Acid-catalysed Condensation of Ethyl 5-Acetoxymethyl-4-acetyl-3-methylpyrrole-2-carboxylate and its Analogues with Aromatic Substrates

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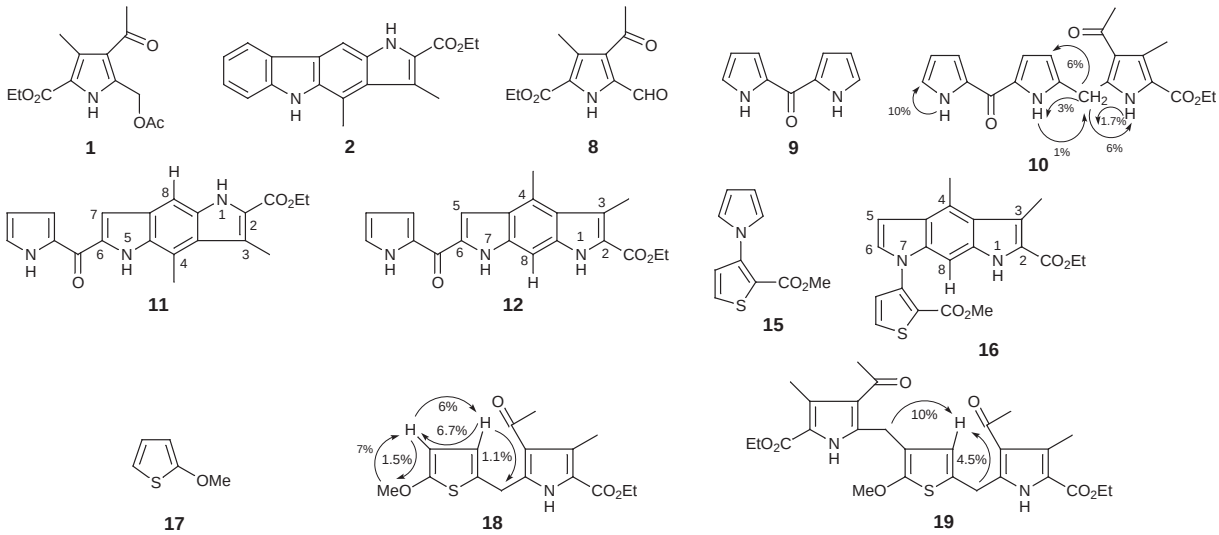
The 5-acetoxy-4-acetylpyrrole **1** and its derivatives show a range of reactivity towards various aromatic substrates giving pyrroloindoles and pyrrolo[3,2-*b*]carbazoles amongst other products.

Earlier work[1–3] showed that acid-catalysed condensation of the pyrrole **1** with indoles, benzothiophene, benzofuran and pyrroles gave pyrrolo[3,2-*b*]carbazoles **2**, and other polycyclic systems. We now describe the products of the acid-catalysed condensation of the pyrrole **1** and its derivative **8** with new aromatic substrates.

Treatment of the pyrrole **1** with pyrrol-2-yl ketone **9**[4] in the presence of K-10 clay gave after chromatography, first, a crystalline complex of ketone **9** and pyrrole **1** of molar ratio 2 : 1, respectively. The second product was the ketone **10** whose structure was confirmed by its spectral features and the NOE intensity enhancements shown. Treatment of the ketone **9** and pyrrole **1** with toluene-*p*-sulfonic acid however gave the deep-red pyrrolo[2,3-*f*]indole **11**. The alternative pyrrolo[3,2-*f*]indole **12** was also formed but was best prepared by cyclisation of the tripyrranone **10** with toluene-*p*-sulfonic acid. The orientation of **12** and of the isomer **11** were supported by the differences between the ^{1}H NMR shifts for the 8-H signals when compared with the values for model compounds.[3] Condensation between the pyrrole **1** and methyl 3-(1-pyrrolyl)thiophene-2-carboxylate **15** gave the *N*-(2-carbomethoxythiophen-3-yl)pyrrolo[3,2-*f*]indole **16**, but with 2-methoxythiophene **17** no annelation was achieved with the pyrrole **1** and clay (or toluene-*p*-sulfonic acid). Instead, the substitution products **18** and **19** were isolated. Neither isomer could be induced to cyclise to a thiophenoindole even under forcing conditions.

Treatment of the pyrrole **1** with toluene-*p*-sulfonic acid and the thiophenes **20** and **21** gave only the dipyrromethane **22**.[5] Although these thiophenes showed insufficient reactivity towards the pyrrole **1**, the 2-*p*-methoxyphenylthiophene **23** paralleled the results with 2-methoxythiophene **17**, giving the products **24** and **25** with toluene-*p*-sulfonic acid. The thiophene **26** showed no aromatic reactivity towards the pyrrole **1** but with toluene-*p*-sulfonic acid it gave the *N*-substituted derivative **27**, and the dipyrromethane **22**. The phenol **28** on acid-catalysed condensation with the pyrrole **1** gave only the monosubstituted phenol **30** which failed to cyclise to a pyrrolonaphthalene with polyphosphoric acid or trifluoroacetic acid/trifluoroacetic anhydride. From 2,4-dimethylphenol **29** two products were isolated. The first was clearly the 2-pyrrolylmethylphenol **31**. The second product showed two pyrrole and two phenolic groups in its ^{1}H NMR spectrum. Singlets at δ 3.79 and 3.94 indicated two methylene groups linking phenol/pyrrole rings. The remaining necessary link between aromatic rings could be inferred from the presence of only seven methyl groups and two singlets at δ 6.19 and 6.24 due to a C=CH$_2$ system. The structure **32** was confirmed by the CI mass spectrum which gave an M + 1 ion at *m/z* 641.321 ($C_{38}H_{44}N_2O_7 + H$ requires *m/z* 641.322). Oxidation of the pyrrole **34**[5] with ceric ammonium nitrate gave the pyrrole-2-aldehyde **8**.[6] Reaction of this with indole **35a** in the presence of K-10 clay gave two products. The first, shown to be the diindolylpyrrolylmethane **36**, was converted with clay into the second, the pyrrolo[3,2-*b*]carbazole **37a**. Similarly, the 5- and 6-halogenoindoles **35b**,**c**,**d** gave the



1 **2** **8** **9** **10** **11** **12** **15** **16** **17** **18** **19**

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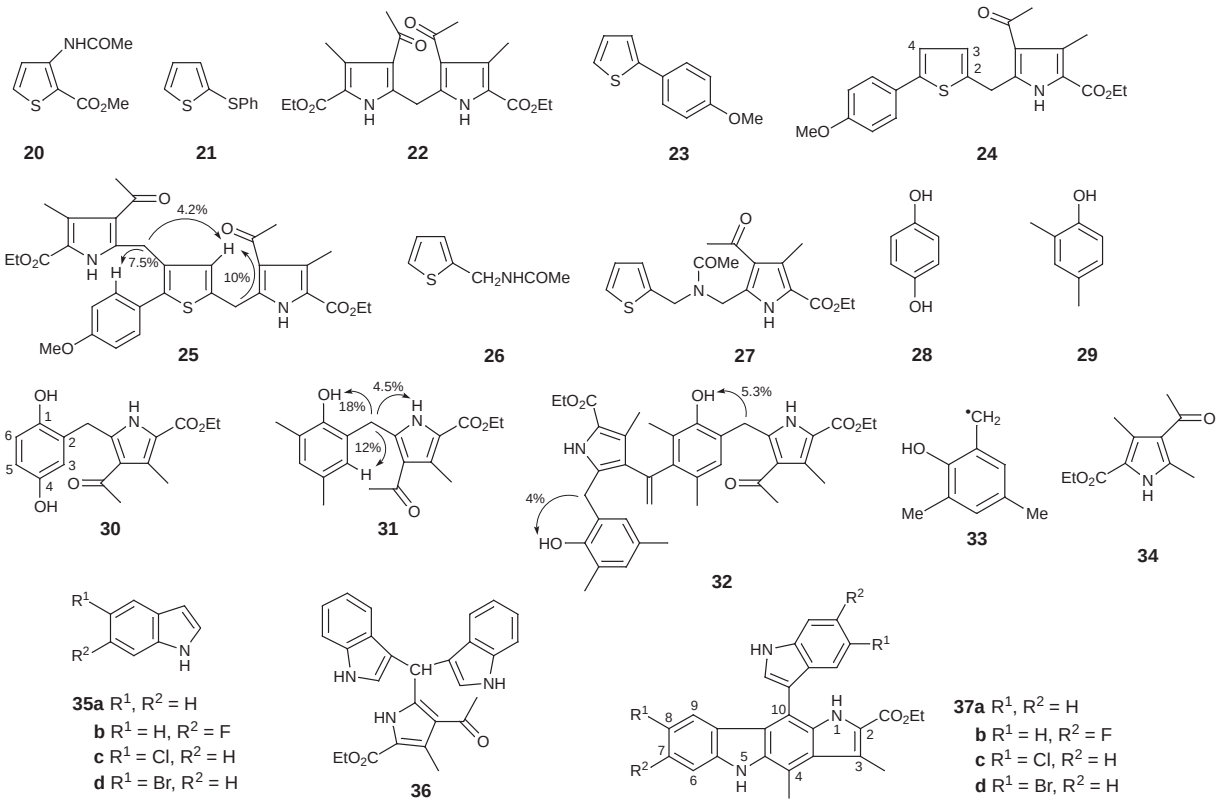

10-indolyl pyrrolocarbazoles **37b**,**c**,**d**. The ^{1}H NMR spectrum of the dichloro derivative **37c** showed the pyrrolocarbazole 9-H and indolyl 4-H signals at δ 6.78 and 6.84, (each d, J 2.04 and 2.14 Hz, respectively) at abnormally high field. This is explained by shielding of these protons as a result of rotation about the C-10–C-3 axis.

These and earlier[1] results show that acid-catalysed condensations of the pyrroles **1** and **8**, are a viable route to polycyclic systems mainly when applied to pyrrole and indole substrates.

Techniques used: ^{1}H NMR

References: 7

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