vents were removed by distillation under reduced pressure and the residue was distributed between water and CH_2Cl_2. The pH was adjusted to 2.0 and several extractions were made with CH_2Cl_2. The organic layer was dried and the solvent was removed *in vacuo*. The residual solid weighed 30 mg and its tlc zone had the same R_f as that of **8**, the preparation of which is described below. The overall yield of **8** from **6** was 14%.

4-(4′-Fluoro-3′-aminophenylsulfonyl)-2-phenylazo-*N*-phenylglycine (8). A mixture of 373 mg (1.0 mmol) of **4**, 168 mg (2.0 mmol) of $NaHCO_3$, 75 mg (1.0 mmol) of glycine, 18 ml of MeOH, and 5 ml of H_2O was heated to the reflux temperature for 10 hr. The solvents were removed by distillation under reduced pressure and the residue was mixed with water and extracted with CH_2Cl_2 at pH 2.0. The organic layer was dried and concentrated *in vacuo* to 170 mg (40%) of **8**. Recrystallization from aqueous EtOH afforded an analytically pure sample: mp 169.0–170.0°; ir (Nujol) 3590, 3470 (NH and NH_2), 1740 (carboxyl carbonyl), 1600 (N=N), 1310, and 1130 cm^{-1} (SO_2).

Anal. Calcd for $C_{20}H_{17}FN_4O_4S$ (**8**): C 56.10; H, 3.97; F, 4.44; N, 13.05; S, 7.47. Found: C, 56.25; H, 4.11; F, 4.31; N, 12.94; S, 7.32.

Reductive Cyclization of 8. Preparation of 7-(4′-Fluoro-3′-aminophenylsulfonyl)-3,4-dihydro-2(1*H*)-quinoxalone (7). A mixture of 227 mg (0.53 mmol) of **8**, 500 mg (9.27 mmol) of KBH_4, 60 mg of 5% Pd/C, and 125 ml of H_2O was stirred at room temperature for 3 hr. More KBH_4 (500 mg) and 5% Pd/C (40 mg) were added to the reaction mixture and stirring was continued for another 1 hr. The catalyst was removed by filtration through a layer of Celite and the pH of the filtrate was adjusted to 2.0. A precipitate separated during a 1-hr storage period. The pH was changed to 8.9 and the mixture was filtered. The solid was recrystallized from C_6H_6-MeOH to afford 120 mg (71%) of **7** which decomposes beginning at 170°. The ir and tlc of this product were identical with those determined on the product from the reduction and subsequent reactions of **6** (see above).

Anal. Calcd for $3C_{14}H_{12}FN_3O_3S \cdot 2C_6H_6$ (benzene solvate of **7**): C, 57.90; H, 4.32; F, 5.09; N, 11.25; S, 8.59. Found: C, 57.76; H, 4.17; F, 4.86; N, 11.36; S, 8.44.

Acknowledgment. Support of this research by the National Science Foundation (Grant GP-33582) is gratefully acknowledged.

Registry No.—**1**, 312-30-1; **2** dihydrochloride, 51472-56-1; **3**, 51472-57-2; **4**, 51472-58-3; **5**, 556-50-3; **6**, 51472-59-4; **7**, 51472-60-7; **8**, 51472-61-8.

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Nucleophilic Cleavage of the 1,2,5-Thia- and -Selenadiazole Rings[1]

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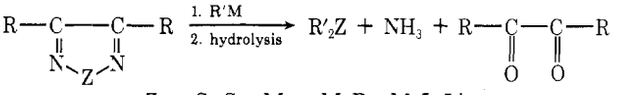
Some years ago we showed that 1,2,5-thiadiazole and its monosubstituted derivatives, but not 1,2,5-selenadiazole,[2] undergo deprotonation with incorporation of deuterium[3,4] when treated by deuterioxide in heavy water solution. As a matter of fact, both 1,2,5-thia- and -selenadiazole rings unsubstituted, or alkyl and aryl mono- and disubstituted, are rather stable when treated with aqueous or alcoholic hydroxide,[2,3,5] but reaction occurs with Grignard reagents and lithium alkyls.[1,4,6] The present work is concerned with the reaction of some alkyl and aryl disubstituted 1,2,5-thia- and -selenadiazoles towards such strong nucleophiles.

Both 1,2,5-thiadiazoles and 1,2,5-selenadiazoles react with Grignard reagents or lithium alkyls at temperatures as low as −70° to yield, after hydrolysis, a thio- or selenoether, ammonia, and 1,2-dicarbonyl compounds (Scheme I). The reaction often yields also small amounts of nitrogen-containing heterocycles such as imidazoles or pyrazines (Table I).

Scheme I



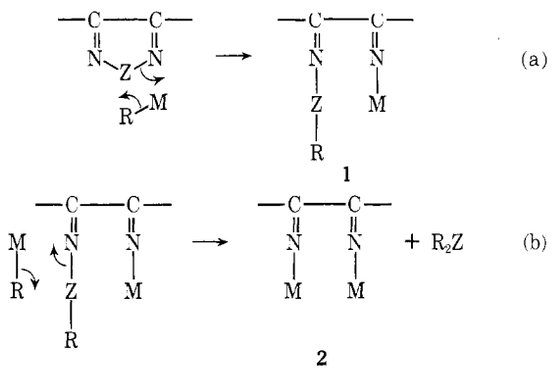
Z = S, Se; M = MgBr, MgI, Li

The reaction of 3,4-diphenyl-1,2,5-thiadiazole and *n*-butylmagnesium bromide give rise to thioalcohol and olefin in place of the thioether. The products derived from the heterocyclic substrate were unchanged.

The formation of thio- or selenoether or thiol suggests the sulfur or selenium atoms as the centers of the nucleophilic attack. Examples of nucleophilic attack at the sulfur atom of an S–N bond are known; the nearest analogy to this study may be found in the reaction between isothiazoles and *n*-butyllithium,[7,8] or between a Grignard reagent and sulfur nitride S_4N_4,[9] where the NSN angle and N–S bond distances[10] are similar to those of the 1,2,5-thiadiazole ring.[3]

We suggest that the first step in the process is insertion of the Grignard reagent or lithium alkyl (R–M) on a S–N or Se–N bond, followed by cleavage of the ring and formation of the intermediate **1** (Scheme IIa). Reaction of **1**

Scheme II



Z = S, Se; M = MgBr, MgI, Li

with a second molecule of organometallic reagent forms thio- or selenoether and the final product **2**, which contains the same —N=C—C=N— system as the starting diazole (Scheme IIb). Production of thiol and olefin with *n*-butyl Grignard reagent is consistent with reduction of intermediate **1** rather than nucleophilic substitution. This reaction course does not affect the formation of **2**, but it requires a further molecule of the organometallic compound to transform the thiol into its magnesium salt. Hydrolysis of the diimines **2** finally leads to the dicarbonyl compound and ammonia.

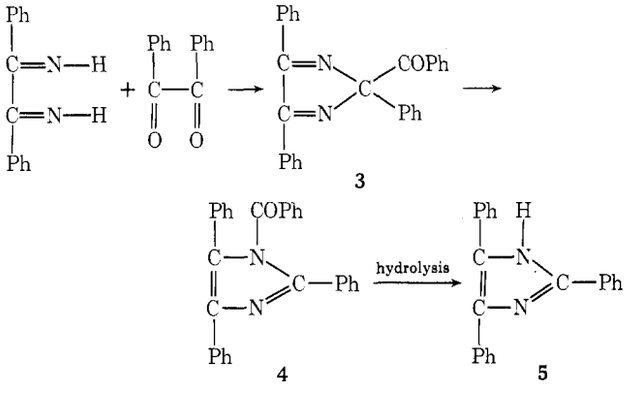
Formation of 2,3,5,6-tetraphenylpyrazine from 3,4-diphenyl-1,2,5-thia- and -selenadiazole, which involves a redox reaction, may take place during hydrolysis. It is significant that the same compound is also formed by reaction between benzil and ammonia.[11] 2,4,5-Triphenylimidazole (**5**) and the easily hydrolyzed 1-benzoyl-2,4,5-triphenylimidazole (**4**) can arise from the 2-isoimidazole (**3**) during the hydrolysis reaction[12] (Scheme III).

Table I
Reagents and Products[a] of the Reactions between 3,4-Disubstituted 1,2,5-Thia- or -Selenadiazole Derivatives and Nucleophiles

Diazole reagent (mmol)	Registry no.	Nucleophile (mmol)	Products (mmol)
Diphenylthia- (4.13)	4057-61-8	CH_3MgI (29.38)	Benzil (1.77); 1-benzoyl-2,4,5-triphenylimidazole (0.99); 2,4,5-triphenylimidazole (0.04); 2,3,5,6-tetraphenylpyrazine (0.03); methyl sulfide (2.80)[b]
Diphenylthia- (4.20)		n-C_4H_9MgBr (30.00)	Benzil (3.42); 2,4,5-triphenylimidazole (0.18); 1-butene (2.35);[c] 1-butanethiol (3.64);[d] ammonia (6.63)
Diphenylthia- (4.20)		CH_3Li (14.70)	Benzil (3.29); 2,4,5-triphenylimidazole (0.21); methyl sulfide (3.11)[b]
Dimethylthia- (22.34)	5728-21-2	C_2H_5MgBr (78.18)	Diacetyl (11.39)
Dimethylthia- (18.83)		n-C_4H_9Li (47.01)	Diacetyl (10.92)
Phenanthro[9,10-c]thia- (0.48)	1143-73-3	C_2H_5MgBr (5.00)	9,10-Phenanthrenedione (0.42)[e]
Diphenylselena- (1.75)	19768-00-4	CH_3MgI (4.39)	Benzil (1.21); 2,4,5-triphenylimidazole (0.22); 2,3,5,6-tetraphenylpyrazine (0.02); methyl selenide (1.35)[f]
Diphenylselana- (1.60)		CH_3Li (6.08)	Benzil (1.23); 2,4,5-triphenylimidazole (0.10)
Dimethylselena- (9.44)	17505-12-3	CH_3MgI (23.60)	Diacetyl (4.34); methyl selenide (7.64)[f]
Dimethylselena- (12.11)		CH_3Li (30.28)	Diacetyl (6.18); methyl selenide (9.45)[f]

[a] Only quantitatively determined products have been reported in the table. [b] Weighed as $2(CH_3)_2S \cdot 3HgCl_2$. [c] Weighed as 1,2-dibromobutane. [d] Weighed partly as C_4H_9SHgCl (1.30 mmol) and partly as $(C_4H_9S)_2Hg$ (1.17 mmol). [e] Data obtained from V. Bertini, A. De Munno, and A. Marraccini, *J. Org. Chem.*, **37**, 2587 (1972). [f] Weighed as $(CH_3)_2Se \cdot HgCl_2$.

Scheme III



A 1:1 molar mixture of 3,4-diphenyl-1,2,5-thiadiazole and 3,4-diphenyl-1,2,5-selenadiazole, allowed to react with methylmagnesium iodide (see Experimental Section), showed that the selenium derivative reacts much faster than the sulfur one. The 1,2,5-selenadiazole ring is also the more susceptible to reducing[2,3] and oxidizing[13] agents and to heat and sunlight.[2]

The reported reactions of the 1,2,5-thia- and -selenadiazole derivatives with carbanionic nucleophiles must be mentioned for their intrinsic interest in the preparation of otherwise not easily obtainable 1,2-diimine derivatives.[14]

Experimental Section

The following reagents were prepared according to known methods from the literature: 3,4-dimethyl-1,2,5-thiadiazole,[15] 3,4-diphenyl-1,2,5-thiadiazole,[15] 3,4-dimethyl-1,2,5-selenadiazole,[2] 3,4-diphenyl-1,2,5-selenadiazole.[2] For comparison purposes, samples were also prepared of 1-benzoyl-2,4,5-triphenylimidazole,[16] 2,4,5-triphenylimidazole,[17] 2,3,5,6-tetraphenylpyrazine,[18] 1-butanethiol,[19] chloromercury n-butylthiol,[20] mercury di-n-butylthiol,[20] methyl sulfide,[21] methyl selenide,[22] the mercury chloride addition products $2(CH_3)_2S \cdot 3HgCl_2$[23] and $(CH_3)_2Se \cdot HgCl_2$,[24] and 1,2-dibromobutane by bromination of commercial 1-butene.

General Procedure for the Reaction between 1,2,5-Thia- or -Selenadiazoles and Grignard Reagents or Lithium Alkyls. An ethereal solution of the 1,2,5-thia- or -selenadiazole compound was slowly added to a stirred ethereal solution of the organometallic reagent, maintained under nitrogen at a selected temperature (from −70 to −30° for lithium alkyls, room temperature for Grignard reagents). After stirring (from 0.5 to 8 hr for Grignard reagents, from 0.2 to 3 hr for lithium alkyls) the reaction mixture was hydrolyzed with iced water, then acidified with hydrochloric acid. The nonhydrosoluble products of the reaction were recovered by extraction with ether and separated by distillation (volatile products) or by preparative layer chromatography on Merck $PF_{254-366}$ silica gel (thickness 1.5 mm; eluent 60:40 benzene–n-pentane). The 1-benzoyl-2,4,5-triphenylimidazole, sparingly soluble in the aqueous layer and in diethyl ether, was separated by filtration. Ammonium salts appeared to be present in the aqueous layer of each examined reaction; its quantitative determination was carried out by alkaline distillation and titration. The 1-butene was collected by a slow stream of nitrogen into a trap cooled at −80° and then treated with a 20% carbon tetrachloride solution of bromine. The 1,2-dibromobutane was then recovered by distillation in the fraction boiling at 58–60° (20 Torr). All products have been identified by comparison with authentic samples on the basis of ir spectra and boiling or melting data. For 1,2-dibromobutane the comparison was also done on the basis of glpc behavior on a 2-m column of polypropylene glycol.

The results of the reactions are summarized in Table I.

Reaction of the Mixture of 3,4-Diphenyl-1,2,5-thiadiazole and 3,4-Diphenyl-1,2,5-selenadiazole with Methylmagnesium Iodide. A mixture of 3,4-diphenyl-1,2,5-thiadiazole (0.70 mmol) and 3,4-diphenyl-1,2,5-selenadiazole (0.70 mmol) in 55 ml of ether, allowed to react 1 hr at 28° with 14 mmol of methylmagnesium iodide in 14 ml of ether, was hydrolyzed by quenching with 1 N hydrochloric acid under vigorous stirring and refrigeration. From the reaction mixture 88.5% of the unreacted 3,4-diphenyl-1,2,5-thiadiazole was recovered while no traces of unreacted 3,4-diphenyl-1,2,5-selenadiazole were detected by tlc. The reaction repeated with the same quantities of thia- and selenadiazole derivatives in 100 ml of ether and with 3.50 mmol of methylmagnesium iodide in 20 ml of ether, at −70° for 6 sec yielded the whole of the unreacted 3,4-diphenyl-1,2,5-thiadiazole and no traces of unreacted 3,4-diphenyl-1,2,5-selenadiazole were detected by tlc.

Acknowledgment. This work was supported by C. N. R., Roma, Italy.

Registry No—Methyl iodide, 74-88-4; butyl bromide, 109-65-9; methyllithium, 917-54-4; ethyl bromide, 74-96-4; butyllithium, 109-72-8.

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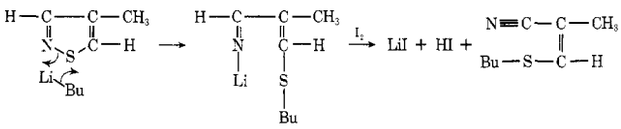

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Reductive Cleavage of Phosphinanilides with Lithium Aluminum Hydride

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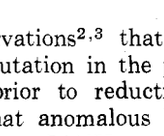
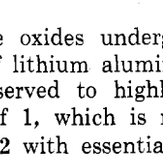
Observations[2,3] that phosphine oxides undergo rapid stereomutation in the presence of lithium aluminum hydride prior to reduction have served to highlight the somewhat anomalous behavior of **1**, which is reported[4] to undergo $LiAlH_4$ reduction to **2** with essentially complete retention of configuration at phosphorus. The behavior of **1** seems even more unusual with our finding that the principal reactions of phosphinanilides **3** and **4** with $LiAlH_4$ produce P–N bond cleavage rather than deoxygenation.



1, X = O
2, X = lone pair



3, R = H
4, R = CH_3

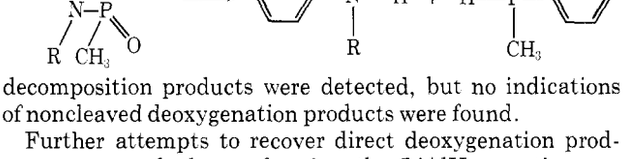
The reduction of optically active **1** to **2** with $LiAlH_4$ afforded the first reported example of a compound whose optical activity could be attributed to a pyramidally stable tervalent phosphorus.[5] Although retention of configuration during the reaction was originally ascribed to the possible formation of an iminophosphorane intermediate which resembles an organophosphorus ylide and might be expected to yield optically active phosphine with retention of configuration,[6] more recent studies[2] have suggested that the lack of stereomutation of **1** probably reflects the presence of barriers to pseudorotation of an intermediately formed phosphorane. Tertiary phosphine oxides are reduced by $LiAlH_4$ with retention of configuration, but yield phosphines of low optical purity owing to the rapid stereomutation of the phosphine oxides. Restraints imposed by the azaphosphorus ring system, the neighboring NH group, or the neighboring nitrogen atom could account for the observed stereochemistry at phosphorus of **1**.

We decided to investigate the reactions of optically active methylphenylphosphinanilide (**3**)[7] and its *N*-methyl derivative (**4**) with $LiAlH_4$, since these compounds provided for a systematic elimination of the alternatives suggested above. Azaphosphorus ring restraints are absent in **3**, and **4** lacks a proton on nitrogen.

The phosphinanilides were synthesized by treating diastereomerically enriched menthyl methylphenylphosphinate[8] with lithium reagents of aniline[9] and *N*-methylaniline, respectively. Both reactions proceeded smoothly, but **4** presented some problems in isolation and purification. It is hygroscopic, crystallizes with some difficulty, and is slightly light sensitive.

Stereomutation probes were performed initially by allowing mixtures of the respective phosphinanilides and $LiAlH_4$ (mole ratios of 2:1) in tetrahydrofuran to stand at room temperature for varying periods of time. Although both **3** and **4** could be recovered[10] without losses in their stereochemical integrities, they differed markedly in their chemical stabilities. Compound **4** is extremely reactive at room temperature, but higher temperatures and increased quantities of $LiAlH_4$ are required to promote a significant reactivity of **3**.

In contrast to expectations based on the reported behavior of **1**, nmr analysis of the reaction mixtures from **3** and **4** demonstrated that the phosphinanilides were undergoing P–N bond cleavage instead of deoxygenation. Aniline and *N*-methylaniline, respectively, could be readily identified and isolated. By comparisons with samples[11] of methylphenylphosphine[12] and methylphenylphosphine oxide,[13] the presence of these organophosphorus cleavage products could be discerned by nmr. They could be isolated in some cases.[14] Small quantities of other unidentified



decomposition products were detected, but no indications of noncleaved deoxygenation products were found.

Further attempts to recover direct deoxygenation products were made by performing the $LiAlH_4$ reactions on larger scales using racemic **3** and **4**. However, again only reaction products reflecting P–N bond cleavage could be discerned. In those cases where starting compounds were recovered, it seems highly unlikely that they resulted from a reoxygenation of reduction products during the reaction work-ups. Extreme care was exercised to minimize exposure of the reaction mixtures to air, and the presence of the easily oxidizable methylphenylphosphine could be ascertained. Also, more vigorous reaction conditions led to complete cleavage of the phosphinanilides.

The increased reactivity of **4** compared to **3** is consistent with the well-known cleavage of carboxylic amides with $LiAlH_4$,[15] but is in reverse to the relative rates of alkaline hydrolysis of phosphinamides.[16] This observation suggests