A NOVEL THERMAL REARRANGEMENT OF 1-TRITYLIMIDAZOLES

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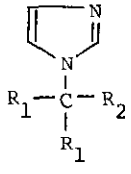
Heating of 1-[(2-chlorophenyl)diphenylmethyl]imidazole (1a) afforded (2-chlorophenyl)-[4-(imidazol-1-yl)phenyl]phenylmethane (2a). Similarly 1-tritylimidazole was converted to diphenyl-[4-(imidazol-1-yl)phenyl]methane (2b).

In the thermal rearrangement of 1-substituted imidazoles,[1] it has been known that the substituents migrate from nitrogen to carbon atoms of the imidazole ring, affording mainly 2-substituted imidazoles, together with 4-substituted isomers as minor products. In the case of 1-tritylimidazoles, Gieseman et al.[2] found that the melting of 4,5-diphenyl-1-tritylimidazole formed 4,5-diphenyl-2-tritylimidazole and that of 2-phenyl-1-tritylimidazole afforded 2-phenyl-4-tritylimidazole.

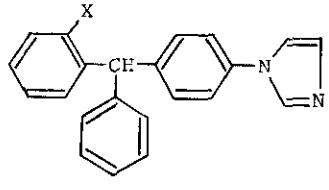
In the course of a study on 1-substituted imidazoles as antimycotics, we found a novel thermal rearrangement of 1-tritylimidazoles. When 1-[(2-chlorophenyl)diphenylmethyl]imidazole (1a)[3] was heated under nitrogen atmosphere at 230°C for 10 hours, there was obtained a mixture consisting of an unexpected product 2a and the starting material 1a with the ratio of 58:7, determined by high performance liquid chromatograpy. Separation by silica-gel column chromatography using chloroform as an effluent, followed by recrystallization from acetonitrile gave 2a, mp 114-116°; pmr ($CDCl_3$-TMS): δ 5.99 (1H, s, CH), 6.8-7.5 (15H, aromatic protons) and 7.88 (1H, s, CH); cmr ($CDCl_3$-TMS) 52.7 ppm (CH) and 117.8-141.8 (aromatic carbons); m/e M^+ 344. From the evidence obtained above, compound 2a was characterized as (2-chlorophenyl)-[4-(imidazol-1-yl)phenyl]phenyl methane.

In order to determine the structure of 2a unambiguously, the compound 2a

was synthesized in a three step sequence starting with 2-chloro-4'-fluorobenzophenone (3)[4] as shown in Scheme 1. Treatment of 3 with imidazole in the presence of sodium carbonate and copper powder in DMF gave 2-chloro-4'-(imidazol-1-yl)benzophenone (4), mp 139-140°; ir (nujol) 1658 cm^{-1}; pmr ($CDCl_3$-TMS) δ 7.2-7.9 (aromatic protons); m/e M^+ 282, in 65% yield. Compound 4 was converted by treatment with 20 equivalents of phenylmagnesium bromide to (2-chlorophenyl)-[4-(imidazol-1-yl)phenyl]phenylmethyl alcohol (5), mp 207-209°; pmr ($CDCl_3$-TMS) δ 4.68 (1H, s, OH), 6.7-7.5 (15H, aromatic protons) and 7.8 (1H, s, CH), m/e M^+ 360, in 31% yield. Reduction of 5 with iodine and red phosphorous in acetic acid and water furnished 2a, mp 114-116°, in 62% yield The compound 2a thus

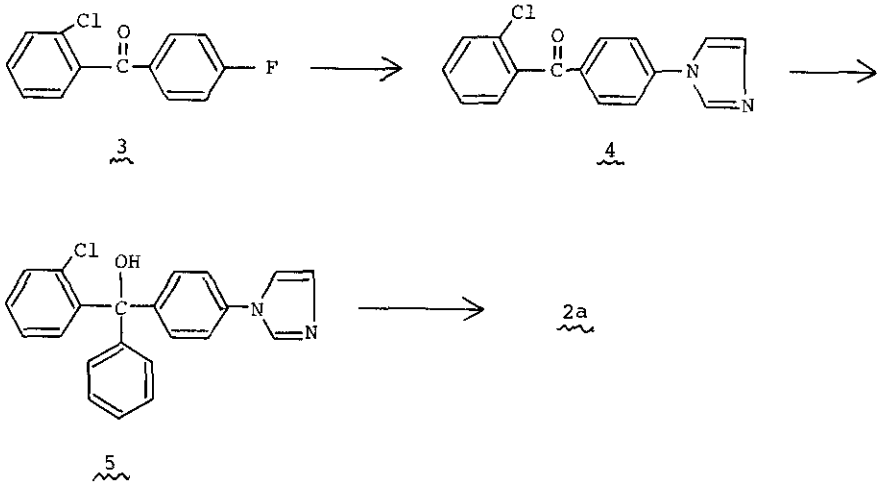


1a R_1=Ph, R_2=2-Cl Ph
1b R_1=R_2=Ph
1c R_1=R_2=4-F Ph
1d R_1=Ph, R_2=H



2a X=Cl
2b X=H

Scheme 1



obtained was identical with the rearrangement product in the mp, ir and pmr spectra. Similarly 1-tritylimidazole (1b) was converted to diphenyl-[4-(imidazol-1-yl)]phenylmethane (2b), mp 119-120°, in 23% yield.

In order to examine whether the migration of the trityl substituent occurs to position 2 of imidazole ring when 4-positions of phenyl rings are completely blocked, 1-[tri(4-fluorophenyl)]imidazole (1c), mp 162-163°C, was synthesized from tri(4-fluorophenyl)methyl alcohol[5] according to the method described in the literture[3]. Heating of 1c at 230°C for 10 hours gave polymeric materials and at 180°C for 10 hours resulted in the recovery of the stating material in 56% yield, together with intractable tar. The same result was obtained in the case of 1-benzhydrylimidazole (1d)[6].

The migration of the substituent from nitrogen atom to position 2 or 4 of imidazole ring was not observed.

REFERENCES

1 C. G. Begg, M. R. Grimmett and P. D. Wethey, Aust. J. Chem., 1973, 26, 2435 and references cited therein.

2 (a) H. Giesemann and G. Hälschke, Chem. Ber., 1959, 92,92. (b) H. Giesemann, H. Lettau and H. -G. Mannsfeldt, Chem. Ber., 1960, 93, 570. (c) H. Giesemann, A. Oelschlägel and H. Pfau. Chem. Ber., 1960, 93, 576.

3 K, H. Büchel, W. Draber, E. Regel and M. Plempel, Arzneim. Forsch., 1972, 22 1260.

4 K. C. Joshi and S. Giri, J. Indian Chem. Soc., 1963, 40, 42.

5 F. Bacon and J. H. Gardner., J. Org. Chem., 1938, 3, 281.

6 H. A. Staab and K. Wendel. Ann. Chem., 1966, 694, 91.

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