Hydrogenation of 9-pyridylmethylene- and 9-benzylidene(aza)fluorenes in the presence of rhenium heptasulfide

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Hydrogenation of 9-pyridylmethylene(aza)fluorenes and 9-benzylidene-4-azafluorene at 250 °C and p_{H_2} = 130 atm in the presence of Re_2S_7 as a catalyst occurs preferably at the exocyclic double bond of the fulvene fragment to yield pyridyl-9-(aza)fluorenylmethanes.

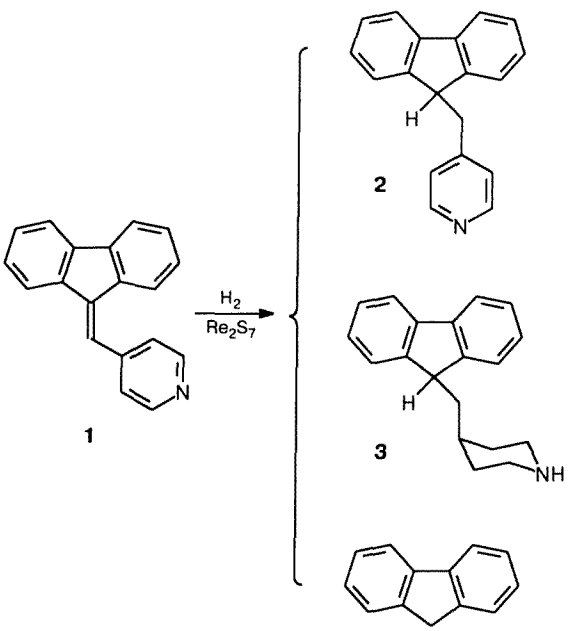
Key words: 9-pyridylmethylene(aza)fluorene, 9-benzylidene-4-azafluorene, hydrogenation; rhenium heptasulfide; 9-(4-pyridylmethyl)fluorene; 9-(4-piperidylmethyl)fluorene.

Previously,[1–3] conditions for the hydrogenation of polynuclear nitrogen-containing heterocycles in the presence of rhenium heptasulfide were found. It was of interest to study the possibility of hydrogenation of the fulvene type exocyclic double bond. For this purpose, we choose 9-pyridylmethylene(aza)fluorenes as objects of the study. Reduction of the double bond in these compounds would give heterocycles containing the so-called "magic grouping" of the $Ar_2CH(CH_2)_nNR^1R^2$ type, which often causes pharmacological activity.[4] We used the previously synthesized 9-(4-pyridylmethylene)fluorene (**1**),[5] 9-(4-pyridylmethylene)-4-azafluorene,[6] and 9-benzylidene-4-azafluorene[7] as starting fulvenes. These substrates were hydrogenated under conditions that are optimal for maintaining a high activity of a catalyst of reduction of pyridine moieties into the corresponding piperidines (Re_2S_7, 250 °C, p_{H_2} = 130 atm).[1–3]

Hydrogenation of fulvene **1** resulted in a high overall yield of a mixture of three compounds: 9-(4-pyridylmethyl)fluorene (**2**), 9-(4-piperidylmethyl)fluorene (**3**), and fluorene (a hydrogenolysis product), which were isolated by column chromatography in 33, 16, and 10 % yields, respectively.

The presence of partially hydrogenated derivative **2** in the mixture suggests that the starting compound **1** is probably first preferably coordinated to acidic centers of the catalyst by its fulvene fragment, where excess π-electron density is located, rather than by the unshared electron pair (UEP) of the N atom in the pyridine ring. Calculations of such fulvene systems confirm the presence of partial negative charges on C atoms of the exocyclic double bond.[6] The product formed after reduction of this bond is coordinated to the active catalyst surface through the UEP of the N atom, which favors hydrogenation of the pyridine ring.

Scheme 1



Hydrogenation of azafluorene systems under similar conditions (transition from fluorenylidene **1** to 9-benzylidene-4-azafluorene (**4**) and 9-(4-pyridylmethylene)-4-azafluorene (**5**)) gives complex mixtures of products, including derivatives hydrogenated at the C(9)=C(10) bond, 9-benzyl-4-azafluorene (**6**) and 9-(γ-pyridylmethyl)-4-azafluorene (**7**) isolated in low yields (10—20 %) (Scheme 2). The formation of compounds **6** and **7** containing non-reduced pyridine rings confirms that azafluorene systems are initially also preferably coordi-

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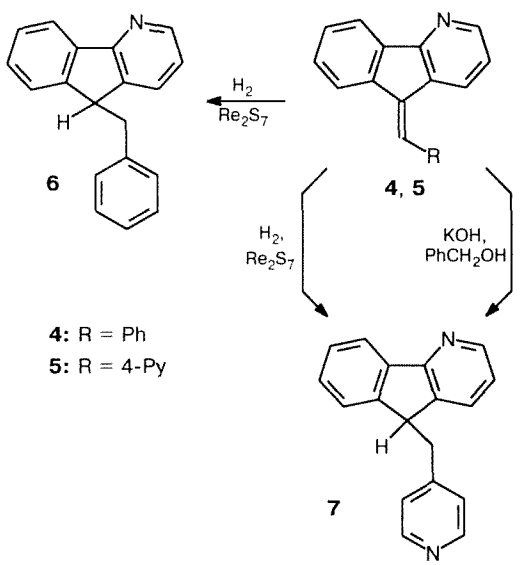
nated to the catalyst by the planar fulvene fragment, even when two N atoms competing for the catalytic centers are present (fulvene **5**). To increase the selectivity of hydrogenation, less drastic conditions are probably required, *i.e.*, a decrease in temperature and shorter duration of contact.

Scheme 2



The structures of all partially reduced compounds were unambiguously determined from ^{1}H NMR and mass spectral data (see Experimental). For example, the presence of the C(9)H—C(10)H$_2$ grouping in compounds **2**, **6**, and **7** was confirmed by the existence of a triplet at δ ~4.0—4.2 (1 H) and a multiplet around ~2.8—3.2 (2 H) in their ^{1}H NMR spectra. The mass spectra of these compounds contain molecular ion peaks, $[M]^+$, along with highly intense ion peaks $[HetAr—CH_2]^{+\cdot}$.

To confirm the structure of compound **7**, it was also obtained by an independent synthesis (see Scheme 2), *i.e.*, by reduction of fulvene **5** with benzyl alcohol in the presence of KOH (yield 66 %).

Experimental

The compounds obtained were isolated by column chromatography on silica gel L 40/100 using TLC control with Silufol UV-254 plates and hexane—ethyl acetate (1 : 1) as the eluent; the plates were visualized by iodine vapors. Mass spectra (EI) were obtained on an MKh-1303 spectrometer (70 eV). ^{1}H NMR spectra were recorded on a Bruker WP-80 spectrometer (80 MHz) in $CDCl_3$ using $SiMe_4$ as the internal standard.

Rhenium heptasulfide was obtained by passing hydrogen sulfide through a solution of ammonium perrhenate (2 g) in distilled water (30 mL) and 6 *N* HCl (60 mL) over a period of 3.5 h on a boiling water bath and then cooling to room temperature in a weak stream of hydrogen sulfide. After ~24 h, the catalyst was filtered off, washed with distilled water until a negative reaction for chloride ions, and dried for 2—3 days over $CaCl_2$ until a constant weight was attained. Yield 100 %. Found (%): Re, 62.5; S, 38.1. Re_2S_7. Calculated (%): Re, 62.5; S, 37.8.[8]

Hydrogenation of pyridylmethylenefluorene (1). A tube containing a solution of compound **1** (1 g, 3.92 mmol) in benzene (15 mL) and rhenium heptasulfide (0.1 g, 10 % of the weight of the compound to be hydrogenated) was placed into a rotating autoclave (150 mL in volume), purged with nitrogen, and filled with hydrogen. The mixture was kept for 4 h at 250 °C and p_{H_2} = 130 atm and then cooled. The catalyst was separated, the solvent was distilled off *in vacuo*, and the residue (0.9 g) was chromatographed on a column with silica gel using hexane—ethyl acetate (1 : 1) as the eluent. Chromatography successively gave 0.067 g (10.3 %) of **fluorene** with m.p. 115—116 °C (the ^{1}H NMR and mass spectra are identical to those of an authentic sample) and 0.33 g (33 %) of **9-(γ-pyridylmethyl)fluorene (2)** as colorless crystals, m.p. 98—99 °C, R_f 0.38. ^{1}H NMR, δ: 2.6—3.1 (m, 2 H, CH_2); 4.02 (t, 1 H, H(9), J = 8 Hz and 7.5 Hz); 7.02 (dd, 2 H, H(3′), H(5′), J = 6.4 Hz and 1.2 Hz); 7.08—7.25 (m, 8 H, H arom.); 8.43 (br.d, 2 H, H(2′), H(6′)). MS, m/z (I_{rel} (%)): 257 $[M]^+$ (25), 165 $[C_{13}H_9]^+$ (100). Found (%): C, 88.9; H, 5.5; N, 5.4. $C_{19}H_{15}N$, M = 257. Calculated (%): C, 88.7; H, 5.8; N, 5.5.

After that, 0.16 g (16 %) of **9-(γ-piperidylmethyl)fluorene (3)** was obtained as a light-yellow heavy oil, R_f 0.18. ^{1}H NMR, δ: 1.5—2.05 (br.m, 9 H, H of piperidine); 4.0—4.45 (m, 4 H, H of piperidine); 7.25—7.8 (m, 8 H, H arom.). MS, m/z (I_{rel} (%)): 263 $[M]^+$ (25), 165 $[C_{13}H_9]^{+\cdot}$ (100), 132.5 $[M]^{2+}$ (2), 85 (98). Found (%): C, 86.5; H, 8.1; N, 5.4. $C_{19}H_{21}N$, M = 263. Calculated (%): C, 86.7; H, 8.0; N, 5.3.

Similarly, hydrogenation of 9-benzylidene-4-azafluorene (**4**) gave 60 mg (20 %) of **9-benzyl-4-azafluorene (6)** isolated by chromatography as a yellow heavy oil. ^{1}H NMR, δ: 2.95 and 3.1 (both q, 1 H, —CH_2—, J = 14.0 Hz, 8.0 Hz, and 7.5 Hz); 4.08 (t, 1 H, H(9), J = 8.0 Hz and 7.5 Hz); 7.08 (q, 1 H, H(2), J = 7.2 Hz and 5.0 Hz); 7.1—7.5 (m, 9 H, H arom.); 8.08 (m, 1 H, H(1)); 8.52 (dd, 1 H, H(3), J = 5.2 Hz and 1.4 Hz). MS, m/z (I_{rel} (%)): 257 $[M]^+$ (50), 181 (10), 167 (21), 166 (50), 91 $[Ph—CH_2]^{+\cdot}$ (100). Found (%): C, 88.8; H, 5.9; N, 5.3. $C_{19}H_{15}N$, M = 257. Calculated (%): C, 88.7; H, 5.8; N, 5.5.

A similar reaction of pyridylmethyleneazafluorene **5** (0.5 g, 1.95 mmol) followed by separation and purification on a chromatographic column gave 50 mg (10 %) of **9-(γ-pyridylmethyl)-4-azafluorene (7)** as colorless crystals, m.p. 120—121.5 °C (from benzine). ^{1}H NMR, δ: 3.1 and 3.2 (both q, 1 H, —CH_2—, J = 14.0 Hz, 8.0 Hz, and 7.5 Hz); 4.24 (t, 1 H, H(9), J = 8.0 Hz and 7.5 Hz); 7.08 (m, 3 H, H(2), H(3′), H(5′)); 7.6—7.83 (m, 4 H, H arom.); 8.08 (m, 1 H, H(1)); 8.52 (m, 3 H, H(3), H(2′), H(6′)). MS, m/z (I_{rel} (%)): 258 $[M]^+$ (1), 196 (2), 181 (100), 92 $[C_5H_4N—CH_2]^{+\cdot}$ (40). Found (%): C, 84.0; H, 5.6; N, 10.6. $C_{18}H_{14}N_2$, M = 258. Calculated (%): C, 83.7; H, 5.4; N, 10.9.

The latter compound was also obtained by an independent synthesis: a mixture of arylidene **5** (1.49 g, 6 mmol) with KOH (0.48 g, 8 mmol) in benzyl alcohol (11 mL) was refluxed for 4 h and cooled, then water (20 mL) was added, and the mixture was extracted with ether to give 0.98 g (66 %) of dihydro derivative **7**, whose melting point, ^{1}H NMR spectrum, and mass spectrum were identical to those of an authentic sample obtained by the above procedure.

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