Synthesis of Indazolo[3,2-*a*]isoquinoline

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Treatment of 1-(2'-nitrophenyl)isoquinoline with hot triethylphosphite afforded indazolo[3,2-*a*]isoquinoline.

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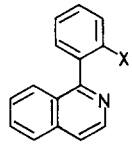
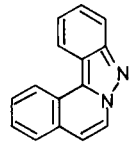
The triethylphosphite mediated intramolecular reductive cyclisation of arylnitro compounds is an established method of synthesising heterocycles and is believed to involve an arylnitrene intermediate or its equivalent [1-3]. We wished to study the intramolecular reductive cyclisation reaction of 1-(2'-nitrophenyl)isoquinoline **1** as a potential route to the indazolo[3,2-*a*]isoquinoline ring system **2**. We recognised that reductive cyclisation of compound **1** could result in formation of either a nitrogen-nitrogen bond giving product **2** or a carbon-nitrogen bond giving product **3** *via* the common electrophilic nitrene intermediate **4**. The triethylphosphite mediated intramolecular reductive cyclisation reactions of aryl-nitro compounds where either nitrogen-nitrogen or carbon-nitrogen bond formation might occur have only been reported occasionally [4-7].

1-(2'-Nitrophenyl)isoquinoline **1** was readily prepared from the known 1-(2'-nitrophenyl)-3,4-dihydroisoquinoline [8] by treatment with *N*-bromosuccinimide in boiling carbon tetrachloride solution in 98% yield. When compound **1** was treated with excess hot triethylphosphite the required indazolo[3,2-*a*]isoquinoline **2** was the only product isolated in 80% yield. The structure of the compound **2** was confirmed from its proton-nmr spectrum. Thus ten aromatic protons with their expected multiplicities were observed whereas in the alternative product **3**, only nine aromatic protons would be expected together with a >NH proton.

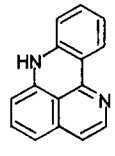
We have thus successfully prepared indazolo[3,2-*a*]isoquinoline **2** and elucidated the preferred mode of intramolecular cyclisation of the arylnitrene **4**.



1 X=NO_2
4 X=$\ddot{N}$:



2



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EXPERIMENTAL

Proton-nmr spectra were determined at 300 MHz in deuteriochloroform solution using tetramethylsilane as an internal standard. Infrared spectra were determined as cesium iodide discs.

1-(2'-Nitrophenyl)isoquinoline **1**.

A mixture of 1-(2'-nitrophenyl)-3,4-dihydroisoquinoline (2.0 g) [8], *N*-bromosuccinimide (1.8 g) and a few crystals of dibenzoyl peroxide was heated in carbon tetrachloride (40 ml) at reflux (3 hours) with stirring. After cooling to room temperature, chloroform (30 ml) and dilute sodium hydroxide solution were added. The mixture was shaken vigorously until all residue had dissolved. The organic layer was separated, washed with water, dried (sodium sulfate) and evaporated giving 1-(2'-nitrophenyl)-isoquinoline **1** (1.90 g, 96%) as pale yellow needles, mp 104° (from ethanol); ir: ν max 1530, 1380 and 1365 cm^{-1}; δ 8.56 (1H, d, J = 6 Hz), 8.18 (1H, dd, J = 8 and 1.5 Hz), 7.90 (1H, d, J = 8 Hz) and 7.80-7.45 (7H, m).

Anal. Calcd. for $C_{15}H_{10}N_2O_2$: C, 72.0; H, 4.0; N, 11.2. Found: C, 71.7; H, 3.9; N, 11.0.

Indazolo[3,2-*a*]isoquinoline **2**.

A mixture of compound **1** (0.4 g) and triethylphosphite (2 ml) was heated (24 hours) in an oil-bath (oil-bath temperature 115-130°) under an atmosphere of nitrogen. After cooling to room temperature the excess triethylphosphite was removed under reduced pressure (Kugelrohr) and the residue was fractionated by column chromatography (silica gel, eluent chloroform-methanol, 9:1) giving indazolo[3,2-*a*]isoquinoline **2** (0.28 g, 80%) as yellow needles, mp 92-93° (from toluene-hexane); ir: ν max 1520, 1350 and 1230 cm^{-1}; δ 8.65 (1H, d, J = 8 Hz), 8.58 (1H, d, J = 8 Hz), 8.43 (1H, d, J = 8 Hz), 7.94 (1H, d, J = 8 Hz), 7.85 (1H, d, J = 8 Hz), 7.74 (1H, td, J = 8 and 1 Hz), 7.60 (1H, td, J = 8 and 1 Hz), 7.54 (1H, td, J = 8 and 1 Hz), 7.38 (1H, d, J = 7 Hz) and 7.32 (1H, td, J = 7 and 1 Hz).

Anal. Calcd. for $C_{15}H_{10}N_2$: C, 82.5; H, 4.6; N, 12.8. Found: C, 82.5; H, 4.6; N, 12.9.

Collection and combination of further fractions from the column afforded a red oil (0.12 g) which was shown to be a complex mixture of products (by tlc) and was not investigated further.

Acknowledgements.

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References and Notes

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