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Nucleophilic aromatic substitutions on 4,5-dicyanopyridazine. Part 2: Nitrogen nucleophiles

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ABSTRACT

As previously reported with pyrrole and indole *C*-nucleophiles, 4,5-dicyanopyridazine (DCP) showed remarkable reactivity as a heterocyclic electrophile at the C–4 carbon toward amino nucleophiles. Aminocyanopyridazines, the formal S_NAr2 products, have been easily synthesized in satisfactory yields through the facile substitution of a CN group of DCP, that behaves as leaving group. Operating in different solvents, the best results were generally obtained with a medium polar solvent, such as THF. The introduction of amino functionalities into the pyridazine system allows a desymmetrization of the starting material and opens the way to further synthetic elaborations.

1. Introduction

In the domain of drug molecules, recent literature data showed that the bioisosteric replacement of phenyl rings with the corresponding pyridazine nucleus opens the way to diaza analogues characterized by significant improvements with respect to receptor interactions, metal coordination, salt formation, and water solubility.[1] Due to their affinity for a great number of receptor proteins, pyridazines can be certainly considered as 'privileged structures' in medicinal chemistry,[1] according to Evans's definition.[2] In this context, aminopyridazine derivatives play a very important role confirmed by the presence of this pharmacophoric moiety in natural and bioactive compounds,[1] such as dopaminergic, serotonergic, cholinergic ligands, monoamine oxidase, and acetylcholine esterase inhibitors,[3] orally active antinociceptive agents,[4] as well as suppressors of glial activation involved in neurodegenerative disorders such as Alzheimer's disease.[5]

On the other hand, nucleophilic displacement of a cyano group in cyano substituted heterocycles is quite unusual and only a few examples involving 1,2,4-triazine-,[6] quinazoline-,[6b,7] pyrazine-,[8] as well as pyridine-[9] and pyridinium-carbonitriles[10] have been reported. Concerning 1,2-diazines, in particular, apart from preliminary data relating to reactions of 1-phthalazine- and 4-cinnoline-carbonitriles with Grignard reagents,[11] the nucleophilic substitution of the CN group has been clearly observed only in the treatment of cinnoline-3,4-dicarbonitrile with ammonia and amines[12] and in the reactions of 4-cyano-3(2*H*)-pyridazinone and tetrazolo[1,5-*b*]pyridazine-8-carbonitrile with phenylmagnesium chloride.[13]

Previous studies from our laboratory showed 4,5-dicyanopyridazine (DCP) (**1**) displayed surprising reactivity as a heterocyclic azadiene in inverse electron-demand Hetero Diels–Alder (HDA) reactions with different dienophiles, allowing facile access to functionalized mono- and polycyclic systems.[14] Furthermore, recent results showed for compound **1** an unprecedented behavior as a very reactive heterocyclic electrophile at the C-4 carbon atom. Depending on the reaction conditions, DCP is able to react with pyrrole and indole counterparts as an azadiene, affording benzoannelated pyrrole and indole systems,[15] as well as an electrophile. In the latter case, cyanopyrrolyl- and cyanoindolylpyridazines have been easily synthesized through formal S_NAr2 processes where pyrrole and indole derivatives act as carbon nucleophiles displacing a CN group of DCP.[16] With the aim of evaluating the applications and limits of this new facet of reactivity of DCP, we decided to investigate its behavior as a heterocyclic electrophile toward different nitrogen nucleophiles, which would provide direct access to aminopyridazine derivatives.

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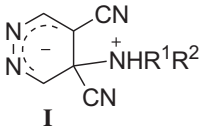
2. Results and discussion

The dinitrile **1** was allowed to react with different primary and secondary amines. The reactions were first performed using chloroform as the solvent, at room temperature and with stoichiometric amounts of amine **2a**–**e**, leading to 5-amino-4-cyanopyridazines **3a**–**e** in 41–80% yields (Table 1, entries 1, 3, 5, 7, 9).

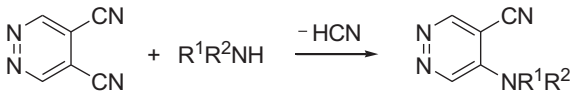
More hindered amines, such as diisopropylamine **2f** and diallylamine **2g**, were less reactive and so the reactions were performed with an excess of reagents (3 equiv) at 50 °C, for longer times, affording compounds **3f** and **3g** in 13 and 48% yields, respectively (Table 1, entries 11 and 16). Due to these poor results (in particular with **2f**), the above reactions were repeated in a more polar solvent, such as MeCN, to favor the nucleophilic substitution processes due to the more efficient stabilization of the Meisenheimer intermediates **I** and then of the near transition states.



I

Operating with a stoichiometric amount of diisopropylamine **2f**, at room temperature, aminopyridazine **3f** was isolated in 35% yield (Table 1, entry 12) while no improvements were observed for **2g** (Table 1, entry 17).

Table 1
Reactions of DCP (**1**) with primary and secondary amines **2a**–**i**



1 **2** **3**

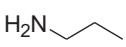
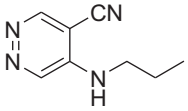
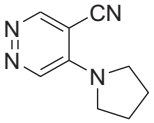
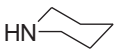
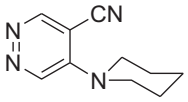
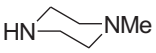
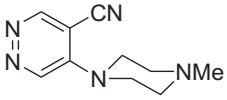
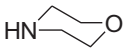
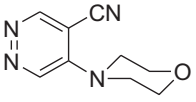
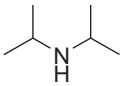
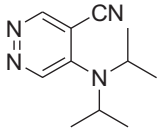
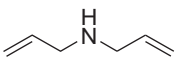
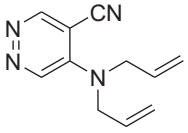
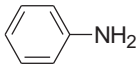
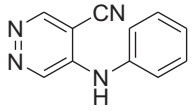
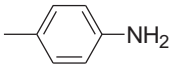
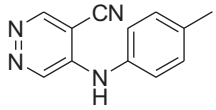
Entry	Reagent	Equiv	Solvent	Temp	Time	Product	Yield[a] (%)
1		1.1	$CHCl_3$	rt	0.5 h		65
2	**2a**	1.1	THF	rt	5 h	**3a**	100
3		1.1	$CHCl_3$	rt	0.5 h		80
4	**2b**	1.1	THF	rt	7 h	**3b**	100
5		1.1	$CHCl_3$	rt	0.5 h		41
6	**2c**	1.5	THF	65 °C	5 h	**3c**	50
7		1.1	$CHCl_3$	rt	5 h		51
8	**2d**	1.1	THF	65 °C	11 h	**3d**	64
9		1.1	$CHCl_3$	rt	24 h		47
10	**2e**	1.5	THF	65 °C	5 h	**3e**	72
11		3	$CHCl_3$	50 °C	72 h		13
12		1.1	MeCN	rt	42 h		35
13		1.1	DMF	rt	63 h		18
14	**2f**	1.1	THF	rt	48 h	**3f**	—[b]
15		1.1	THF	65 °C	5 d		—[c]
16		3	$CHCl_3$	50 °C	25 h		48
17		1.1	MeCN	rt	72 h		17
18	**2g**	1.5	THF	110 °C[d]	50 h	**3g**	30[e]

Table 1 (*continued*)

Entry	Reagent	Equiv	Solvent	Temp	Time	Product	Yield[a] (%)
19	 **2h**	1.5	THF	110 °C[d]	82 h	 **3h**	78
20	 **2i**	1.5	THF	110 °C[d]	60 h	 **3i**	96

[a] Isolated yields.
[b] No reactivity.
[c] Complex reaction mixture containing both DCP and **3f**.
[d] Reactions performed in a screw-cap tube (Pyrex N° 13).
[e] Yield based on the recovery of unreacted **1**.

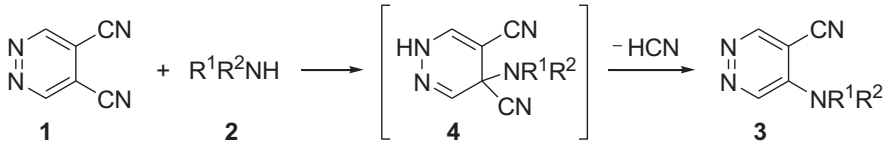
To evaluate the solvent effect, the reaction of **2f** with DCP was studied in a highly polar solvent (DMF) and a less polar solvent (THF). Unfortunately, in the former case compound **3f** was isolated in only 18% yield from a complex reaction mixture (Table 1, entry 13) and in the latter DCP was absolutely inert toward **2f** at room temperature while, after heating at 65 °C for five days, a complex mixture was obtained preventing the isolation of the reaction product (Table 1, entries 14 and 15). In the case of **2g** the reaction rate in THF was very low at 65 °C and so the reaction was then performed at 110 °C, in a screw-cap Pyrex tube, but compound **3g** was isolated in only 30% yield (Table 1, entry 18).

These reactions were often characterized by the formation of complex reaction mixtures containing black residues, insoluble for the most part in organic solvents, likely associated with polymerization and/or decomposition processes. Scarcely reactive nucleophiles and highly polar solvents can then favor nucleophilic attacks of the Meisenheimer intermediates **I** on the highly electrophilic DCP, leading to disappearance of the starting pyridazine without significant formation of substitution products.

Despite the problems observed in the reactions of DCP with **2f** and **2g** in tetrahydrofuran, with all the other tested amines the use of THF, at room temperature or under heating, led to improved results. In particular, when a solution of DCP in THF was slowly added to a solution of the amine (in almost stoichiometric amount) in the same solvent, the reaction rates were decreased with respect to the corresponding reactions in chloroform but this drawback was balanced by the achievement of cleaner reactions from which the substitution products were more easily recovered and in higher yields. This procedure guarantees a low concentration of DCP in the solution and this situation seems to promote the nucleophilic attack of the amino reagent on **1**, disfavoring the competitive polymerization/decomposition processes. Following this procedure, compounds **3a**,**b** were isolated in quantitative yields operating at room temperature for 5–7 h (Table 1, entries 2 and 4) while **3c**–**e** were recovered in 50–72% yields, by heating for 5–11 h at 65 °C (Table 1, entries 6, 8, 10).

Even less reactive aromatic amines, such as aniline (**2h**) and *p*-toluidine (**2i**), were able to react with DCP in THF but at higher temperature and for longer reaction times. These reactions were then performed in a screw-cap Pyrex tube, by simple heating a THF solution of both the reagents at 110 °C, leading to the formation of derivatives **3h**,**i** in 78 and 96% yields, respectively (Table 1, entries 19 and 20).

On the basis of the previous results obtained with pyrrole and indole *C*-nucleophiles,[16] providing evidence for the formation of 1,4-dihydropyridazine intermediates, the formation of nucleophilic aromatic substitution products **3a**–**i** is likely the result of an addition–elimination (A–E) mechanism (Scheme 1). Certainly, in this case, the use of basic reagents strongly favors the HCN elimination step, that gives rise to aromatic derivatives, preventing the isolation of 1,4-dihydropyridazine adducts of type **4**.



Scheme 1. Proposed reaction mechanism.

3. Conclusions

In conclusion, these results clearly show that DCP (**1**) displays remarkable reactivity as a heterocyclic electrophile toward amino counterparts. Aminocyanopyridazines **3a**–**i** have been easily synthesized in satisfactory yields from the starting pyridazine, confirming the facile substitution of a CN group that behaves as leaving group. On the other hand, the CN group in derivatives **3a**–**i**, certainly due to the presence of the amino function, is no longer activated toward nucleophilic substitution and as such the reaction products are stable even in the presence of an excess of nucleophile. Performing the above reactions in different solvents, apart from a few cases, the best results were obtained with a medium polar solvent, such as THF, through a slow addition of DCP to disfavor competing reactions. The introduction of amino functionalities into the pyridazine skeleton appears very promising from both synthetic and biological viewpoints: in fact, it allows a desymmetrization of the starting material and makes possible further synthetic elaborations, especially oriented to the synthesis of bioactive compounds. In particular, the use of

suitable bis-nucleophiles could open the way to the synthesis of new condensed polynuclear pyridazine derivatives. The study of synthetic applications of this new methodology is now in progress in our laboratory.

4. Experimental section

4.1. General

Melting points were taken on a Stuart Scientific SIMP3 apparatus and are uncorrected. Silica gel plates (Merck F_{254}) and silica gel 60 (Merck, 230–400 mesh) were used for TLC and flash chromatographies (FC), respectively. Petroleum ether (PE) employed for crystallizations and chromatographic workup refers to the fractions of bp 30–50 and 40–70 °C, respectively. IR spectra were recorded with a Perkin–Elmer Spectrum BX FT-IR System spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Mercuryplus 400 instrument, operating at 400 and 100 MHz, respectively. Elemental analyzes were performed with a Perkin–Elmer 2400 analyzer. Accurate mass spectra were recorded on a LTQ-Orbitrap high-resolution mass spectrometer (Thermo, San Jose, CA, USA), equipped with a conventional ESI source.

4.2. Reactions of DCP (1)[14] with amines 2a–e. General procedures

(A) A mixture of DCP (**1**) (65.0 mg, 0.50 mmol) and the amine (0.55 mmol) in $CHCl_3$ (1 mL) was kept at room temperature under magnetic stirring in a screw-cap tube (Pyrex N. 13) for the reported time. Chromatographic purification of the crude reaction mixture obtained by evaporation of the solvent under reduced pressure, allowed the isolation of the aminopyridazine derivative.

(B) Unless otherwise stated, operating with the same amounts of reagents, a solution of DCP in anhydrous THF (4 mL) was slowly added (ca. 1 h) to a solution of the amine in the same solvent (1 mL). The resulting solution was kept at room temperature or heated to reflux under magnetic stirring for the reported time.

*4.2.1. Reactions of DCP (**1**) with n-propylamine (**2a**).* (A) After 0.5 h, chromatographic resolution (PE/EtOAc 1:5) of the reaction mixture obtained from DCP and **2a** (32.5 mg, 45 μL, 0.55 mmol) allowed the isolation of 4-cyano-5-propylaminopyridazine (**3a**) (53.0 mg, 65%) as a pale yellow solid, R_f (PE/EtOAc 1:5) 0.31, mp 100–101 °C (from Et_2O/acetone); [found: C, 59.03; H, 6.01; N, 34.74. $C_8H_{10}N_4$ requires: C, 59.24; H, 6.21; N, 34.54%]. IR (KBr) 3232, 3172, 3030, 2967, 2862, 2219, 1610, 1587 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.84 (s, 1H, H-6), 8.70 (br s, 1H, H-3), 5.86 (br s, 1H, NH), 3.45–3.40 (m, 2H, NCH_2CH$_2$CH$_3$), 1.75 (sextet, J=7.3 Hz, 2H, NCH$_2$CH_2CH$_3$), 1.04 (t, J=7.3 Hz, 3H, NCH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 149.5 (d),[17] 145.1 (s), 138.7 (d),[17] 114.1 (s), 92.3 (s),[17] 44.4 (t), 22.4 (t), 11.1 (q).

(B) Operating for 5 h at room temperature, compound **3a** (81.0 mg, 100%) was recovered by evaporation to dryness of the ethereal solution.

*4.2.2. Reactions of DCP (**1**) with pyrrolidine (**2b**).* (A) After 0.5 h, FC separation (PE/EtOAc 1:1) of the crude reaction mixture obtained from DCP and **2b** (39.1 mg, 46 μL, 0.55 mmol) afforded 4-cyano-5-(pyrrolidin-1-yl)pyridazine (**3b**) (70.0 mg, 80%) that crystallized from Et_2O/acetone as pale yellow needles, R_f (PE/EtOAc 1:1) 0.34, mp 160–161 °C; [found: C, 61.79; H, 5.76; N, 32.02. $C_9H_{10}N_4$ requires: C, 62.05; H, 5.79; N, 32.16]. IR (KBr) 3065, 3028, 2981, 2950, 2875, 2215, 1571, 1553, 1453 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.63–8.62 (m, 2H, H-3 and H-6), 3.82–3.67 (m, 4H, 2′-CH_2 and 5′-CH_2), 2.09–2.06 (m, 4H, 3′-CH_2 and 4′-CH_2); ^{13}C NMR ($CDCl_3$) δ 151.3 (d), 142.4 (s), 140.8 (d), 117.3 (s), 90.4 (s), 49.2 (t), 25.1 (t).

(B) Operating for 7 h at room temperature, compound **3b** (87.0 mg, 100%) was recovered by evaporation to dryness of the ethereal solution.

*4.2.3. Reactions of DCP (**1**) with piperidine (**2c**).* (A) After 0.5 h, the mixture obtained from DCP and **2c** (46.8 mg, 54 μL, 0.55 mmol) was subjected to FC resolution (EtOAc) affording 4-cyano-5-(piperidin-1-yl)pyridazine (**3c**) (39.0 mg, 41%) as a brown solid, R_f (EtOAc) 0.21, mp 116–117 °C (from Et_2O/PE); [found: C, 63.53; H, 6.21; N, 29.56. $C_{10}H_{12}N_4$ requires: C, 63.81; H, 6.43; N, 29.77]. IR (KBr) 3060, 2925, 2856, 2212, 1560 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 9.02 (d, J=0.7 Hz, 1H, H-6), 8.70 (d, J=0.7 Hz, 1H, H-3), 3.83–3.81 (m, 4H, 2′-CH_2 and 6′-CH_2), 1.78–1.75 (m, 6H, 3′-CH_2, 4′-CH_2 and 5′-CH_2); ^{13}C NMR (acetone-d_6) δ 152.2 (d), 146.3 (s), 143.0 (d), 117.7 (s), 93.2 (s), 49.8 (t), 26.4 (t), 24.4 (t).

(B) Operating for 5 h at 65 °C with 1.5 equiv of **2c** (63.9 mg, 74 μL, 0.75 mmol), chromatographic separation afforded **3c** (47.0 mg, 50%).

*4.2.4. Reactions of DCP (**1**) with N-methylpiperazine (**2d**).* (A) After DCP was allowed to react with **2d** (55.1 mg, 61 μL, 0.55 mmol) for 5 h, FC separation (EtOAc/MeOH/Et_3N 90:5:5) gave 4-cyano-5-(4-methylpiperazin-1-yl)pyridazine (**3d**) (52.0 mg, 51%) that crystallized from Et_2O/PE in orange needles, R_f (EtOAc/MeOH/Et_3N 90:5:5) 0.18, mp 122–123 °C; [found: C, 58.79; H, 6.25; N, 34.12. $C_{10}H_{13}N_5$ requires: C, 59.10; H, 6.45; N, 34.46]. IR (KBr) 3067, 2940, 2804, 2216, 1574 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.88 (d, J=0.7 Hz, 1H, H-6), 8.73 (d, J=0.7 Hz, 1H, H-3), 3.80 (t, J=5.1 Hz, 4H, 2′-CH_2 and 6′-CH_2), 2.60 (t, J=5.1 Hz, 4H, 3′-CH_2, and 5′-CH_2), 2.36 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$) δ 151.7 (d), 145.5 (s), 141.7 (d), 116.4 (s), 93.8 (s), 54.3 (t), 47.8 (t), 45.7 (q).

(B) After heating at 65 °C for 11 h, FC resolution led to **3d** (65.0 mg, 64%).

*4.2.5. Reactions of DCP (**1**) with morpholine (**2e**).* (A) After reaction of DCP with **2e** (47.9 mg, 48 μL, 0.55 mmol) for 24 h, chromatographic separation (EtOAc/MeOH 95:5) afforded 4-cyano-5-morpholinopyridazine (**3e**) (45.0 mg, 47%) as a red solid, R_f (EtOAc/MeOH 95:5) 0.29, mp 168–169 °C (from Et_2O/$CHCl_3$); [found: C, 56.89; H, 5.52; N, 29.77. $C_9H_{10}N_4O$ requires: C, 56.83; H, 5.30; N, 29.46]. IR (KBr) 3070, 2970, 2924, 2219, 1563 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 9.08 (d, J=0.8 Hz, 1H, H-6), 8.78 (d, J=0.8 Hz, 1H, H-3), 3.86 (s, 8H, 2′-CH_2, 3′-CH_2, 5′-CH_2, and 6′-CH_2); ^{13}C NMR (acetone-d_6) δ 152.1 (d), 146.7 (s), 142.9 (d), 117.5 (s), 94.1 (s), 66.8 (t), 48.7 (t).

(B) Operating for 5 h at 65 °C with 1.5 equiv of **2e** (65.3 mg, 66 μL, 0.75 mmol), chromatographic separation afforded **3e** (68.7 mg, 72%).

4.3. Reactions of DCP (1) with amines 2f–i. General procedure

A mixture of DCP (**1**) (65.0 mg, 0.50 mmol) and the amine in the reported solvent (1 mL) was kept at the specified temperature under magnetic stirring in a screw-cap tube (Pyrex N. 13) for the reported time. Chromatographic resolution of the crude reaction mixture obtained by evaporation of the solvent under reduced pressure allowed the isolation of the corresponding aminopyridazine derivative.

*4.3.1. Reaction of DCP (**1**) with diisopropylamine (**2f**).* FC resolution (EtOAc/MeOH 20:1) of the crude obtained by treatment of DCP with amine **2f** (55.6 mg, 77 μL, 0.55 mmol) in MeCN at room temperature for 42 h, led to 4-cyano-5-diisopropylaminopyridazine (**3f**) (36.0 mg, 35%) as a brown sticky product, R_f (EtOAc/MeOH 20:1) 0.33. IR (KBr) 3070, 2972, 2920, 2229, 1608 cm^{-1}; ^{1}H NMR (DMSO-

d_6) δ 8.31 (d, J=0.7 Hz, 1H, H-3), 8.08 (d, J=0.7 Hz, 1H, H-6), 3.29 (septet, J=6.5 Hz, 2H, 2× CH), 1.22 (d, J=6.5 Hz, 12H, 4× CH_3); ^{13}C NMR (DMSO-d_6) δ 166.9 (s), 152.1 (d), 150.8 (d), 118.5 (s), 96.2 (s), 46.2 (d), 18.9 (q). HRMS (ESI): MH^+, found 205.1445, $C_{11}H_{17}N_4$ requires 205.1448.

*4.3.2. Reaction of DCP (**1**) with diallylamine (**2g**).* Operating in $CHCl_3$ at 50 °C for 25 h with 3 equiv of **2g** (145.7 mg, 185 μL, 1.50 mmol), 4-cyano-5-diallylaminopyridazine (**3g**) (48.1 mg, 48%) was isolated by FC resolution (PE/EtOAc 2:3) as an orange oil, R_f (PE/EtOAc 2:3) 0.33. IR (liquid film) 3085, 2927, 2218, 1566 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.75 (d, J=0.8 Hz, 1H, H-6), 8.68 (d, J=0.8 Hz, 1H, H-3), 5.94–5.85 (ddt, J=17.2, 10.3 and 4.8 Hz, 2H, 2× CH_2CH=CH_2), 5.36–5.33 (m, 2H, 2× CH_2CH=CH_2), 5.23–5.18 (m, 2H, 2× CH_2CH=CH_2), 4.24–4.22 (m, 4H, 2× CH_2CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 152.0 (d), 143.9 (s), 140.7 (d), 130.4 (d), 118.5 (t), 116.9 (s), 90.8 (s), 52.8 (t). HRMS (ESI): MH^+, found 201.1132, $C_{11}H_{13}N_4$ requires 201.1135.

*4.3.3. Reaction of DCP (**1**) with aniline (**2h**).* Operating in THF at 110 °C (screw-cap tube Pyrex N. 13) for 82 h with 1.5 equiv of **2h** (69.8 mg, 68 μL, 0.75 mmol), 5-anilino-4-cyanopyridazine (**3h**) (76.8 mg, 78%) was isolated by FC resolution (PE/EtOAc 1:1) and crystallized from PE/acetone as pale orange needles, R_f (PE/EtOAc 1:1) 0.28, mp 186–187 °C; [found: C, 66.99; H, 3.81; N, 28.24. $C_{11}H_8N_4$ requires: C, 67.34; H, 4.11; N, 28.55]. IR (KBr) 3229, 3129, 2227, 1608, 1561 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 8.95 (s, 1H, H-6), 8.87 (br s, 2H, H-3 and NH), 7.53–7.49 (m, 2H, Ar–2H), 7.45–7.44 (m, 2H, Ar–2H), 7.35 (t, J=7.4 Hz, 1H, Ar–1H); ^{13}C NMR (acetone-d_6) δ 151.2 (d), 144.7 (s), 141.1 (d), 137.8 (s), 130.6 (d), 127.7 (d), 125.5 (d), 114.8 (s), 94.3 (s).

*4.3.4. Reaction of DCP (**1**) with p-toluidine (**2i**).* FC resolution (PE/EtOAc 1:1) of the reaction crude obtained by heating DCP and *p*-toluidine (**2i**) (80.4 mg, 0.75 mmol) in THF at 110 °C in a screw-cap tube (Pyrex N. 13) for 60 h gave rise to 4-cyano-5-(4-toluidino) pyridazine (**3i**) (101.0 mg, 96%) as ivory flakes, R_f (PE/EtOAc 1:1) 0.35, mp 226–227 °C (from Et_2O/acetone); [found: C, 68.21; H, 4.89; N, 26.72. $C_{12}H_{10}N_4$ requires: C, 68.56; H, 4.79; N, 26.65]. IR (KBr) 3221, 3116, 2914, 2223, 1605, 1560 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 8.88 (d, J=0.8 Hz, 1H, H-6), 8.84 (d, J=0.8 Hz, 1H, H-3), 8.79 (br s, 1H, NH), 7.32 (s, 4H, Ar–4H), 2.38 (s, 3H, CH_3); ^{13}C NMR (acetone-d_6) δ 151.2 (d), 144.9 (s), 141.0 (d), 137.7 (s), 135.1 (s), 131.1 (d), 125.7 (d), 114.8 (s), 93.9 (s), 21.0 (q).

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