

Quantitative Gas–Solid Reactions with ClCN and BrCN: Synthesis of Cyanamides, Cyanates, Thiocyanates, and Their Derivatives

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Abstract: Gas–solid reaction techniques allow quantitative cyanations with ClCN and BrCN. Three primary and four secondary cyanamides, a cyanimide, four cyanates, and four thiocyanates were all prepared as solids in 100 % yield from solid anilines, benzimidazoles, imides, phenolates, and thiolates, respectively. Intramolecular solid-state reactions of cyanated *o*-aminophenol and of cyanated hydrazides gave heterocyclic compounds. When comparable reactions were performed in sol-

ution the reported product yields were considerably less than 100 % in all cases. The reasons for the success of the environmentally benign solid-state syntheses are discussed in terms of phase rebuilding, phase transformation, and crystal disintegration. Atomic force mi-

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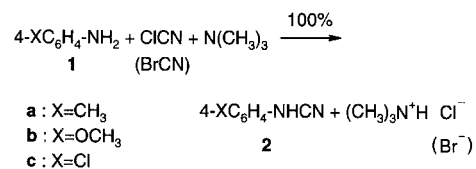
croscopy (AFM) of selected systems indicates the occurrence of long-range molecular movements which are governed by the crystal packing. This is evident from the obvious correlations between the molecular movements and the known crystal packing data. A new type of geometric surface feature, a rectangular and a rhombic depression which resembles a swimming-pool basin, was found in the cyanation of *o*-aminophenol and benzohydrazide.

Introduction

The title compounds are known as tumor inhibitors;^[1] they are also intermediates in the synthesis of herbicides,^[2] and are important precursors in the synthesis of *N*-alkyl or *N*-aryl imides.^[3] Their structural properties are well established. Although their syntheses are straightforward, they do not produce quantitative yields and require tedious purification procedures. This leads to a great expenditure of time, energy, and expensive materials, in addition to the production of large amounts of dangerous wastes. Thus, it appears expedient to utilize the now well-understood gas–solid reaction technique, which makes use of the crystal packing initially present in the substrate, to produce a 100 % yield in reactions with amines, hydrazides, imides, phenols, phenolates, and thiolates. We report on the quantitative synthesis of numerous cyanamides, cyanimides, cyanates, and thiocyanates, as well as on some of their reaction products.

Results

Cyanamides: Various types of cyanamides can be prepared by the interaction of gaseous cyanogen chloride or cyanogen bromide with crystalline primary or secondary amines and with imide salts. While all of our reactions with the NH bases may be performed without the aid of additional base, it is advisable to perform them in the presence of gaseous trimethylamine in order to bind the acid formed and to achieve the quantitative use of the reacting base (Scheme 1).



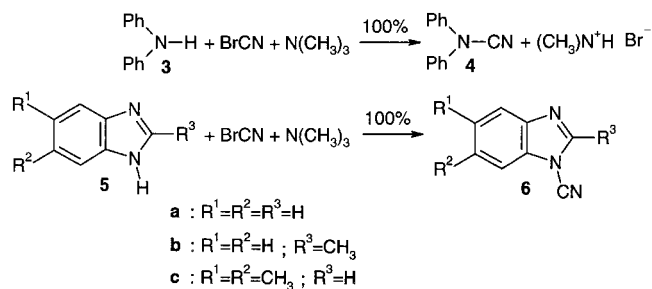
Scheme 1. Gas–solid synthesis of cyanamides from primary amines and ClCN or BrCN.

Control experiments showed that preformed solid hydrochlorides of **1** did not react with ClCN under our conditions. Thus, in the absence of a stronger base, only 1:1 mixtures of cyanamide and amine hydrohalogenide were formed. For technical reasons, a magnetic spin bar was rotated in the solid in order to mix in the gases, although overhead rotation of the flask is equally suitable.

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The cyanamides were formed quantitatively together with trimethylamine hydrohalogenide, which was then simply washed out with water. In larger runs, trimethylamine can be recovered from the aqueous washings by the use of known procedures. The reaction products remained solid. The corresponding yields of **2a–c** from reactions in solution were reported to be as low as 43 %, [4] 19 %, [5] and unspecified. [6]

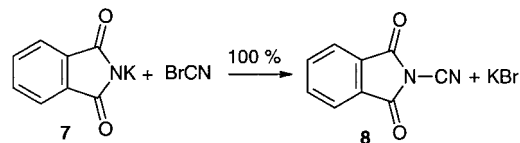
Even solid secondary aromatic amines, such as diphenylamine **3** or benzimidazoles **5**, reacted quantitatively with BrCN to give **4** and **6**, respectively (Scheme 2). Because the hydrochlorides of **5** proved to be unreactive, N(CH₃)₃ was employed again in order to make full use of the starting materials. The reaction products remained solid without intermediate melting.



Scheme 2. Gas–solid synthesis of cyanamides from secondary amines and BrCN.

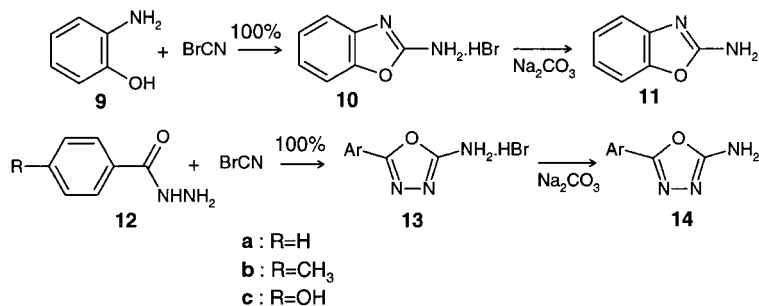
In contrast to our quantitative reactions, liquid-phase syntheses gave **4** in only 45 % yield (pressure reaction of the melt)^[2] or 54 % yield in solution,^[7] while syntheses of **6a,b** were reported to give yields of only 88 % (BrCN, benzene)^[8] or were unspecified.^[9] Thus, our gas–solid technique is clearly superior and should replace the earlier techniques inasmuch as it is performed more easily and more safely (poisonous gases) than the liquid-state reactions.

An extension of the reactions to succinimide and phthalimide (in the absence of a base) was not possible. However, finely powdered potassium phthalimide (**7**) reacted quantitatively with BrCN to give **8** and KBr (Scheme 3). The corresponding reaction in acetone solution in the presence of triethylamine afforded only a 77 % yield of **8**.^[10] Thus, the potential of **8** as a starting material for the synthesis of *N*-arylphthalimides^[3] has considerably increased.



Scheme 3. Synthesis of **8** from potassium phthalimide (**7**) and BrCN.

Cyanamides are susceptible to nucleophilic attack, which provides a possible route to the synthesis of heterocycles in the presence of suitable substituents. For example, the cyanation of solid *o*-aminophenol (**9**) with BrCN afforded quantitative yields of 2-aminobenzoxazole hydrobromide (**10**) in an intramolecular solid-state reaction: the hydroxy group added to the presumed intermediate cyanamide functionality (solid phenols do not react; see *Cyanates* below), and no additional base was necessary in this case (Scheme 4). The



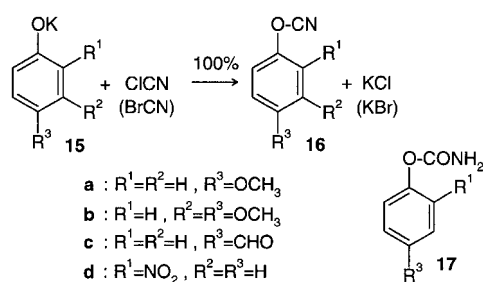
Scheme 4. Synthesis of heterocycles **11** and **14**.

Abstract in German: Gas/Festkörper-Reaktionstechniken ermöglichen quantitative Cyanierungen mit ClCN und BrCN. Drei primäre und vier sekundäre Cyanamide, ein Cyanimid, vier Cyanate und vier Thiocyanate werden aus Anilinen, Benzimidazolen, Imiden, Phenolaten und Thiolaten mit 100 % Ausbeute synthetisiert, wobei alle Edukte und Produkte Feststoffe sind. Intramolekulare Festkörperreaktionen von cyaniertem *o*-Aminophenol und von cyanierten Hydraziden liefern Heterocyklen. Wenn vergleichbare Reaktionen in Lösung durchgeführt werden, betragen die publizierten Ausbeuten in allen bekannten Fällen weit weniger als 100 %. Die Gründe für den Erfolg der umweltschonenden Festkörpersynthesen werden auf der experimentellen Grundlage von Phasenumbildung, Phasenumwandlung und Kristallzerfall diskutiert. Die Kristallpackung bestimmt die kraftmikroskopisch beobachteten, weitreichenden Molekülwanderungen. Diese korrelieren mit den bekannten Kristallpackungen. Bei der Cyanierung von *o*-Aminophenol und Benzhydrazid wird ein neuer Typ von Oberflächenstrukturen gefunden, deren geometrische Form kleinen Schwimmbecken ähnelt.

free base **11** was obtained quantitatively after washing **10** with Na₂CO₃ solution. Hitherto, **11** had only been obtained in solution with 82 % yield.^[11]

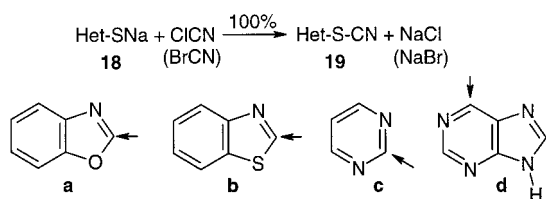
The gas–solid cyanations of the hydrazides **12** are equally clear. They most probably start at the primary amino group followed by a [1,3]-H shift and cyclization to give solid **13** (Scheme 4). All three systems **12a–c** gave a 100 % yield. The free bases **14a–c** were isolated by washing **13** with aqueous Na₂CO₃. Similar reactions in solution gave compounds **14a,c** with only 81 %^[12] and 35 % yield, respectively.^[13] Cyanamides are very useful reagents for a multitude of intermolecular syntheses.^[14] Thus, their quantitative production is of particular value.

Cyanates: Crystalline phenols did not react with ClCN or BrCN at room temperature. However, quantitative reactions were obtained by the use of potassium phenolates (**15**) (Scheme 5). The gas–solid synthesis of **16a,b** is a significant improvement compared with liquid-state reactions (yield of **16a**: 94 %^[15]), as the inorganic salt product (KBr, KCl) may

Scheme 5. Gas–solid cyanation of potassium phenolates (**15**).

be simply washed away with water. However, **16c,d** are highly hydrolyzable so that washing with water was unsuitable as it produced the urethanes **17c,d**. This reaction can easily be brought to completion but is of limited value. It is better to postpone the separation from the salt until preparative use has been made of the particularly versatile cyanate function^[14] of **16c,d** in the presence of the salts.

Thiocyanates: While it was not possible to react a number of solid heterocyclic thiols with ClCN or BrCN, the reactions of their sodium salts **18a–d** provided the desired thiocyanates **19** in quantitative yields (Scheme 6). The inorganic products, NaCl or NaBr, were removed by washing with water.

Scheme 6. Reaction of the sodium salts of solid heterocyclic thiols **18a–d** with ClCN or BrCN to afford thiocyanates **19a–d**.

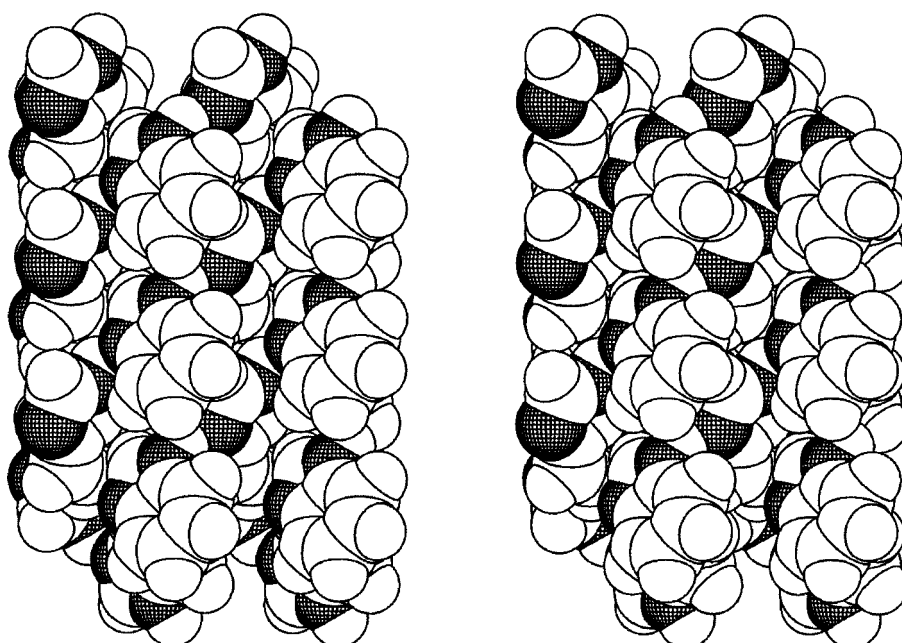
All of these heterocyclic thiocyanates have already been synthesized in solution (**19a–c**: no yield given,^[16–18] **19d**: 88 %^[19]) and their usefulness as drugs and synthetic building blocks (e.g. as antitumor agents^[1] or antimicrobials^[20]) has been demonstrated. Their quantitative synthesis considerably improves the future prospects of these drugs.

Structure elucidation: None of the products that were obtained in this work by solid-state cyanation with gaseous ClCN or BrCN rearranged to their corresponding *iso* forms (i.e. carbodiimides, isocyanates, isothiocyanates). This is clearly evidenced by the structure of the cyclization products **10** and **13**, the fair stability towards hydrolysis (except **16c,d**), the comparison with literature data of some already known compounds,

and by the characteristic IR bands of the C≡N bonds. All C≡N frequencies of the cyanamides **2**, **4**, **6**, and **8** are found between $\tilde{\nu} = 2210$ and 2260 cm^{-1} , whereas carbodiimides at $\tilde{\nu} = 2130$ – 2155 cm^{-1} .^[21] In the case of aryl cyanates and aryl isocyanates, the expected ranges overlap ($\tilde{\nu} = 2280$ – 2240 and 2290 – 2240 cm^{-1}). However, only cyanates would have split bands and a characteristic C–O–C vibration at $\tilde{\nu} = 1235$ – 1160 cm^{-1} .^[22] Indeed, the splitting and the latter band are found in the spectra of **16a–d**. Thus, we can be sure that also the readily hydrolyzable **16c,d** have a cyanate structure. The thiocyanates **19** exhibit IR frequencies close to $\tilde{\nu} = 2170\text{ cm}^{-1}$ as expected,^[22] whereas arylisothiocyanates would have bands at $\tilde{\nu} = 2100$ – 2040 cm^{-1} .^[22]

Mechanistic investigations with AFM: The striking superiority of the gas–solid reactions is related to the quality of the crystal packing according to the well-established three-stage mechanism: 1) phase rebuilding with long-range molecular movements, 2) phase transformation into the product lattice, and 3) crystal disintegration.^[23] Such a correlation with the crystal packing was demonstrated for single crystals of known crystal structure by the use of AFM.

Reaction with ClCN generates islands^[24] on the (100)-face of benzimidazole (**5a**) because there is efficient shielding of all the nitrogen functions on that face, as the crystal packing^[25] indicates (Figure 1). Therefore, the reaction cannot start on (100) except at defect sites. Reaction continues around these sites until the crystal disintegrates. Prominent defect sites are, of course, the slopes of the terraces on the (100)-face of **5a** where the functional groups are available (see top and left side in Figure 1). Thus, the slope of the 6+2 nm terrace in Figure 2a was the principal site of reaction in this experiment. The reaction continued from the initial starting points to produce the islands visible in Figure 2b. It is highly gratifying

Figure 1. Space-filling stereoscopic view onto the (100)-face of **5a** (*Pna*₂₁)^[25] showing the shielding of the functional groups; N atoms are shaded.

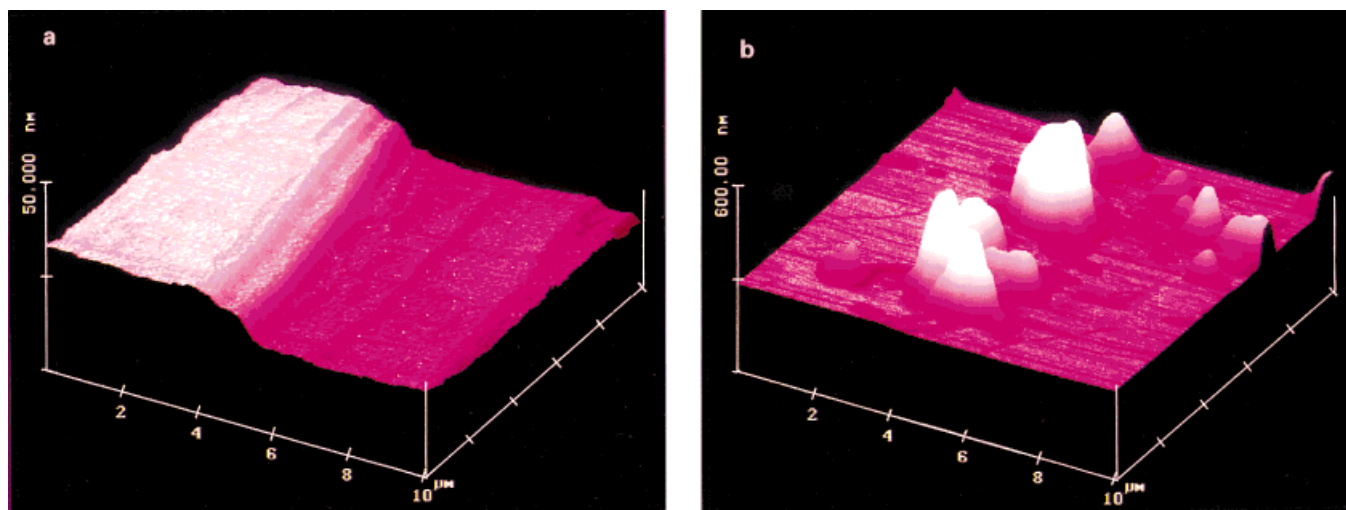


Figure 2. AFM topographies of **5a** on the (100)-face at a step site: a) fresh surface, b) same site after application of ClCN (3 mL, 20%), which shows the development of the features at the slope sites.

to see that it is the crystal packing that determines the reactivity which manifests itself in the long-range molecular movements. Even the smaller islands were initiated at defect sites on the surface (Figure 2a).

The reaction of BrCN gas with the (001)-face of crystals of **9** started with the formation of shallow craters and terraces (Figure 3b). The next step was the formation of nearly square or rectangular depressions that resemble the basins of swimming pools (Figure 3c,d) prior to crystal disintegration. The edges of the basins lie at $\pm 45^\circ$ with respect to the long crystal axis [100]. This correlates nicely with the crystal packing^[26] (Figure 4; see p. 2472): half of the steeply (73°) inclined molecules are at the $+45^\circ$ diagonal across the face and the other half are at the -45° diagonal. Clearly, the product molecules **10** move and align themselves along these two directions of preference during phase transformation (stage 2) in an epitaxial manner. The depth of the rectangular basins reaches 120 nm, while the depth of the initial square depression in Figure 3c is only 11 nm. The initial reaction stage (phase rebuilding; Figure 3b) produces terraces 2–2.5 nm high along with isolated craters 0.6 or 1.2 nm deep, as is expected for a hindered double-layer reaction with two lateral directions of preference. In fact, the functional groups of the double layers point inwards and are well shielded by the benzene rings.

Even the multistep reaction of BrCN with the (100)-face of **12a** gave very distinct AFM features. Initially the reaction was hindered: the reaction sites were double-layer steps of 1.5 nm in height and these changed position and height (1.0–1.8 nm) with respect to the fresh surface (Figure 5a; see p. 2472). Upon continuation of the reaction there were still molecular steps, and isolated upright cones with heights of up to 88 nm grew on that face (Figure 5b). The number and volume of the island volcanoes increased and some craters (15 of them, 30–60 nm deep) formed (Figure 5c). Later on in the reaction the cones grew together and reached heights of up to 250 nm prior to the phase transformation step, which produced wide rhombic (66°) basins. The horizontal edges of these basins are parallel to the long crystal axis of **12a** (Figure 5d). The

correlation with the crystal structure is striking: the packing^[27] of **12a** on (100) is shown in Figure 6 (see p. 2473). The molecules are inclined at an angle of 71° on that face in four orientations and form double layers. All multiply H-bonded functional groups lie inside the double layer and are shielded against attack by BrCN, in a similar manner to that in **9** or in α - and β -cinnamic acid.^[23, 28] As the functional groups of **12a** are only available at the slopes of the terraces, that is more or less from the single double-layer (010)- and (001)-faces, it is easily understood that we see an initial layer mechanism followed by the formation of islands around nucleation points with long-range molecular transport above the initial surface through several double layers. At increased local defect concentration the reaction proceeds, leaving some craters, while still in the phase rebuilding stage. The interlocking does impede lateral movements. Thus, even the sudden phase transformation to give the rhombic basins of Figure 5d is evidently epitaxial in nature; the horizontal edges are parallel to the long crystal axis. The angle of $66^\circ/114^\circ$ is not available on (100) of **12a**. However, the very complicated intramolecular rearrangement steps with formation of the salt **13a** does change the product lattice considerably. The layer-by-layer reaction occurs in a dissimilar manner to the reaction of **9** at the beginning, but in a similar manner at the end. Again, upon further reaction after the phase transformation the crystal disintegrates and thus forms a fresh surface. It is highly gratifying that even in a very complicated series of chemical reactions a straightforward correlation with the packing in the crystal is still present.

Discussion

None of the gas–solid reactions described here (except the reaction of **7** to give **8** where some surface passivation—probably impeding step 3, crystal disintegration—required ball-milling) required grinding or other pretreatment of the dry crystals, and all of them gave 100% yield. They are greatly superior to liquid-state reactions which do not give a

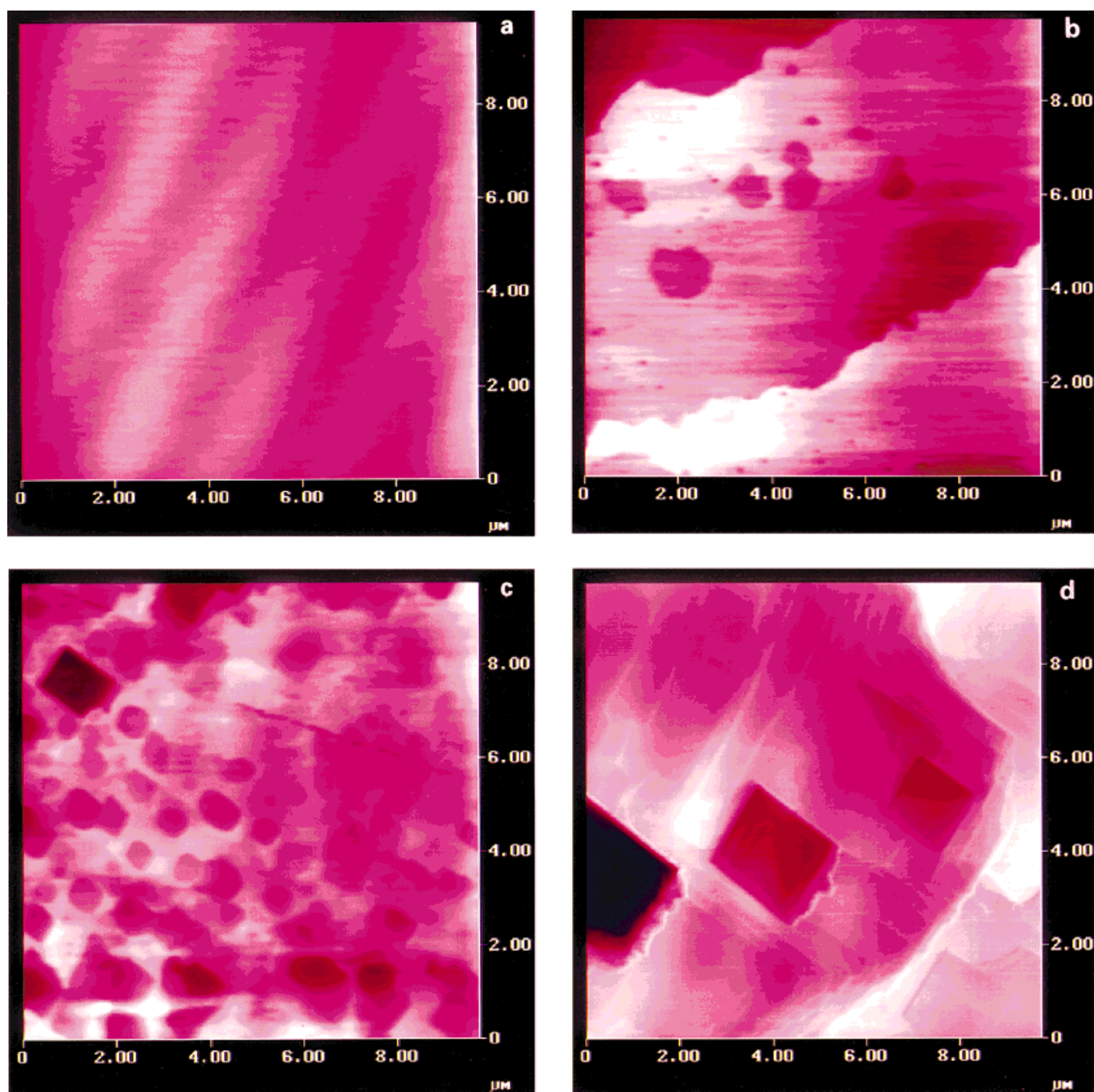


Figure 3. AFM topographies on the (001)-face of **9**: a) fresh surface, b) after the first, c) after the second, d) after the sixth treatment with BrCN gas. The scan direction from left to right was at $5-10^\circ$ to the long crystal axis; the Z scale is a) 10 nm, b) 10 nm, c) 30 nm, and d) 100 nm.

quantitative yield and require costly separation techniques in the workup. If simple salts of alkaline bases or of trimethylamine are also formed as end products, these are simply removed by washing and no further waste is formed.

The crystal packing of our starting materials is the major reason for the quantitative syntheses. It permits the undisturbed occurrence of the three necessary stages: 1) phase rebuilding with long-range molecular movements, 2) phase transformation into the product lattice, and 3) crystal disintegration to form fresh surfaces.^[23] This experimental mechanism has again been verified by AFM measurements and correlated with the known crystal structures. A new type

of feature was found: rectangular and rhombic depressions that resemble swimming-pool basins, a term that we use for a versatile geometric classification. This new type of feature complements the eight types already known.^[23]

Further prerequisites that must be met in 100 % solid-state syntheses are, of course, thermodynamical feasibility and the lack of (nano)liquid phases during the reaction.^[23]

If quantitative reactions are desired, then starting materials should be of sufficient purity. For practical purposes it can be more profitable to allow some impurities in the starting material if these do not enforce melting towards the end of reaction and thus prevent its completion. Such strategies are

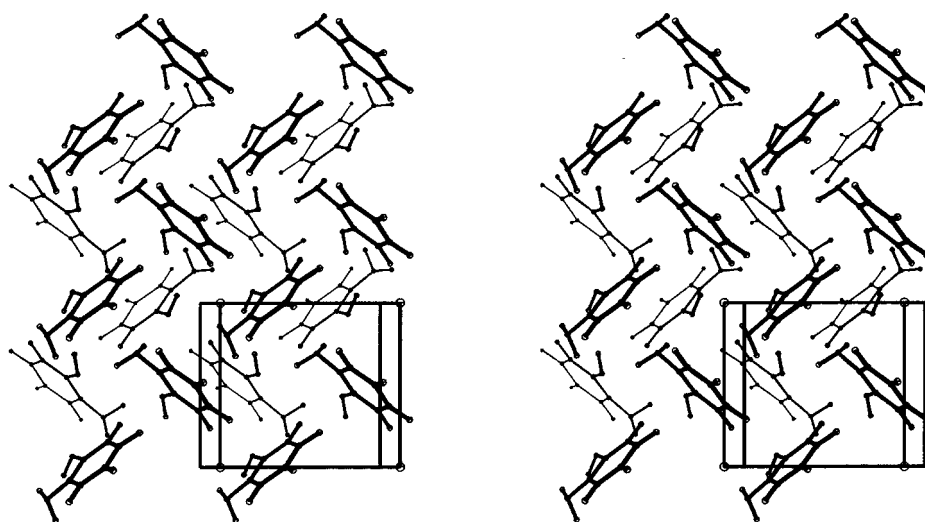


Figure 4. Stereoscopic view of the crystal packing of **9** onto the (001)-face showing one of the infinite double layers (thickness: 1.2 nm). All the molecules are inclined at 73° and lie at $\pm 45^\circ$ diagonally across that surface.

frequently successful if the melting points are sufficiently high. They are particularly valuable if the impurities can be removed more easily at a later stage of a reaction sequence.^[29]

The now facile and quantitative synthesis of cyanamides, cyanates, and thiocyanates increases both the availability of these interesting classes of compounds and their synthetic

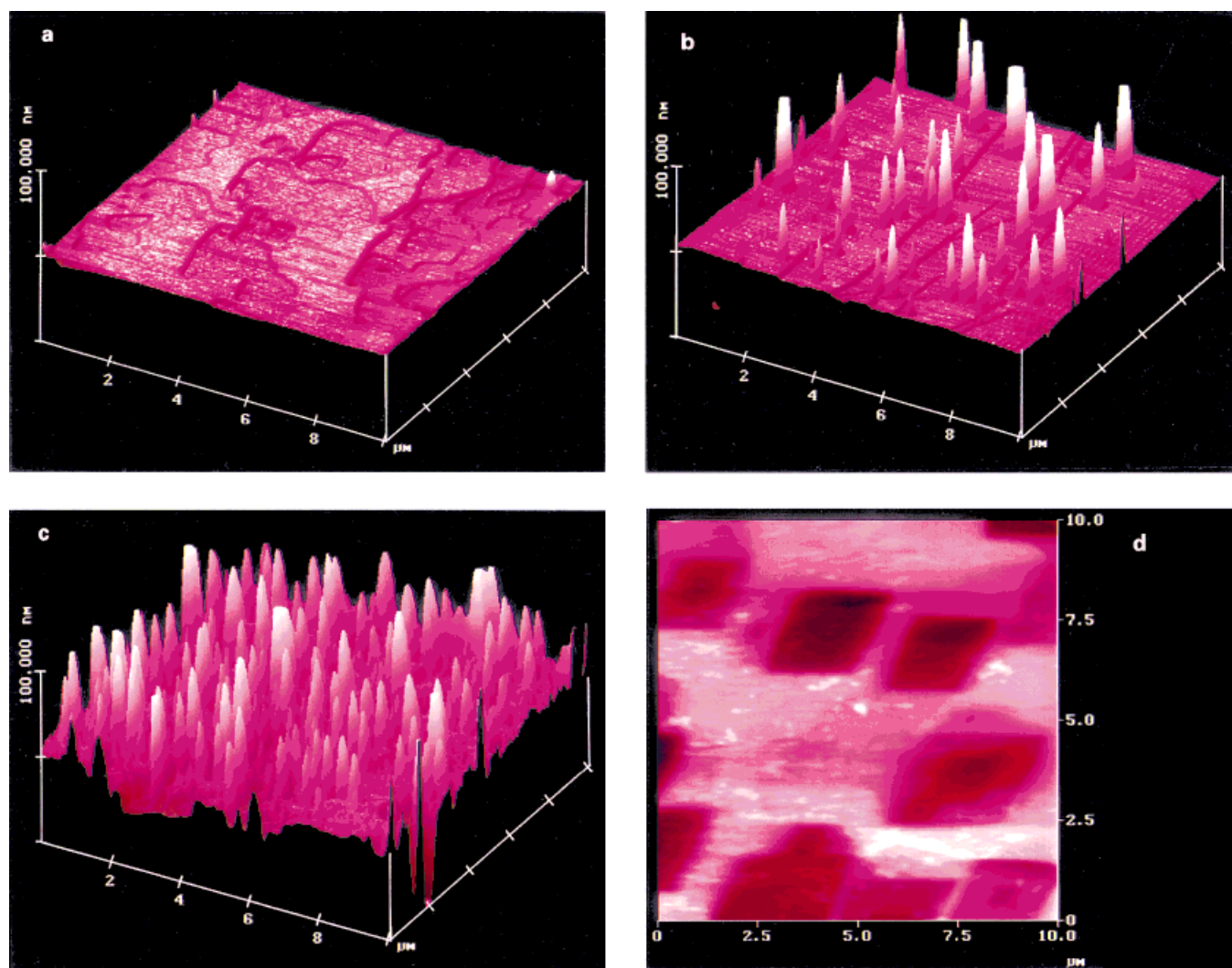


Figure 5. AFM topographies of **12a** on the (100)-face. a) Flat surface after application of 0.1 mL BrCN, showing molecular terraces, b) after application of 0.2 mL BrCN, c) after application of 0.4 mL BrCN, and d) phase transformation after application of 1 mL BrCN gas, showing rhombic pool basins of 60–100 nm depth; the Z scale in d) is 400 nm.

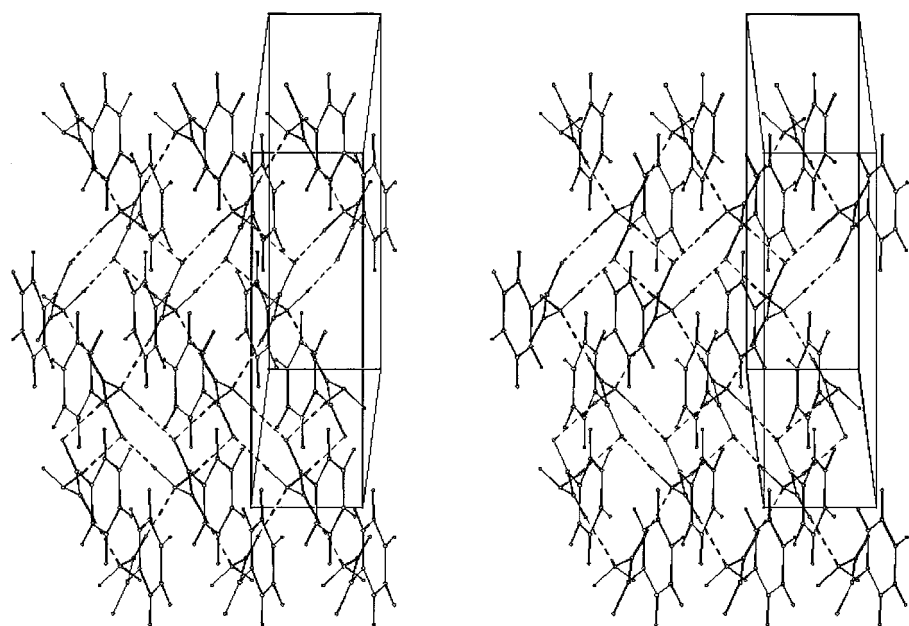


Figure 6. Stereoscopic view of the crystal packing of **12a** ($P2_1/c$)^[27] onto the (100)-face showing one double layer with the 3D network of hydrogen bonds (dashed) between the functional groups. These groups are shielded by the phenyl groups which penetrate the face at angles of 71° in two directions; the (001)-face lies on the top of the model, while (010) is to the right.

value for all kinds of practical applications in an environmentally benign way that cannot be attained by any other technique. As in principle no obstacles oppose the scaling up of our reactions,^[30] they are of interest for production and education.

Experimental Section

The product yields were detected by the weight increase measured after evaporation of the excess gas in a high vacuum. The purity of commercial or freshly synthesized anilines, phenols, thiols, hydrazides, and benzimidazoles was checked by their melting points, ^1H NMR, and thin-layer chromatography. Any residual solvents in the starting materials were removed by an appropriate drying procedure and water of hydration was removed as much as possible. The success of solvent removal was controlled by TGA. The experimental error in the determination of the yields is judged to be $\pm 1\%$. The gas/solid^[23, 30, 31] and AFM techniques^[23, 30, 32] have been described in detail elsewhere. Surface scraping was avoided^[33] and all AFM images were stable for at least 10 scans. Single crystals of **5a**, **9**, and **12a** were obtained from methanol, acetone, and acetone, respectively, by slow evaporation. The ClCN and BrCN gases were applied by syringe from ca. 1 cm distance to the sample surface. ClCN was diluted to about 10% in air, the applied BrCN concentration was 3.3 mmol L^{-1} in air. After 1 min exposure the gas was flushed away with air. Aliphatic amines and cyanogen chloride were taken from lecture bottles (Aldrich); cyanogen bromide was sublimed prior to use.

Only $\text{C}\equiv\text{N}$ bands and some other particularly relevant vibrations are given in the FT-IR data. The NMR spectra were recorded with a Bruker WP 300 spectrometer and the mass spectra with a Finnigan MAT 212 instrument. Thiolates and phenolates were prepared under inert gas by the dissolution of equivalent amounts of thiols or phenols with NaOH or KOH in ethanol, followed by evaporation and drying at 80°C under vacuum.

General procedure: The crystalline substrate (10.0 mmol: anilines **1**, **3**, **9** [with 20 mmol $\text{N}(\text{CH}_3)_3$]; benzimidazoles **5** [with 20 mmol $\text{N}(\text{CH}_3)_3$]; hydrazides **12**; potassium phthalimide **7** (2.0 mmol, ball-milled); phenolates **15**; thiolates **18**) was placed in a flask (250 mL) which was filled with ClCN (1 bar, 11.2 mmol) or connected to a vacuum line with a flask (250 mL) containing BrCN (1.17 g, 11.0 mmol). The mixtures were left

overnight at room temperature. In all reactions with added $\text{N}(\text{CH}_3)_3$ gas, a magnetic spin bar was rotated in the flask. After the reaction was complete, the slight excess of gas was recovered in a cold trap at 77 K, the solid residue was weighed and then liberated from the salts.

4-Methylphenylcyanamide (2a): Solid *p*-toluidine (**1a**) was treated with ClCN (or BrCN) according to the general procedure and the trimethylammonium chloride (bromide) was then removed by washing. Yield: 100% (100%); m.p. 70°C (ref. [4]); m.p. $70\text{--}71^\circ\text{C}$; IR (KBr): $\tilde{\nu} = 2223\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR (CDCl_3): $\delta = 7.13$ (AA'BB', 2H), 6.92 (BB'AA', 2H), 6.69 (brs, 1NH), 2.32 (s, 3H).

4-Methoxyphenylcyanamide (2b): Solid *p*-anisidine (**1b**) was treated with ClCN (or BrCN) and the trimethylammonium chloride (bromide) was then removed by washing. Yield: 100% (100%); m.p. $87\text{--}88^\circ\text{C}$ (ref. [5]; m.p. $87\text{--}89^\circ\text{C}$); IR (KBr): $\tilde{\nu} = 2219\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR (CDCl_3): $\delta = 6.95$ (AA'BB', 2H); 6.84 (BB'AA', 2H), 3.80 (s, 3H).

4-Chlorophenylcyanamide (2c): Solid *p*-chloroaniline (**1c**) was treated with ClCN (or BrCN) and the trimethylammonium chloride (bromide) was then removed by washing. Yield: 100% (100%); m.p. 107°C (ref. [34];

m.p. $108\text{--}109^\circ\text{C}$); IR (KBr): $\tilde{\nu} = 2239\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR (CDCl_3): $\delta = 7.02$ (AA'BB', 2H), 6.71 (BB'AA', 2H).

N-Cyanodiphenylamine (4): Solid diphenylamine (**3**) was treated with BrCN and the trimethylammonium bromide was then removed by washing. Yield: 100%; m.p. 73°C (ref. [2]; m.p. 74°C); IR (KBr): $\tilde{\nu} = 2224\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR: $\delta = 7.23$ (m, 6H), 7.42 (m, 4H).

1-Cyanobenzimidazole (6a): Solid benzimidazole (**5a**) was treated with BrCN and the trimethylammonium bromide was then removed by washing. Yield: 100%; m.p. 104°C (ref. [8]; m.p. $104\text{--}105^\circ\text{C}$); IR (KBr): $\tilde{\nu} = 2260\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR (CDCl_3): $\delta = 8.0$ (s, 1H), 7.56 (m, 2H), 7.20 (m, 2H).

1-Cyano-2-methylbenzimidazole (6b): Solid 2-methylbenzimidazole (**5b**) was treated with BrCN and the trimethylammonium bromide was then removed by washing. Yield: 100%; m.p. 110°C (ref. [9]; m.p. 112°C); IR (KBr): $\tilde{\nu} = 2256\text{ cm}^{-1}$; ^1H NMR (CDCl_3): $\delta = 7.70$ (m, 1H), 7.51 (m, 1H), 7.41 (m, 2H), 2.78 (s, 3H).

1-Cyano-5,6-dimethylbenzimidazole (6c): Solid 5,6-dimethylbenzimidazole (**5c**) was treated with BrCN and the trimethylammonium bromide was then removed by washing. Yield: 100%; m.p. 127°C ; IR (KBr): $\tilde{\nu} = 2249\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR (CDCl_3): $\delta = 8.05$ (s, 1H), 7.60 (s, 1H), 7.41 (s, 1H), 2.41 (s, 3H), 2.39 (s, 3H); HR-MS (CI, isobutane) calcd for $\text{C}_{10}\text{H}_{10}\text{N}_3$: 172.0869; found 172.0868.

N-Cyanophthalimide (8): Potassium phthalimide (**7**, 370 mg, 2.0 mmol) was ball-milled (30 min, particle size: $< 1\text{ }\mu\text{m}$) and then treated with gaseous BrCN (225 mg, 2.1 mmol) for 24 h. KBr was removed by washing and the residue dried. Yield: 340 mg (99%); m.p. 73°C (ref. [10]; m.p. 74°C); IR (KBr): $\tilde{\nu} = 2245\text{ cm}^{-1}$ ($\text{C}\equiv\text{N}$); ^1H NMR ($[\text{D}_6]\text{DMSO}$): $\delta = 8.05\text{--}8.00$ (AA'BB'); MS (CI, isobutane): $m/z = 173$ [$M+1$].

2-Aminobenzoxazole (11) and its hydrobromide (10): Solid *o*-aminophenol (**9**) was treated with BrCN to give 100% of the hydrobromide **10**; m.p. 132°C (decomp). The salt was washed with 5% Na_2CO_3 solution to afford **11** in pure form. Yield: 100%; m.p. 127°C (ref. [11]; m.p. $128\text{--}129^\circ\text{C}$); IR (KBr): no $\text{C}\equiv\text{N}$ band; ^1H NMR (CDCl_3): $\delta = 7.30$ (m, 1H), 7.24 (m, 1H), 7.18 (m, 1H), 7.05 (m, 1H).

2-Amino-5-phenyl-1,3,4-oxadiazole (14a) and its hydrobromide (13): Solid benzohydrazide (**12a**) was treated with BrCN to give 100% of the hydrobromide **13a**; m.p. $> 300^\circ\text{C}$. The salt was washed with 5% Na_2CO_3 solution to afford **14a** in pure form. Yield: 100%; m.p. 243°C (ref. [12]; m.p.

246–248 °C); ¹H NMR (CDCl₃/[D₆]DMSO): δ = 7.76 (m, 2H), 7.41 (m, 3H), 7.04 (s, 2H).

2-Amino-5-(p-tolyl)-1,3,4-oxadiazole (14b): Solid 4-methylbenzohydrazide (12b) was treated with BrCN to give 100% of the hydrobromide 13b which was washed with 5% Na₂CO₃ solution to give 14b. Yield: 100%; m.p. 277–279 °C (ref. [13]; m.p. 278–280 °C); ¹H NMR (CDCl₃/[D₆]DMSO): δ = 7.65 (AA'BB', 2H), 7.22 (BB'AA', 2H), 6.89 (s, 2H), 2.34 (s, 3H).

2-Amino-5-(p-hydroxyphenyl)-1,3,4-oxadiazole (14c): Solid 4-hydroxybenzohydrazide (12c) was treated with BrCN to give 100% of the hydrobromide 13c which was washed with 5% Na₂CO₃ solution to give 14c. Yield: 99%; m.p. 273 °C (ref. [13]; m.p. 274–276 °C); ¹H NMR (CDCl₃/[D₆]DMSO): δ = 7.61 (AA'BB', 2H), 6.80 (BB'AA', 2H), 6.08 (s, 2H).

4-Methoxyphenylcyanate (16a): Solid potassium 4-methoxyphenolate (15a) was treated with ClCN (or BrCN) to give a mixture of KCl (KBr) and 16a; yield: 100% (100%). Pure 16a was obtained after removal of KCl (KBr) by washing with water. M.p. 32 °C (ref. [15]; m.p. 29–31 °C); IR (KBr): ν̄ = 2278, 2238 (C≡N), 1176 cm⁻¹ (C–O–C).

3,4-Dimethoxyphenylcyanate (16b): Solid potassium 3,4-dimethoxyphenolate (15b) was treated with ClCN (or BrCN) to give a mixture of 16b and KCl (KBr); yield: 100% (100%). Pure 16b was obtained after removal of KCl (KBr) by washing with water. M.p. 60–62 °C; IR (KBr): ν̄ = 2273, 2238 (C≡N), 1172 cm⁻¹ (C–O–C); ¹H NMR (CDCl₃): δ = 6.88 (m, 2H), 6.80 (s, 1H), 3.79 (s, 6H); ¹³C NMR (CDCl₃): δ = 150.13, 147.60, 146.76, 111.37, 109.17, 106.25, 99.88, 56.32, 56.29; HR-MS (CI, isobutane) calcd for C₉H₉NO₃+H: 180.0643; found 180.0641.

4-Cyanatobenzaldehyde (16c): Solid potassium 4-formylphenolate (15c) was treated with ClCN (or BrCN) to give a mixture of 16c and KCl (KBr); yield: 100% (100%). The mixture was extracted with dry CH₂Cl₂, the solvent evaporated, and the residue dried in a vacuum to give pure 16c. Yield: 98%; m.p. 53 °C (ref. [35]; m.p. 54 °C); IR (KBr): ν̄ = 2268, 2153 (C≡N), 1214 cm⁻¹ (C–O–C).

4-Formylphenylurethane (17c): A mixture of 16c and KCl (280 mg) from the above experiment was stirred for 10 min with water (20 mL). The mixture was filtered and dried to give 17c. Yield: 204 mg (99%); m.p. 227 °C; IR (KBr): ν̄ = 3278 (N–H), 1665, 1605 cm⁻¹ (C=O); ¹H NMR (CDCl₃): δ = 9.60 (s, 1H), 7.51 (d, 2H), 6.68 (d, 2H); HR-MS calcd for C₈H₇NO₃: 165.0424; found 165.0426.

2-Nitrophenylcyanate (16d) and 2-nitrophenylurethane (17d): Solid potassium 2-nitrophenolate hemihydrate (15d) was treated with ClCN (or BrCN) to give a mixture of 16d and KCl (KBr) that contained small quantities of 17d; IR (KBr): ν̄ = 2237, 2203 (C≡N), 1203 cm⁻¹ (C–O–C). If the mixture was stirred with water for 5 min then 17d was obtained after filtration and drying. Yield: 99%; m.p. 131–132 (ref. [36]; m.p. 134–136 °C); IR (KBr): ν̄ = 3351 (N–H), 1703 cm⁻¹ (C=O).

Benzoxazole-2-thiocyanate (19a): Solid sodium benzoxazole-2-thiolate (18a) was treated with ClCN (or BrCN). The product was washed with water and dried to give pure 19a. Yield: 100% (100%); m.p. 73 °C (ref. [16]; m.p. 74–75 °C); IR (KBr): ν̄ = 2176 cm⁻¹ (C≡N).

Benzothiazole-2-thiocyanate (19b): Solid sodium benzothiazole-2-thiolate (18b) was treated with ClCN (or BrCN). The product was washed with water and dried to give pure 19b. Yield: 100% (100%); m.p. 84 °C (ref. [17]; m.p. 85–87 °C); IR (KBr): ν̄ = 2167 cm⁻¹ (C≡N); ¹H NMR (CDCl₃): δ = 7.96 (1H), 7.83 (1H), 7.51 (1H), 7.41 (1H).

Pyrimidine-2-thiocyanate (19c): Solid sodium pyrimidine-2-thiolate (18c) was treated with ClCN (or BrCN). The product was washed with water and dried to give pure 19c. Yield: 100% (100%); m.p. 106 °C (ref. [18]; m.p. 107–109 °C); IR (KBr): ν̄ = 2173 (C≡N); ¹H NMR (CDCl₃): δ = 8.58 (d, 2H), 7.08 (t, 1H).

Purine-6-thiocyanate (19d): Solid sodium purine-6-thiolate (18d) was treated with ClCN (or BrCN). The product was washed with water and dried to give pure 19d. Yield: 100% (100%); m.p. > 220 °C (decomp) (ref. [19]; m.p. 225–226 °C); IR (KBr): ν̄ = 2182 cm⁻¹ (C≡N); ¹H NMR (CDCl₃/[D₆]DMSO): δ = 8.82 (s, 1H), 8.48 (s, 1H).

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