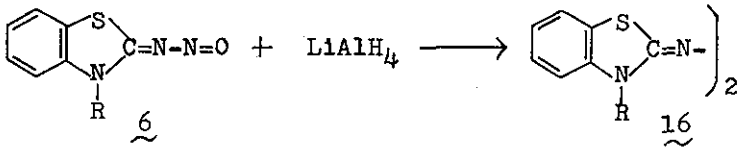
1

$$\xrightarrow{\text{LAH}} (4\text{-X-2,6-Me}_2\text{C}_6\text{H}_2)_2\overset{+}{\text{C}}\text{=}\overset{-}{\text{N}}\text{=N} \qquad (12)$$

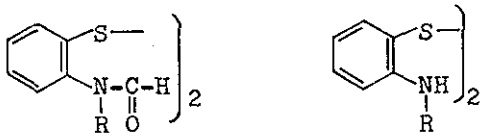
15

g) X=Me, 53 % and h) X=MeO, 46 %

Based on this description, 6 were allowed to react with LAH to prepare hitherto unknown diazo compounds (B) but three kinds of main products (16, 17, and 18) were obtained in the yields shown in Table 4.[19]



6 16



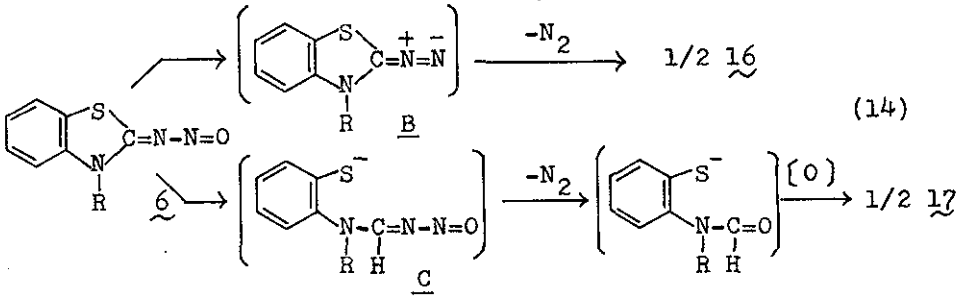
(13)

17 18

Table 4 Reduction Products (mole %) of 6 with Lithium Aluminum Hydride (excess)

6	16	17	18
a) R=Me	27	22	24
b) R=Ph	16	30	20
c) R=Et	30	28	18

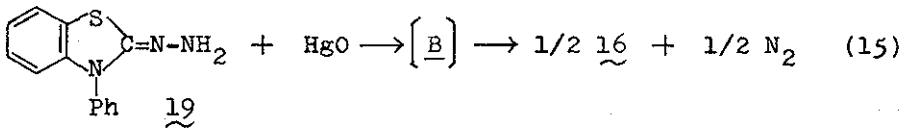
The formation of 16 is explained by attack of hydride at the nitrogen of nitroso group to give the expected diazo compound (B) as an intermediate and that of 17 by attack at C-2 of the ring to afford the ring opened nitrosoimine (C) as an intermediate. Further reduction of 17 in situ could yield 18.



(14)

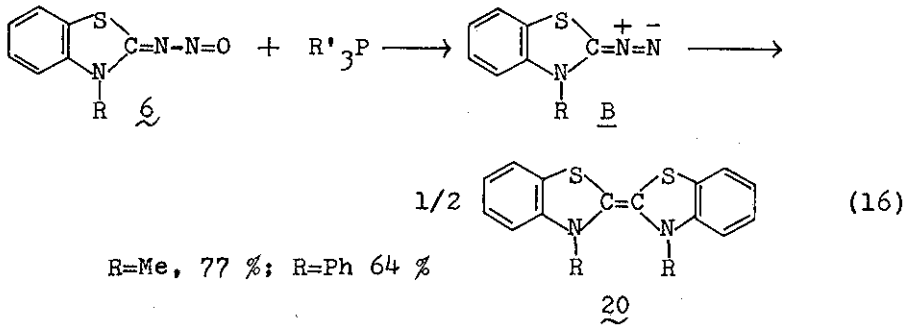
In order to prepare B, 2-hydrazono-3-phenyl-2,3-dihydrobenzothiazole (19) was oxidized with mercuric oxide. The reaction took place very slowly at 0 °C as compared with that of

benzophenone hydrazone, giving 16 as the major product (ca. 70 %).



(15)

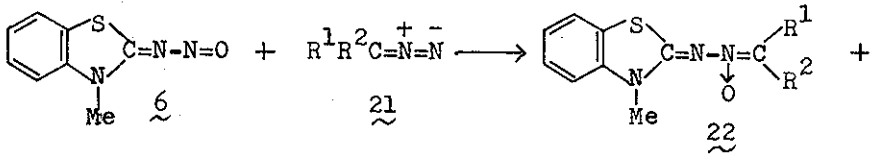
Deoxygenation of 6 with tertiary phosphines gave bis-benzothiazolidene (20) in high yield, which should proceed via the diazo compound (B).[20] Until now, diazo compounds contained in heterocycles such as benzothiazoline and benzimidazoline have not been characterized yet.

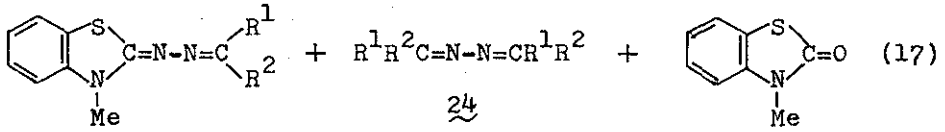


(16)

R=Me, 77 %; R=Ph 64 %

In connection with the reaction of nitrosoimines with diazo compounds, phenyl-, methylphenyl-, and diphenyldiazomethanes (21) were allowed to react with 6 to give unsymmetrical azine N-monoxide (22) and unsymmetrical azine (23) as shown below (see Table 5). Unsymmetrical azine (23) is the deoxygenated product of N-monoxide (22).





23 + $R^1R^2C{=}N{-}N{=}CR^1R^2$ (24) + 25a (17)

a) $R^1{=}R^2{=}Ph$, b) $R^1{=}Ph$, $R^2{=}Me$, c) $R^1{=}Ph$, $R^2{=}H$

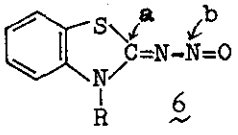
Table 5 Reaction of 6a with Diazo Compounds (21)[*1)]

21	22	23	24	25a	6a recovery
a) $Ph_2C{=}N_2$	16	—	42	80	—
b) $MePhC{=}N_2$	—	34	39	—	88
c) $PhCH{=}N_2$	11	—	46[*2)]	—	90

*1) The yields (mol %) of 22, 23, and 25a were calculated based on the amount of 6a consumed. The yield of 24 was calculated based on the amount of initially charged 21.

*2) PhCOCHPhN=NCHPhCOPh (11 %), probably the by-product in the preparation of 21c, was obtained.

Reactions with Grignard Reagents Reactions of 6 with aryl, benzyl, and alkyl Grignard reagents were investigated in detail to see the reactivity of 6 toward nucleophiles.

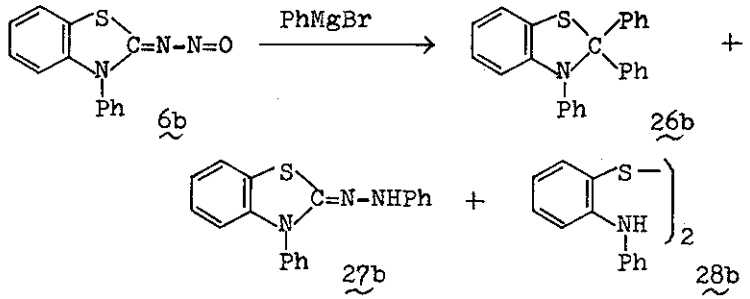


6

Reaction took place by initial attack via path a and b and the ratio of final products were determined according to the structure of Grignard reagents.

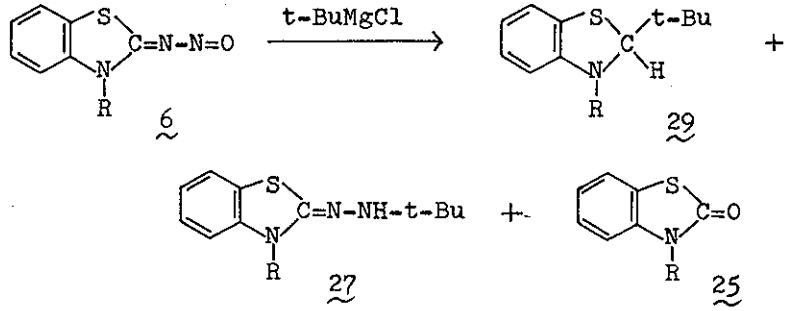
When excess phenylmagnesium bromide was allowed to react with 2-nitrosoimino-3-phenyl-2,3-dihydrobenzothiazole (6b),

the following products were obtained:[21] 2,2,3-triphenyl-2,3-dihydrobenzothiazole (26b, 48 %), 3-phenyl-2-N'-phenylhydrazono-2,3-dihydrobenzothiazole (27b, 17 %), and a small amount of bis(o-anilinophenyl) disulfide (28b).



(18)

When t-butylmagnesium chloride was allowed to react with 6, main product was 2-t-butyl-2,3-dihydrobenzothiazole (29) as shown below.



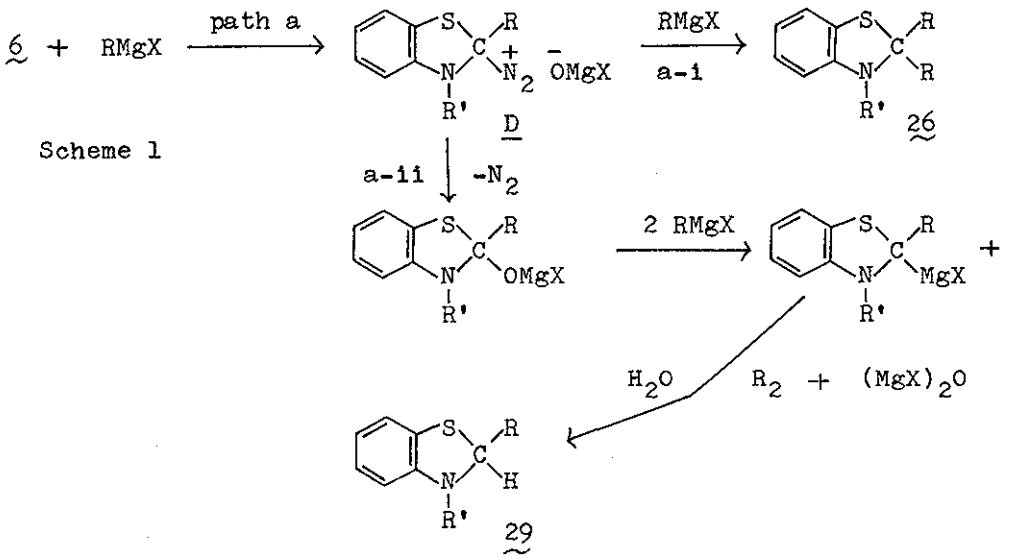
(19)

	29 (%)	27 (%)	25 (%)
6a	39	8	13
6b	50	15	22

Mesitylmagnesium bromide gave similar results to t-butyl magnesium chloride showing the presence of steric hindrance at the second attack of Grignard reagent on the diazonium in-

termediate (D). Production of 2-disubstituted (26) and 2-monosubstituted 2,3-dihydrobenzothiazoles (29) can be explained as shown in Scheme 1.

Scheme 1

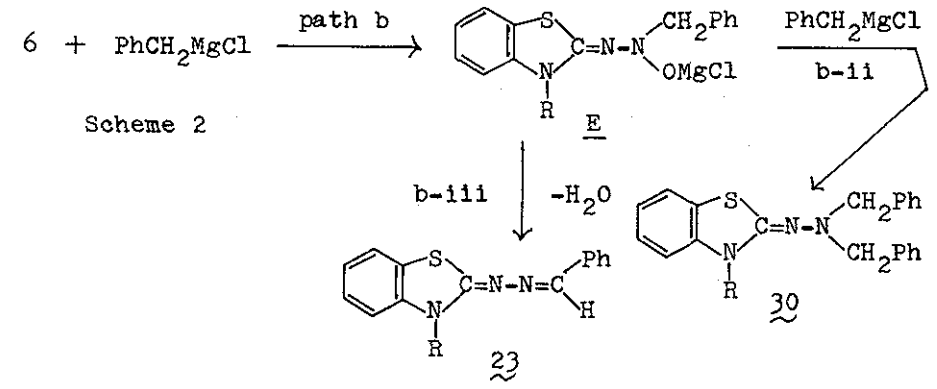


In the reaction of benzylmagnesium chloride with 6a, the type of the products was essentially the same as in reaction (18), but the main reaction took place on the nitrogen of nitroso group to give unsymmetrical azine (23) and hydrazone (30a, 19 %).[22]

The yield of the hydrazone (30a, 31 %) increased by refluxing the solvent accompanied by decrease of the azine (23c, 14 %). This result shows that the intermediate (E) was alkylated by benzylmagnesium chloride to give the hydrazone (30). (see Scheme 2)

Reactions of alkyl Grignard reagents with 6 followed essentially the same reaction paths and the results are

summarized in Table 6 and general reaction scheme is shown in Scheme 3.[23]



Scheme 2

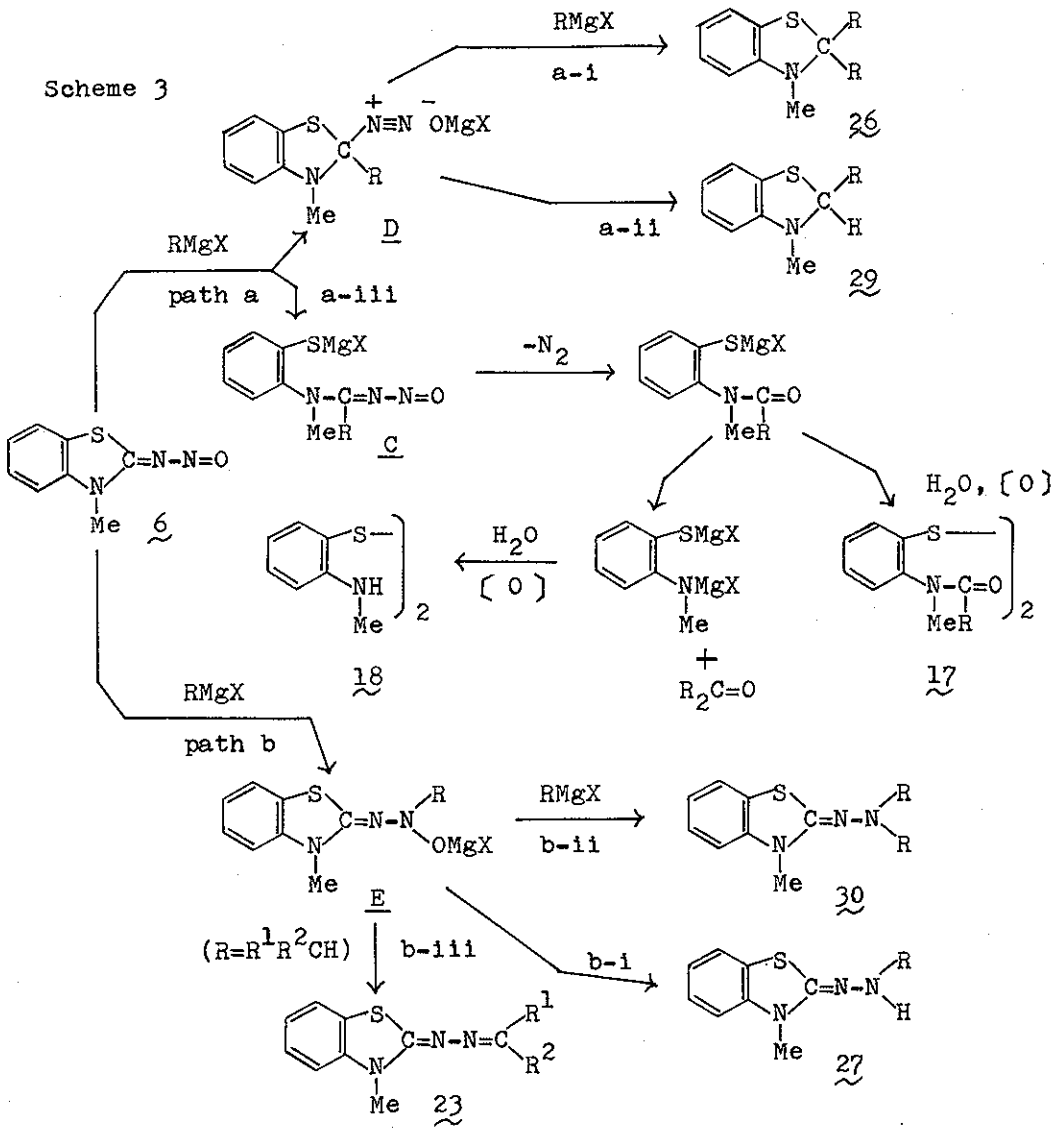
Table 6 Yields of Reaction Products of 6a with RMgX*1)

R	X	Reaction path*2) a-i	a-ii	a-iii	a	Reaction path*2) b-i	b-ii	b-iii	b
a) $PhCH_2$	Cl	8	—	—	8	—	19	44	63
b) $n\text{-}PrCH_2$	Br	7	—	23	30	20	15	—	35
c) MeEtCH	Br	—	—	13	13	18	—	22	40
d) $cyclo\text{-}C_6H_{11}$	Cl	—	—	8	8	20	6	14	40
e) Me_3C	Cl	—	39	—	39	8	—	—	8
f) $p\text{-}MeC_6H_4$	Br	66	—	—	66	17	—	—	17
g) $2,4,6\text{-}Me_3C_6H_2$	Br	—	46	—	46	18	—	—	18

*1) Numerical values show the yield (mol %) of products based on initially charged 6a.

*2) Reaction paths correspond to those shown in scheme 3.

Scheme 3


RMgX
a-i
26
D
a-ii
29
RMgX
path a
a-iii
C
-N2
6
H2O
[O]
18
H2O, [O]
17
R2C=O
RMgX
path b
E
RMgX
b-ii
30
(R=R1R2CH)
b-iii
b-i
23
27

It is apparent from Table 6 that Grignard reagents can be classified into two groups:

group α (more reactive), consisting of aryl and t-butyl groups (e-g) and

group β (less reactive), consisting of primary and secondary alkyl groups (a-d). General features of the reaction are summarized and rationalized as follows:

1) The main path of group α is path a and that of group β is path b. It is well known that Grignard reagents add almost exclusively on the carbon of Schiff's base but not on the nitrogen,[24] therefore path a is expected to be the main path for all Grignard reagents. Since very large contribution of charge separated canonical forms to the ground state of 6 has been shown by spectroscopic studies[7,10] for the present system, path a should be of a higher energy process than path b, because the entire conjugation between the benzothiazoline ring and the nitrosoimino group being cut off in the former but the conjugation between the ring and the imino group is retained in the latter. Therefore, the results are reflection of competition of these factors according to the reactivty of Grignard reagents.
2) For path a, group α reacts exclusively through diazonium intermediate (D), whereas path a-iii is preferred by group β except benzylmagnesium chloride. This can be realized mainly by the electronic effect of the substituent (R), where R can stabilize positive charge on the C-2 more effectively,

paths through D become predominant. It is noteworthy to mention that paths a-i and a-ii were not observed with Grignard reagents derived from secondary alkyl halides, probably because of the balance between electronic and steric effects.

3) For path b, group α reacts exclusively through path b-i, whereas path b-i, b-ii, and b-iii are competitive for group β. When the intermediate (E) is stabilized thermodynamically by dehydration, path b-iii is preferred shown as a typical one for benzylmagnesium chloride. Path b-ii, alkylation of Grignard type reagent of hydroxylamine by Grignard reagent, has not been observed so for. However, this was substantiated by the increase of the product of this path by refluxing the solvent in the case of benzylmagnesium chloride. The reason is not clear why group α does not follow path b-ii at all. However, it is understandable if we consider the difference of nature of R-$\overset{|}{N}$-OMgX bond in the intermediate B among group α and group β Grignard reagents (Ar-$\overset{|}{N}$-OMgX and t-Bu-$\overset{|}{N}$-OMgX compared with Alkyl-$\overset{|}{N}$-OMgX).

A uniue example of the reaction of 6 with Grignard reagents is that of 6 with Grignard type reagent of the corresponding imine (14) which proceeded via path a-ii to afford the azamonomethine-cyanine perchlorates in almost quantitative yields.[25] This can be understood by large stabilization of the resulting carbonium ion as shown in Scheme 4.

The results are summarized in Table 7.

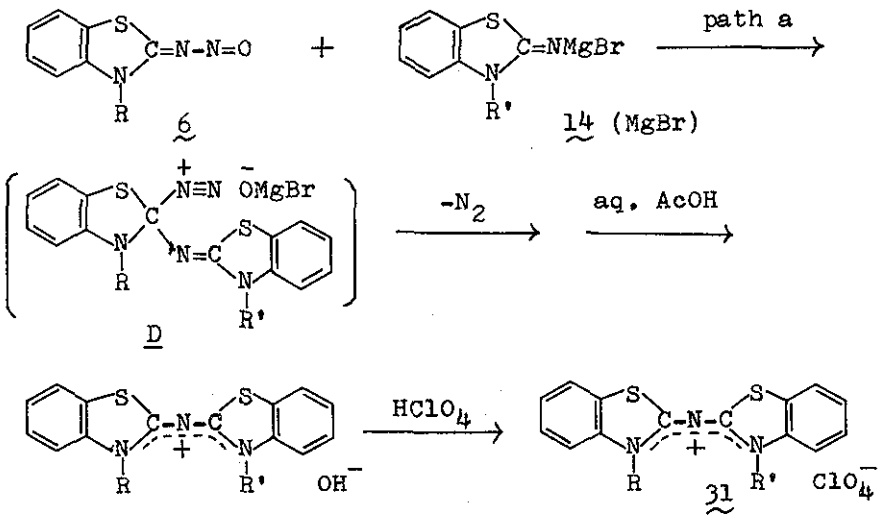
Table 7 Yields and Melting Points of Azamonomethine-cyanine Perchlorates (31)[25]

6	14 (MgBr)	31	Yield(%)*	Mp (°C)
R=Me	R'=Me	a,a*2	84.5	319.0-320.0 (dec)
Me	Et	a,c	89.8	276.8-278.0
Et	Me	c,a	95.8	276.8-278.0
Et	Et	c,c	89.3	275.0-276.5
Ph	Me	b,a	70.9	312.0-314.0 (dec)
Ph	Et	b,c	78.0	253.5-255.0
Ph	Ph	b,b	80.0	316.0-317.3 (dec)

* Isolated yields are shown after recrystallization from ethanol once and are calculated based on 6 initially charged.

*2 Small letter a stands for Me, b does for Ph, and c does for Et. So, c,a, for example, shows that 31 has R=Et and R'=Me.

Scheme 4



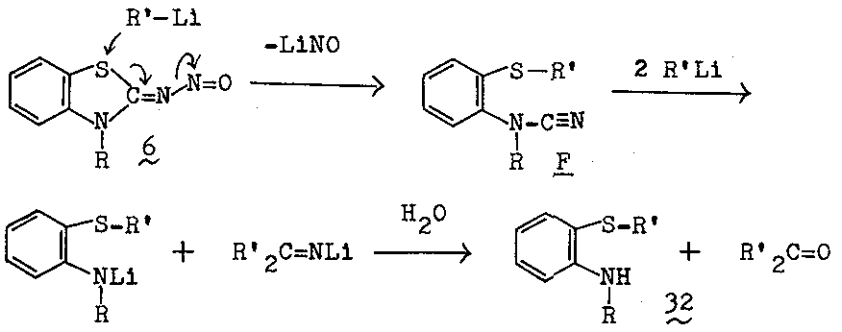
6 + 14 (MgBr) → D → 31

Reactions with Organolithiums When excess n-butyllithium was added to a suspension of 6b in ether, 2,2-di-n-butyl-3-phenyl-2,3-dihydrobenzothiazole (26d, 10 %), bis(o-anilinophenyl) disulfide (18b, 3 %), o-anilinophenyl n-butyl sulfide (32c, 43 %), and 2-N'-n-butylidenehydrazono-3-phenyl-2,3-dihydrobenzothiazole (23d, 10 %) were obtained. The same type of compound, phenyl (N-substituted o-amino)phenyl sulfide (32), was also the main product in the reaction of 6 with phenyllithium, i.e., the yields were 36 % (32a) and 38 % (32b) when N-substituents of 6 were methyl and phenyl, respectively, and benzophenone (52-58 %) was also obtained.[26]

The main product (32) is a new type of product which was not obtained in the reactions of 6 with Grignard reagents and benzyllithium. The reaction path of formation of 32 is explained

in Scheme 5.

Scheme 5



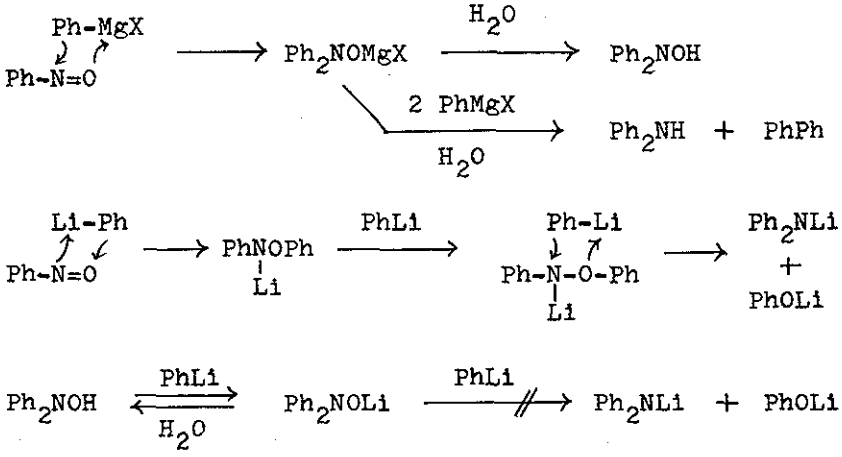
Phenyl- and n-butyllithiums directly attack the sulfur atom of the benzothiazoline ring via lithium-nitrogen coordination and cleavage of the carbon-sulfur linkage followed by loss of NO^- anion to give the corresponding phenyl and n-butyl (N-substituted o-cyanamino)phenyl sulfides (F) as a primary product. F reacts further with excess organolithium to produce 32 and the corresponding ketone after hydrolysis.

Discussion on the Difference of Reactivities between Grignard Reagents and Organolithiums Based on the results of the spectral studies on 6,[7,10] the reactions of 6 with nucleophiles are expected to take place on three possible reaction centers, i.e., the C-2 position of the benzothiazoline ring (a), the nitrogen atom of the nitroso group (b) and the sulfur atom of the ring (c).

The difference between the reactions of 6 with Grignard reagents and those with organolithiums can primarily be attributed to the difference in the coordination position of organomagne-

sium and organolithium compounds to the nitrosoimino group of 6.

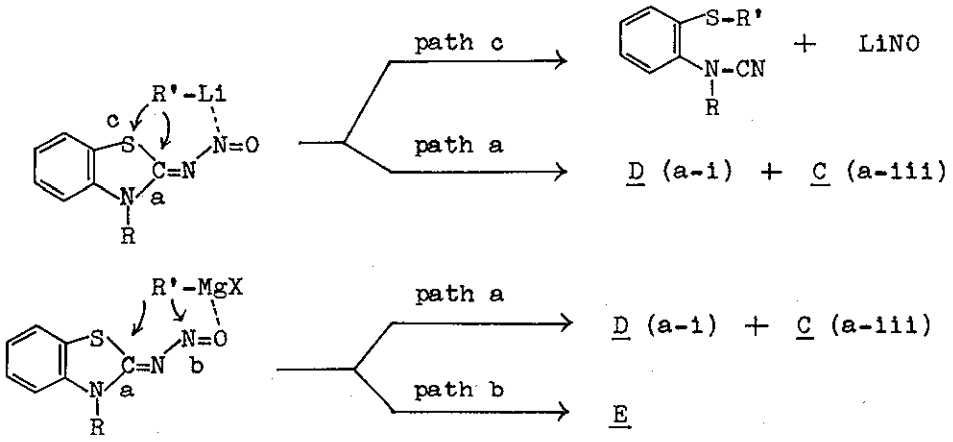
This postulate is supported by the reactions of nitrosobenzene with Grignard reagents[27-30] and phenyllithium.[31] The reaction with an equimolar amount of phenylmegnesium bromide has been shown to give the corresponding hydroxylamine,[27,29,30] which reacts successively with excess Grignard reagent to give diphenylamine and biphenyl.[29] On the other hand, nitrosobenzene reacts with excess phenyllithium to give diphenylamine and phenol, but the reaction of N,N-diphenylhydroxylamine with excess phenyllithium does not produce diphenylamine and phenol, recovering the hydroxylamine.[31]



It was proposed from the results that the reaction of nitrosobenzene with phenyllithium initially gives not O-lithio compound but N-lithio compound, which is then attacked by another phenyllithium to give diphenylamine and phenol.[31]

Let us propose that organolithiums are coordinated by the nitrogen atom of the nitroso group and attack the sulfur atom of the benzothiazoline ring (path c) and competitively the C-2 position of the ring (path a). Path c may be a process of higher energy than path a, since benzyllithium follows path a exclusively.

On the other hand, we propose that Grignard reagents are coordinated by the oxygen atom of the nitroso group and attack the C-2 position of the ring to give the corresponding diazonium salt (path a-i) and/or the ring-opened nitrosoimine (path a-iii) and competitively the nitrogen of nitroso group to produce the magnesium salt of the corresponding hydrazono derivative (path b).



It should be kept in mind that addition of Grignard reagents and organolithiums occurs exclusively on the carbon atom of Schiff's base[24,32] and that organolithiums are usually more reactive than Grignard reagents as shown by the addition of methyllithium to N-benzylidene-t-butylamine which is inert

to methylmagnesium bromide.[33]

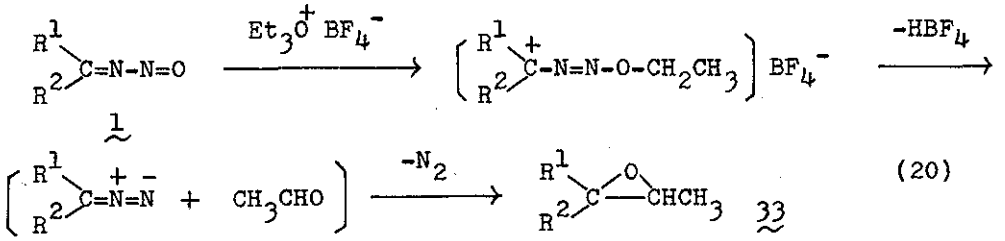
There may be another factor contributing to the difference in reactivity of Grignard reagents and organolithiums, viz., thiophilicity.

Organometallics have been shown to attack the sulfur of thioketones[34] and thioketenes,[35] generating the corresponding carbanions. There is no definite comparison of thiophilicity of organolithiums and Grignard reagents. However, the fact that the yield of benzhydryl phenyl sulfide was 70 % (isolated yield) and 37 % (glc yield), respectively, when thiobenzophenone reacted with phenyllithium and phenylmagnesium bromide[34] shows greater thiophilicity of phenyllithium than that of phenylmagnesium bromide. However, there had been no other decisive evidence on thiophilic attack of organolithiums at divalent sulfur (R-S-R') than the present result, but the same type of reactivity was reported by us recently in the reaction of phosphinodithioate esters with organolithiums.[36]

Thus, the difference in reactivity between organolithiums and Grignard reagents can be ascribed to three factors, i.e., i) coordination site, ii) thiophilicity, and iii) ionic character of both reagents.[37]

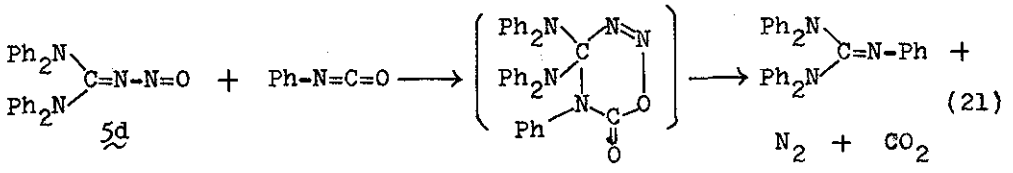
Miscellaneous Reactions Some reactions of open-chain nitrosoimines were reported. Epoxides (33) were obtained in moderate yields (26-69 %) when four examples of 1 were ethylated with Meerwein reagent ,whose reaction was effected by

initial ethylation of the oxygen of nitroso group.[3]



(20)

Reaction of 2-nitroso-1,1,3,3-tetraphenylguanidine (5d) with phenyl isocyanate gave pentaphenylguanidine in 38 % yield, where 1,4-cycloaddition of 5d was proposed.[5]



(21)

Reactivities of open-chain nitrosoimines have not been investigated extensively due to their thermal instability.

ACKNOWLEDGEMENT Authors are very grateful to their former students who are named as coauthors in original papers for their sincere efforts and positive attitude which made the present research possible.

REFERENCES

1. K. Akiba, M. Imanari, and N. Inamoto, Chem. Commun., 1969, 168.

2. H. Balli and F. Kersting, Ann. Chem., 1961, 647, 1; 1963, 663, 97, 103.
H. Balli, Angew. Chem., 1964, 76 995.
H. Quast and S. Huenig, Angew. Chem., 1964, 76, 989.
3. C. J. Thoman, S. J. and I. M. Hunsberger, J. Org. Chem., 1968, 33, 2852.
4. H. Zimmerman and D. H. Paskovich, J. Am. Chem. Soc., 1964, 86, 2149.
5. K. Akiba, S. Matsunami, C. Eguchi, and N. Inamoto, Bull. Chem. Soc. Jpn., 1974, 47,935.
6. J. Jappy and P. N. Preston, Tetrahedron Lett., 1970, 1157.
7. K. Akiba, I. Fukawa, N. Nomura, and N. Inamoto, Bull. Chem. Soc. Jpn., 1972, 45, 1867.
8. K. Akiba, T. Tsuchiya, I. Fukawa, and N. Inamoto, Bull. Chem. Soc. Jpn., 1976, 49, 550.
9. S. F. Mason, Quart. Rev., 1961, 15, 314.
10. K. Akiba, M. Hisaoka, N. Inamoto, T. Ohta, and H. Kuroda, Chem. Lett., 1975, 347.
11. J. H. Vis and P. Meinke, J. Heterocyclic Chem., 1970, 7, 1417.
12. K. Akiba,K. Ishikawa, and N. Inamoto, unpublished results.
13. K. Akiba and N. Inamoto, Chem. Commun., 1973, 13.
14. H. Kato, M. Hashimoto, and M. Ohta, Nippon Kagaku Zasshi, 1957, 78, 707.
15. K. Akiba, I. Fukawa, K. Mashita, and N. Inamoto, Tetrahedron Lett., 1968, 2859.

16. M. Akhtor and D. H. R. Barton, J. Am. Chem. Soc., 1964, 86, 1528; M. Akhtor, "Advances in Photochemistry", 1964, Vol. 2, 263.

17. K. D. Anderson, C. J. Crumpler, and D. L. Hammick, J. Chem. Soc., 1935, 1679; J. G. Calvert and J. N. Pitts, Jr., "Photochemistry", 1966, John Wiley & Sons, N. Y., p. 475-485.

18. K. Akiba, T. Tsuchiya, I. Fukawa, and N. Inamoto, Bull. Chem. Soc. Jpn., 1976, 49, 550.

19. K. Akiba, T. Kawamura, M. Ochiumi, and N. Inamoto, Heterocycles, 1973, 1, 35.
K. Akiba, T. Kawamura, M. Ochiumi, and N. Inamoto, Bull. Chem. Soc. Jpn., 1976, 49, 1913.

20. H. J. Kleiner, Ann. Chem., 1969, 724, 221.

21. K. Akiba, T. Kawamura, M. Hisaoka, and N. Inamoto, Chem. Lett., 1973, 201.
K. Akiba, T. Kawamura, M. Hisaoka, and N. Inamoto, Bull. Chem. Soc. Jpn., 1975, 48, 3262.

22. M. Hisaoka, K. Akiba, and N. Inamoto, Bull. Chem. Soc. Jpn., 1975, 48, 3266.

23. K. Akiba, M. Hisaoka, T. Kawamura, and N. Inamoto, Bull. Chem. Soc. Jpn., 1975, 48, 3270.

24. R. B. Moffett and W. M. Hoehn, J. Am. Chem. Soc., 1947, 69, 1792.

25. K. Akiba, K. Ishikawa, and N. Inamoto, Heterocycles, 1974, 2, 555; K. Akiba, K. Ishikawa, and N. Inamoto, to be published in Bull. Chem. Soc. Jpn.

26. K. Akiba, M. Hisaoka, and N. Inamoto, Chem. Lett., 1974, 1267. M. Hisaoka, K. Akiba, and N. Inamoto, Bull. Chem. Soc. Jpn., 1975, 48, 3274.
27. H. Wieland and A. Roseeu, Ber., 1912, 45, 494.
28. H. Wieland and A. Roseeu, Ber., 1915, 48, 1117.
29. H. Gilman and R. McCracken, J. Am. Chem. Soc., 1927, 49, 1052.
30. K. Maruyama, Bull. Chem. Soc. Jpn., 1964, 37, 1013.
31. P. Buck and G. Koebrich, Tetrahedron Lett., 1967, 1563.
32. H. Gilman and R. H. Kirby, J. Am. Chem. Soc., 1933, 55, 1265.
33. B. L. Embing, R. J. Horvath, A. J. Saraceno, E. F. Ellermeyer, L. Hail, and L. D. Hudac, J. Org. Chem., 1959, 24, 657.
34. P. Beak and J. W. Warley, J. Am. Chem. Soc., 1972, 94, 597. M. Dagonneau and J. Vialle, Tetrahedron, 1974, 30, 3119.
35. E. Schaumann and W. Walter, Chem. Ber., 1974, 107, 3562.
36. K. Goda, R. Okazaki, K. Akiba, and N. Inamoto, Tetrahedron Lett., 1976, 181; K. Goda and N. Inamoto, Chem. Lett., 1975, 1009.
37. L. Pauling, "The Nature of the Chemical Bond", Chap. 3, Cornell University Press, 1960.

Received, 5th August, 1977