Selective Acylation of Oxygenated Naphthalenes

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The synthesis of 1,4,5,7-tetraoxygenated naphthalenes is described, as well as their selective acylation at either C-3 or C-8 using either trifluoroacetic anhydride or acetic acid and trifluoroacetic anhydride; the potential of these reactions in the synthesis of naturally occurring naphthoquinones is referred to.

Naphthalenes oxygenated at C-1, -4, -5, and -7 are useful synthetic precursors to a variety of naturally occurring naphthoquinones of polyketide origin.[1] Specific acylation at C-3[2] would provide entry to the naphthopyranquinones such as the aphid pigments protoaphins-*fb* and -*sl*, and eleutherin analogues (*e.g.* frenolicin). Alternative specific acylation at C-8 should give access to the naphthalene-based ansamycin antibiotics.[3] We report here both the synthesis of such naphthalenes with readily removable protection at O-7 and also their specific acylation at either C-3 or C-8 under relatively mild conditions.

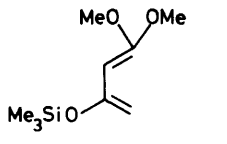
Diels–Alder addition of Brassard's diene (**1**)[4] to benzoquinone and subsequent alkylation of the crude adduct (**2**) with isopropyl bromide and potassium carbonate in dimethylformamide gave the naphthol (**3**)† (69% after chromatography), the more hindered, hydrogen-bonded hydroxy group remaining unprotected. Similar alkylation of adduct (**2**) with benzyl bromide afforded the naphthol (**4**)† (42%) together with some of the tribenzyl ether (9%).†

Acetylation of naphthol (**3**) with premixed acetic acid and trifluoroacetic anhydride[5] in boiling chloroform gave very predominantly the acetyl acetate (**8**)† (70%), with C-acylation as required at C-3. Mild basic hydrolysis provided the *ortho*-acetylnaphthol (**5**)† (90%). Similar acetylation of the naphthol (**4**) with acetic acid–trifluoroacetic anhydride gave rise to the acetyl acetate (**9**)† (51%) which also underwent hydrolysis to the *ortho*-acetylnaphthol (**6**)† (60%).

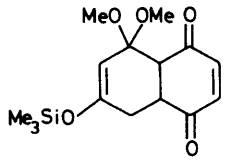
Alternatively, acetylation of naphthol (**3**) with pyridine and acetic anhydride afforded the acetate (**10**)† (87%). Subsequent acylation with acetic acid–trifluoroacetic anhydride in dichloromethane at room temperature gave (**11**)† as the sole product (80%), arising from acetylation at C-8, the assignment being based on a comparison of the ^{1}H n.m.r. spectra of (**10**) and (**11**).

Acylation of the naphthol (**3**) with trifluoroacetic anhydride alone in dichloromethane at room temperature yielded the

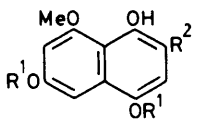
† All new compounds gave satisfactory elemental analyses and their spectroscopic data were in accord with the assigned structures.



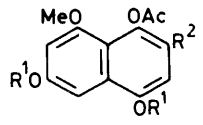
(**1**)



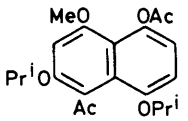
(**2**)



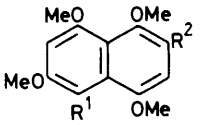
(**3**) $R^1 = Pr^i$, $R^2 = H$
(**4**) $R^1 = CH_2Ph$, $R^2 = H$
(**5**) $R^1 = Pr^i$, $R^2 = Ac$
(**6**) $R^1 = CH_2Ph$, $R^2 = Ac$
(**7**) $R^1 = Pr^i$, $R^2 = COCF_3$



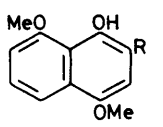
(**8**) $R^1 = Pr^i$, $R^2 = Ac$
(**9**) $R^1 = CH_2Ph$, $R^2 = Ac$
(**10**) $R^1 = Pr^i$, $R^2 = H$



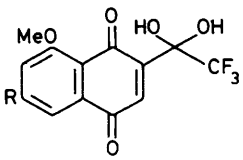
(**11**)



(**12**) $R^1 = R^2 = H$
(**13**) $R^1 = COCF_3$, $R^2 = H$
(**14**) $R^1 = Ac$, $R^2 = H$
(**15**) $R^1 = H$, $R^2 = Ac$



(**16**) R = H
(**17**) $R = COCF_3$



(**18**) $R = OPr^i$
(**19**) R = H

ortho-trifluoroacetylnaphthol (**7**)† (85%) directly. In contrast, treatment of naphthalene 1,4,5,7-tetramethyl ether (**12**)‡[2,6] with this anhydride afforded only the 8-trifluoroacetyl derivative (**13**)† (67%). However, addition of premixed acetic acid–trifluoroacetic anhydride to (**12**) gave not only the 8-acetyl compound (**14**)† as the major compound (66%) but also the 3-isomer (**15**)† (22%). Trifluoroacetylation of the dimethoxynaphthol (**16**)[2] was also readily achieved to afford the *ortho*-acylnaphthol (**17**)† (79%).

The trifluoroacetylnaphthols (**7**) and (**17**) underwent clean oxidation to the respective dihydroxytrifluoroethyl-1,4-naphthoquinones (**18**)† (90%) and (**19**)† (86%) with cerium(IV) ammonium nitrate in a water–acetonitrile mixture.

We are currently investigating the synthesis of naphthopyranquinones *via* the C-3 acylated compounds described above, as well as the potential of the C-8 acylation reactions in the construction of ansamycin analogues.

‡ 1,4,5,7-tetramethoxynaphthalene is also readily available by exhaustive methylation of the adduct (**2**) with potassium carbonate and dimethyl sulphate in acetone.

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References

1 R. H. Thomson, 'Naturally Occurring Quinones,' Academic Press, London, 1971.
2 T. A. Chorn, R. G. F. Giles, I. R. Green, V. I. Hugo, P. R. K. Mitchell, and S. C. Yorke, *J. Chem. Soc., Perkin Trans. 1*, 1984 in the press.
3 *E.g.* V. Prelog and W. Oppolzer, *Helv. Chim. Acta*, 1973, **56**, 2279.
4 P. Brassard and J. Banville, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1852.
5 E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *J. Chem. Soc.*, 1951, 718.
6 A. J. Birch, D. N. Butler, and J. B. Siddall, *J. Chem. Soc.*, 1964, 2941.