Monatshefte für Chemie 138, 771–776 (2007)
DOI 10.1007/s00706-007-0665-7
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Waste-Free Solid-State Organic Syntheses: Solvent-Free Alkylation, Heterocyclization, and Azo-Coupling Reactions

Ehab Abdel-Latif* and **Mohamed A. Metwally**

Department of Chemistry, Faculty of Science, Mansoura University, Mansoura, Egypt

Received January 15, 2007; accepted (revised) February 12, 2007; published online May 23, 2007

Summary. Solid-state techniques allow for waste-free quantitative syntheses. The solid–solid reactions of α-haloketones with several pyrazolones and with thiosemicarbazones were shown to afford the corresponding pyrazolyl ethers and 4-substituted 2-(arylidenehydrazino)thiazoles. The product yields are quantitative in all cases and the products do not require purifying workup. Therefore, these reactions are truly solvent-free, sustainable, and no wastes are produced. A diazonium nitrate is quantitatively accessible by gas–solid reaction of the corresponding amine with NO_2 gas. It is a useful material for environmental synthesis of azo dyes through solid-state coupling with a variety of coupling compounds, as *e.g.* β-naphthol, acetoacetanilide, pyrazolones, and barbituric acid.

Keywords. Environmentally benign; Ball-milling; Thiazole; Solid-state reactions; Gas–solid diazotization.

Introduction

Waste-free environmentally benign solid-state reactions mean 100% yield of one product without any necessity for purifying workup by recrystallization, chromatography, *etc*. Organic solid-state reactions in the gas–solid and stoichiometric solid–solid versions are highly promising new tools for solvent-free sustainable synthesis. More than thousand waste-free quantitative syntheses in organic solid-state chemistry are already known and have been reported in a review article that covers more than 25 reaction types [1]. These include solvent-free salt formations, complexations, condensations of amines, heterocyclic syntheses, *Knoevenagel* condensations, cascade reactions, halogen additions, stereo- and regiospecific protective reactions, and redox reactions. All of these may be of technical importance. Some of these involve now easily obtainable products that cannot be produced by solution reactions.

The solid-state mechanism, which involves phase rebuilding, phase transformation, and crystal disintegration, has been elucidated by atomic force microscopy (AFM), scanning near-field optical microscopy (SNOM), and grazing incidence diffraction (GID) for very different situations and has been comprehensively described [2].

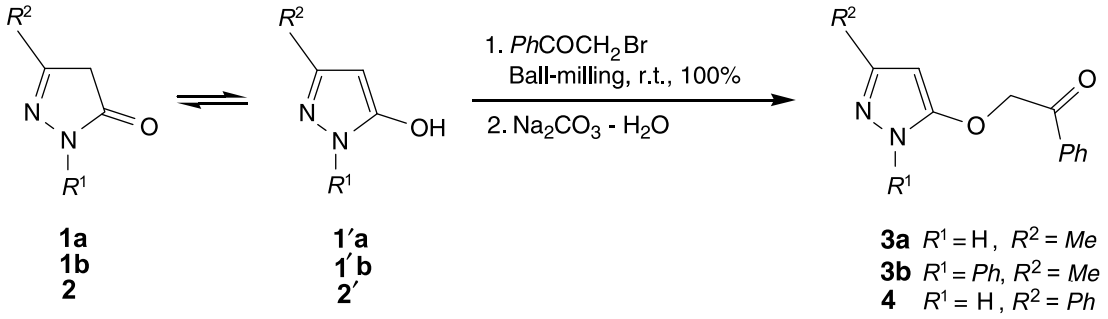
Results and Discussion

We report here on various examples of quantitative solid–solid and gas–solid reactions that proceed with unsurmounted efficiency, much better than in solutions or melts. For example, solid–solid reactions of α-haloketones with several pyrazolones (O-alkylation), with thiosemicarbazone derivatives (heterocyclization), and solid-state azo-coupling reactions of the diazonium nitrate derived from a 2-(2-aminophenylthio)nicotinonitrile derivative with a variety of diazocoupling components. While no mechanical treatment is required in most gas–solid reactions, solid–solid reactions require cogrinding, ultrasound treatment, or most easily reactive milling.

*Solid-State Synthesis of Pyrazolyl Ethers **3** and **4***

The quantitative solid-state synthesis of the pyrazolyl ethers **3** and **4** was achieved by ball-milling an equi-

* Corresponding author. E-mail: ehabattia00@gmx.net



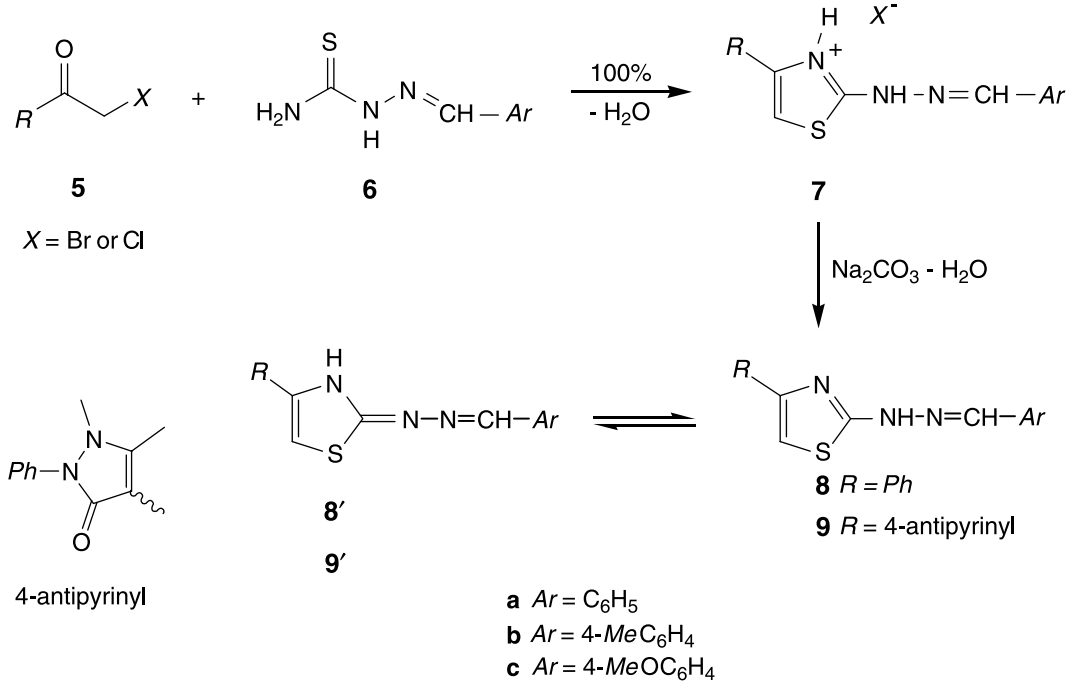
Scheme 1

molar ratio of pyrazolone derivatives **1** and **2** with phenacyl bromide. It is unnecessary to use base catalysis, solvents, or liquid phases and the highly versatile ether products **3** and **4** were obtained with 100% yield at room temperature after washing with sodium carbonate solution (Scheme 1). The reactivity of phenacyl bromide towards O-alkylation in **3** and **4** can be accounted for by the contribution of tautomers **1′** and **2′**. The formation of **3** and **4** finds support from their correct analytical and spectral data.

Pyrazoles and 4,5-dihydropyrazoles are important biological agents with a wide range of pharmaceutical (anti-inflammatory, antifungal, antibacterial, antitumor, and antiviral) and agrochemical activities [3, 4]. Thus, our waste-free access to pyrazolyl ethers may be of pharmacological importance.

*Solid-State Synthesis of 4-substituted 2-(Arylidenehydrazino)thiazoles **8** and **9***

The technique of waste-free solid-state reaction could be applied to prepare the 4-substituted 2-(arylidenehydrazino)thiazoles **8** and **9**. Stoichiometric runs by ball-milling of α-haloketones **5** with the arylidenethiosemicarbazone derivatives **6** afforded the corresponding iminium salts **7** with 100% yield without the aid of basic catalysts and solvents. The water of the reaction can be removed by evapora-



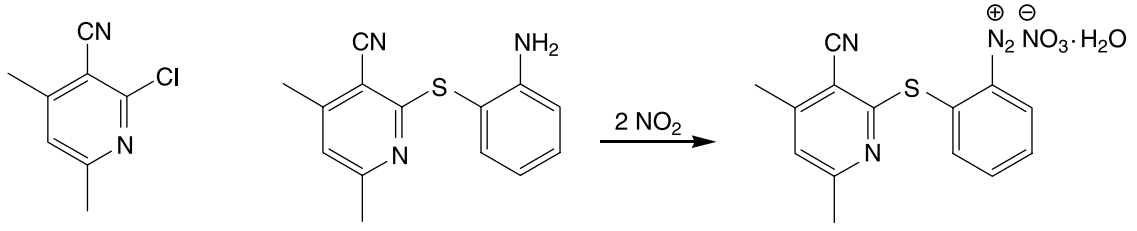
Scheme 2

tion at 80°C in vacuum without loss by hydrolysis. Washings with aqueous Na_2CO_3 can easily liberate the free bases **8** and **9** (Scheme 2). All of the isolated products **8** and **9** gave satisfactory elemental analyses and spectroscopic data (IR, ^{1}H NMR, and MS) consistent with their assigned structures.

The ball-milling reaction of phenacyl bromide to produce the corresponding 2-(arylidenehydrazino)-4-phenylthiazoles **8** proceeds more easily at room temperature while the corresponding reaction of 4-(chloroacetyl)antipyrine requires ball-milling at higher temperatures (50°C) for a quantitative yield.

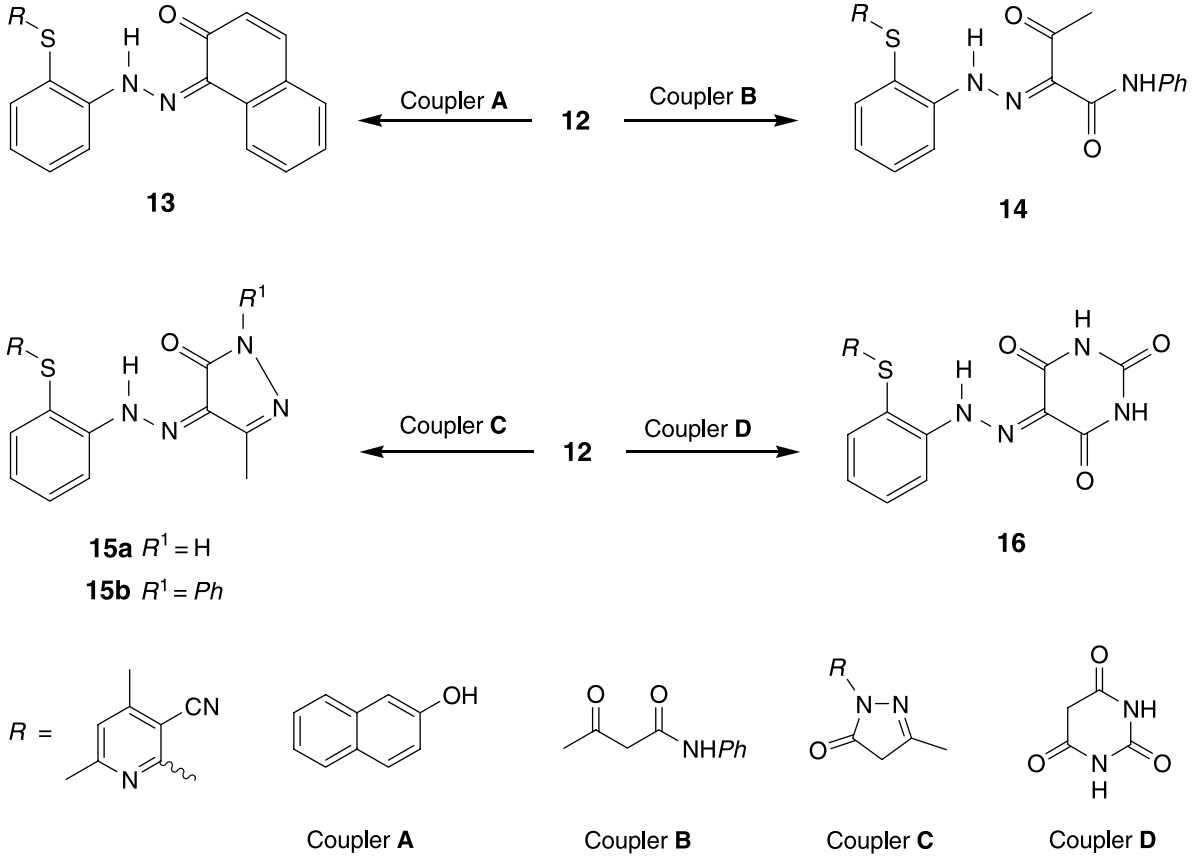
Semiempirical PM3 calculations predict the azine structure **8′** to be 14.4 kJ mol^{-1} more stable than the hydrazone structure **8**. However, DFT calculations (*B3LYP*/6-31G*) predict the unsubstituted hydrazone lower in energy by 20.5 kJ mol^{-1}.

Large numbers of thiazole derivatives have emerged as active pharmaceutical ingredients in several drugs for their potential anti-inflammatory [5],



10 **11** **12**

Scheme 3



Scheme 4

anti-tumour [6], anti-hyperlipidemic [7], and several other biological properties [8, 9].

Solid-State Azo-Coupling Reactions Using a Variety of Coupler Components

2-Chloro-4,6-dimethylnicotinonitrile (**10**) was reacted with *o*-aminothiophenol in ethanol to afford 2-(2-aminophenylthio)-4,6-dimethylnicotinonitrile (**11**). The diazotization of **11** with gaseous NO_2 gave quantitatively the monohydrate of the diazonium nitrate **12**. The solid compound **12** can be safely handled at room temperature, but it explodes upon melting and should not be exposed to mechanical shock or ball-milled or ground at sharp edges for safety reasons.

Azo couplings were achieved with quantitative yields by cautious co-grinding of the solid diazonium salt **12** with different classes of azo coupling components. The azo coupling with β-naphthol (coupler **A**) is preparatively useful and the azo dye **13** is obtained in quantitative yield after neutralization (Scheme 4).

The azo-couplings with active methylene components either an acyclic component, *e.g.* acetoacetanilide (coupler **B**), or cyclic components, *e.g.* 5-methylpyrazol-3-ones (coupler **C**) and barbituric acid (coupler **D**) furnished the corresponding azo dyes **14**, **15**, and **16**, respectively. The azo dyes were quantitatively obtained by the action of gaseous trimethylamine and washings with water. The constitution of the compounds was secured by their IR, NMR, and MS spectra.

Experimental

Melting points were determined with a Gallenkamp melting point apparatus (capillary method). Elemental analyses were carried out at the Microanalytical Unit of the Faculty of Science, Cairo University; the results were in satisfactory agreement with the calculated values. IR spectra (KBr) were recorded with a Matteson 5000 FTIR spectrometer (not all frequencies are reported). The ^1H and ^{13}C NMR spectra were acquired using a Bruker WP 300 spectrometer at 300 MHz (^1H) or 75.5 MHz (^{13}C) in broad band mode. Mass spectra were obtained at a Finnigan MAT 212 instrument by electron impact at 70 eV. The ball-mill was a Retsch MM 2000 swing mill with a 10 cm^3 stainless steel, double-walled beaker with fittings for circulating coolants. Two stainless steel balls of 12 mm diameter were used. Ball-milling was performed at 20225 Hz frequency, usually at room temperature (without circulating liquid the temperature did not rise above 30°C). Water or methanol of the appropriate temperature was circulated for heating or cooling.

*Solid-State Synthesis of the Pyrazolyl Ethers **3** and **4***

A mixture of 2.00 mmol **1** or **2** and 398 mg phenacyl bromide (2.00 mmol) was ball-milled at room temperature for 1 h. The solid powders were washed with 5% Na_2CO_3 solution, followed by H_2O, and drying at 0.01 bar at 80°C in vacuum to liberate the free ethers **3** and **4**.

(5-Methyl-2H-pyrazol-3-yl) (2-oxa-2-phenylethyl) ether (**3a**, $C_{12}H_{12}N_2O_2$)

Yield 100%; mp 187–188°C; IR (KBr): $\bar{\nu} = 3216$ (NH), 1694 (C=O), 1615 (C=N) cm^{-1}; ^1H NMR ($CDCl_3/CF_3COOD$): $\delta = 2.40$ (s, CH_3), 4.50 (s, CH_2), 5.75 (s, C=CH), 7.50–8.00 (m, Ar′H) ppm; ^{13}C NMR ($CDCl_3/CF_3COOD$): $\delta = 11.66$, 30.24, 92.39, 129.13 (2C), 129.37 (2C), 133.46, 135.04, 147.36, 157.10, 195.03 ppm.

(5-Methyl-2-phenyl-2H-pyrazol-3-yl) (2-oxa-2-phenylethyl) ether (**3b**, $C_{18}H_{16}N_2O_2$)

Yield 100%; mp 211–212°C; IR (KBr): $\bar{\nu} = 1687$ (C=O), 1609 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.20$ (s, CH_3), 4.45 (s, CH_2), 5.90 (s, C=CH), 7.10–8.00 (m, Ar′H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 16.95$, 43.06, 92.34, 118.87 (2C), 125.01, 128.82 (2C), 128.89 (2C), 129.85 (2C), 133.90, 138.03, 147.11, 156.22, 170.54, 191.25 ppm.

(5-Phenyl-2,5-dihydro-1H-pyrazol-3-yl) (2-oxa-2-phenylethyl) ether (**4**, $C_{17}H_{16}N_2O_2$)

Yield 100%; mp 167–168°C; IR (KBr): $\bar{\nu} = 3417$ (NH), 3270 (NH), 1688 (C=O) cm^{-1}; ^1H NMR ($CDCl_3/CF_3COOD$): $\delta = 3.25$ (d, CH), 4.50 (s, CH_2), 5.50 (d, C=CH), 7.35–8.00 (m, Ar′H) ppm.

*Solid-State Preparation of 2-(Arylidenehydrazino)-4-phenylthiazoles **8***

A mixture of 398 mg phenacyl bromide (2.00 mmol) and 2.00 mmol **6** was ball-milled at room temperature for 1 h. After drying at 0.01 bar at 80°C quantitative yields of the hydrobromide salts **7** were obtained. The free bases **8** were obtained by washing the fine powder of the hydrobromide with 5% Na_2CO_3 solution, followed by water, and drying at 80°C in vacuum.

2-(Benzylidenehydrazino)-4-phenylthiazole (**8a**, $C_{16}H_{13}N_3S$)

Yield 100%; mp 192–193°C (Ref. [10] 191–192°C; IR (KBr): $\bar{\nu} = 3270$ (NH), 1620 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 7.15$ (s, thiazole H-5), 7.30–8.00 (m, Ar′H), 8.35 (s, N=CH), 10.25 (s, NH) ppm; MS: m/z (%) = 279 (65), 202 (92), 188 (20), 172 (15), 121 (20), 104 (24), 83 (30), 77 (40), 56 (100).

2-(p-Methylbenzylidenehydrazino)-4-phenylthiazole (**8b**, $C_{17}H_{15}N_3S$)

Yield 100%; mp 203–204°C (Ref. [11] 202–205°C; IR (KBr): $\bar{\nu} = 3295$ (NH), 1631 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 2.40$ (s, CH_3), 7.25–7.90 (m, Ar′H and thiazole H-5), 8.25 (s, N=CH), 9.70 (s, NH) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 19.33$, 101.93, 124.08 (2C), 124.92

(2C), 126.42, 126.77 (2C), 127.52 (2C), 129.32, 130.44, 137.91, 143.12, 144.72, 166.80 ppm.

2-(p-Methoxybenzylidenehydrazino)-4-phenylthiazole (**8c**, $C_{17}H_{15}N_3OS$)
Yield 100%; mp 210–212°C (Ref. [11] 213–217°C; IR (KBr): $\bar{\nu} = 3279$ (NH), 1626 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$/CF_3COOD): $\delta = 3.90$ (s, OCH_3), 7.20–7.90 (m, Ar′H and thiazole H-5), 8.30 (s, N=CH) ppm.

Solid-State Preparation of 2-(Arylidenehydrazino)-4-antipyrinylthiazoles ***9***
A mixture of 529 mg 4-chloroacetylantipyrine (2.00 mmol) and 2.00 mmol **6** was ball-milled at 50°C for 1 h. After drying at 0.01 bar at 80°C quantitative yields of the hydrochloride salts **9** were obtained. The free bases **9** were obtained by washing the fine powder of the hydrochloride with 5% Na_2CO_3 solution, followed by H_2O, and drying at 80°C in vacuum.

2-(Benzylidenehydrazino)-4-antipyrinylthiazole (**9a**, $C_{21}H_{19}N_5OS$)
Yield 100%; mp 218–219°C; IR (KBr): $\bar{\nu} = 3437$ (NH), 1625 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.60$ (s, CH_3), 3.25 (s, CH_3), 6.90 (s, thiazole H-5), 7.20–7.70 (m, Ar′H), 8.30 (1H, s, N=CH), 9.50 (1H, s, NH) ppm; MS: m/z (%) = 389 (100), 286 (35), 243 (28), 103 (50), 77 (36), 56 (58).

2-(p-Methylbenzylidenehydrazino)-4-antipyrinylthiazole (**9b**, $C_{22}H_{21}N_5OS$)
Yield 100%; mp 228–229°C; IR (KBr): $\bar{\nu} = 3391$ (NH), 1609 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 2.40$ (s, CH_3), 2.65 (s, CH_3), 3.35 (s, CH_3), 7.10 (s, thiazole H-5), 7.25–7.70 (m, Ar′H), 8.35 (s, N=CH), 9.75 (s, NH) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 10.76$, 19.71, 33.11, 96.38, 99.51, 124.11 (2C), 125.68 (2C), 126.39, 127.72 (2C), 127.87 (2C), 128.98, 132.28, 133.58, 139.13, 146.47, 149.25, 161.06, 165.20 ppm.

2-(p-Methoxybenzylidenehydrazino)-4-antipyrinylthiazole (**9c**, $C_{22}H_{21}N_5O_2S$)
Yield 100%; mp 226–227°C; IR (KBr): $\bar{\nu} = 3398$ (NH), 1606 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$/CF_3COOD): $\delta = 2.50$ (s, CH_3), 3.40 (s, CH_3), 3.85 (s, OCH_3), 6.70 (s, thiazole H-5), 6.90–7.60 (m, Ar′H), 8.10 (s, N=CH) ppm.

2-(2-Aminophenylthio)-3-cyano-4,6-dimethylpyridine (**11**, $C_{14}H_{13}N_3S$)
A solution of 1.66 g 2-chloro-4,6-dimethylnicotinonitrile (**10**) (10.0 mmol), 1.25 g aminothiophenol (10.0 mmol), and 1.38 g anhydrous K_2CO_3 in 50 cm^3 ethanol was heated under reflux for 2 h. The precipitate which formed on cooling was filtered off, washed with H_2O, dried, and recrystallized from ethanol. Yield 88%; mp 163–164°C; IR (KBr): $\bar{\nu} = 3411$ and 3309 (NH_2), 2212 (C≡N), 1620 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.35$ (s, CH_3), 2.45 (s, CH_3), 4.45 (s, NH_2), 6.75–7.45 (m, Ar′H and pyridine H-5) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.18$, 24.76, 105.90, 112.47, 115.17, 115.66, 118.59, 120.98, 131.48, 137.76, 149.61, 152.23, 161.34, 161.86 ppm; MS: m/z (%) = 255 (88), 222 (100), 136 (24), 80 (28).

2-(4,6-Dimethyl-3-cyano-2-pyridinylthio)benzenediazonium nitrate hydrate (**12**)
Compound **11** (510 mg, 2.00 mmol) was evacuated in a 250 cm^3 flask and then exposed to 360 mg NO_2 (7.8 mmol) at 0.7 bar for 6 h at room temperature with occasional careful shaking. The excess gas was recovered from a trap at 77 K. Yield 100%; mp 106–107°C; IR (KBr): $\bar{\nu} = 2292$ (N≡N), 2218 (C≡N) cm^{-1}; ^1H NMR (CF_3COOD): $\delta = 2.90$ (s, CH_3), 3.00 (s, CH_3), 7.90 (s, pyridine H-5), 8.20–8.95 (m, Ar′H) ppm; ^{13}C NMR (CF_3COOD): $\delta = 20.87$, 20.98, 109.61, 112.01, 115.29, 119.83, 129.78, 134.42, 135.89, 138.85, 143.81, 152.29, 163.01, 163.72 ppm.

Solid-State Azo-Coupling of ***12*** *with β-Naphthol*

Naphthalene-1,2-dione 1-[2-(4′,6′-dimethyl-3′-cyano-2′-pyridinylthio)phenyl]hydrazone (**13**, $C_{24}H_{18}N_4OS$)
β-Naphthol (coupler **A**, 288 mg, 2.00 mmol) was ground in an agate mortar, and 694 mg **12** (3.00 mmol) were added and co-ground in five portions for 10 min each. Most of the diazonium band at $\bar{\nu} = 2292\ cm^{-1}$ disappeared, but the completion of the reaction was achieved by 24 h ultrasound application in a test tube. The solid product was neutralized with 20 cm^3 0.5 *N* NaOH, washed with H_2O, and dried. Yield 100%; mp 157–158°C; IR (KBr): $\bar{\nu} = 2215$ (C≡N), 1619 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.20$ (s, CH_3), 2.40 (s, CH_3), 6.60–8.45 (m, Ar′H and pyridine H-5), 16.00 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.21$, 24.57, 105.66, 115.06, 116.92, 119.38, 121.06, 121.91, 125.77, 126.16, 126.41, 128.16, 128.66, 128.98, 130.75, 131.32, 133.61, 137.14, 140.87, 146.70, 152.23, 160.24, 161.76, 175.17 ppm; MS: m/z (%) = 410 (24), 279 (100), 254 (45), 239 (84), 115 (56).

Solid-State Azo-Coupling of ***12*** *with Acetoacetanilide, Pyrazolones, and Barbituric Acid*
Acetoacetanilide (coupler **B**), 5-methylpyrazol-3-ones (coupler **C**), or barbituric acid (coupler **D**) (2.00 mmol) and the solid diazonium salt **12** (2.00 mmol) were cautiously co-ground in an agate mortar for 5 min. The mixture was transferred to a 100 cm^3 flask, which was then evacuated. The mixture was exposed to $(CH_3)_3N$ (0.5 bar) for 12 h at room temperature. After condensation of the gas into a remote trap at 77 K, the trimethylammonium nitrate was washed away with 20 cm^3 H_2O, and the residual solid was dried.

2-[(4′,6′-Dimethyl-3′-cyano-2′-pyridinylthio)-2-phenylhydrazono]-3-oxo-N-phenylbutanamide (**14**, $C_{24}H_{21}N_5O_2S$)
Yield 100%; mp 204–205°C; IR (KBr): $\bar{\nu} = 3429$ (NH), 2220 (C≡N), 1667 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.20$

(s, CH_3), 2.40 (s, CH_3), 2.55 (s, CH_3), 6.75 (s, pyridine H-5), 7.00–7.90 (m, Ar′H), 11.25 (s, NH), 14.90 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.08$, 24.57, 26.07, 105.80, 114.98, 115.63, 117.05, 120.36 (2C), 121.07, 124.39, 125.11, 127.30, 128.83 (2C), 131.39, 137.26, 137.37, 144.25, 152.18, 159.97, 161.77, 162.01, 199.54 ppm; MS: m/z (%) = 443 (8), 400 (28), 324 (16), 281 (32), 254 (95), 239 (45), 222 (72), 93 (94), 77 (46), 43 (100).

4-[(4′,6′-Dimethyl-3′-cyano-2′-pyridinylthio)-2-phenylhydrazono]-5-methyl-2,4-dihydropyrazole-3-one
(**15a**, $C_{18}H_{16}N_6OS$)
Yield 100%; mp 208–209°C; IR (KBr): $\bar{\nu} = 3212$ (NH), 2218 (C≡N), 1663 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 2.20$ (s, CH_3), 2.25 (s, CH_3), 2.45 (s, CH_3), 6.90 (s, pyridine H-5), 7.10–7.90 (m, Ar′H), 10.90 (s, NH), 13.60 (s, NH) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 10.83$, 19.15, 23.62, 104.13, 113.99, 114.55, 114.69, 120.32, 123.99, 128.95, 130.75, 136.33, 143.33, 146.33, 151.24, 158.57, 159.47, 160.91 ppm; MS: m/z (%) = 364 (44), 254 (100), 239 (98), 233 (54), 222 (22), 78 (30), 63 (31).

4-[(4′,6′-Dimethyl-3′-cyano-2′-pyridinylthio)-2-phenylhydrazono]-5-methyl-2-phenyl-2,4-dihydropyrazole-3-one
(**15b**, $C_{24}H_{20}N_6OS$)
Yield 100%; mp 218–219°C; IR (KBr): $\bar{\nu} = 2217$ (C≡N), 1657 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$/CF_3COOD): $\delta = 2.30$ (s, CH_3), 2.70 (s, CH_3), 2.75 (s, CH_3), 7.40–8.15 (m, Ar′H and pyridine H-5) ppm; ^{13}C NMR ($CDCl_3$/CF_3COOD): $\delta =$ 10.44, 19.92, 21.55, 110.31, 111.39, 112.12, 118.36, 123.89 (2C), 127.01, 129.07, 129.72, 129.86, 129.98 (2C), 133.98, 135.74, 138.30, 143.59, 151.98, 156.65, 157.81, 159.24, 164.67 ppm; MS: m/z (%) = 440 (10), 309 (32), 254 (100), 239 (68), 222 (25), 93 (18), 77 (68).

5-[(4′,6′-Dimethyl-3′-cyano-2′-pyridinylthio)-2-phenylhydrazono]pyrimidine-2,4,6-(1H,3H,5H)-trione
(**16**, $C_{18}H_{14}N_6O_3S$)
Yield 100%; mp > 300°C; IR (KBr): $\bar{\nu} = 3377$ (NH), 2220 (C≡N), 1743 (C=O), 1702 (C=O), 1666 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 2.25$ (s, CH_3), 2.50 (s, CH_3), 6.90 (s, pyridine H-5), 7.25–8.00 (m, Ar′H), 11.30 (s, NH), 11.45 (s, NH), 14.70 (s, NH) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6): $\delta = 18.55$, 23.06, 103.28, 113.32, 115.27, 115.36, 116.94, 119.99, 125.00, 130.43, 135.89, 142.45, 148.18, 150.90, 157.66, 158.54, 160.47, 160.62 ppm; MS: m/z (%) = 394 (5), 254 (10), 239 (100), 222 (16), 49 (10), 44 (26).

References

[1] Kaupp G (2005) Top Curr Chem **254**: 95
[2] Kaupp G (2003) Cryst Eng Comm **5**: 117
[3] Azarifar D, Ghasemnejad H (2003) Molecules **8**: 642
[4] Elguero J (1996) In: Katritzky AR, Ress CW, Scriven EF (eds) Comprehensive Heterocyclic Chemistry II. Vol. 3. Pergamon press, Oxford, UK, p 70
[5] Miwatashi S, Arikawa Y, Kotani E, Miyamoto M, Naruo K-I, Kimura H, Tanaka T, Asahi S, Ohkawa S (2005) J Med Chem **48**: 5966
[6] El-Subbagh HI, Al-Obaid AM (1996) Eur J Med Chem **31**: 1017
[7] Pereira R, Gaudon C, Iglesias B, Germain P, Gronemeyer H, de Lera AR (2006) Bioorg Med Chem Lett **16**: 49
[8] Millan DS, Prager RH, Brand C, Hart PH (2000) Tetrahedron **56**: 811
[9] Wang W-L, Yao D-Y, Gu M, Fan M-Z, Li J-Y, Xing Y-C, Nan F-J (2005) Bioorg Med Chem Lett **15**: 5284
[10] Yamazaki C (1980) Bull Chem Soc Jpn **53**: 3289
[11] Maccioni E, Cardia MC, Distinto S, Bonsignore L, De Logu A (2003) Farmaco **58**: 951