Conversion of Anilines into *N*-Methyl-2-quinolones *via* [2,3] Sigmatropic Rearrangements

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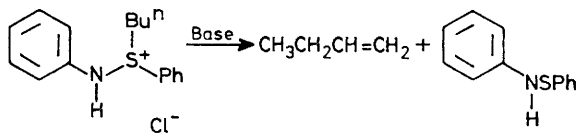
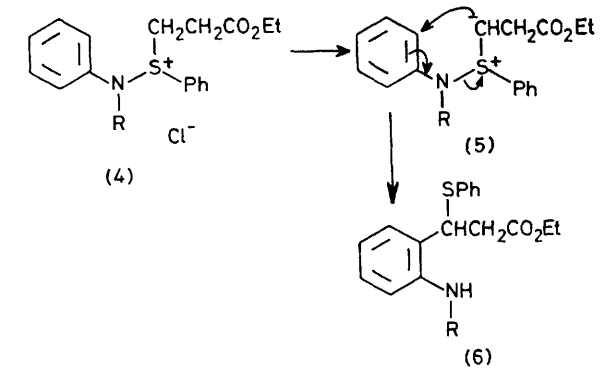
Summary A new general synthesis of *o*-(*N*-methylamino)-cinnamic acid, *N*-methyl-2-quinolone, and **3**,4-dihydo-*N*-methyl-2-quinolone has been developed, which involves the sequential reaction of *N*-methylaniline with (i) t-butyl hypochlorite, (ii) ethyl 3-phenylthiopropionate, and (iii) sodium methoxide to produce the reactive intermediate *o*-(2-ethoxycarbonyl-1-phenylthioethyl)-*N*-methyl aniline, which is readily converted into the aforementioned products.

THE [2,3] sigmatropic rearrangement of ylides derived from *N*-arylazasulphonium salts has proved to be an extremely useful reaction for the exclusive *ortho*-substitution of aromatic amines.[1] In addition, modifications of this procedure have been used to derive new and general syntheses of indoles[2] and oxindoles.[3] A major limitation on this synthetic methodology is the tendency for olefin formation if the aliphatic species bonded to the sulphur atom of the azasulphonium salt bears a β-hydrogen.[1] Thus, treatment of the azasulphonium salt (**1**) with base gives the olefin (**2**) together with (**3**).[1] This precedent indicates that

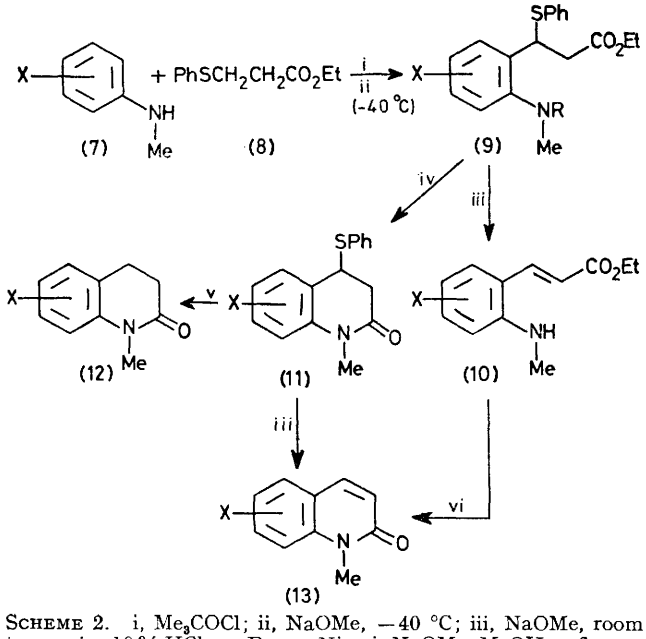


(1) (2) (3)

the azasulphonium salt (**4**) would be unlikely to yield the ylide (**5**), which, if formed, would undergo a spontaneous [2,3] sigmatropic rearrangement and rearomatization to give (**6**). We now report that the general conversion of (**4**) into (**6**) can be accomplished when R = Me (Scheme 1).



SCHEME 1



SCHEME 2. i, Me_3COCl; ii, NaOMe, −40 °C; iii, NaOMe, room temp.; iv, 10% HCl; v, Raney Ni; vi, NaOMe, MeOH, reflux.

In a general procedure (Scheme 2), an *N*-methylaniline (**7**) (1 equiv.) and ethyl 3-phenylthiopropionate (**8**) (1·2 equiv.) were dissolved in $MeCN–CH_2Cl_2$ (3:1) and the solution was cooled to −40 °C. A solution of t-butyl hypochlorite (1·1 equiv.) in CH_2Cl_2 was added dropwise and the reaction mixture was stirred for *ca.* 4 h at −40 °C. A methanolic solution of sodium methoxide (2·0 equiv.) was added dropwise at a rate which permitted the reaction mixture to be maintained below −35 °C and the reaction mixture was stirred for a further 3 h at −40 °C.

If the reaction mixture was allowed to warm to room temperature in the presence of excess of base, ethyl *o*-(*N*-methylamino)cinnamate (**10**; X = H) was obtained in 73% yield. The highly reactive intermediate (**9**; X = H, R = H) could be isolated in 51% yield if the reaction mixture was neutralized at −40 °C with an excess of saturated ammonium chloride solution. This intermediate was characterized as its stable acetyl derivative (**9**; X = H, R = COMe).

When the reaction mixture was quenched at −40 °C with an excess of saturated ammonium chloride solution, and then treated with 10% hydrochloric acid solution, work-up gave (**11**; X = Me-*p*, 65%; X = H, 60%; X=Cl-*p*, 51%; X = CO_2Et-*p*, 20%; yields are of purified products based on the starting *N*-methylaniline). Treatment of (**11**) with Raney nickel afforded 3,4-dihydro-*N*-methyl-2-quinolone (**12**; X = H) in 95% yield. Excess of sodium methoxide at room temperature converted (**11**) into *N*-methyl-2-quinolone (**13**; X = H) in 96% yield. Similarly, refluxing of (**10**) in methanolic sodium methoxide for 24 h gave a 69% yield of (**13**; X = H).

We thank the National Cancer Institute and the Institute of General Medical Sciences of the Public Health Service for support.

(*Received*, 23*rd June* 1977; *Com.* 628.)

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[3] P. G. Gassman and T. J. van Bergen, *J. Amer. Chem. Soc.*, 1974, **96**, 5508.