The *ortho*-Acetoxylation of Phenols by Copper(II) Acetate

Yasuomi Takizawa,* Akira Tateishi, Junichi Sugiyama, Hiroyuki Yoshida and Nobutoshi Yoshihara

Department of Chemistry, Tokyo Gakugei University, Nukuikita Machi, Koganei-shi, Tokyo 184, Japan

Oxidation of *p*-methoxyphenols and 6-chromanols by copper(II) acetate in acetic acid gave the corresponding *o*-acetoxyphenols and 5-acetoxy-6-chromanols, which were easily hydrolysed in MeOH–H_2O containing HCl to give catechol-type phenols.

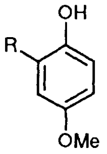
In recent years increasing interest has been shown in the chemistry of the oxidation of phenols using copper(II)-mediated oxidation processes[1] and copper(II)-based oxidation systems.[2] *o*-Acetoxyphenols are of interest because of their connection with naturally occurring compounds such as monospermoside,[3] dopa melanin[4] and tocopherols.

However, no easy and simple method for the preparation of *o*-acetoxyphenols has been found, although Hewgill *et al.*[5] have reported the synthesis of quinone *via* the acetoxylation of phenols with lead tetraacetate. We now find that oxidation of *p*-alkoxyphenols **1a–c** and **3a–e** by copper(II) acetate in acetic acid gives the corresponding *o*-acetoxyphenols **2a–c** and **4a–e**. A solution of 2-t-butyl 4-methoxyphenol **1a** and an equimolar amount of copper(II) acetate in acetic acid was refluxed under argon for 24 h. The mixture was poured into water and extracted with dichloromethane. The extracts were evaporated to give a dark red oily residue which was chromatographed on silica gel to give **2a**, m.p. 121 °C in 70% yield.† The structure of **2a** was confirmed spectroscopically by nuclear Overhauser enhancement (NOE) experiments. Thus, in **2a**,

---

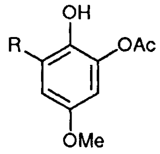
† New compounds were fully characterised by elemental analysis, NMR, IR and mass spectroscopy. **2a**: IR(KBr) ν/cm^{-1} 3330 and 1740; ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 9H, Bu^t), 2.36 (s, 3H, COMe), 3.71 (s, 3H, OMe), 5.50 (br, 1H, OH), 6.36 (d, 1H, *J* 2 Hz, ArH), 6.53 (d, 1H, *J* 2 Hz, ArH), ^{13}C NMR ($CDCl_3$) δ 21.13 (q), 30.34 (q), 34.89 (s), 55.32 (q), 101.15 (d), 105.92 (d), 143.25 (s), 148.67 (s), 157.45 (s), 169.91 (s). MS (M^+) *m/z* 238 (for $C_{13}H_{18}O_4$); **2c**: IR(KBr) ν/cm^{-1} 3330 and 1740; ^{1}H NMR($CDCl_3$) δ 2.11 (s, 3H, Me), 2.33 (s, 3H, COMe), 3.73 (s, 3H, OMe), 5.60 (br, 1H, OH), 6.34 (s, 2H, ArH), ^{13}C NMR($CDCl_3$) δ 16.47 (q), 20.37 (q), 55.54 (q), 101.10 (d), 108.47 (d), 131.82 (s), 148.12 (s), 157.99 (s), 169.42 (s). MS (M^+) *m/z* 196 (for $C_{10}H_{12}O_4$).

The percentage yields took into account the recovered starting materials.



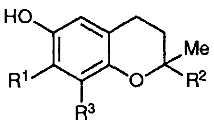
1

a; R = Bu^t
b; R = H
c; R = Me
d; R = Cl
e; R = OAc



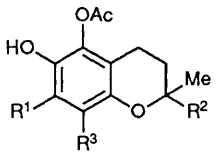
2

a; R = Bu^t
b; R = H
c; R = Me
d; R = Cl



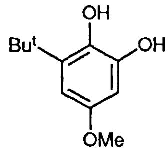
3

a; R^1 = H, R^2 = Me, R^3 = H
b; R^1 = Me, R^2 = Me, R^3 = H
c; R^1 = H, R^2 = $C_{16}H_{33}$, R^3 = H
d; R^1 = H, R^2 = $C_{16}H_{33}$, R^3 = Me
e; R^1 = Cl, R^2 = Me, R^3 = H
f; R^1 = OAc, R^2 = Me, R^3 = H



4

a; R^1 = H, R^2 = Me, R^3 = H
b; R^1 = Me, R^2 = Me, R^3 = H
c; R^1 = H, R^2 = $C_{16}H_{33}$, R^3 = H
d; R^1 = H, R^2 = $C_{16}H_{33}$, R^3 = Me
e; R^1 = Cl, R^2 = Me, R^3 = H



5

distinct NOEs were observed both on the aromatic proton (δ 6.53, d, *J* 2 Hz) by irradiation at the frequency of the Bu^t proton (δ 1.31, s) and on the aromatic proton (δ 6.36, d, *J* 2 Hz) by irradiation at the frequency of the acetoxy proton (δ 2.36, s). This establishes that acetoxylation has occurred at the 6-position, and that the possibility of transesterification involving the 1-hydroxy group can be ruled out in this example. Under similar conditions *p*-methoxyphenols **1b–c** and 6-chromanols **3a–d** reacted to give **2b**, m.p. 80 °C (yield 40%); **2c**, m.p. 104 °C (45%); **4a**, oil (46%); **4b**, m.p. 151 °C (65%); **4c** oil (60%) and **4d**, oil (80%), respectively.† However, acetoxylation of *p*-methylphenols and *p*-phenylphenols failed under similar conditions. In an effort to determine the effect of halogen on acetoxylation of phenols, the oxidation of 2-chloro-4-methoxyphenol **1d** and 7-chloro-2,2-dimethyl-6-chromanol **3e** by copper(II) acetate was investigated. The expected compounds **2d** (yield 20%) and **4e** (yield 30%) were obtained, as well as the unexpected compounds **1e** (yield 35%) and **3f** (yield 17%). Treatment of **2a** in MeOH–H_2O with HCl under argon at 90 °C for 45 min gave **5**, m.p. 70–71 °C in 80% yield. Under similar conditions, other acetoxyphenols were hydrolysed easily.

We thank Professors K. Yamada, Chiba University, T. Nishio and H. Aoyama, Tsukuba University, and H. Yamamoto, Ibaraki University, for mass spectral and/or elemental analyses and Mrs J. Takizawa, Tokyo University of Agriculture and Technology, for discussions of NOE experiments.

Received, 24th May 1990; Com. 0/02331K

References

1 O. Reinaud, P. Capdeviell and M. Maumy, *J. Chem. Soc., Chem. Commun.*, 1990, 566.
2 Y. Takizawa, T. Munakata, Y. Iwasa, T. Suzuki and T. Mitsuhashi, *J. Org. Chem.*, 1985, **50**, 4383.
3 S. R. Gupta, B. Ravindranath and T. R. Seshadri, *Phytochem.*, 1970, **9**, 2231.
4 B. R. Brown in *Biochemical Aspects of Oxidative Coupling of Phenols*, eds. W. I. Taylor and A. R. Battersby, Dekker, New York, 1967, p. 167.
5 F. R. Hewgill, B. Kennedy and D. Kilpin, *J. Chem. Soc.*, 1965, 2904.