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THE *N*,*N'*-DIACYL-4,5-DIHYDROIMIDAZOLIUM ION AS AN ELECTROPHILE

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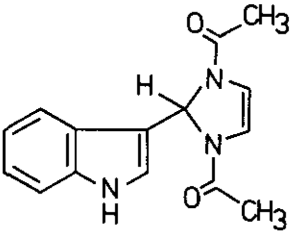
Abstract - 2-Methyl-4,5-dihydroimidazole/acetic anhydride reacts smoothly with indole at room temperature giving *N*,*N'*-diacetyl-2-methyl-2-(3-indolyl)-imidazolidine. This adduct can be hydrolysed to 3-acetylindole. Other aromatics, like 1,3-dimethoxybenzene, undergo similar reactions.

When heated with an imidazole/acetic anhydride reagent, indole afforded[1,2] the adduct 1. The more reactive reagent imidazole/trifluoroacetic anhydride similarly yielded *e.g.* the adducts 2 and 3 with thiophene and 1,3-dimethoxybenzene, respectively.[3] The electrophilic species attacking the aromatic ring was assumed to have the structure 4. We therefore felt that it would be of interest to generate the less stabilized and hence more reactive ion 5 from 4,5-dihydroimidazoles and suitable anhydrides in the presence of aromatic compounds. The results of such a study are reported herein.



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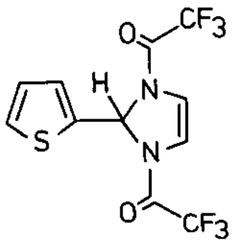

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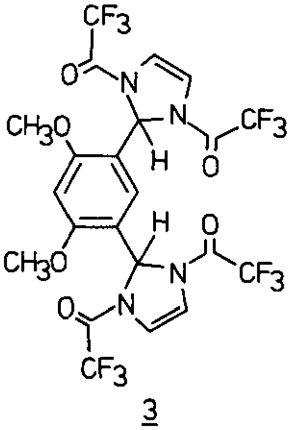

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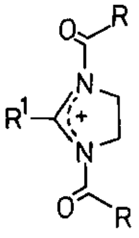

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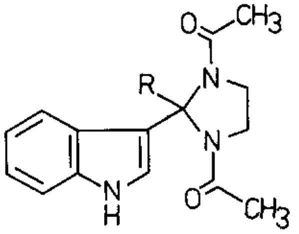
Indole reacted smoothly at room temperature[4] with the 2-methyl-4,5-dihydroimidazole/acetic anhydride reagent yielding 6a. 2-Ethyl-4,5-dihydroimidazole and 2-phenyl-4,5-dihydroimidazole similarly (55°, 5 h) gave 6b and 6c, respectively. In contrast, reactions at reflux temperature (140°C) yielded the ring opened product 7. Compounds 6a and 7 could be readily hydrolysed (5% sodium hydroxide in ethanol/water) to 3-acetylindole in high yield. Compound 6c similarly yielded 3-benzoylindole[5], whereas treatment with sodium borohydride in hot methanol smoothly yielded 3-benzylindole in 93% yield. The yields of 6a - 6c were in the range 85-95%, whereas the yield of 7 was 62%.

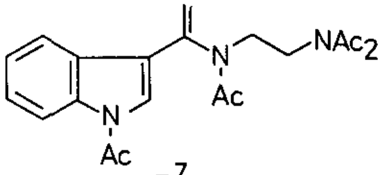
Our interest in precursors[6] to the indole alkaloid ellipticine and related compounds also induced us to treat various indoles with 2-(3-pyridyl)-4,5-dihydroimidazoles and acetic anhydride. The yields of 8 as well as 9 were good to excellent. The hydrolysis of the adduct 8d was in contrast to 8a-c extremely sluggish, a fact that seems to indicate that deprotonation of 8a-c, followed by indolenine-formation (*i.e.* ring-cleavage of the tetrahydroimidazole ring) are important steps preceding the hydrolysis.

From these results, *it appears that the ion* 5, *as expected, is a more powerful electrophile* than the ion 4. However, the ion 5 ($R_1=CH_3$) seems to decompose under more forcing conditions and in several attempts to substitute 1,3-dimethoxybenzene, compound 10a and even 10b were the only products.

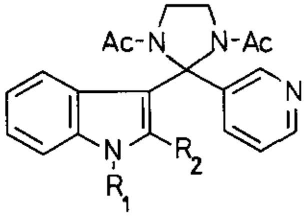
Adducts 11a and 11b could however be prepared from 1,3-dimethoxybenzene and the appropriate 4,5-dihydroimidazole with trifluoroacetic anhydride in acetonitrile (yields 80-90%).



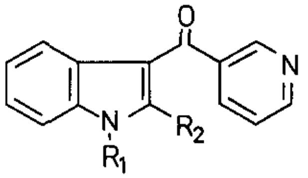
6 a $R=CH_3$
b $R=C_2H_5$
c $R=C_6H_5$



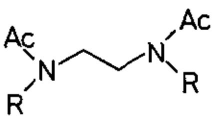
7[7]



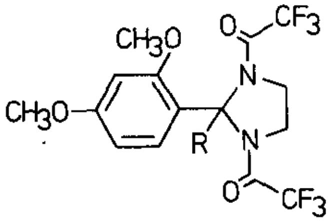
8 a $R_1=R_2=H$
b $R_1=H, R_2=C_2H_5$
c $R_1=H, R_2=CH(CH_3)_2$
d $R_1=R_2=CH_3$



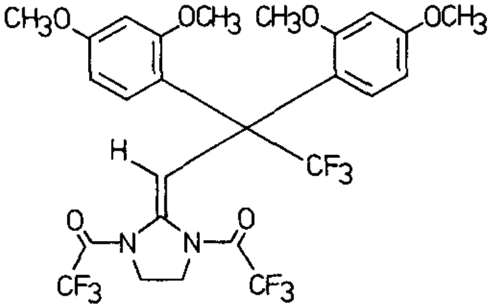
9 a $R_1=R_2=H$
b $R_1=H, R_2=C_2H_5$
c $R_1=H, R_2=CH(CH_3)_2$



10 a R=H
   b R=Ac



11 a $R=C_6H_5$[8]
   b $R=C_2H_5$
   c $R=CH_3$



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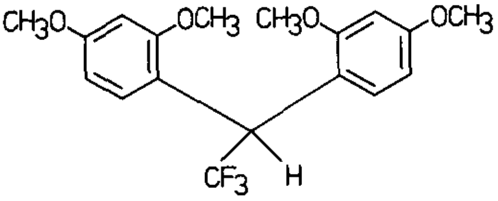

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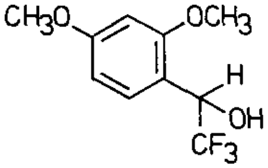

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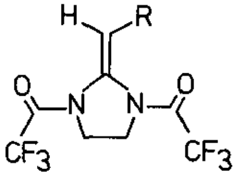
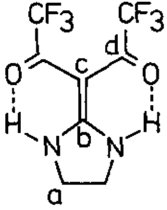


15 a R=H
   b $R=COCF_3$
   c $R=C_6H_5$
   d $R=C_2H_5$



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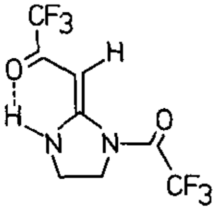

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In contrast 2-methyl-4,5-dihydroimidazole with the same reactants at the same conditions yielded quite a different product assigned structure **12**.[9] This assignment is based on MS and NMR data[10], as well as degradation studies. Alkaline hydrolysis yielded compound **13**, whose structure was confirmed by an independent condensation of the carbinol **14** with 1,3-dimethoxybenzene. Furthermore it was found that 2-methyl-4,5-dihydroimidazole and trifluoroacetic anhydride could be converted to compounds **15a** and **15b** and 2-phenyl- and 2-ethyl-4,5-dihydroimidazoles similarly yielded **15c** and **15d**, respectively. Compound **15b** could be readily hydrolysed to the strongly hydrogen-bonded compound **16**. When 2-methyl-4,5-dihydroimidazole was refluxed with $(CF_3CO)_2O$ in acetonitrile for 2 h, the related *C*-di-$COCF_3$-substituted compound **17**[11] could be immediately isolated in high yield as a stable crystalline solid when the reaction mixture was poured into water.

REFERENCES AND NOTES

1. J. Bergman, *Tetrahedron Letters* 4723 (1972).
2. J. Bergman, B. Sjöberg and L. Renström, *Tetrahedron* **36**, 2505 (1980).
3. These adducts can readily be converted[2] to the corresponding aldehydes.
4. In contrast indole fails to give an adduct with the 2-methylimidazole/acetic anhydride reagent even at reflux temperature.

5a. This route to 3-benzoylindole is much more convenient than the route given by Stütz and Stadler[5b], involving attack of indole with a 1,3-dithiolium ion in the first step.

5b. P. Stütz and P.A. Stadler, *Org. Synth.* **56**, 8 (1977).

6. J. Bergman and R. Carlsson, *Tetrahedron Letters*, 4663 (1977).
7. Compound **7**; m.p. 130-131°C; MS, *m/e* (% relative intensity): 370 (23), 369 (100), 327 (17), 285 (24), 268 (17), 267 (16), 266 (23), 255 (20) and 253 (14). Only peaks stronger than 10% of the base peak and *m/e* above 250 are given; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.18$ (s, 3 H, $COCH_3$), 2.46 (s, 6 H, $COCH_3$), 2.65 (s, 3 H, $COCH_3$), 3.63 (dd, 2 H, CH_2), 3.96 (dd, 2 H, CH_2), 5.36 (s, 1 H, $C = CH_2$), 5.83 (s, 1 H, $C = CH_2$), 7.35-7.69 (several peaks, 4 H) and 8.51 (d, 1 H).
8. Compound **11a**; m.p. 145-146°C; MS, *m/e* (% relative intensity): 477 (25), 476 (100), 408 (10), 407 (42), 399 (11) and 350 (17). Only peaks stronger than 10% of the base peak and above *m/e* 250 are given.

9a. Compound **11c** was not formed at all.

9b. Thiophene yielded an adduct analogous with **12**.

10a. Compound **12**; m.p. 139-140°C; MS, *m/e* (% relative intensity): 631 (28.8), 630 (100), 590 (16.7), 423 (25.4), 411 (14.3), 219 (14.3), 70 (56.0); Calculated for M.w. $C_{26}H_{24}F_9N_2O_6$; 630.1412. Found: 630.1414. The yield of this compound was 84%.

10b. We thank Dr G. Höhne, Technische Universität, Berlin, for this measurement.

11. Compound **17**; m.p. 213-214°C; $IR_{(KBr)}$: 3360 (NH), 1603 (C = 0); ^{13}C-NMR ($CDCl_3$): a = 43.4, b = 163.4, c = 87.8, d = 175.5 (J_{FC_d} = 36 Hz), e = 116.8 (J_{FC_e} = 292 Hz). The yield of this compound was 92%.

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