Using ring strain to inhibit a decomposition path: first synthesis of an Alkyl-BIAN ligand (Alkyl-BIAN = bis(alkyl)acenaphthenequinonediimine)†

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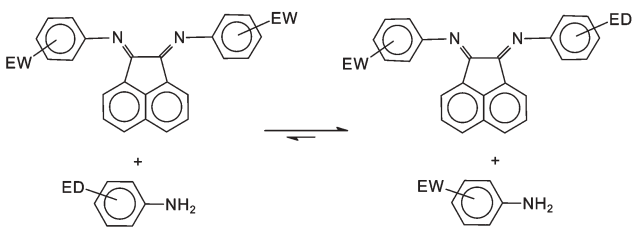
Received (in Cambridge, UK) 13th October 2004, Accepted 16th November 2004
First published as an Advance Article on the web 10th January 2005
DOI: 10.1039/b415767b

***N*-Alkyl imines of acenaphthenequinone are not stable because an isomerization occurs that releases part of the ring strain of the initially formed imine by changing the hybridization of one of the ring carbon atoms from sp^2 to sp^3; however, if an even more strained ring is present in the alkyl group, the isomerization becomes unfavorable and the compound is stable.**

Compounds of the family Ar-BIAN (Ar-BIAN = bis(aryl)-acenaphthenequinonediimine) (Scheme 1) have been known for some time,[1,2] but have been brought to general attention only in recent years by Elsevier and his group.[3] Since then, they have found widespread use as ligands and the corresponding complexes have been employed as catalysts for a wide variety of reactions.[4] For some of these syntheses, the use of the Ar-BIAN ligands was instrumental in achieving high performance of the catalytic system. However, BIAN derivatives having alkyl groups in place of aryl ones have not yet been reported. This is at first sight surprising since imines derived from alkylamines are generally even easier to prepare than those derived from arylamines. The earliest investigations of the reactivity of acenaphthenequinone with aliphatic amines date back almost 70 years.[5,6] Other works were published later,[3,7–11] but Alkyl-BIAN derivatives were never obtained. In general, a reaction always occurs, but mixtures of products are obtained and the desired bis-imine is never among them. The reactions of acenaphthenequinone with nitrogen nucleophiles have been recently reviewed.[12]

We have recently employed a transimination strategy to synthesize mixed Ar,Ar′-BIAN derivatives (Scheme 1).[5]

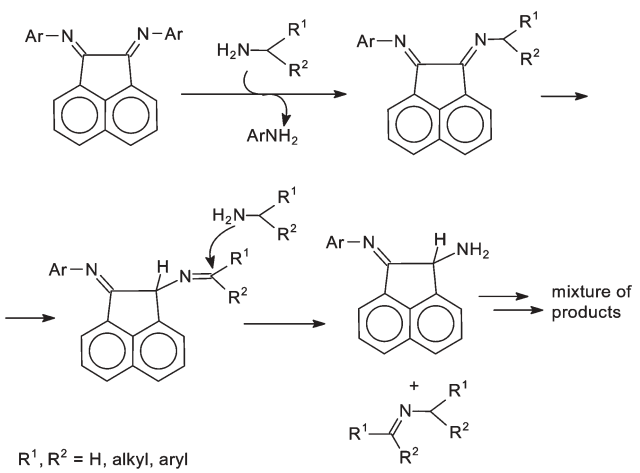
The reaction does not occur under mild conditions in the absence of a promoter, but proceeds easily in the presence of protic or Lewis acids, such as $ZnCl_2$. The exchange reaction in Scheme 1 occurs under milder conditions than the direct synthesis of the same compound from acenaphthenequinone and we hoped to avoid any decomposition in the synthesis of Alkyl-BIAN derivatives by use of this protocol. However, when we reacted $ZnCl_2$(Ar-BIAN) (Ar = 3,5-$Cl_2C_6H_3$, 4-$O_2NC_6H_4$, 3,5-$(CF_3)_2C_6H_3$) with several alkylamines, mixtures of products were obtained. A complete identification of all the products is underway, but a product that is always present and clearly identifiable in the GC-MS spectrum of the solution after the reaction of a generic amine $R^1R^2CHNH_2$ is the imine $R^1R^2C{=}NCHR^1R^2$. The only reasonable explanation for the formation of these imines is that transimination initially affords the desired $C{=}N{-}CHR^1R^2$ moiety, but this then isomerizes to $CH{-}N{=}CR^1R^2$ and the so formed iminic carbon is involved in a second transimination reaction with the alkylamine to afford the observed $R^1R^2CH{-}N{=}CR^1R^2$ (Scheme 2).



Scheme 1

The most obvious way of avoiding this isomerization would be to employ an amine lacking any hydrogen atom on the carbon atom α to nitrogen. However, no reaction was observed between either *tert*-butylamine or 1-aminoadamantane with acenaphthenequinone either directly or by a transimination procedure. This kind of amine appears to be too sterically hindered to form Alkyl-BIAN derivatives and this strategy cannot be used to solve the problem. A deeper understanding of the source of the problem is needed.

An isomerization of the kind shown in Scheme 2 can in principle occur during the synthesis of most imines, but is apparently not a problem in the synthesis of alkyldiazabutadienes or related ligands, likely because during the isomerization the conjugation between



Scheme 2

† Electronic supplementary information (ESI) available: experimental procedures and crystallographic data for [Pd(Cypr-BIAN)(η^3-$CH_2C(CH_3)CH_2$)][PF_6]. See http://www.rsc.org/suppdata/cc/b4/b415767b/

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the two double bonds is lost and the reaction is thus thermodynamically unfavorable.

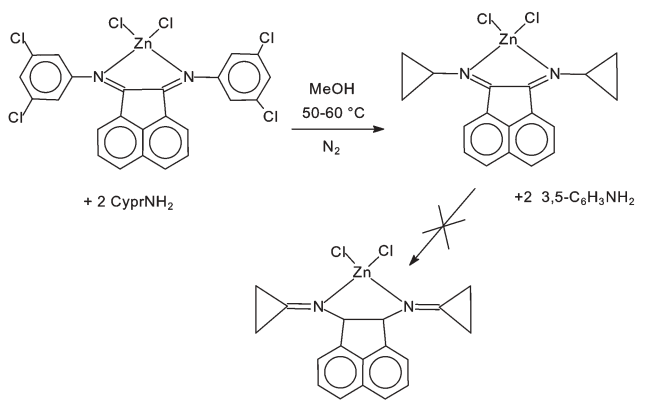
We deemed the reason for the high efficiency of the isomerization reaction under examination is to be found in the strain of the five-membered ring of all BIAN-type ligands. Five-membered rings are usually little strained because the ideal angle for an sp^3 hybridized atom is very close to that of a regular pentagon, although repulsion between the substituents deforms the ideal geometry. However, all five carbon atoms of the nitrogen-bearing ring of a BIAN ligand are sp^2 hybridized, a very unfavorable situation. Isomerization of the imine double bond rehybridizes one of the ring carbons from sp^2 to sp^3, thus partly releasing this hybridization-induced ring strain. The energy gain so obtained apparently overwhelms the loss due to the interruption of the conjugation between the two double bonds.

If we are correct in identifying the strain release as the initial cause for isomerization, then the solution is to employ an amine such that isomerization would eventually lead to a "total" final strain even higher than the one that is released. The ideal amine from this point of view is cyclopropylamine, since isomerization would generate an sp^2 carbon atom on a three-membered ring and this is very unfavorable for what we mentioned before on ideal angles. The approach was successful and the desired complex was obtained by transimination in a 95% yield without any detectable amount of isomerized product or of compounds deriving from ring opening of the three-membered ring (Scheme 3).

The free ligand was obtained in an overall 80% yield by shaking a CH_2Cl_2 suspension of $ZnCl_2$(Cypr-BIAN) (Cypr = cyclopropyl) with a saturated oxalate aqueous solution (see Supplementary Information).

That the isomerization and not the experimental conditions is responsible for previous failures to obtain Alkyl-BIAN derivatives is indicated by the fact that Cypr-BIAN can be obtained almost quantitatively even from the quinone and the amine in the presence of molecular sieves (in methanol, at 60 °C, in a closed vessel), although some product is lost in the purification (see Supporting Information). The presence of $ZnCl_2$ is not required.

Much has been written about strained systems in organic chemistry.[13] Strained systems are generally considered to be more reactive than their non-strained analogues and this increase in reactivity is employed as a synthetic tool. The present is a very rare case in which strain is employed to inhibit an unwanted decomposition which occurs with any unstrained group.‡



Scheme 3

We have recently introduced a method to measure the relative coordination strength of a chelating nitrogen ligand based on the position of an equilibrium reaction in which the tested ligand displaces Ph-BIAN from a complex.[4,5,14] Preliminary measurements indicate that Cypr-BIAN is a much stronger ligand for palladium than any Ar-BIAN compound and stronger even than phenanthroline.

A palladium π-allyl complex of Cypr-BIAN, [Pd(Cypr-BIAN)-(η^3-$CH_2C(CH_3)CH_2$)][PF_6], has been synthesized and its single crystal X-ray structure solved (Fig. 1).§ Details of the structure are included in the Supplementary Information. The most noteworthy feature is that the two cyclopropyl groups adopt two different conformations, and hence an asymmetric coordination to palladium, that is quite unusual in other BIAN complexes. The conformation of the C201–203 cyclopropyl ring hinders coordination to Pd and, as a result, the Pd–N2 distance is significantly longer than Pd–N1 (2.156(4) *vs.* 2.106(4) Å). The same effect is reflected in the Pd coordination to the allyl group. Preliminary calculations and intuition suggest that the conformation adopted by C101–C103 is more favorable, but cyclopropyl C201–C203 cannot assume the same conformation as the other group, because of being hampered by BIAN molecules of a symmetry related complex molecule, while the other cyclopropyl has free room available. In solution at RT the compound appears to be symmetric on the ^{1}H NMR timescale.

Now that an hybridization induced strain has been identified as both the cause and a possible remedy for the instability of "usual" Alkyl-BIAN compounds, other molecules can be designed which may be stable, keeping in mind that strained rings can be present not only in 3 or 4 membered cycles, but also in bi- or tri-cyclic molecules. Preliminary experiments indicate that Alkyl-BIAN ligands can also be obtained from cyclobutylamine, 2-aminonorbornane (bicyclic) and 2-aminoadamantane (tricyclic). However, these compounds are less stable than Cypr-BIAN and optimization of the conditions for their synthesis is in progress.

In this work we have shown that strained systems can impart stability, instead of instability, when included in a more complex system in cases where the decomposition would generate an additional strain in the already strained moiety. This principle is clearly not limited to the synthesis of Alkyl-BIAN compounds and not even to organic chemistry in general. For example, many transition metal alkylamido and alkoxo complexes are unstable because of easy β-hydrogen elimination. Use of strained amines and alcohols should inhibit this latter reaction and may constitute

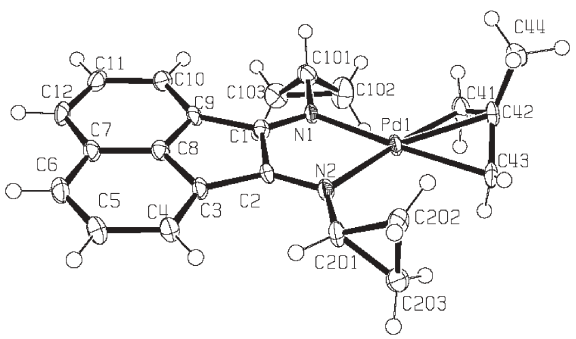


Fig. 1 ORTEP drawing of the cationic part of [Pd(Cypr-BIAN)(η^3-$CH_2C(CH_3)CH_2$)][PF_6].

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an entrance to a new chemistry of this type of complex. Attempts in this direction are in progress.

We thank P. Parma and S. Morelato for experimental assistance, Prof. S. Cenini for helpful discussions, and the MIUR (PRIN 2003033857) for financial support.

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Notes and references

‡ It has long been known[15] that SN1 substitution reactions on cyclopropyl derivatives are slower than those of unstrained molecules. However, we are not aware of any case in which this effect has been developed into a synthetic tool to prepare otherwise unstable molecules.

§ Crystal data for $[PF_6][Pd(C_3H_5)_2C_{12}H_8(C_4H_7)]$: monoclinic, $P2_1/n$, a = 8.600(1), b = 13.217(2), c = 18.918(3) Å, β = 91.575(4)°, V = 2149.6(7) Å^3, T = 120(2) K, Z = 4, MW = 566.79, μ = 1.0 mm^{-1}, 3804 independent reflections, R_{int} = 0.066, R_1 = 0.046 ($I > 2\sigma(I)$). CCDC 243009. See http://www.rsc.org/suppdata/cc/b4/b415767b/ for crystallographic data in .cif or other electronic format.

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