The Structure of the Diazonium Coupling Products of Phenacyl Thiocyanate and Phenacyl Selenocyanate with Diazotized 3-Phenyl-5-Aminopyrazole

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The reaction of diazotized 3-phenyl-5-aminopyrazole with phenacyl thiocyanate **1a** and phenacyl selenocyanate **1b** afforded directly 2-imino-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-2,3-dihydro-1,3,4-thiadiazole monohydrate **9a** and 2-imino-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-2,3-dihydro-1,3,4-selenadiazole monohydrate **9b**, respectively. The products **9a** and **9b** were also obtained from the reaction of *C*-benzoyl-*N*-(3-phenyl-5-pyrazolyl)formohydrazidoyl bromide **10** with potassium thiocyanate and potassium selenocyanate, respectively. Acetylation, benzoylation, and nitrosation of **9** afforded the corresponding diacetyl, dibenzoyl, and nitroso derivatives **11-13**, respectively. Cyclization of *C*-benzoyl-*N*-(3-phenyl-5-pyrazolyl)-nitrilimine **6** was shown to give the pyrazolo [5,1-*d*]triazole **8** and not the pyrazolo[5,1-*c*]-*as*-triazine derivative **7**, as previously reported.

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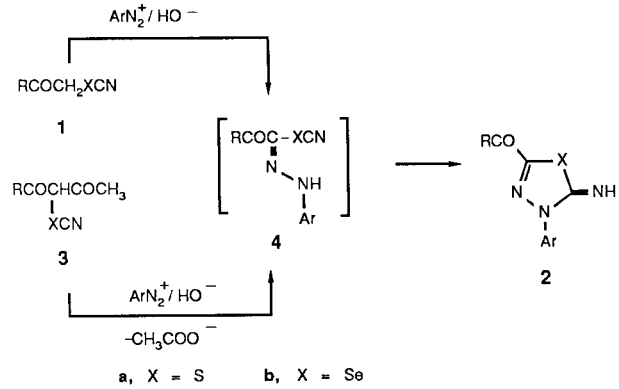
Introduction.

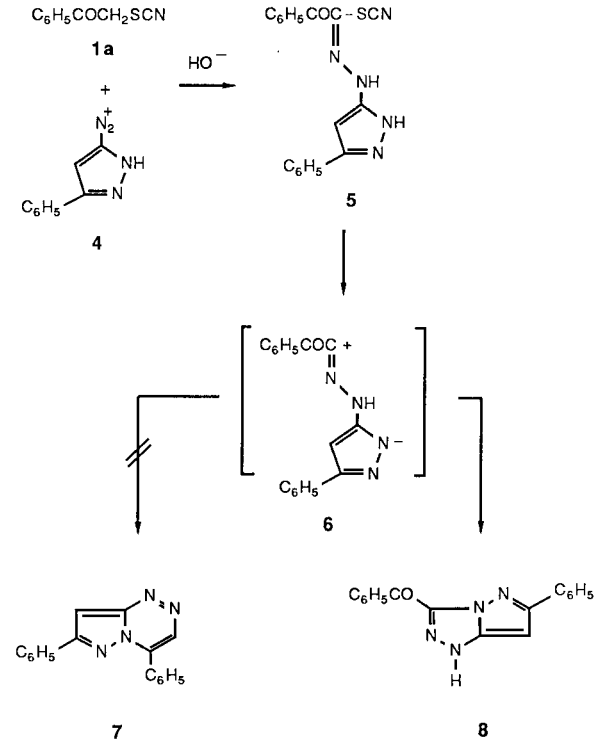
Active methylene thiocyanates **1a** and selenocyanates **1b** were reported from our laboratory and others [2-5] to undergo coupling with aromatic diazonium salts and yield the corresponding 2-imino-2,3-dihydro-1,3,4-thiadiazoles **2a** and 2-imino-2,3-dihydro-1,3,4-selenadiazoles **2b**, respectively (Scheme 1). Similarly, the reaction of active methine thiocyanates **3a** and selenocyanates **3b** with diazotized arylamines led to one-step synthesis of **2a** and **2b** respectively (Scheme 1) [6-9]. In all cases, the acyclic hydrazone intermediate **4** seems to undergo cyclization as it is formed.

Scheme 1



Diazotized 3-phenyl-5-aminopyrazole was claimed to react with phenacyl thiocyanate **1a** to give the acyclic hydrazone **5**, although its infrared spectrum does not reveal an absorption band due to a free thiocyanato group [10] (Scheme 2). Furthermore, it was reported by the same authors [10] that treatment of **5** with concentrated sulfuric acid yields a product which, on the basis of its elemental analysis only, was assigned the structure of the pyrazolo-[5,1-*c*]-*as*-triazine derivative **7** (Scheme 2). The formation

Scheme 2



of **7** from **5** was assumed to result from initial elimination of thiocyanic acid leading to the formation of the nitrilimine intermediate **6**, which cyclizes then to afford **7** [10]. As the cyclization of **6** is expected to give **8** and not **7**, by analogy to the behaviour of other nitrilimines with *N*-heterocyclic moieties [11,12], it was thought necessary to re-examine the structures of the products from the diazonium coupling reaction of **1a** with diazotized 3-phenyl-5-aminopyrazole, and the cyclization of **6**.

We now wish to report the results of the study of the reactions of 3-phenyl-5-pyrazolediazonium chloride with **1a** and its selenium analog **1b**, and the alternate synthesis of the products of these reactions from *C*-benzoyl-*N*-(3-phenyl-5-pyrazolyl)formohydrazidoyl bromide **10** and potassium thiocyanate and selenocyanate respectively. Also, the generation of **6** from **10** and its cyclization to **8** are outlined (Scheme 3).

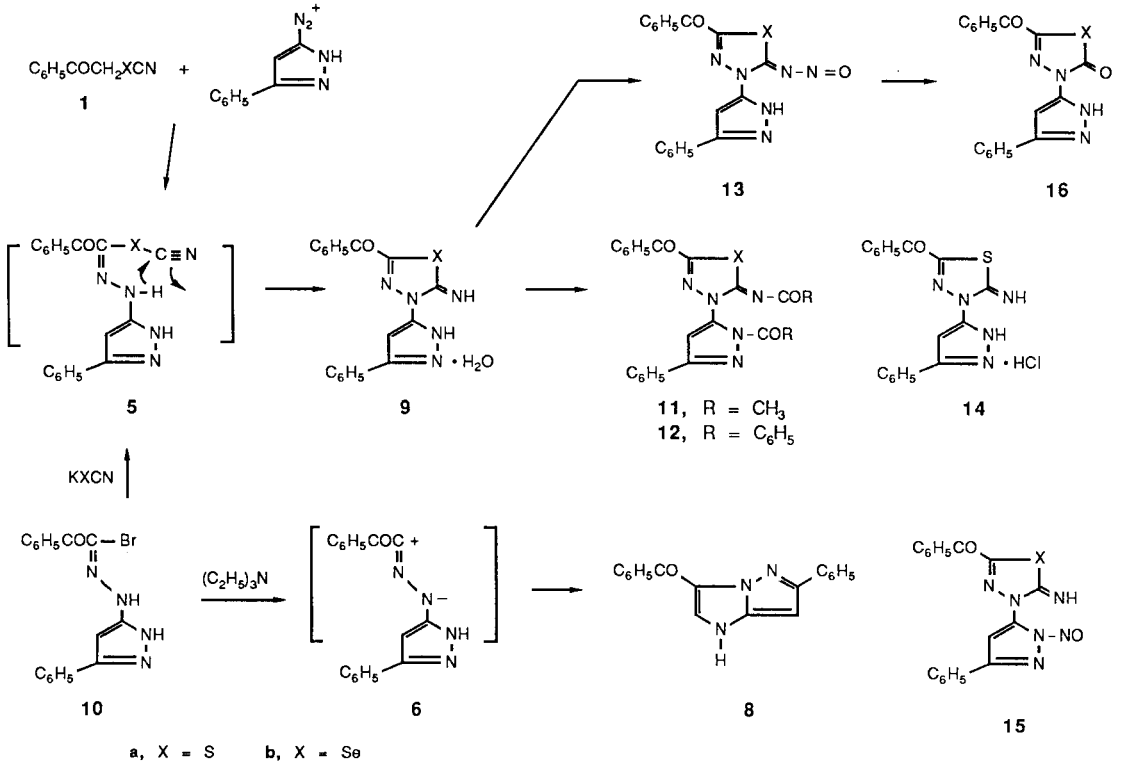
Results and Discussion.

The treatment of phenacyl thiocyanate **1a** with diazotized 3-phenyl-5-aminopyrazole in ethanol in the presence of sodium acetate gave a product which analyzed correctly for $C_{18}H_{15}N_5O_2S$. Its infrared spectrum showed no band in the region 2125-2200 cm^{-1} assignable to a free thiocyanato group, thus excluding the possibility of the acyclic structure **5a**. The spectrum revealed, however, NH absorption bands at 3250 and 3320 cm^{-1} and an OH band near 3450 cm^{-1}. The appearance of the latter absorption together with the elemental analysis data indicate that the product isolated was the monohydrate of 2-imino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole **9a**. Treatment of the latter in ether with hydrogen chloride gas yielded the corresponding hydrochloride salt **14** which analyzed correctly for $C_{18}H_{14}ClN_5OS$. The structure of **9a** was further confirmed by its alternate synthesis from the reaction of the hydrazidoyl bromide **10** and potassium thiocyanate at room temperature. The chemical reactions of **9a** outlined in Scheme 3 are also consistent with its assigned structure.

Phenacyl selenocyanate **1b** reacted similarly with diazotized 3-phenyl-5-aminopyrazole in ethanol in the presence of sodium acetate and gave 2-imino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-selenadiazole monohydrate **9b**. The structure of the latter was elucidated on the basis of its spectra, elemental analytical data, alternate synthesis from the hydrazidoyl bromide **10** and potassium selenocyanate, and by its chemical reactions shown in Scheme 3 (see Experimental).

The reflux of **9a** and **9b** in acetic anhydride afforded the corresponding diacetyl derivatives **11a** and **11b**, respectively. The infrared spectra of **11** showed in each case no NH absorption, but exhibited three carbonyl bands near 1645, 1630 and 1750 cm^{-1}. In their pmr spectra, each of **11a** and **11b** exhibited two singlets assignable

Scheme 3



to the resonances of the protons of the two acetyl groups near δ 2.35 and 2.45 ppm. These spectral data together with the satisfactory elemental analyses are consistent with the assigned structures of **11a** and **11b**.

Reaction of **9a** and **9b** in acetic acid with sodium nitrite gave the reddish products **13a** and **13b** respectively. The structures of the latter, which were formulated as *N*-nitrosoimines rather than *N*-nitrosopyrazoles **15**, were deduced from their electronic and infrared spectra. Thus, if the nitrosation products had structure **15**, the nitroso group would not be in conjugation with the C=N group, and the color of the products would be expected to be more like that of most nitroso derivatives of pyrazoles. The electronic absorption spectra of **13** in ethanol showed, however, two maxima in the 500-470 (log e > 2) and 340-360 (log e > 4) nm regions. These bands are assigned to the n-π^* and π-π^* transitions of the nitrosoimino group. Further support for structure **13** comes from a comparison of the infrared spectra of **9** and **13**. Thus, while the infrared spectrum of **9** showed two bands at 3320 and 3250 cm^{-1} assignable to the imino NH and pyrazole NH groups respectively, the spectra of **13** revealed only the pyrazole NH band at 3200 cm^{-1}. The shift of this band to lower frequency probably results from intramolecular hydrogen bonding between the nitroso and pyrazole NH groups. The formation of **13** is also consistent with the fact that electrophilic attack on systems having both imino and pyrazole NH groups occurs preferentially on the imino nitrogen [13]. The reflux of **13a** in xylene afforded the corresponding 2-oxo-2,3-dihydro-1,3,4-thiadiazole derivative **16a** (Scheme 3).

Next to confirm that the cyclization of the nitrilimine intermediate of type **6** would yield the pyrazolo[5,1-*d*]triazole derivative **8** and not the pyrazolo[5,1-*c*]-*as*-triazine derivative **7**, we investigated the base catalyzed dehydrobromination of the hydrazidoyl bromide **10**. Thus treatment of **10** with triethylamine in benzene gave **8** in almost quantitative yield (Scheme 3). The structure of **8** followed from its elemental analysis and spectral data. The infrared spectrum of **8** showed bands near 1640 and 3200 cm^{-1} assignable to benzoyl and NH groups respectively. Similar cyclizations of hydrazidoyl halides with *N*-heterocyclic moities have been reported [11,12]. It is worthy to mention that, in our hands, compound **9a** was recovered unchanged after being treated with concentrated sulfuric acid at room temperature for three days.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra (potassium bromide) were recorded on a Unicam SP1000 infrared spectrophotometer. Ultraviolet spectra (ethanol) were recorded using a Unicam SP8000 spectrophotometer. The nmr spectra (deuterated chloroform) were recorded with a T60-A spectrometer using tetramethylsilane as internal reference. Phenacyl thiocyanate (**1a**) [14] and phenacyl selenocyanate (**1b** [15] and 3-phenyl-5-aminopyrazole [16] were prepared as previously described.

C-Benzoyl-*N*-(3-phenyl-5-pyrazolyl)formohydrazidoyl bromide (**10**).

To a stirred cold solution of phenacyldimethylsulfonium bromide [17] (1.3 g, 0.005 mole) in ethanol (40 ml) was added an equivalent amount (0.005 mole) of 3-phenyl-5-pyrazolediazonium chloride [16] portionwise over a period of 30 minutes. After stirring the reaction mixture for further 2 hours, the solid that precipitated was filtered and washed with water. Crystallization from ethanol gave the pure hydrazidoyl bromide **10** in 72% yield, mp 128°; ir: ν NH 3200, ν CO 1685 cm^{-1}; pmr: δ 9.8 (s, 1H), 7.3-8.2 ppm (m, 12H).

Anal. Calcd. for $C_{17}H_{13}BrN_4O$: C, 55.30; H, 3.55; N, 15.17. Found: C, 55.22; H, 3.79; N, 15.22.

3-Benzoyl-6-phenyl-1*H*-pyrazolo[5,1-*d*]triazole (**8**).

To a solution of **10** (0.005 mole) in dry benzene (30 ml) was added triethylamine (0.7 ml, 0.005 mole) and the mixture was refluxed for 2 hours, then cooled. The precipitated triethylammonium hydrobromide was filtered and the filtrate was evaporated under vacuum. The crude residue solidified upon trituration with petroleum ether (40/60°). The crude solid was collected and crystallized from ethanol to give **8** in 78% yield, mp 165°; ir: ν NH 3200, ν CO 1640 cm^{-1}; pmr: δ 7.3-8.2 ppm (m).

Anal. Calcd. for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.19; N, 19.43. Found: C, 70.39; H, 4.49; N, 19.71.

General Procedure of the Reaction of Phenacyl Thiocyanate (**1a**) and Phenacyl Selenocyanate (**1b**) with 3-Phenyl-5-pyrazolediazonium Chloride.

A cold solution of the appropriate phenacyl ester **1** (0.005 mole) and sodium acetate trihydrate (1.3 g, 0.005 mole) in ethanol (30 ml) was treated while stirring with an equimolar amount of 3-phenyl-5-pyrazolediazonium chloride [16] and left in the ice bath for 4 hours. The solid that precipitated was collected and washed with water. Crystallization from aqueous ethanol gave the corresponding **9**.

2-Imino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole Monohydrate (**9a**).

This compound was obtained in 60% yield, mp 179°; ir: ν OH 3450, ν NH 3250, 3320, ν CO 1650 cm^{-1}; pmr: δ 3.0 (s, 2H, H_2O), 6.85 (s, 1H, pyrazole H-4), 7.3-8.0 (m, 10H, ArH), 8.2 (s, 1H, NH), 8.3 (s, 1H, NH) ppm.

Anal. Calcd. for $C_{18}H_{15}N_5O_2S$: C, 59.16; H, 4.13; N, 19.16. Found: C, 59.28; H, 3.93; N, 19.25.

2-Imino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-selenadiazole Monohydrate (**9b**).

This compound was obtained in 54% yield, mp 165°; ir: νOH 3430, ν NH 3240, 3310, ν CO 1650 cm^{-1}; pmr: δ 3.2 (broad s, 2H, H_2O), 7.3 (s, 1H, pyrazole H-4), 7.4-7.9 (m, 10H, ArH), 8.5 (s, 1H, NH), 8.6 (s, 1H, NH) ppm.

Anal. Calcd. for $C_{18}H_{15}N_5O_2Se$: C, 52.43; H, 3.66; N, 16.98. Found: C, 51.92; H, 3.28; N, 16.48.

General Procedure for the Reaction of **C**-Benzoyl-*N*-(3-phenyl-5-pyrazolyl)formohydrazidoyl Bromide (**10**) with Potassium Thiocyanate and Potassium Selenocyanate.

To a suspension of **10** (0.005 mole) in ethanol (30 ml), was added potassium thiocyanate (0.005 mole) and the mixture was stirred for 24 hours at room temperature. During this period, compound **10** dissolved and the crude **9a** precipitated. The latter was collected and washed with water. Crystallization from aqueous ethanol gave pure **9a** in 75%, mp 179°, not depressed when mixed with a sample of **9a** prepared above from **1a** and 3-phenyl-5-pyrazolediazonium chloride.

Reaction of equimolar amounts of **10** and potassium selenocyanate following the same procedure gave the product **9b** in 70% yield, identical in all respects (mp, mixture mp, and spectra) with that obtained from coupling of phenacyl selenocyanate **1b** and 3-phenyl-5-pyrazolediazonium chloride.

2-Imino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole Hydrochloride (**14**).

Hydrogen chloride was bubbled for one hour into a suspension of **9a** (0.5 g, 0.001 mole) in dry ether. The solid was then filtered and crystallized from dioxane to give **14** in 85% yield.

Anal. Calcd. for $C_{18}H_{14}ClN_5OS$: C, 56.32; H, 3.67; N, 18.24. Found: C, 55.93; H, 3.48; N, 17.95.

Acetylation of Thiadiazole and Selenadiazole Derivatives **9a,b**.

A solution of the appropriate **9** (0.005 mole) in acetic anhydride (25 ml) was refluxed for 1 hour. The excess solvent was then distilled and the residue was triturated with cold water. The crude solid that formed was collected and crystallized from acetic acid to give the corresponding diacetyl derivative **11**.

2-Acetylimino-2,3-dihydro-3-(1-acetyl-3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole (**11a**).

This compound was obtained 90% yield, mp 214°; ir: ν CO 1750, 1645, 1630 cm^{-1}; pmr: δ 2.30 (s, 3H), 2.43 (s, 3H), 7.3-8.4 ppm (m, 11H).

Anal. Calcd. for $C_{22}H_{17}N_5O_3S$: C, 61.23; H, 3.97; N, 16.23. Found: C, 60.87; H, 3.77; N, 15.88.

2-Acetylimino-2,3-dihydro-3-(1-acetyl-3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-selenadiazole (**11b**).

This compound was obtained in 88% yield, mp 240°; ir: ν CO 1745, 1640, 1630 cm^{-1}; pmr: δ 2.32 (s, 3H), 2.41 (s, 3H), 7.2-8.3 ppm (m, 11H).

Anal. Calcd. for $C_{22}H_{17}N_5O_3Se$: C, 55.23; H, 3.58; N, 14.64. Found: C, 55.04; H, 3.40; H, 15.03.

Nitrosation of Thiadiazole and Selenadiazole Derivatives **9a,b**.

To a stirred cold solution of the appropriate **9** (0.005 mole) in acetic acid (20 ml) was added an ice-cold solution of sodium nitrite (0.7 g in 10 ml water) dropwise over a period of 20 minutes. The mixture was then left in a refrigerator for 6 hours. The colored solid that precipitated was filtered, washed with water and crystallized from aqueous ethanol to give the nitroso derivative **13**.

2-Nitrosoimino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole (**13a**).

This compound was obtained in 77% yield, mp 150° dec; ir: ν NH 3200, ν CO 1640 cm^{-1}; uv: λ max (log e) 442 (1.7), 348 (4.1), 256 nm (4.49); pmr: δ 7.3-8.2 ppm (m).

Anal. Calcd. for $C_{18}H_{12}N_6O_2S$: C, 57.43; H, 3.21; N, 22.32. Found: C, 57.64; H, 3.21; N, 21.94.

2-Nitrosoimino-2,3-dihydro-3-(3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-selenadiazole (**13b**).

This compound was obtained in 70% yield, mp 172° dec; ir: ν NH 3200, ν CO 1645 cm^{-1}; uv: λ max (log e) 445 (1.5), 345 (4.3), 260 (4.8) nm; pmr: δ 7.2-8.3 ppm (m).

Anal. Calcd. for $C_{18}H_{12}N_6O_2Se$: C, 51.07; H, 2.85; N, 19.85. Found: C, 50.70; H, 2.88; N, 19.95.

2,3-Dihydro-2-oxo-5-benzoyl-3-(3-phenyl-5-pyrazolyl)-1,3,4-thiadiazole (**16a**).

The nitrosoimine derivative **13a** (0.44 g, 0.005 mole) was refluxed in dry xylene (20 ml) for 1 hour. The solvent was then distilled under vacuum and the residue was triturated with petroleum ether (40/60°). The solid product was filtered and crystallized from ethanol to give **16a** in 85% yield, mp 230°; ir: ν NH 3200, ν CO 1700, 1645 cm^{-1}; pmr: δ 7.3-8.2 ppm (m).

Anal. Calcd. for $C_{18}H_{12}N_4O_2S$: 62.05; H, 3.47; N, 16.08. Found: C, 61.55; H, 3.47; N, 16.27.

Benzoylation of Thiadiazole and Selenadiazole Derivatives **9a,b**.

A mixture of the appropriate **9** (0.001 mole) and benzoyl chloride (0.001 mole) in pyridine (15 ml) was refluxed for 15 minutes. The reaction mixture was then poured into ice cold hydrochloric acid solution. The solid that precipitated was filtered, washed with dilute hydrochloric acid and then with water. Crystallization from ethanol gave the corresponding dibenzoyl derivative **12**.

2-Benzoylimino-2,3-dihydro-3-(1-benzoyl-3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-thiadiazole (**12a**).

This compound was obtained in 89% yield, mp 175°; ir: ν CO 1645, 1665, 1670 cm^{-1}; pmr: δ 7.3-8.2 ppm (m).

Anal. Calcd. for $C_{32}H_{21}N_5O_3S$: C, 69.17; H, 3.80; N, 12.60. Found: C, 68.16; H, 3.57; N, 12.26.

2-Benzoylimino-2,3-dihydro-3-(1-benzoyl-3-phenyl-5-pyrazolyl)-5-benzoyl-1,3,4-selenadiazole (**12b**).

This compound was obtained in 80% yield, mp 193°; ir: ν CO 1650, 1660, 1665 cm^{-1}; pmr: δ 7.2-8.3 ppm (m).

Anal. Calcd. for $C_{32}H_{21}N_5O_3Se$: C, 63.80; H, 3.51; N, 11.63. Found: C, 63.32; H, 3.50; N, 11.54.

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