Nitration of Phenols by Silver Nitrate on Silica Gel

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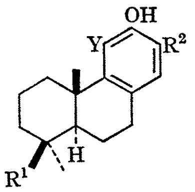
Summary The interaction of solutions of phenols in hydrocarbon or other inert solvents with silica gel impregnated with silver nitrate produces nitro-phenols.

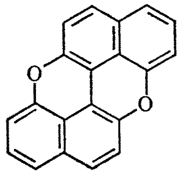
IN light of the widespread use of adsorption chromatography on silica gel impregnated with silver nitrate for the separation of mixtures of unsaturated substances, the following experience suggests the need for caution in the use of this technique especially in phytochemical research. Chromatography of a plant extract, containing an appreciable quantity of (+)-ferruginol (I), on a column of 100—200 mesh silica gel impregnated with 10% silver nitrate[1] and elution with ether–petroleum yielded *inter alia* an orange solid, m.p. 149—150°, λ_{max} (EtOH) 278 nm (ϵ 1560), δ($CDCl_3$) 0·91 (s. 6H, C-4 methyls), 1·11 (d, J 7 Hz, 6H, isopropyl), 1·43 (s, 3H, C-10 methyl), 6·95 (s, 1H, 14-H), *m/e* 331, o.r.d. (*c* 0·06, MeOH) $[\alpha]_{210}^{25}$ + 1670°, $[\alpha]_{220}$ + 2830, $[\alpha]_{230}$ + 2940, $[\alpha]_{240}$ + 2075, $[\alpha]_{250}$ 0, $[\alpha]_{260}$ −850, $[\alpha]_{290}$ −1075, $[\alpha]_{316}$ −750, $[\alpha]_{320}$ −1700, $[\alpha]_{354}$ 0, $[\alpha]_{385}$ +925, $[\alpha]_{400}$ +900, $[\alpha]_{425}$ +575, $[\alpha]_{500}$ +200, $[\alpha]_{589}$ +125, $[\alpha]_{600}$ +113, $[\alpha]_{700}$ +50 . Analytical figures (C,H,N) were satisfactory for $C_{20}H_{29}O_3N$. This compound proved to be 11-nitroferruginol (II) in view of its identity with the product of nitration (nitric acid in 1-nitropropane[2]) of ferruginol. Suspect as a natural product, it seemed likely to be an artifact produced during the chromatography. When as a consequence a sample of pure ferruginol (I) was chromatographed in the above manner, recovered (I) was accompanied by 7% of (II). This unprecedented nitration could be accomplished also by refluxing petroleum, methylene chloride, or benzene solutions of (I) in which the $AgNO_3$–SiO_2 reagent was suspended. Such treatment of suspensions of 40 : 1 reagent : solute for 1—24 hr. yielded up to 12% of (II). (No effort to optimize conditions was expended.)

On 8 hr. exposure of methyl podocarpate (III) to

$AgNO_3$–SiO_2 in refluxing benzene, 7% of methyl 13-nitropodocarpate (IV)[3], m.p. 129—130°, was obtained while similar treatment of β-naphthol yielded a complex mixture from which 1-nitro-2-naphthol[4] could be isolated. The importance of the silica support and inert medium was emphasized by the observation of the interaction of β-naphthol with silver nitrate (in two-fold excess) in buffered aqueous solution at pH 7 leading to 1,1′-bis-2-hydroxynaphthyl[5] (42%), but to no nitration product.



(I) R^1=Me, R^2=Pr^i, Y=H
(II) R^1=Me, R^2=Pr^i, Y=NO_2
(III) R^1=CO_2Me, R^2=Y=H
(IV) R^1=CO_2Me, R^2=NO_2, Y=H



(V)

Exposure of β-naphthol to AgOAc–SiO_2 (obtained in the same manner in which the $AgNO_3$–SiO_2 reagent had been prepared) in refluxing benzene yielded a complex mixture of products containing no acetoxynaphthol. Some *peri*-xanthenoxanthene (V)[6] (1%) could be isolated.

All these exploratory experiments indicate that silver salts on inert solid support may prove to be useful reagents for aromatic substitution. But more work will be needed to improve the efficiency of the new method and to overcome the competitive oxidation processes.

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