The Structure of *N*-(Azol-*N*-yl)formamides: A Crystallographic and Dynamic NMR Spectroscopy Study

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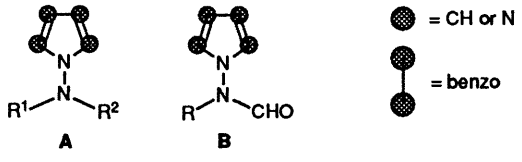
The molecular structures of *N*-(pyrazol-1-yl)formamide **1** [$C_4H_5N_3O$, orthorhombic, space group $P2_12_12_1$, $a = 5.269(8)$, $b = 8.039(8)$, $c = 12.79(2)$, $Z = 4$] and *N*-(indazol-1-yl)formamide **5** [$C_8H_7N_3O$, monoclinic, space group $P2_1/c$, $a = 9.065(2)$, $b = 11.089(7)$, $c = 8.463(7)$, $Z = 4$] have been solved by X-ray crystallography. Regarding the amide bond, both compounds exist in the *Z* configuration, a configuration which also prevails in solution for all the *N*-H azolyl formamides whilst the *N*-substituted derivatives prefer the *E* configuration. The rotation barriers about the amide bond are similar although a little lower than those of *N*-phenylformamide and *N*-methyl-*N*-phenylformamide, a fact that may be related to the electronic properties of the *N*-azolyl substituent.

During the synthesis of *N*-aminoazoles bearing alkyl substituents on the amino group, **A**,[1] two *N*-(azol-*N*-yl)formamides **B** (**1** and **5**) were used as intermediates. These compounds appear to be mixtures of *E* and *Z* isomers (see footnote 22 in ref. 1). We report here the synthesis of four more such compounds, the X-ray molecular structures of **1** and **5**, and the experimental barriers to rotation about the amide bond for **1**, **3**, **4** and **5**.



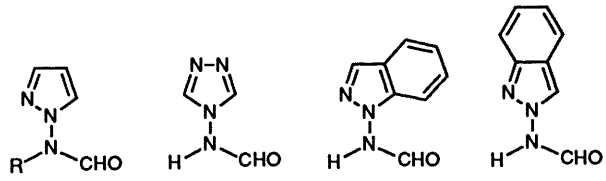
A B

Results and Discussion

N-(Azol-*N*-yl)formamides **B** are a new class of amides characterized by the presence on the amide nitrogen of an aromatic azole linked to it by the nitrogen. Since this substituent is very peculiar (no counterpart in aromatic nor in six-membered heterocyclic chemistry)[2] it was decided to study the properties of these amides including the *E*/*Z* isomerism in the solid state by crystallography and in solution by ^1H, ^{13}C and ^{15}N NMR spectroscopy, *i.e.* their static properties, as well as their dynamic behaviour in solution by ^1H DNMR spectroscopy.

X-Ray Crystallography.—Table 1 summarizes the results obtained with compounds **1** and **5**, while Figs. 1 and 2 correspond to a view (drawn with PLUTO)[3] of these compounds with the atomic numbering scheme. Table 2 contains a selection of geometrical parameters.

The structure of formamide **1** is characterized by two almost perfect planar systems, the pyrazole ring and the *Z*-amide group; these planes [N(1), N(2), C(1), C(2), C(3) *vs.* N(1), N(3), C(4), O(1)] are related by a dihedral angle of 85.5(2)°. In this respect, the structure of the other formamide **5** is very similar, the amide is still of *Z*-configuration and the dihedral angle between the N(1), N(2), C(1), C(2), C(3), C(5), C(6), C(7), C(8) (the indazole ring) and the N(1), N(3), C(4), O(1) (the amide



1; R = H
2; R = CH_3
3; R = $CH_2C_6H_5$

4 **5** **6**

group) planes is 96.1(2)°, *i.e.* both structures deviate by about 5° from orthogonality. This situation is to be compared with that of *N*-aminoazoles **A** ($R^1 = R^2 = H$),[9] where the nitrogen atom of the amino group is of sp^3 character, and where the conformation is such that its lone pair eclipses the azole plane (the so-called planar conformation). The geometries of the heterocyclic rings are similar to those described for pyrazoles in the case of compound **1**,[10] and to that of 1*H*-indazole in the case of compound **5**.[11]

Another interesting comparison would be with *N*-phenylformamide (formanilide), but the crystal structure of this compound is unknown. Fortunately, three derivatives of *N*-phenylformamide have been studied by Boeyens.[12] These compounds have a methyl group in the *ortho* position of the phenyl ring (both *E* and *Z* isomers) or an *ortho* phenyl group (*Z* isomer). The two more interesting conclusions of this comparison are: (i) the *ortho*-substituted phenyl ring forms a mean angle of 29° with the amide plane whereas in the case of the azole this angle is of 85°; (ii) the bond distances of the averaged amide geometry are very similar [*N*-phenylformamides, N–C = 1.338 Å, C–O = 1.211 Å; *N*-azolylformamides, N–C = 1.331(7) Å, C–O = 1.217(7) Å]. The first result corresponds to the tendency of the amino nitrogen to delocalize into the phenyl ring, a phenomenon that cannot occur in the case of *N*-substituted azoles; however, this delocalization is a minor effect compared with the amide delocalization and, consequently, both classes of amides are very similar in geometry and, as we will show later, in electronic properties.

The main features of the crystallographic packing are shown

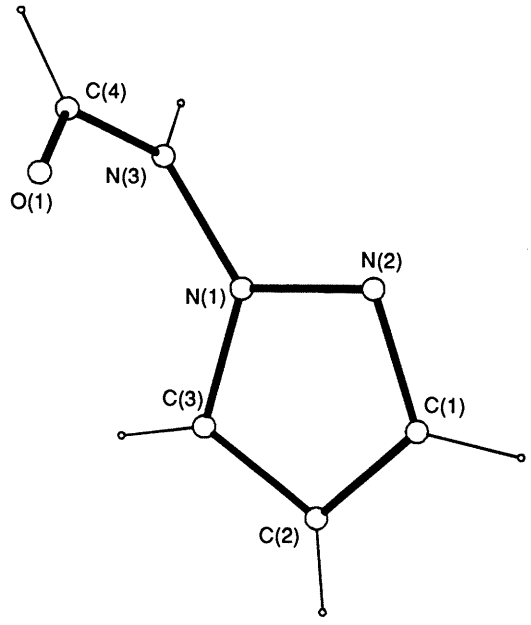


Fig. 1 A view of the crystal structure of **1** showing the atomic numbering

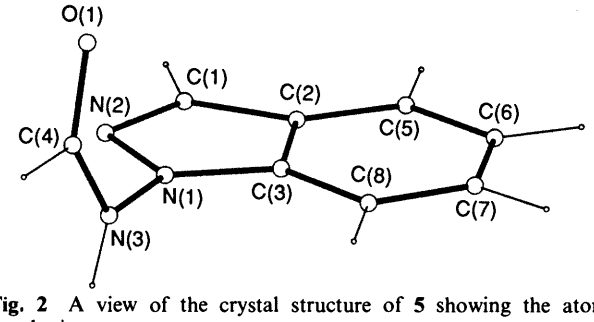


Fig. 2 A view of the crystal structure of **5** showing the atomic numbering

in Table 3, where only one strong intermolecular H-bond was found for **1**, while no intermolecular H-bonds were observed for compound **5**. Other intermolecular contacts are C–H • • • O contacts, observed for both compounds, with an average C • • • O distance of 3.376(4) Å.

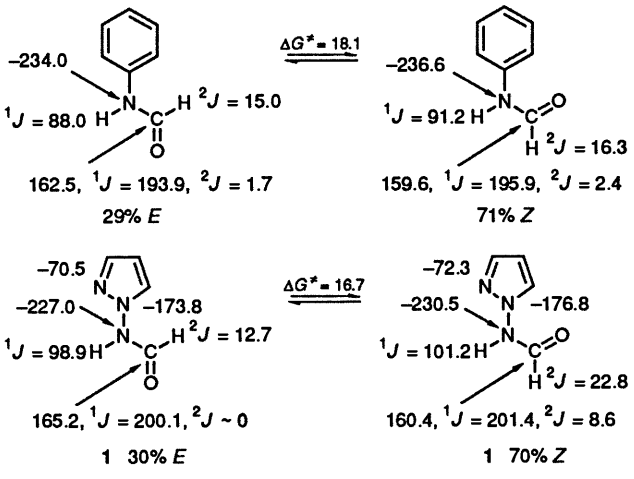
Considering that the barriers to rotation about the amide bond increase when its double bond character increases,[13] and assuming a positive relationship between bond order and bond length,[14] then, since in the pyrazole derivative **1**, N(3)–N(4) = 1.336(7) Å, and in the indazole derivative **5**, N(3)–C(4) = 1.326(7) Å, the barrier of the latter should be the higher.

In conventional amides having at least one N–H, the H-bond network involves N–H • • • O=C interactions.[15] In compound **1**, and presumably **4**, the strong hydrogen bond acceptor character of the pyridine-like nitrogen atom of the azole,[16] replaces these interactions by N(3)–H • • • N(2) ones.

NMR Spectroscopy.—E/Z *Equilibrium.* The data concerning compounds **1–6** are collected in Tables 4 (^{1}H NMR of azoles **1–4**), 5 (^{1}H NMR of indazoles **5** and **6**), 6 (^{13}C NMR of azoles) and 7 (^{13}C NMR of indazoles).

To assign the *E*/*Z* configuration to each isomer, several techniques have been used. In the case of compound **1**, the ^{13}C NMR signals of both isomers are quite similar, with the exception of the carbonyl group which appears at 160.4 ppm for the major isomer (70% from the ^{1}H NMR spectrum) and at 165.2 ppm for the minor one (30%). In the solid state (^{13}C CP/MAS technique), where the configuration is *Z*, this signal appears at 160.8 ppm [the three pyrazole carbons resonate at 137.9, C(3), 108.0, C(4) and 132.6 ppm, C(5)]. Therefore, the major isomer present in solution has the same *Z* configuration as that existing in the crystal. This method has been successfully used in the case of (*Z*)-*N*-phenylbenzamide and (*E*)-*N*-methyl-*N*-phenylbenzamide.[17]

The resulting assignment is consistent with other criteria found in the literature for amides. Thus, Barboiu and Petrescu[18] have shown that the carbon of the carbonyl group in formamide presents a larger ^2J coupling with the N–H proton *anti* to the carbonyl group (5.2 Hz) than with the *syn* N–H proton (2.9 Hz). The major isomer of pyrazole **1** presents such a coupling (8.6 Hz) whereas the coupling is absent in the minor isomer, which is consistent with them being respectively the *Z* and *E* isomers. In the case of *N*-methylformamide,[19] the carbonyl signal appears at 165.5 and 168.7 ppm for the *Z* and *E* isomers, respectively, and the signal of the *N*-methyl group at 25.4 and 29.4 ppm, for the same isomers. Both observations (δ C=O and δ N–R) are consistent with the assignments of compound **1** in Table 6. ^{15}N NMR spectroscopy is another useful tool to assign *E*/*Z* isomers in amides, using not only the chemical shifts,[20–22] but also the ^{1}H–^{15}N coupling constants. Those of *N*-phenylformamide were determined from the ^{1}H NMR spectrum of an enriched sample.[23] We summarized in Scheme 1 the comparison of *N*-phenylformamide (^{13}C chemical shifts and ^{1}H–^{13}C coupling constants from this work, the chemical shifts being consistent with a previous publication)[20] and *N*-(pyrazol-1-yl)formamide **1**. The only criteria that cannot be used are the ^3J(H–N–C–H) coupling constants (in *N*-phenylformamide, for the *E*-isomer, 11.0 Hz and for the *Z*-isomer, 2.0 Hz)[20,23] since they are not observed in azolylformamides, probably owing to the catalytic effect of the azole on the N–H exchange rate.



Scheme 1 *J* in Hz; $\Delta G^{\ddagger}$ in kcal mol^{-1}*

The *E*/*Z* ratios for compounds **1–6** as well as for *N*-phenylformamide and *N*-methyl-*N*-phenylformamide, are summarized in Table 8. No attempt has been made to study the effect of the concentration on the *E*/*Z* ratio, but it is much less sensitive in the case of azolylformamides than in the case of *N*-phenylformamide.[23,24] Nevertheless, each class of spectra has been recorded at the same concentration, 0.2 mol dm^{-3} for ^{1}H NMR and 0.5 mol dm^{-3} for ^{13}C NMR spectroscopy.

The population inversion when the last N–H is replaced by an alkyl group (compare **1** with **2** and **3**, or *N*-phenylformamide with its *N*-methyl derivative) is well documented.[17,24,27] The variation of the percentage of the *E* isomer as a function of the aromatic ring (pyrazole **1**, 30%, 4*H*-1,2,4-triazole **4**, 12%, 1*H*-indazole **5**, 30%, 2*H*-indazole **6**, 23%, phenyl, 29%) may be

* (1 cal = 4.184 J)

Table 1 Crystal analysis parameters at room temperature

	1	5
Crystal data		
Formula	$C_4H_5N_3O$	$C_8H_7N_3O$
Crystal habit	Colourless needles	Colourless needles
Crystal size/mm	0.15 × 0.09 × 0.03	0.17 × 0.07 × 0.03
Symmetry	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1/c$
Unit-cell determination:	Least-squares fit from 25 reflections ($5° < \theta < 15°$)	Least-squares fit from 25 reflections ($5° < \theta < 12°$)
Unit cell dimension/Å, °	a = 5.269(8)	a = 9.065(2)
	b = 8.039(8)	b = 11.089(7)
	c = 12.79(2)	c = 8.463(7)
		β = 112.63(5)
Packing: V/Å, Z	542(1), 4	785.2(9), 4
D_c/g cm^{-3}, M, F(000)	1.36, 111.10, 232	1.36, 161.16, 336
μ/cm^{-1}	0.97	0.89
λ/Å	0.710 73	
Experimental data		
Technique	Diffractometer: Enraf–Nonius CAD-4 single-crystal Graphite crystal monochromator: Mo-Kα, ω–2θ scans, 1 min per reflection	
Number of reflections:		
Measured	2116	1607
Independent	946	1373
Observed	410[2$\sigma(I)$ criterion]	457[3$\sigma(I)$ criterion]
Standard reflections:	3 reflections every 60 min	
Range hkl	0, −11, −18 to 7, 11, 18	−10, 0, 0 to 9, 13, 10
Drift correction	0.99–1.41	0.95–1.02
Absorption correction:		
Difabs	0.59–1.21	0.69–1.24
Solution and refinement:		
Solution	Direct methods	
Refinement	Full matrix least-squares on F_o	
Parameters:		
Number of variables	93	116
Degrees of freedom	317	341
Ratio of freedom	4.4	3.9
H atoms	Difference Fourier synthesis	
Final shift/error	0.07	0.001
Weighting scheme	$\Sigma w(F_o - F_c)^2$, $w = 1/[\sigma^2(F_o) + gF_o^2]$ with $\sigma(F_o)$ from counting statistics	
g	0.000 30	0.000 35
Max. thermal value	U22[O(1)] = 0.077(3) Å^2	U33[C(6)] = 0.100(5) Å^2
Final ΔF peaks	0.29, −0.26 e Å^{-3}	0.14, −0.19 e Å^{-3}
Final R and R_w	0.043, 0.035	0.043, 0.041
Computer and programs	MicroVAX-3400, SHELXS86,[4] SHELX76,[5] DIFABS,[6] PLUTO,[3] PARST[7]	
Scattering factors	*Int. Tables for X-Ray Crystallography*[8]	

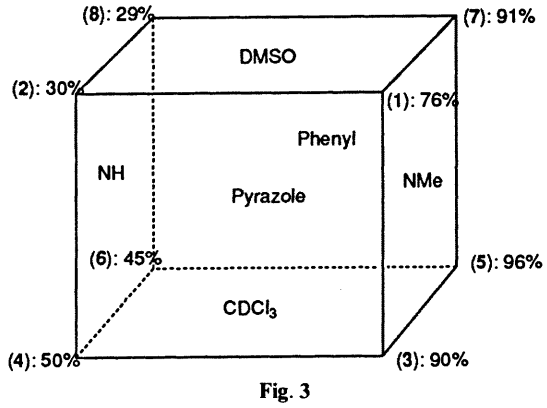


Fig. 3

related to some property of the heterocycle; for instance with the dipole moment of the corresponding *N*-aminoazole A (R^1 = R^2 = H, INDO calculations)[9] and aniline (μ = 1.48 D):[28] $\%E = 30.175 - 0.608\,\mu^2$, $n = 5$, $r^2 = 0.999$.

There is a clear solvent effect on the E/Z ratio. A way to discuss this effect is to put together the effects of the substituent on the nitrogen and the solvent for pyrazole **1** and for the phenyl group (*N*-phenylformamide, PF, and *N*-methyl-*N*-phenylformamide, NMPF) in a tridimensional display (Fig. 3).

This representation can be analysed as a classical 2^3 factorial design.[29] Variable X_1 corresponds to the aromatic substituent (phenyl, −1; pyrazol-1-yl, +1), variable X_2 corresponds to the substituent on the nitrogen (none, −1; methyl, +1) and variable X_3 represents the solvent [$CDCl_3$, −1; $(CD_3)_2SO$, +1]. Thus the eight vertices of the cube correspond to (1), compound **2** in $(CD_3)_2SO$; (2), compound **1** in $(CD_3)_2SO$; (3), compound **2** in $CDCl_3$; (4), compound **1** in $CDCl_3$; (5), NMPF in $CDCl_3$; (6), PF in $CDCl_3$; (7), NMPF in $(CD_3)_2SO$ and (8), PF in $(CD_3)_2SO$. From the corresponding values of the percentage of *E* isomer, the following effects can be calculated:

a_1 (effect of the aromatic substituent) = −1.88 which means that the $\%E$ decreases by 2 × 1.88 when the phenyl ring is replaced by a pyrazolyl, an effect that we have related to the dipole moments of aniline (μ_{exp} = 1.48 D) and 1-aminopyrazole (μ_{INDO} = 0.56 D).

a_2 (effect of *N*–R) = 24.88 which means that the $\%E$ increases by 2 × 24.88 when the N–H is replaced by an N–CH_3, an effect that we have commented upon previously.

a_3 (solvent effect) = −6.88 which corresponds to a decrease of 2 × 6.88 of the %E when $CDCl_3$ is replaced by $(CD_3)_2SO$, the more polar solvent stabilizing the Z isomer.

Nevertheless, these conclusions must be treated with caution since the interaction terms are important: a_{12} = −3.38, a_{13} = −1.62, and a_{23} = 2.12 (all in %E units).

Rotational barriers about the amide bond. To a first approximation, and considering all the problems with amide rotational barriers,[13,24,30] azolylformamides behave like *N*-phenylformamides. The lower barriers of these last compounds compared with formamides have been attributed to the fact that the conjugation of the nitrogen atom lone pair with the phenyl ring (aniline-type delocalization) decreases the double bond character of the amide bond. In the case of *N*-aminoazoles the lone pair cannot be delocalized in the azole ring since it is an N–N bond instead of an N–C bond.[9] Nevertheless the barriers are lower and this is not related to the presence of a second nitrogen, since the barriers of hydrazides are very similar to those of amides.[31]

Table 2 Bond lengths/Å and bond angles/° for compounds **1** and **5**

1		**5**	
N(1)–N(2)	1.367(5)	N(1)–N(2)	1.361(5)
N(1)–C(3)	1.360(6)	N(1)–C(3)	1.359(6)
N(1)–N(3)	1.371(5)	N(1)–N(3)	1.377(6)
N(2)–C(1)	1.334(6)	N(2)–C(1)	1.318(6)
C(1)–C(2)	1.392(8)	C(1)–C(2)	1.413(7)
C(2)–C(3)	1.353(8)	C(2)–C(3)	1.401(7)
N(3)–C(4)	1.336(7)	N(3)–C(4)	1.326(7)
C(4)–O(1)	1.213(6)	C(4)–O(1)	1.221(7)
		C(2)–C(5)	1.397(6)
		C(5)–C(6)	1.383(8)
		C(6)–C(7)	1.410(8)
		C(7)–C(8)	1.364(8)
		C(8)–C(3)	1.389(6)
N(2)–N(1)–C(3)	112.5(5)	N(2)–N(1)–C(3)	113.5(5)
N(2)–N(1)–N(3)	119.5(5)	N(2)–N(1)–N(3)	120.2(4)
C(3)–N(1)–N(3)	128.0(5)	C(3)–N(1)–N(3)	126.2(5)
N(1)–N(2)–C(1)	103.7(4)	N(1)–N(2)–C(1)	104.1(4)
N(2)–C(1)–C(2)	111.3(5)	N(2)–C(1)–C(2)	112.6(5)
C(1)–C(2)–C(3)	106.7(6)	C(1)–C(2)–C(3)	104.5(5)
N(1)–C(3)–C(2)	105.8(6)	N(1)–C(3)–C(2)	105.3(5)
N(1)–N(3)–C(4)	120.1(5)	N(1)–N(3)–C(4)	121.6(5)
N(3)–C(4)–O(1)	125.7(5)	N(3)–C(4)–O(1)	124.6(6)
		C(1)–C(2)–C(5)	136.5(6)
		C(3)–C(2)–C(5)	119.0(5)
		C(2)–C(5)–C(6)	118.2(6)
		C(5)–C(6)–C(7)	120.9(6)
		C(6)–C(7)–C(8)	122.2(6)
		C(7)–C(8)–C(3)	116.2(6)
		C(8)–C(3)–C(2)	123.6(5)
		C(8)–C(3)–N(1)	131.1(6)

N-Azolyl substituents are similar to pseudo-halogens [σ_p(pyrazole) = 0.19, σ_p(4*H*-1,2,4-triazole) = 0.33, σ_p(halogens) = 0.25].[32] Thus, the barrier should be compared with that of *N*-halogenoamides but no data are available. The only related information concerns *N*-trifluoromethyl amides, but these compounds appear to have much lower barriers than *N*-methyl amides [however $\sigma_p(CF_3)$ is 0.54].[33]

A final point concerning the barriers reported in Table 8 is that the prediction based on X-ray geometries [$\Delta G^{\ddagger}$(**5**) > $\Delta G^{\ddagger}$(**1**)] is fulfilled.

Experimental

M.p.s were determined with a Reichert model 723 hot-stage microscope and are uncorrected. Spectral studies were carried out with the following instruments: IR, Perkin-Elmer 577; ^1H, ^{13}C and ^{15}N NMR, Bruker AC-200. Combustion analyses were performed with a Perkin-Elmer 2400 CHN instrument.

Crystal-structure determination of Compounds **1** *and* **5**.—Cell parameters and orientation matrices were obtained by least-squares refinement using 25 reflections in the range 5° < θ < 15° (**1**) and 5 < θ < 12° (**5**). The data collection was performed for the two compounds using the techniques and references shown in Table 1. On all reflections profile analysis was performed.[34,35] The reflections were corrected for Lorentz and polarization; absorption corrections were applied for both compounds. The absolute configuration of amide **1** was assigned using a new version of the program BIJVOET[36] giving a Bijvoet coefficient of 0.24(9) for the ten strongest Friedel pairs. Selected bond distances and bond angles are given in Table 2. All calculations were made on the MicroVAX-3400 at the Scientific Computer Center of the University of Oviedo.

Tables of atomic coordinates, bond lengths and angles and thermal parameters for compounds **1** and **5** have been deposited at the Cambridge Crystallographic Data Centre.*

^1H *and* ^{13}C *NMR Spectroscopy.*—The ^1H, ^{13}C and ^{15}N NMR spectra (see ref. 9 for experimental details) were recorded on a Bruker AC 200 instrument working at 200.14, 50.32 and 20.29 MHz, respectively. Chemical shifts (δ) are given from internal tetramethylsilane for ^1H and ^{13}C nuclei and from external nitromethane for the ^{15}N nucleus (no corrections for bulk differences were applied) with an accuracy of ±0.1 ppm. Coupling constants (J in Hz) were measured with digital resolution of 0.2 Hz. In all cases standard conditions and Bruker microprograms were used for the homonuclear (^1H–^1H) and

* For details of the deposition scheme see 'Instruction for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

Table 3 Intermolecular H-bonds and shortest contacts for compounds **1** and **5**

	Donor-H	Donor ··· Acceptor	H ··· Acceptor	Donor-H ··· Acceptor
	Compound **1**			
	N(3)–H(3′)	N(3) ··· N(2)[a]	H(3′) ··· N(2)[a]	N(3)–H(3′) ··· N(2)[a]
	0.90(6)	2.884(7)	2.04(6)	156(5)
	C(1)–H(1)	C(1) ··· O(1)[b]	H(1) ··· O(1)[b]	C(1)–H(1) ··· O(1)[b]
	1.05(6)	3.384(8)	2.44(6)	149(4)
	C(3)–H(3)	C(3) ··· O(1)[c]	H(3) ··· O(1)[c]	C(3)–H(3) ···· O(1)[c]
	0.87(6)	3.374(8)	2.56(5)	158(5)
	Compound **5**			
	C(6)–H(6)	C(3) ··· O(1)[d]	H(3) ··· O(1)[d]	C(3)–H(3) ··· O(10)[d]
	1.08(1)	3.369(8)	2.680(8)	121.3

Symmetry codes: [a] $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$. [b] $-x - \frac{1}{2}, -y + 1, z + \frac{1}{2}$. [c] $x + 1, y, z$. [d] $-x + 1, y - \frac{1}{2}, -z + \frac{1}{2}$.

Table 4 ^{1}H NMR data of *N*-azolylformamides **1–4** (δ in ppm from $SiMe_4$, ^{1}H–^{1}H coupling constants in Hz)

Compound	Solvent	Conformer	H-3	H-4	H-5	CHO	N-H	N-R
1	$CDCl_3$	*Z*(50%)	7.52	6.36	7.52	8.28		
		E(50%)	7.52	6.36	7.52	8.36		
1	$(CD_3)_2SO$	*Z*(70%)	7.49	6.34	7.72	8.29	11.71(br)	—
			J_{34} = 1.7	J_{45} = 2.4	J_{35} = 0.7			
		E(30%)	7.53	6.39	7.90	8.32	11.71(br)	—
			J_{34} = 1.3	J_{45} = 2.3	J_{35} = 0.7			
1	CD_3OD	*Z*(68%)	7.72	6.58	7.80	8.49	—	—
				J_{45} = 2.5	J_{35} = 0.6			
		E(32%)	7.72	6.60	7.93	8.53	—	—
				J_{45} = 2.0				
2	$CDCl_3$	*Z*(10%)	7.65	6.38	7.30	8.09	—	3.52
			J_{34} = 2.1	J_{45} = 2.5				
		E(90%)	7.56	6.38	7.51	8.32	—	3.37
			J_{34} = 2.1	J_{45} = 2.5	J_{35} = 0.7			
2	$(CD_3)_2SO$	*Z*(24%)	7.52	6.35	7.77	8.13	—	3.39
			J_{34} = 2.1	J_{45} = 2.5				
		E(76%)	7.58	6.42	8.02	8.33	—	3.22
			J_{34} = 2.1	J_{45} = 2.5				
3	$CDCl_3$	*Z*(20%)	7.53	6.17	6.91	8.38	—	4.92(CH_2)
			J_{34} = 2.1	J_{45} = 2.4	J_{35} = 0.7			
		E(80%)	7.53	6.18	6.95	8.38	—	4.92(CH_2)
			J_{34} = 2.1	J_{45} = 2.5	J_{35} = 0.8			
3	$(CD_3)_2SO$	*Z*(23%)	7.49	6.21	7.62	8.65	—	4.98(CH_2)
				J_{45} = 2.2				
		E(77%)	7.53	6.29	7.66	8.46	—	4.98(CH_2)
			J_{34} = 2.0	J_{45} = 2.4				
4	$(CD_3)_2SO$	*Z*(88%)	8.69	—	8.69	8.39	11.67(br)	—
		E(12%)	8.84	—	8.84	8.33	11.67(br)	—

Table 5 ^{1}H NMR data of *N*-indazolylformamides **5** and **6** (δ in ppm from $SiMe_4$, ^{1}H–^{1}H coupling constants in Hz)

Compound	Solvent	Conformer	H-3	H-4	H-5	H-6	H-7	CHO	N-H
5	$CDCl_3$	*Z*(70%)	8.00	[—7.56–7.18—]		7.73	[7.56–7.18]	8.42	9.23(br)
		E(30%)	8.03	[—7.56–7.18—]		7.73	[7.56–7.18]	8.45	8.84(br)
5	$(CD_3)_2SO$	*Z*(34%)	8.13	7.80	7.21	7.50	7.41	8.46	9.0(br)
			J_{37} = 0.8	J_{45} = 7.7	J_{56} = 6.1	J_{46} = 1.0	J_{67} = 8.0		
							J_{57} = 1.8		
		E(66%)	8.18	7.83	7.25	7.50	7.41	8.45	9.0(br)
6	$(CD_3)_2SO$	*Z*(75%)	8.42	7.70	7.12	7.29	7.61	8.45	12.4(br)
		E(25%)	8.42	7.70	7.12	7.29	7.61	8.57	12.4(br)

heteronuclear (^{1}H–^{13}C) correlation experiments carried out on compounds **1** and **6**.[37]

Rotational barriers were measured by line-shape analysis[13,38] of formyl and methyl protons (the same values were obtained using pyrazole and indazole protons). The high-resolution solid-state ^{13}C NMR spectrum was recorded on a Bruker CXP400 (*Instituto de Materiales*, CSIC) working at 100.63 MHz.

Synthesis of Azolylformamides **B**.—*General procedure.* To a solution of 10 mmol of *N*-aminoazole in 40 cm^3 of anhydrous isopropyl ether was added 0.8 cm^3 (20 mmol) of 98% formic acid. The mixture was heated at reflux with a Dean-Stark trap until no more water was collected. The solvent was removed under vacuum and the residue purified. Column chromatography was always carried out using silica gel (240–300 mesh). Compounds **1** and **5** have already been described.[1]

N-*Methyl*-N-(*pyrazol*-1-*yl*)*formamide* **2**. Prepared from 1-(methylamino)pyrazole[1] and purified by column chromatography using ethyl acetate/light petroleum (40–65 °C) (8:2) as eluent. Yield (oil) 52% (Found: C, 47.7; H, 5.5; N, 33.8. $C_5H_7N_3O$ requires: C, 48.0; H, 5.64; N, 33.58); ν_{max}(film)/cm^{-1} 3120, 2930, 2880, 1700, 1520, 1480, 1450, 1400, 1350, 1330, 1270, 1200, 1140, 1080, 1040, 975, 940, 910, 890, 840 and 750.

N-*Benzyl*-N-(*pyrazol*-1-*yl*)*formamide* **3**. Prepared from 1-(benzylamino)pyrazole[1] and purified by column chromatography using ethyl acetate/light petroleum (2:1) as eluent. Yield (oil) 66% (Found: C, 65.35; H, 5.6; N, 20.6. $C_{11}H_{11}N_3O$ requires: C, 65.66; H, 5.51; N, 20.88); ν_{max}(film)/cm^{-1} 3120, 3060, 3030, 2930, 2880, 1700, 1520, 1500, 1450, 1390, 1360, 1320, 1270, 1200, 1100, 1080, 1060, 1050, 950, 910, 740 and 700.

N-(1,2,4-*Triazol*-4-*yl*)*formamide* **4**. Prepared from 4-amino-1,2,4-triazole (commercially available) and purified by crystallization from tetrahydrofuran/ethanol, m.p. 115–117 °C. Yield 75% (Found: C, 32.05; H, 3.6; N, 49.75. $C_3H_4N_4O$ requires: C, 32.15; H, 3.59; N, 49.98); ν_{max}(KBr)/cm^{-1} 3360, 3120, 3090, 1690, 1540, 1500, 1460, 1450, 1380, 1360, 1310, 1200, 1105, 1050, 940, 860 and 835.

N-(*Indazol*-2-*yl*)*formamide* **6**. Prepared from 2-aminoindazole[39] and purified by column chromatography using chloroform/ethanol (9:1) as eluent. M.p. 119–120 °C. Yield 42% (Found: C, 59.9; H, 4.4; N, 25.9. $C_8H_7N_3O$ requires: C, 59.62; H, 4.38; N, 26.07); ν_{max}(KBr)/cm^{-1} 3150, 3120, 3060, 2900, 1710, 1630, 1550, 1520, 1420, 1390, 1360, 1325, 1295, 1240, 1200, 1150, 1110, 1010, 980, 920, 880, 800 and 750.

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Table 6 ^{13}C NMR data of *N*-azolylformamides **1–4** (δ in ppm from $SiMe_4$, ^1H–^{13}C coupling constants in Hz)

Compound	Solvent	Conformer	C-3	C-4	C-5	CHO	N-R
1	$(CD_3)_2SO$	*Z*	137.6 ^1J = 187.0 ^2J = 5.1 ^3J = 8.4	105.4 ^1J = 178.2 ^2J = 9.6 ^2J = 8.7	130.8 ^1J = 193.0 ^2J = 9.1 ^3J = 4.0	160.4 ^1J = 201.4 ^2J = 8.6	—
		E	138.4 ^1J = 187.3 ^2J = 5.1 ^3J = 9.0	106.2 ^1J = 178.5 ^2J = 9.2 ^2J = 9.2	131.3 ^1J = 193.4 ^2J = 9.1 ^3J = 4.0	165.2 ^1J = 200.1	—
2	$CDCl_3$	*Z*	138.3	105.4	129.1	160.3	37.3
		E	138.9 ^1J = 188.4 ^2J = 5.0 ^3J = 8.9	106.2 ^1J = 179.5 ^2J = 9.5 ^2J = 8.4	129.1 ^1J = 192.1 ^2J = 9.0 ^3J = 3.9	162.2 ^1J = 204.8 ^3J = 1.8	34.4 ^1J = 141.4 ^3J = 3.2
2	$(CD_3)_2SO$	*Z*	137.9 ^1J = 187.3 ^2J = 5.1 ^3J = 8.9	105.4 ^1J = 178.5 ^2J = 9.1 ^2J = 9.1	129.9 ^1J = 193.1 ^2J = 9.0 ^3J = 4.4	161.5 ^1J = 205.8 ^3J = 2.5	37.7 ^1J = 140.9
		E	138.8 ^1J = 188.1 ^2J = 5.0 ^3J = 8.8	106.2 ^1J = 179.1 ^2J = 9.1 ^2J = 9.1	130.6 ^1J = 194.2 ^2J = 9.3 ^3J = 3.7	163.0 ^1J = 206.1 ^3J = 1.6	34.4 ^1J = 141.2 ^3J = 3.1
3	$CDCl_3$	*Z*	138.8 ^1J = 188.2	105.6 ^1J = 179.0	130.3 ^1J = 192.7	159.7 ^1J = 204.0	52.1(CH_2) ^1J = 140.7
		E	139.2 ^1J = 188.3 ^2J = 4.8 ^3J = 8.8	105.8 ^1J = 179.4 ^2J = 9.1 ^2J = 9.1	130.5 ^1J = 192.5 ^2J = 9.1 ^3J = 3.4	161.9 ^1J = 205.7	50.8(CH_2) ^1J = 141.3 ^3J = 3.1
3	$(CD_3)_2SO$	*Z*	137.9 ^1J = 187.5	105.0 ^1J = 178.6	130.8 ^1J = 193.0	161.4 ^1J = 207.0	53.5(CH_2) ^1J = 141.3
		E	138.7 ^1J = 188.1 ^2J = 5.1 ^3J = 8.8	105.9 ^1J = 179.2 ^2J = 9.0 ^2J = 9.0	131.2 ^1J = 194.2 ^2J = 9.4 ^3J = 3.7	162.9 ^1J = 207.6 ^3J = 1.5	50.3(CH_2) ^1J = 141.1
4	$(CD_3)_2SO$	*Z*	143.6 ^1J = 216.4 ^3J = 3.8	—	143.6 ^1J = 216.4 ^3J = 3.8	160.6 ^1J = 205.1	—
		E	144.3 ^1J = 216.8 ^3J = 3.4	—	144.3 ^1J = 216.8 ^3J = 3.4	165.0 ^1J = 203.3	—

Table 7 ^{13}C NMR data of *N*-indazolylformamides **5** and **6** (δ in ppm from $SiMe_4$, ^1H–^{13}C coupling constants in Hz)[a]

Compound	Conformer	C-3	C-4	C-5	C-6	C-7	C-3a	C-7a	CHO
5	*Z*	132.3 ^1J = 191.5 ^3J = 2.7	121.2 ^1J = 163.0 ^2J = 2.3 ^3J = 6.1	121.5 ^1J = 160.6 ^2J = 2.3 ^3J = 7.4	127.3 ^1J = 161.2 ^2J = 1.5 ^3J = 8.0	108.9 ^1J = 166.4	122.4	138.9	160.8 ^1J = 201.4
	E	133.0 ^1J = 192.1 ^3J = 2.7	121.3*	122.0* ^1J = 162.0	127.9 ^1J = 161.2	109.0 ^1J = 166.5	122.6	139.6	166.2 ^1J = 200.4
6	*Z*	124.6	120.7	121.9	126.5	117.2	120.4	145.9	160.0
	E	124.6	120.7	122.3	126.9	117.2	120.7	146.3	164.8

[a] In $(CD_3)_2SO$.

Table 8 *E*/*Z* ratios and rotational barriers (in kcal mol^{-1}, error ±0.5 kcal mol^{-1})

	E/*Z* ratio		Barriers ($\Delta G^{\ddagger}$)	
Compound	$(CD_3)_2SO$	$CDCl_3$	$E \longrightarrow Z$	$Z \longrightarrow E$
1	30/70	50/50	16.7	17.2
2	76/24	90/10	—	—
3	77/23	80/20	16.9	16.1
4	12/88	—	16.1	17.5
5	30/70	66/34	17.5	17.9
6	23/77	—	—	—
N-Phenylformamide	29/71	45/55[a]	18.1[b]	18.3[b]
N-Methyl-*N*-phenylformamide	91/9	96/4[c]	18.7[d]	17.1[d]

[a] 40/60 in ref. 20, 23. [b] From ref. 25 (solvent: $CDCl_3$). [c] 90/10 in ref. 26, 27. [d] From ref. 27 (solvent: C_6H_5Cl).

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