Regioselectivity in Dipolar Cycloaddition Reactions of *N*-Phenylcinnamonitrilimine

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The regioselectivity of the cycloadditions of α,β-unsaturated nitrilimine derived from *N*-phenylcinnamohydrazidoyl chloride **2** to C=Se, C=S and C=C double bonds of the resonance stabilized selenocyanate and thiocyanate anions, enol tautomer of dibenzoylmethane and benzalacetophenone was investigated. The results indicate that the reactions studied are dipole-LUMO-dipolarophile-HOMO controlled and that the larger orbital coefficient in the LUMO of *N*-phenylcinnamonitrilimine is on the carbon atom bearing the styryl group. The structures of the cycloadducts were assigned and confirmed on the basis of their elemental analyses and spectra.

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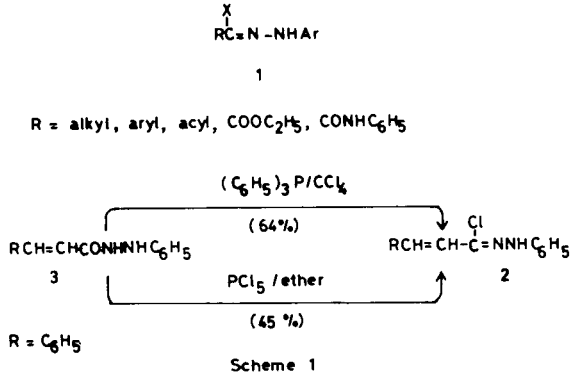
Introduction.

In continuation of our previous studies [2-5] directed towards exploring the synthetic potentialities of hydrazidoyl halides **1**, we have now prepared *N*-phenylcinnamohydrazidoyl chloride **2** and investigated its 1,3-dipolar cycloaddition as well as nucleophilic substitution reactions. The chemistry of **2** has not been explored until recently. Our interest in the study of **2** is to evaluate the effect of extending conjugation of the cationic center of nitrilimine with C=C double bond on the regioselectivity in the cycloaddition reactions. Furthermore, the *N*-phenylcinnamonitrilimine is expected to lead to the synthesis of functional heterocyclic compounds that may have synthetic utility in the preparation of other heterocyclic systems.

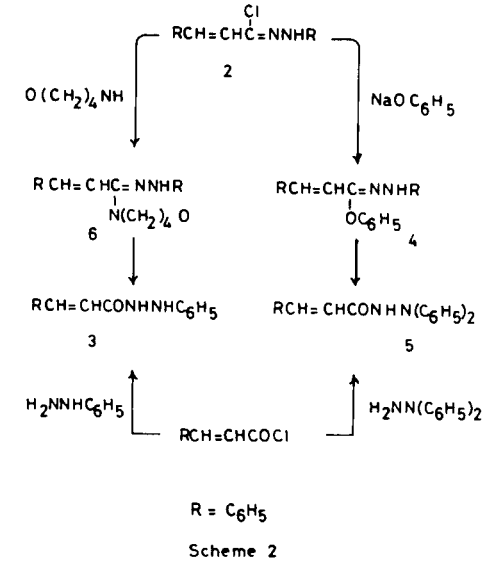
Results and Discussion.

The work of Appel and co-workers [6,7] in transforming secondary amides into the corresponding imidoyl halides by the use of triphenylphosphine-carbon tetrachloride system was extended to the preparation of the hydrazidoyl chloride **2**. Thus addition of carbon tetrachloride to a stirred suspension of the hydrazide **3** and triphenylphosphine in acetonitrile and workup of the reaction mixture gave **2** in 64% yield. The product from this reaction was identical in all respects with an authentic sample prepared from **3** and phosphorus pentachloride [8] (Scheme 1).



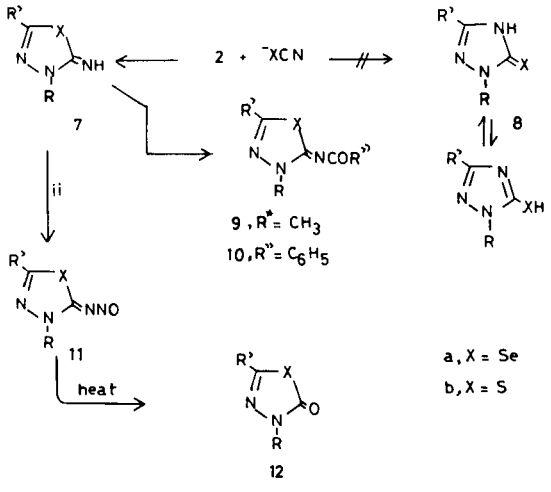
Scheme 1

Compound **2** was found to be readily attacked by nucleophilic reagents. Thus, when equivalent amounts of **2** and sodium phenolate in ethanol were stirred at room temperature, one product, identified as the hydrazonate ester **4** was obtained. The latter ester rearranged smoothly into the hydrazide **5** when heated in xylene. The structure of **5** was confirmed by its alternate synthesis from cinnamoyl chloride and *N,N*-diphenylhydrazine (Scheme 2). Morpholinolysis of **2** in ethanol gave the amidrazone **6** which was found to undergo hydrolytic cleavage in acetic acid to give the hydrazide **3**. The identity of **3** was established by its alternate synthesis from cinnamoyl chloride and phenylhydrazine.



Scheme 2

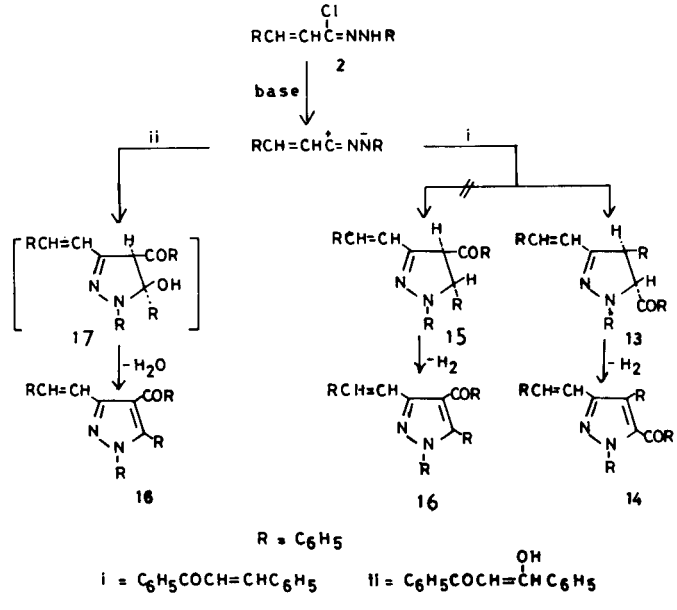
Treatment of **2** with selenocyanate and thiocyanate anions in aqueous ethanol yielded the selenadiazoline and thiadiazoline derivatives **7a** and **7b**, respectively. The structures of these products were deduced from their spectra and elemental analyses together with their chemical reactions summarized in Scheme 3. Thus, the infrared



Scheme 3

spectra of **7a,b** revealed the absence of absorption bands in the region 2000-2250 cm^{-1} due to free SeCN and SCN group [9]. However, they showed an imino NH band near 3345 cm^{-1}. The exclusive formation of **7** can be rationalized in terms of the frontier orbital treatment as follows. As the thiocyanate (or selenocyanate) anion is electron rich dipolarophile, its reaction with *N*-phenylcinnamonitrilimine is expected to be controlled by the dipole-LUMO dipolarophile-HOMO interaction. Furthermore, as the biggest HOMO coefficient of XCN has been shown to be on the X-arom [10,11], the formation of **7** indicates that the larger orbital coefficient in the *N*-phenylcinnamonitrilimine LUMO is at the carbon atom bearing the styryl group. This conclusion is substantiated by the results obtained from the reaction of **2** with benzalacetophenone and the enolate anion of dibenzoylmethane outlined below.

The product obtained from the reaction of **2** and benzalacetophenone in benzene in the presence of triethylamine was identified as 5-benzoyl-3-styryl-1,4-diphenyl-Δ^2-pyrazoline **13** (Scheme 4). The other regioisomer **15** was not identified in the reaction mixture as evidenced by tlc analysis. The structure of **13** was elucidated from its spectra and elemental analysis (Experimental). Oxidation of **13** by chloranil yielded the pyrazole derivative **14**.



Scheme 4

The reaction of **2** with dibenzoylmethane in ethanol in the presence of sodium ethoxide at room temperature yielded the pyrazole derivative **16**, probably through the intermediacy of the pyrazoline derivative **17** which seems to lose water as it is formed [2,12,13]. These results indicate that the regioselectivity; in the cycloaddition reactions of *N*-phenylcinnamonitrilimine is similar to that of diphenylnitrilimine [12-14].

Thus, by analogy to diphenylnitrilimine, the cycloadditions of *N*-phenylcinnamonitrilimine to benzalacetophenone and the enolate anion of dibenzoylmethane are dipole HOMO and dipolarophile-HOMO controlled respectively. Recent calculations of frontier molecular orbital energies and coefficients of benzalacetophenone [14] and enol tautomer of dibenzoylmethane [15] show that the orbital coefficient of the carbon atom carrying the benzoyl group in the LUMO of benzalacetophenone is smaller than that of the carbon carrying the phenyl group, whereas the reverse is true in the HOMO of dibenzoylmethane enol tautomer. Obviously such differences would lead to opposite regiochemical results in agreement with experiment. Furthermore, the exclusive formation of **13** and **16** in the reactions of *N*-phenylcinnamonitrilimine with benzalacetophenone and dibenzoylmethane enol tautomer respectively substantiates the foregoing conclusion that the larger orbital coefficient in the LUMO of the studied nitrilimine is on the carbon atom bearing the styryl residue.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra (potassium bromide disc) were recorded on Perkin Elmer 257 spectrophotometer and the

electronic absorption spectra were obtained in ethanol using Beckman DK2 spectrophotometer. The pmr spectra in deuterated chloroform were recorded on a Varian T 60-A spectrometer using tetramethylsilane as the internal reference. Elemental analyses were performed by Galbraith Laboratory, Knoxville, Tennessee, USA.

N-Phenylcinnamohydrazidoyl Chloride **2**.

Carbon tetrachloride (1.95 ml, 20 mmoles) was added to a stirred suspension of *N*-phenyl-*N'*-cinnamoylhydrazine **3** (4.24 g, 20 mmoles) and triphenylphosphine (6.55 g, 25 mmoles) in acetonitrile (40 ml), dried by passage through an alumina column and introduced directly from the column into the reaction flask. After 5 hours water (20 ml) was added. The crude product was collected and washed with water. Crystallization from acetic acid gave compound **2** in 65% yield, mp 151° (lit mp 150-151°) [8].

Phenyl *N*-Phenylcinnamohydrazonate **4** and Amidrazone **6**.

General Procedure.

Equimolecular quantities (0.005 mole each) of **4** and sodium phenoxide (or morpholine) in ethanol (50 ml) were stirred for 3 hours at room temperature and the mixture was left overnight. The solid that precipitated was collected, washed with water and crystallized from ethanol.

Compound **4** had mp 162°; ir (potassium bromide): cm^{-1} 1250, 1050; uv (ethanol): λ max (log ε) 380 (4.45) nm.

Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.22; H, 5.70; N, 8.98.

Compound **6** had mp 172°.

Anal. Calcd. for $C_{19}H_{21}N_3O$: C, 74.23; H, 6.89; N, 13.67. Found: C, 72.11; H, 6.79; N, 13.55.

Thermolysis of **4**.

The hydrazonate ester **4** (0.5 g) was refluxed in xylene (15 ml) for 5 hours. The pale yellow solid that separated upon cooling (0.51 g) was collected and crystallized from methanol. The hydrazide **5** had mp 132°; ir (potassium bromide): cm^{-1} 3250 (NH), 1660 (CO), 1620 (C=C), 1590 (C=N); the mixture mp of this product with an authentic sample prepared from *N,N*-diphenylhydrazine and cinnamoyl chloride in pyridine was 132°.

Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.16; H, 5.72; N, 8.92.

Hydrolysis of the Amidrazone **6**.

A solution of amidrazone **6** (0.75 g) in 90% acetic acid (20 ml) was refluxed for 30 minutes, left to cool and diluted with water. The solid that separated was collected and crystallized from dilute acetic acid. The hydrazide **3** was obtained in 70% yield, mp 190° (lit mp 191°) [16]; mixed mp of this product with an authentic sample of **3** prepared from phenylhydrazine and cinnamoyl chloride showed no depression.

Selena- and Thiadiazoline Derivatives **7a,b**.

General Procedure.

Potassium selenocyanate (0.28 g, 0.002 mole) or potassium thiocyanate (0.19 g, 0.002 mole) in ethanol was added to a warm solution of **2** (0.25 g, 0.001 mole) in the same solvent (50 ml). The mixture was refluxed for 15 minutes and then cooled. The crude product was collected, washed with water and finally crystallized from ethanol. Compound **7a** was obtained in 85% yield, mp 115°; ir (potassium bromide): cm^{-1} 3225 (NH), 1610 (C=N); uv (ethanol): λ max (log ε) 335 (4.55), 260 (4.33) nm.

Anal. Calcd. for $C_{16}H_{13}N_3Se$: C, 58.89; H, 4.02; N, 12.88. Found: C, 58.72; H, 4.10; N, 12.88.

Compound **7b** had mp 116° and was obtained in 80% yield; ir (potassium bromide): cm^{-1} 3220 (NH), 1607 (C=N); uv (ethanol): λ max (log ε) 342 (4.32), 277 (4.22), nm.

Anal. Calcd. for $C_{16}H_{13}N_3S$: C, 68.80; H, 4.64; N, 15.04. Found: C, 68.77; H, 4.61; N, 15.03.

Acetylation of **7a,b**.

This was effected by refluxing **7a** (or **7b**) (0.7 g) in excess acetic anhydride (20 ml) and the mixture was poured on crushed ice with stirring. The crude product was collected, washed with water and then crystallized from acetic acid.

Compound **9a** had mp 155°; ir (potassium bromide): cm^{-1} 1630 (CO); uv (ethanol): λ max (log ε) 355 (4.55), 260 (4.33); pmr (deuteriochloroform): δ ppm 2.45 (s, 3H, CH_3CO), 6.5 (d, 1H, J = 9 Hz, $CH=CHC_6H_5$), 7.3-8.3 (m, 11H, ArH and $CH=CHC_6H_5$).

Anal. Calcd. for $C_{18}H_{15}N_3OSe$: C, 58.69; H, 4.10; N, 11.41. Found: C, 58.55; H, 4.21; N, 11.33.

Compound **9b** had mp 145°; ir (potassium bromide): cm^{-1} 1630 (CO), 1610, (C=C); uv (ethanol): λ max (log ε) 340 (4.48), 290 (4.44), 230 (4.31) nm; pmr (deuteriochloroform): δ ppm 2.45 (s, 3H, CH_3CO), 6.45 (d, 1H, J = 9 Hz, $-CH=CHC_6H_5$), 7.2-8.3 (m, 11H, ArH, $-CH=CHC_6H_5$).

Anal. Calcd. for $C_{18}H_{15}N_3OS$: C, 67.28; H, 4.70; N, 13.08. Found: C, 67.22; H, 4.61; N, 13.10.

Benzoylation of **7a,b**.

This was effected by refluxing equimolecular quantities of **7** and benzoyl chloride (0.005 mole each) in pyridine (30 ml) for 1 hour. Upon cooling and pouring the reaction mixture on ice, the crude benzoyl derivative precipitated. It was collected and crystallized from acetic acid.

Compound **10a** had mp 180°; ir (potassium bromide): cm^{-1} 1625, 1610; uv (ethanol): λ max (log ε) 350 (4.61), 305 (4.46) 250 (4.35) nm.

Anal. Calcd. for $C_{23}H_{17}N_3OSe$: C, 64.18; H, 3.98; N, 9.76. Found: C, 64.20; H, 3.87; N, 9.86.

Compound **10b** had mp 165°; ir (potassium bromide): cm^{-1} 1625, 1605; uv (ethanol): λ max (log ε) 350 (4.61), 303 (4.48), 257 (4.47) nm.

Anal. Calcd. for $C_{23}H_{17}N_3OS$: C, 72.05; H, 4.47; N, 10.96. Found: C, 72.00; H, 4.41; N, 10.90.

Nitrosation of **7a,b**.

A solution of **7a** (or **7b**) (0.001 mole) in acetic acid (10 ml) was treated with sodium nitrite solution (0.4 g, 0.002 mole) in water (2 ml) while stirring. The reddish product, which precipitated was collected and crystallized from acetic acid.

Compound **11a** had mp 155°; uv (ethanol): λ max (log ε) 480 (1.92), 365 (4.42), 240 (4.22) nm.

Anal. Calcd. for $C_{16}H_{12}N_4OSe$: C, 54.08; H, 3.40; N, 15.77. Found: C, 54.21; H, 3.41; N, 15.71.

Compound **11b** had mp 140°; uv (ethanol): λ max (log ε) 420 (2.01), 365 (4.32), 303 (4.40), 230 (4.25) nm.

Anal. Calcd. for $C_{16}H_{12}N_4OS$: C, 62.33; H, 3.92; N, 18.16. Found: C, 62.25; H, 3.88; N, 18.12.

Thermolysis of **11a,b**

A solution of the appropriate nitroso derivative **11** (0.5 g) in xylene (20 ml) was refluxed for 20 minutes. The solvent was then evaporated and the residue was triturated with petroleum ether (40/60°). The solid formed was collected and crystallized from methanol.

Compound **12a** had mp 135°; ir (potassium bromide): cm^{-1} 1680; uv (ethanol): λ max (log ε) 325 (4.41), 230 (4.32) nm.

Anal. Calcd. for $C_{16}H_{12}N_2OSe$: C, 58.71; H, 3.70; N, 8.56. Found: C, 58.66; H, 3.65; N, 8.58.

Compound **12b** had mp 126°; ir (potassium bromide): cm^{-1} 1685; uv (ethanol): λ max (log ε) 320 (4.58), 268 (4.21), 230 (4.23) nm.

Anal. Calcd. for $C_{16}H_{12}N_2OS$: C, 68.55; H, 4.31; N, 9.99. Found: C, 68.51; H, 4.32; N, 9.97.

Reaction of **2** with Benzalacetophenone.

To a mixture of two equivalent amounts of **2** and benzalacetophenone (0.005 mole each) in benzene (30 ml), triethylamine (0.005 mole) was added. The reaction mixture was refluxed for 4 hours and triethylamine hydrochloride that precipitated was filtered. The excess solvent was distilled off and the residue was triturated with petroleum ether (40/60°). The solid formed was collected, washed with water and finally crystallized from acetic acid. Thin layer chromatographic analysis of the pro-

duct obtained using silica gel as adsorbent and benzene as eluent indicated the presence of one component which was identified as the pyrazoline derivative **13**. Compound **13** had mp 192°; ir (potassium bromide): cm^{-1} 1690, 1620; uv (ethanol): λ max (log ε) 372 (4.38), 254 (4.37) nm; pmr (deuteriochloroform): δ ppm 4.5 (d, 1H, J = 6 Hz, -CH-CHC_6H_5), 5.6 (d, 1H, J = 6 Hz, -CH-$CHCOC_6H_5$), 6.8-8.0 (m, 21H, ArH, CH-CHC_6H_5).

Anal. Calcd. for $C_{30}H_{24}N_2O$: C, 84.08; H, 5.64; N, 6.54. Found: C, 84.01; H, 5.50; N, 6.41.

Dehydrogenation of **13**.

To a solution of **13** (0.003 mole) in dry xylene (30 ml) chloranil (0.004 mole) was added and the reaction mixture was refluxed for 64 hours. The mixture was cooled and then extracted with sodium hydroxide solution (5%) three times and then dried over anhydrous sodium sulfate. The solvent was distilled off and the residue was triturated with petroleum ether (40/60°). The crude solid was collected and crystallization from methanol gave **14** in 55% yield.

Compound **14** had mp 146°; pmr (deuteriochloroform): δ ppm 6.6 (d, 1H, J = 9 Hz, -CH = CHC_6H_5), 7.1-7.9 (m, 21H, ArH and -CH = CHC_6H_5).

Anal. Calcd. for $C_{30}H_{22}N_2O$: C, 84.48; H, 5.20; N, 6.57. Found: C, 84.62; H, 5.18; N, 6.49.

1,5-Diphenyl-3-styryl-4-benzoylpyrazole **16**.

To an ethanolic solution of sodium ethoxide (prepared from sodium (0.1 g, 0.005 g-atom) and absolute ethanol (20 ml) was added dibenzoylmethane (1.1 g, 0.005 mole) with stirring. To the resulting solution, compound **2** (0.005 mole) was added and the mixture was stirred for 4 hours during which the chloride **2** dissolved and the crude pyrazole precipitated. The latter was collected and crystallized from methanol to give 80% yield of **16a**.

Compound **16a** had mp 177°; ir (potassium bromide): cm^{-1} 1635 (CO); uv (ethanol): λ max (log ε) 350-275 (4.48), 257 (4.49) nm; pmr (deuteriochloroform): ppm 6.55 (d, 1H, J = 9 Hz, -CH = CHC_6H_5), 7.1-7.8 (m, 21H, ArH and -CH = CHC_6H_5).

Anal. Calcd. for $C_{30}H_{22}N_2O$: C, 84.48; H, 5.20; N, 6.57. Found: C, 84.50; H, 5.19; N, 6.62.

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