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Azines and Imines of 4- and 5-t-Bu-Pyrrole-2-aldehyde. A Useful Synthesis of the Aldehydes

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AZINES AND IMINES OF 4- AND 5-t-Bu-PYRROLE-2-ALDEHYDE. A USEFUL SYNTHESIS OF THE ALDEHYDES

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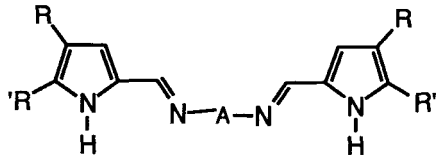
Abstract: The preparation of 4- and 5-t-Bu-pyrrole-2-aldehyde can be brought about in a high yield and purity using Vilsmeier-Haack type reactions as conclusions to reaction sequences involving a 1-benzenesulfonyl directing group on pyrrole (4-substitution) or the formamidinium salt of pyrrole (5-substitution). Azines/imines were prepared and characterised.

The azines **1**, **3**, **5** and the imines **2**, **4**, **6** are potential ligands in the preparation of planar, bimetallic complexes which have utility as low dimensional magnets or conductors.[2] For this reason we recently required **1** - **6** as pure substances in 10 - 30 g quantities. While **1** and **2** are known[3,4] (they can be produced by the reaction of commercially available pyrrole-2-aldehyde with the requisite diamine), significant disparities exist in their reported characterisation.



1; A = single bond, R = H, R' = H
2; A = $(CH_2)_3$, R = H, R' = H
3; A = single bond, R = t-Bu, R' = H
4; A = $(CH_3)_2$, R = t-Bu, R' =H
5; A = single bond, R = H, R' = t-Bu
6; A = $(CH_3)_2$, R = H, R' = t-Bu

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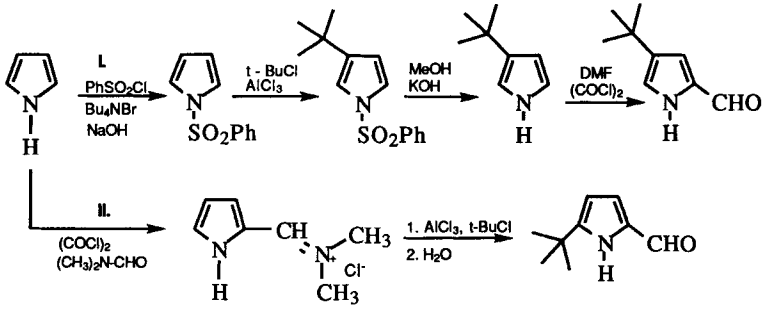
The preparation of **3** - **6** requires the precusors 4- and 5-t-Bu-pyrrole-2-aldehyde. Preparation reactions of alkyl-pyrrole-2-aldehydes, especially those involving external heating, are almost inevitably accompanied by partial decomposition of the aldehyde producing dark oils which are not always simply and conveniently purified.[5,6] Reactions which avoid such decomposition can consequently be useful in producing high yields and large amounts of substituted pyrrole-2-aldehydes requiring relatively little further purification.

In the synthesis of 4-t-Bu-aldehyde; only a few useful reaction sequences to even simple 4-alkyl-pyrrole-2-aldehydes are known.[6,7] Anderson and Loader[5] have, however, also mentioned (as an "unpublished observation") a route to 3-t-Bu-pyrrole, via the introduction and later removal of a 1-benzenesulfonyl group.



We have found the latter preparation, followed by a Vilsmeier-Haack formylation (route **I.** above) to be most useful in the preparation of the desired 4-t-Bu-pyrrole-2-aldehyde. Unlike previous preparations the reaction occurs without significant decomposition of the product. As a result single batches, in excess of 10 g of aldehyde, could be produced without the need for extensive purification. The starting material, 1-benzenesulfonyl pyrrole was readily prepared in 100 g amounts from pyrrole using a phase transfer catalyst.[8] The electrophilic substitution step[5] proceeded in high yield (88%) with no observed 2-substitution product, while the directing group could be removed by reflux in a KOH/H_2O-methanol medium (quantitatively).[5] A Vilsmeier-Haack formylation then produced the desired 2,4-substitution product with no observed 2,5-product (83% yield). Two simple purification sequences were required. In the first of these small amounts of unreacted t-BuCl in the substitution step had to be removed (column

chromatography on silica gel: elution with hexane, followed by washing with 1:1 hexane/CH_2Cl_2 mix) to avoid interference with the later purification of 4-t-Bu-pyrrole-2-aldehyde (filtration through a silica gel column: CH_2Cl_2, and recrystallisation). Addition of hydrazine to the aldehyde led to 4,4'-bis(t-Bu)-pyrrole-2-aldehyde-azine, **3**, while reaction with 1,3-diaminopropane produced propane-1,3-bis-(4-t-Bu-pyrrole-2-aldehyde)-imine, **4**.

Another 'interrupted' Vilsmeier-Haack type synthesis (route **II.** above) successfully utilised in the production of 4-acyl-pyrrole-2-aldehydes[5] (viz. the formation of the Vilsmeier, formamidinium salt of pyrrole followed by a Friedel-Crafts acylation and hydrolysis) led, in reactions with t-BuCl, to substitution entirely at the 5-position. Again the aldehyde was prepared with relatively little decomposition and could be purified by filtration through a silica gel column (eluant: 1:1 hexane:CH_2Cl_2) and recrystallisation. Single batches of up to 30 g of pure 5,5'-bis(t-Bu)-pyrrole-2-aldehydes were thus produced. Conversion to the desired azine/imine by addition of the diamine produced 5,5'-bis(t-Bu)-pyrrole-2-aldehyde-azine, **5**, and propane-1,3-bis(5-t-Bu-pyrrole-2-aldehyde)-imine, **6**.

The above routes were unsuccessful in the preparation of azines and imines containing large alkyl groups. Attempts to substitute a decyl- or dodecyl- group, as well as the tertiary carbocations, $C_{10}H_{21}C(CH_3)_2$- and $C_{12}H_{26}C(CH_3)_2$-, using route **I.** led instead to chain cleavage reactions in the substitution step with 4-t-Bu-1-benzenesulfonyl pyrrole as the major product in all cases (as observed using GC/MS and ^1H NMR). Thus if the products of any of these reactions were carried through the entire process, followed by addition of hydrazine, 4-t-Bu-pyrrole-2-aldehyde azine was obtained (as evidenced by melting point, E.A., N.M.R. and M.S.).

Characterisation of azines and imines:

1; m.p. 172-173°C (hydrated and anhydrous form). U.V./Vis.(nm): 200-400. Analysis: $C_{10}H_{10}N_4.H_2O$, % found (% theory): C: 58.79 (58.51), H: 5.94 (5.92), N: 27.43 (27.43), O: 7.84 (7.83). I.R.(cm^{-1})(KBr disk): 3480[N-H], 3105[C-H], 1633[C=N]. ^1H NMR (DMSO): δ 3.38 (s, 2H, H_2O), 6.10 (m, 2H, ArH), 6.50 (m, 2H, ArH), 6.90 (m, 2H, ArH), 8.28 (s, 2H, -CH=N), 11.40 (b, 2H, N-H).

2; m.p. 122.5°C. U.V./Vis.(nm): 200-320. Analysis: $C_{13}H_{16}N_4$, % found (% theory): C: 68.91 (68.39), H: 6.95 (7.06), N: 24.18 (24.54); I.R. (cm^{-1})(KBr disk): 3120[C-H, aromatic], 3059, 2945, 2847[C-H, non-aromatic], 1633[C=N]. ^1H NMR ($CDCl_3$): δ 1.92 (m, 2H, $-CH_2-$), 3.56 (t, 4H, N-CH_2-), 6.13 (m, 2H, ArH), 6.36 (m, 2H, ArH), 6.75 (m, 2H, ArH), 7.92 (s, 2H, -CH=N).

3; m.p. 182-183°C. U.V./Vis. (nm): 200-400. Analysis: $C_{18}H_{26}N_4$, % found (% theory): C: 72.14 (72.44), H: 8.81 (8.78), N: 18.57 (18.77). I.R.(cm^{-1})(KBr disk): 3480[N-H], 3105[C-H], 2965[C-H, t-Bu], 1629[C=N]. ^1H NMR ($CDCl_3$): δ 1.20 (s, 18H, t-Bu), 6.44 (m, 2H, ArH), 6.68 (m, 2H, ArH), 8.23 (s, 2H, -CH=N), 9.04 (b, 2H, N-H).

4; m.p. 165-166°C. U.V./Vis (nm): 240-330. Analysis: $C_{21}H_{32}N_4$, % found (%theory): C: 73.78 (74.10), H: 9.54 (9.40) N: 16.73 (16.50). I.R. (cm^{-1})(KBr disk): 3120, 3059[C-H, aromatic], 2964[C-H, t-Bu], 2945, 2847[C-H, non-aromatic], 1633[C=N]. ^1H NMR ($CDCl_3$): δ 1.23 (s, 18H, t-Bu), 1.92 (m, 2H, $-CH_2-$), 3.56 (m, 4H, N-CH_2-), 6.47 (m, 2H, ArH), 6.59 (m, 2H, ArH), 8.03 (s, 2H, -CH=N).

5; m.p. 236-236.5°C. U.V./Vis (nm): 280-420, 250. Analysis: $C_{18}H_{26}N_4$, % found (% theory): C: 72.58 (72.44), H: 8.76 (8.78), N: 18.77 (18.77). I.R.(cm^{-1})(KBr disk): 3480[N-H], 3143, 3107[C-H], 2964[C-H, t-Bu], 1616[C=N]. ^1H NMR ($CDCl_3$): δ 1.25 (s, 18H, t-Bu), 5.93 (m, 2H, ArH), 6.37 (m, 2, ArH), 8.24 (s, 2H, -CH=N), 8.80 (b, 2H, N-H).

6; m.p. 125°C; U.V./Vis. (nm): 220-340. Analysis: $C_{21}H_{32}N_4.0.5H_2O$, % found (% theory): C: 72.38 (72.16), H: 9.49 (9.52), N: 16.18 (16.03). I.R.(nm)(KBr disk): 3140, 3120, 3059[C-H, aromatic], 2964[C-H, t-Bu], 2945, 2850[C-H, non-aromatic],1618[C=N]. ^1H NMR ($CDCl_3$): δ 1.24 (s, 18H, t-Bu), 1.92 (m, 2H, $-CH_2-$), 3.54 (m, 4H, N-CH_2-), 6.08 (m, 2H, ArH), 6.40 (m, 2H, ArH), 7.98 (s, 2H, -CH=N).

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