The [1,2,3]Triazolo[1,5-*a*]pyridine ring: A sensitive sensor for the electronic profile of phosphorus substituents†

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The unique nature of the [1,2,3]triazolo[1,5-*a*]pyridine reveals without any external perturbation the electronic contribution of various substituents to the phosphorus atom in phosphines, based on the equilibrium of two possible ring-chain isomers.

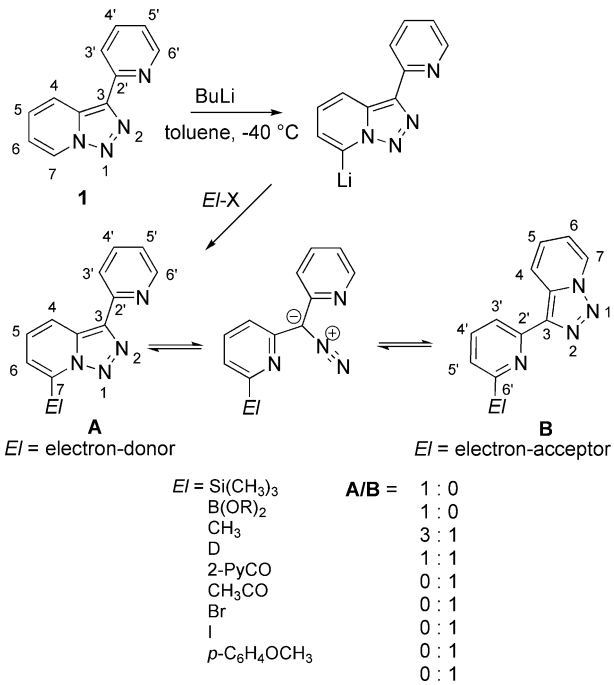
In the context of our study on the chemistry of [1,2,3]triazolo[1,5-*a*]pyridines we have reported their importance in coordination chemistry.[1] Their use in the field of magnetic materials,[2] and as fluorophores[3] that allow the formation of molecular chemosensors have been documented.[4] Quite recently, we could experimentally and theoretically show that 3-(2′-pyridyl)[1,2,3]triazolo[1,5-*a*]pyridine (**1**)[5] undergoes a regioselective metalation at C7. However, after trapping with an electrophile, a ring-chain isomerisation between the two regioisomers **A** and **B** *via* a diazo form occurs (Scheme 1).

We proved that the **A**–**B** ratio depends exclusively on the electronic properties of the *El* substituent.[5] Electron-donating substituents favour the **A** form, electron-withdrawing substituents favour the **B** form, and only in the case where *El* = Me both forms are present (75% of **A**, 25% of **B**).

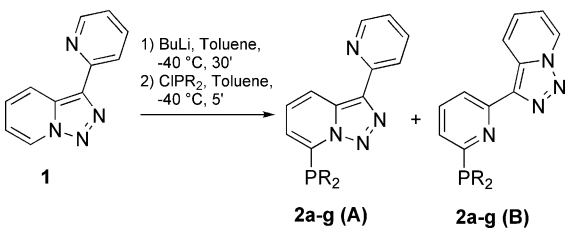
Substituents having both variable acceptor and donor character are expected to provide a mixture of these two structures. Thus, the ratio between structures **A** and **B** should reflect the relative value of the global electronic effect. For example, with **A**/**B** > 1 the substituent has essentially donor properties, while with **A**/**B** < 1, the acceptor capacity dominates.

Phosphines are typical substituents owing an "amphoteric" electronic character as they have both σ-donor- and π-acceptor properties. Therefore, we became interested in the synthesis of phosphine ligands based on the [1,2,3]triazolo[1,5-*a*]pyridine moiety due to its unusual electronic and chemical properties.

3-(2′-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (**1**) was treated with butyllithium in toluene at –40 °C, followed by trapping of the 7-lithiated intermediate with various aliphatic and aromatic chlorophosphines. In each case, a different ratio between the two regioisomers **A** and **B** was obtained (Scheme 2 and Table 1). The



Scheme 1 Triazole-ring rearrangement.



Scheme 2 Synthesis of triazolopyridine-based phosphines.

different isomers cannot be isolated separately, but can be perfectly identified by ^{1}H NMR as they show distinct signals (see ESI†).

When the phosphine acts essentially as an electron-donor, the 2′-phosphino-pyridyl ring-nitrogen is more nucleophilic and can attack the diazo intermediate giving rise to the triazole according to structure **A**. However, with phosphines withdrawing the electron density, the ring-nitrogen of the unsubstituted pyridine in the diazo intermediate is the most nucleophilic one leading to triazole structure **B** (Fig. 1).

The results obtained with the dicyclohexyl-, di-*iso*-propyl- and diphenyl phosphines (entries 1, 3 and 4 in Table 1) reflect the σ-donor properties of alkyl phosphines which are superior to those of aryl phosphines. However, the triazolopyridine system reflects

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† Electronic supplementary information (ESI) available: Experimental details, characterization data, as well as X-ray crystallographic data for **2d** (**B**) and **3e** (**B**). CCDC reference numbers 705762 & 705763. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b906034k

Table 1 Ratios of the donor/acceptor structures **A** and **B**

Entry	PR_2	A/B[a]	A/B[b]	Yield (%)
1	PCy_2 (**2a**)	1.39	1.00	22
2	$P(p\text{-}PhOCH_3)_2$ (**2b**)	1.23	0.88	10
3	$Pi\text{-}Pr_2$ (**2c**)	1.04	0.75	13
4	PPh_2 (**2d**)	0.72	0.52	40
5	$P(p\text{-}PhCH_3)_2$ (**2e**)	0.71	0.51	22
6	$P(p\text{-}PhF)_2$ (**2f**)	0.40	0.28	66
7	$P(p\text{-}PhCF_3)_2$ (**2g**)	0.18	0.13	46

[a] Ratio determined by ^{1}H-NMR before and after purification. [b] Normalized A/B ratio.

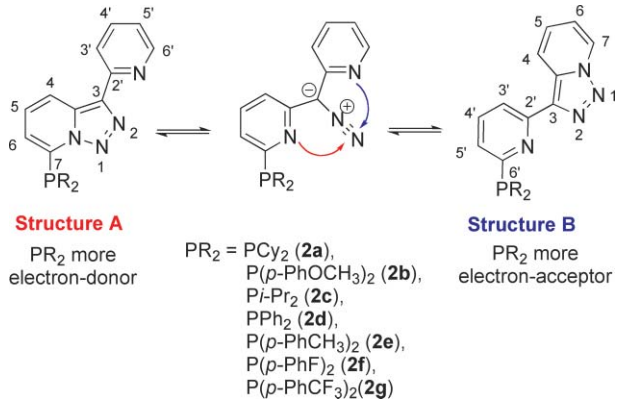

Fig. 1 Influence on the ring-chain isomers depending on the donor/acceptor-properties of the phosphines.

at the same time the dual property of phosphines. For instance, in the case of di-*iso*-propyl phosphine, there is no preferential structure. **A** and **B** are in equilibrium with a ratio of 1.04:1.00 (entry 3 in Table 1). In terms of electron density, this phosphine has equal properties of an acceptor and a donor. This observation is in accordance with calculations by Pacchioni and Bagus revealing that the π-acidity of PR_3 increases along the series $PMe_3 < PH_3 < P(OMe)_3 < PF_3$ with PMe_3 having a "remarkable" π-acidity.[6] When the phenyl-ring in diphenyl phosphine is substituted in the *para* position by electron-accepting groups like F or CF_3, the triazolopyridine **B** is obtained as the major compound. Thus, the acceptor capacity dominates largely. The presence of a methyl group in the *para* position has almost no influence on the global properties of the phosphine (entries 4 and 5 in Table 1). However, our study revealed that a *para*-methoxy diphenyl phosphine provides higher electron density to the triazole system, than di-*iso*-propyl phosphine (entries 2 and 3 in Table 1).

We were able to isolate a single crystal from the ring-chain isomer **2d** (**B**) and confirm its structure by single crystal X-ray analysis (Fig. 2). In solution, the pure isomer **2d** (**B**) undergoes once again equilibration and affords the equilibrium ratio with isomer **2d** (**A**) reported in Table 1 (entry 4).

The σ-donor ability of phosphine ligands is most often determined by measuring the magnitude of the $^1J(^{31}P\text{–}^{77}Se)$ in the ^{77}Se isotopomer of the corresponding selenide. According to Allen and Taylor, an increase in this coupling constant indicates an increase in the s character of the phosphorus lone-pair orbital (*i.e.*, a less basic phosphine = lower σ-donor ability).[7]

As expected, when the phosphines **2a–g** were converted into their selenides **3a–g**, the equilibrium was completely shifted

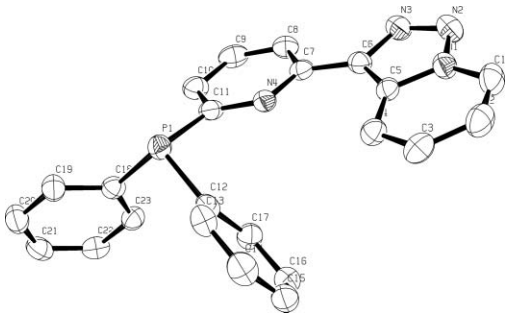

Fig. 2 Solid-state molecular structure of **2d** (**B**). Hydrogen atoms are omitted for clarity. For details see ESI.†

towards the electron-acceptor structure **B**. This allowed us to determine the σ-donor properties of these phosphines according to the selenide method. The structure of these selenides could also be confirmed by single crystal X-ray analysis (Fig. 3).

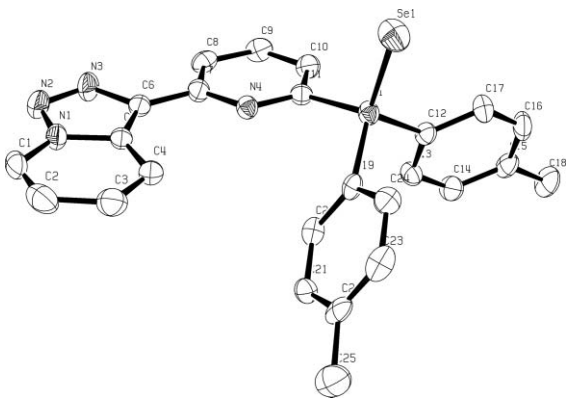

Fig. 3 Solid-state molecular structure of **3e** (**B**). Hydrogen atoms are omitted for clarity. For details see ESI.†

The range of selenium coupling constants is relatively small having the highest value for the smallest σ-donor effect (R = *p*-$PhCF_3$, entry 7 in Table 2) of $^1J(^{31}P\text{–}^{77}Se) = 1.00$ (normalized) and the lowest value (R = Cy, entry 1 in Table 2) for the highest σ-donor effect of $^1J(^{31}P\text{–}^{77}Se) = 0.93$. Thus, the method is less sensitive than the triazolopyridine moiety (Fig. 4).

The studies described here reveal the high sensitivity of the [1,2,3]triazolo[1,5-*a*]pyridine ring towards electronic perturbation. The electronic influence of different alkyl and aryl substituents on phosphorus was shown without any external perturbation (as is the case for the selenide method). For the first time different

Table 2 ^{31}P–^{77}Se coupling constants measured in $CDCl_3$ of the selenides **3a–g**

Entry	PR_2	$^1J_{P\text{-}Se}$ (Hz)[a]	$^1J_{P\text{-}Se}$[b]
1	PCy_2 (**3a**)	705.5	0.93
2	$P(p\text{-}PhOCH_3)_2$ (**3b**)	725.4	0.95
3	$Pi\text{-}Pr_2$ (**3c**)	713.5	0.94
4	PPh_2 (**3d**)	736.4	0.97
5	$P(p\text{-}PhCH_3)_2$ (**3e**)	729.6	0.96
6	$P(p\text{-}PhF)_2$ (**3f**)	744.4	0.98
7	$P(p\text{-}PhCF_3)_2$ (**3g**)	760.6	1.00

[a] Selenides were prepared according to the procedure described in the literature. [b] Normalized $^1J_{P,Se}$ values.

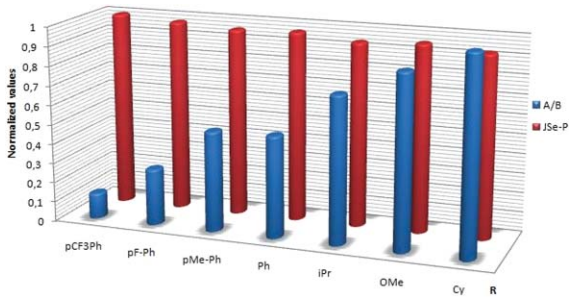

Fig. 4 Comparison between normalized $^{1}J_{P\text{-}Se}$ and normalized **A/B** ratio for the different couple of phosphines **2a–g**.

ratios of the ring-chain equilibrium were obtained with respect to the σ-donor/π-acceptor properties of the investigated phosphines. Further experimental and computational studies are in progress and will be reported soon.

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