Unexpected Formation of Bis(1*H*-7-azaindol-3-yl)(2,4,5-trimethylphenyl)methane by Erbium Metal-Induced C–H Activation

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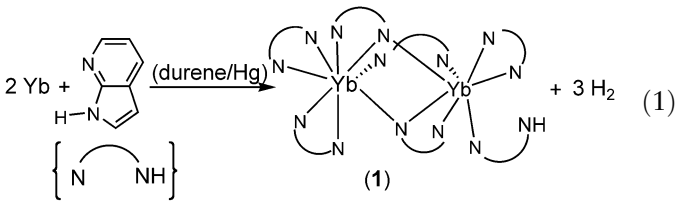
Abstract: Reaction of 7-azaindole (azinH) and 1,2,4,5-tetramethylbenzene (durene) in the presence of erbium metal and mercury at 170 °C under vacuum induced an unusual C–C bond formation between a methyl group of durene and C3 of two azinH molecules yielding bis(1*H*-7-azaindol-3-yl)(2,4,5-trimethylphenyl)methane {**2:** IUPAC name 3-[1*H*-pyrrolo[2,3-*b*]pyridin-3-yl(2,4,5-trimethylphenyl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine}. The structure of **2** was established by X-ray crystallography and supported by IR, NMR and mass spectroscopy.

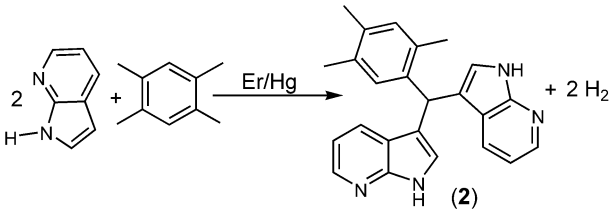
Keywords: catalysis; C–C bond formation; C–H activation; crystallography; erbium; lanthanide

Lanthanoid salts and complexes are widely used in organic synthesis.[1–4] Use of free lanthanoid metals is less widespread[4,5] though mischmetal (alloy mainly of La, Ce, Pr and Nd) has recently been used as a co-reactant in the formation of tertiary alcohols in the presence of a SmI_2 catalyst,[6] and desulphurisation of thiocarbonyl compounds has been effected by ytterbium metal.[7] However, lanthanoid metals are increasingly being used as reagents in the synthesis of organometallics, alkoxides, aryloxides and organoamides.[5,8,9] For example, the direct reaction of lanthanoid metals with weak protic acids at elevated temperatures provides a range of reactive homoleptic lanthanoid organoamides and aryloxides.[8–11] Thus, mercury-activated ytterbium metal reacts with 7-azaindole (azinH) (with and without a durene flux) to give $[Yb_2(azin)_6(azinH)]$ (**1**) with three different azin coordination modes established by X-ray crystallography.[12]



(1)

In attempting the analogous reaction of 7-azaindole with erbium and mercury in durene, the outcome was so surprising that it is reported now, even though the scope is not yet known. Instead of obtaining an erbium 7-azaindolate complex, C–C bond formation occurred giving bis(1*H*-7-azaindol-3-yl)(2,4,5-trimethylphenyl)-methane (**2**), Eq. (2).



(**2**)

Upon slow cooling of the reaction mixture, large rectangular colourless crystals of **2** were observed and the structure was elucidated by X-ray crystallography (Figure 1a), indicating the formation of two C–C bonds of normal single carbon-bond length (*ca.* 1.50 Å) between a methyl carbon of durene and two 7-azaindole molecules through C(3). Hydrogen atoms on the N (indole) of the 7-azaindol-3-yl groups were located on the difference map and are involved in H-bonding through interaction with pyridyl nitrogens on adjacent molecules resulting in a 3-D network (Figure 1b). All other hydrogens were refined in calculated positions.

The highest yield (yet to be optimised) was obtained with a substantial excess of durene (see Experimental Section). Use of less durene or stoichiometric amounts, Eq. (2), lowered the yield. Confirmation of the identity of the bulk product was provided by mass and NMR spectroscopy and unit cell determinations on further crystals. Noteworthy in the ^{1}H NMR spectrum of **2** was the loss of the H-3 resonance of 7-azaindole (6.42 ppm), formation of three separate methyl resonances and a methine peak at 5.90 ppm consistent with a triarylmethane. Retention of the pyrrole hydrogen was indicated by a singlet at 11.32 ppm and a strong ν(NH) absorption in the IR spectrum at 3140 cm^{-1}. The outcome of the present reaction giving **2** is reminiscent of reactions of indoles,[13] including 7-azaindole,[14] with

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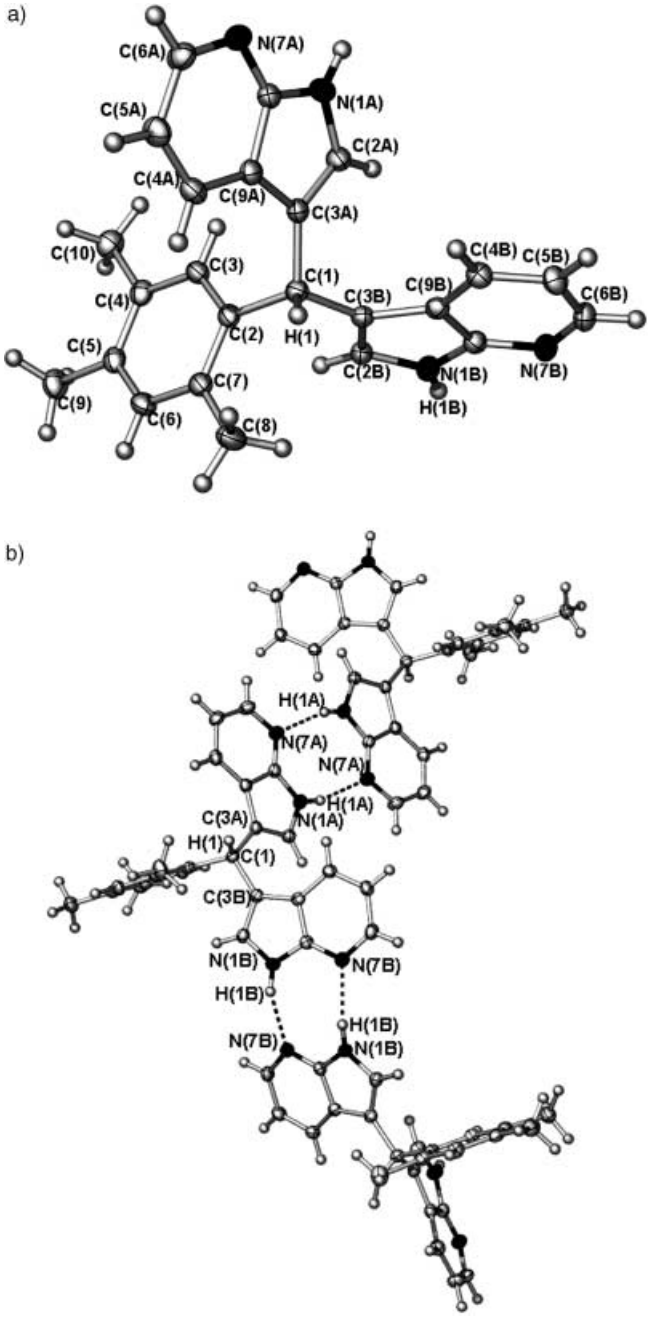

Figure 1. a. X-ray crystal structure of **1**. Thermal ellipsoids are shown at the 50% level. Selected bond distances and angles C(1)–C(3A) 1.504(2), C(1)–C(3B) 1.517(2), C(1)–C(2) 1.530(2) Å. C(3A)–C(1)–C(3B) 113.11(14), C(3A)–C(1)–C(2) 113.03(13), C(3B)–C(1)–C(2) 110.21(14)°.
b. Hydrogen bonding N–H···N in **2** between pyrrole and pyridine nitrogens of adjacent molecules. N···N intermolecular separations range from 2.879(2) to 2.886(2) Å for 1*H*-7-azaindol-3-yl A and B, respectively.

aldehydes to give C-3 substituted bis(1*H*-indol-3-yl)-methanes[15] by electrophilic aromatic substitution. A recent example utilises heterogeneous catalysis with $NaHSO_4$ supported on silica and amberlyst-15.[16] However, it seems implausible that erbium can promote electrophilic substitution, requiring the formation of trialkylphenylmethyl cations at 170 °C. A more likely mechanism under these conditions is a free radical process where C-3 of azinH is likely to be attacked.[17] Activation of durene through transitory formation of an erbium hydride species may generate an arylmethyl radical which then attacks C-3 of azinH. The resulting 1*H*-7-azaindol-3-yl-methane is then further activated giving a more stable arylheteroarylmethyl radical which attacks another azinH to form the product **2**.

In conclusion, unusual C–C formation can be achieved by reaction of a mixture of 7-azaindole and durene in the presence of erbium metal. Triple substitution of the methyl group was not achieved presumably due to steric crowding. The scope of the reaction is being determined but as yet similar behaviour has not been observed for indole and 2-phenylindole nor any interaction achieved between azinH and toluene or hexamethylbenzene.

Experimental Section

Bis(1*H*-7-azaindol-3-yl)(2,4,5-trimethylphenyl)methane (2)

Erbium metal (0.10 g, 0.597 mmol), 7-azaindole (0.08 g, 0.684 mmol), durene (0.50 g, 3.73 mmol) and elemental mercury (several drops) were placed in a Carius tube, which was evacuated and sealed. The tube was then heated to 150 °C for 4 days then at 170 °C for 2 days. The contents were extracted out of the tube using toluene, resulting in a mixture of colourless crystals, mercury and excess metal in a light brown/orange solution. The solution was then filtered and the colourless crystals of 2 were hand picked from the erbium metal and some were used for X-ray crystallography. Yield (residual crystals): 0.049 g (40%); mp 256–259 °C. IR (Nujol mull): $\nu = 3140$ (s), 1651 (s), 1600 (s), 1584 (s), 1507 (vs), 1422 (s), 1343 (s), 1282 (vs), 1202 (s), 1107 (s), 1065 (s), 1024 (vs), 999 (vs), 956 (s), 901 (s), 866 (vs), 796 (vs), 769 (vs), 721 (vs) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 2.01$ (s, 3H, *p*-CH_3), 2.14 (s, 3H, *m*-CH_3), 2.26 (s, 3H, *o*-CH_3), 5.90 (s, 1H, methine), 6.80 [s, 1H, H3(Ph)], 6.81 [s, 2H, H2(azin)], 6.92 [dd, $^3J = 8.0$ Hz, $^3J = 4.7$ Hz, 2H, H5(azin)], 6.96 [s, 1H, H2(Ph)], 7.55 [dd, $^3J = 7.8$ Hz, $^4J = 1.0$ Hz, 2H, H4(azin)], 8.16 [dd, $^3J = 4.6$ Hz, $^4J = 1.3$ Hz, 2H, H6(azin)], 11.32 (br s, 2H, N-H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 400 MHz): $\delta = 18.52$ [*o*-$\underline{C}H_3$(Ph)], 18.74 [*p*-$\underline{C}H_3$(Ph)], 19.10 [*m*-$\underline{C}H_3$(Ph)], 35.46 (methine C), 114.81 [C5(azin)], 116.01 [C3(azin)], 118.85 [C9(azin)], 124.04 [C2(azin)], 126.95 [C2(Ph)], 128.89 [C4(Ph)], 131.51 [C4(azin)], 132.41 [C6(Ph)], 132.83 [C5(Ph)], 133.43 [C3(Ph)], 138.95 [C6(azin)], 142.34 [C1(Ph)], 148.82 [C8(azin)]; ES-MS (DMSO-d_6): *m/z* (%) = 367.1903 (calcd. 367.1928) (100) $[M+H]^+$, 385.1911 (calcd. 385.2028) (20) $[M+H+H_2O]^+$, 451.2411 (calcd. 451.2433) (78) $[M+H+$DMSO-$d_6]^+$, 473.2228 (calcd. 473.2252) (17) $[M+Na+$DMSO-$d_6]^+$. A reaction in the absence of erbium metal gave only reactants (TLC analysis).

Crystal Data for 2

$C_{24}H_{22}N_4$, $M = 366.46$, crystal dimensions $0.30 \times 0.30 \times 0.25$ mm, monoclinic, $C2/c$, $a = 18.295(4)$, $b = 10.862(2)$, $c = 20.334(4)$ Å, $\beta = 105.97(3)^\circ$, $V = 3884.8(14)$ Å^3, $Z = 8$, $D_c = 1.253$ g/cm^3.[18] The structure was solved and refined using the SHELX suite of programs.[19] The program X-Seed[20] was used as an interface to the SHELX programs, and to prepare the figures.

Acknowledgements

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[18] Crystallographic data (excluding structure factors) for **2** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 210469. Copies of the data can be obtained free on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. Code +44(1223)336 – 033; E-mail:deposit@ccdc.cam.ac.uk].
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