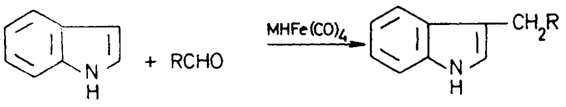
Alkali Metal Tetracarbonylhydridoferrate. A New Route to 3-Alkyl- or 3-Aryl-indoles

By G. P. Boldrini, M. Panunzio, and A. Umani-Ronchi

(*Istituto Chimico 'G. Ciamician', Via Selmi 2, Bologna, Italy*)

Summary 3-Alkyl- and 3-aryl-indoles may be obtained by treating aldehydes in alcoholic or aqueous–alcoholic solution with indole in the presence of $MHFe(CO)_4$.

Recently we reported[1] that treatment of an aqueous or aqueous–alcoholic solution of an aldehyde or a ketone containing the partial structure Me–CO–R[1] or R^2CH_2–CO–R[1] with formaldehyde in the presence of $KHFe(CO)_4$[2] gives high yields of the corresponding α-methyl derivatives. We have now found that indole can be reductively alkylated or arylated in position 3 by aliphatic or aromatic aldehydes by the same procedure (Scheme). Formaldehyde, benzaldehyde, *p*-chlorobenzaldehyde and *p*-methylbenzaldehyde give *ca.* 65% yields (pure isolated product) of the corresponding 3-substituted indoles while acetaldehyde and butanal lead to 3-ethyl- and 3-butyl-indole, respectively, in *ca.* 30% yield. The difference in the yield is due to simultaneous self-condensation of acetaldehyde and butanal induced by the alkalinity of the medium.

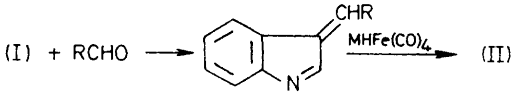


(I) (II)

Scheme

M = Na or K.
R = H, Me, Pr^n, Ph, *p*-ClC_6H_4, or *p*-MeC_6H_4.

In a typical procedure, $Fe(CO)_5$ (11 mmol) was added to a solution of MeONa (33 mmol) in MeOH (50 ml) under argon. The mixture was refluxed for 2 h, then the aldehyde and indole (11 mmol each in 5 ml of MeOH) were added dropwise separately.



In contrast, 3-methylindole was prepared in aqueous–alcoholic $KHFe(CO)_4$[2] from formaldehyde (40% aqueous solution). The mixture was heated under reflux for 6 h, poured into ice–water, and extracted with hexane or ether. The organic layer was dried (Na_2SO_4) and evaporated and the residue chromatographed on silica gel.

This novel reaction may take place *via* 3-arylidene- or 3-alkylidene-indolenines followed by irreversible attack by $MHFe(CO)_4$.

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