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STUDIES ON QUINONES. VI. ACID-CATALIZED REARRANGEMENTS IN SOME 4-ACETYL-2,3-DIHYDROBENZO[*b*]FURANS[1]

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The reaction of 2-acetyl- and 5-acetyl-2-methoxy-1,4-benzoquinone (1a, 1c) with N-propenylpiperidine gave the corresponding 2,3-dihydrobenzo[*b*]furans, 2b and 2c, containing the acetyl group at C-4. Acid treatment of these dihydrofurans rearranged to 8-methyl- and 2-methoxy-8-methyljuglone (4a, 4b). Juglone (4c) and 2,3-dihydrojuglone (6) were obtained in fair yields from 4-acetyl-2,5-dihydroxy-2,3-dihydrobenzo[*b*]furan (2e).

It is known that 2-acetyl-1,4-benzoquinone (1a) and related compounds such as 2-methoxycarbonyl-1,4-benzoquinone (1b) are very reactive at the C-3 position to various nucleophiles.[2-7] In a recent communication[8] we have described the reaction of quinones 1a and 1b with enamines giving substituted furans. These are formed by attack of the nucleophile at C-3 followed by cyclization; i.e. the addition of N-(2-methyl-1-propenyl)-piperidine to 1a gives 4-acetyl-5-hydroxy-3,3-dimethyl-2-piperidino-2,3-dihydrobenzo[*b*]furan (2a).

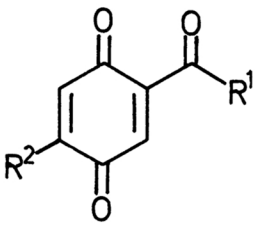
It is interesting to note that the O,N-acetal 2a experiments a ring opening under acidic conditions (ethanol-aqueous HCl) followed by the formation[8] of the 1(4H)-naphthalenone 3. This reaction occurs due to the presence of a potential C=O group at C-2 and the acetyl group in 2a.

These results promted us to study the formation of juglones (5-hydroxy-1,4-naphthoquinones) from benzo[*b*]furans capable to experiment the above rearrangement, followed by aromatization of the newly formed carboxyclic ring.

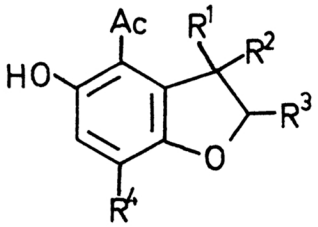
Reaction of 1a and N-propenylpiperidine in benzene solution at room temperature gave 4-acetyl-5-hydroxy-3-methyl-2-piperidino-2,3-dihydrobenzo[*b*]furan (2b) in 80% yield, as an orange oily liquid: IR (film): 1625 cm^{-1}; ^1H-NMR[9] δ;

6.98 (d, 1H, J~9Hz), 6.81 (d, 1H, J~9Hz), 4.96 (d, 1H, J~1.8Hz), 3.63 (dq, 1H, J~1.8Hz), 2.40-2.84 (m, 4H), 2.70 (s, 3H), 1.40-1.70 (m, 4H), 1.38 (d, 3H). Treatment of 2b in the same experimental conditions as those for the transformation 2a → 3 afforded 5-hydroxy-8-methyl-1,4-naphthoquinone (4a) in low yield[10] (15%): m.p. 162-163° [from cyclohexane (lit.[11] 160-163°)] ^{1}H-NMR: δ; 12.47 (s, 1H), 7.43 (d, 1H, J~9Hz), 7.16 (d, 1H, J~9Hz), 6.89 (s, 2H), 2.64 (s, 3H).

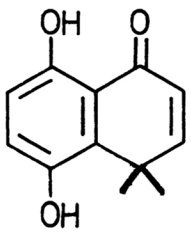
Better results were obtained when 2b was rearranged in refluxing acetone-10% sulfuric acid solution (1:1) which gave 4a in 60% yield. On the other hand treatment of 2b with benzoyl chloride in pyridine produced 1,4,5-tribenzoyloxy-8-methylnaphthalene (5) in 50% yield. IR (Nujol): 1754 and 1740 cm^{-1}; ^{1}H-NMR: δ; 8.40-6.80 (m, 19H), 2.80 (s, 3H).



1a. R^1=Me, R^2=H
b. R^2=OMe, R^2=H
c. R^3=Me, R^2=OMe



2a. R^1=R^2=Me, R^3=Pip., R^4=H
b. R^1=Me, R^2=R^4=H, R^3=Pip.
c. R^1=Me, R^2=H, R^3=Pip., R^4=OMe
d. R^1=Me, R^2=H, R^3=OH, R^4=OMe
e. R^1=R^2=R^4=H, R^3=OH



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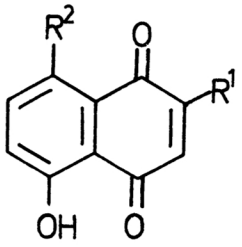
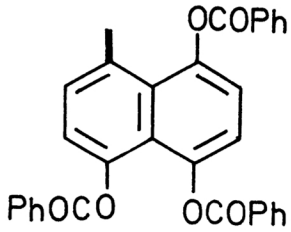


4a. R^1=H, R^2=Me
b. R^1=OMe, R^2=Me
c. R^1=R^2=H



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In order to obtain a substituted juglone in the quinone ring in a similar fashion to that presented above, the reaction of 5-acetyl-2-methoxy-1,4-benzoquinone[12] (1c) and N-propenylpiperidine was carried out, isolating the corresponding 2,3-dihydrobenzo[*b*]furan 2c in 59% yield. IR (KBr): 1610 cm^{-1}; ^{1}H-NMR: δ; 12.95 (s, 1H), 6.36 (s, 1H), 6.05 (s,3H), 5.02 (d, 1H, J~1.8Hz), 3.60 (dq, 1H,

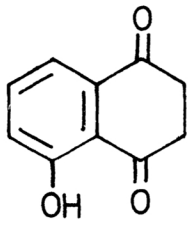
J~1.8Hz), 3.00-2.40 (m, 4H), 2.66 (s, 3H), 1.70-1.35 (m, 4H), 1.37 (d, 3H).

Although two chiral centers appeared at C-2 and C-3 in the formation of the furans 2b and 2c, only one product was isolated in both cases. According to the proton coupling constant C_2-H and C_3-H (~1.8Hz), it seems reasonable to attribute, in principle, stereochemistry *trans* to those heterocycles[13,14], notwithstanding the finding of Zalkow and Thosal[15,16].

Prolonged heating of the furan 2c in 10% sulfuric acid gave 5-hydroxy-2-methoxy-8-methyl-1,4-naphthoquinone (4b) in low yield (21%). IR (KBr): 1670 and 1630 cm^{-1}; ^{1}H-NMR: δ; 12.71 (s, 1H), 7.24 (2d, 2H, J~9Hz), 6.04 (s, 1H), 3.90 (s, 3H), 2.62 (s, 3H). During the acid treatment of compound 2c, it was possible to isolate a reaction product characterized by its ^{1}H-NMR spectrum as the hemiacetal 2d, which by treatment with 10% sulfuric acid gave the juglone 4b.

From these results it was supposed that the transformation 2b → 4a and 2c → 4b is initiated by hydrolysis of the O,N-acetalic grouping followed by cyclization, in an aldol type fashion, of the open form of the hemiacetals, aromatization and, finally, air oxidation.

Taking into account the participation of hemiacetals in the formation of juglones 4a and 4b, acid treatment of hemiacetal 2e[3] gave 2,3-dihydrojuglone (6) in fair yield (44%) m.p. 96-97° [from cyclohexane (lit.[17] 96-97°)] and juglone (4c) in low yield (15%). The latter was identified by comparison with an authentic sample. When the above reaction was carried out in the presence of diluted hydrogen peroxide, only juglone was isolated in 62% yield.



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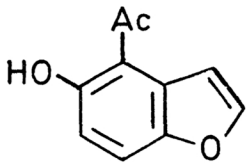

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It is interesting to note that the dihydrofuran 2e by treatment with p-toluenesulfonic acid in benzene solution produced quantitatively 4-acetyl-5-hydroxybenzo[*b*]furan (7). IR (KBr): 1620 cm^{-1}; ^{1}H-NMR: δ; 12.95 (s, 1H), 7.72 (d, 1H, J~2Hz), 7.60 (d, 1H, J~9Hz), 6.95 (d, 1H, J~2Hz), 6.90 (d, 1H, J~9Hz), 2.80 (s, 1H).

References

1. a) Presented at the 10th. National Meeting of the Chemical Society of Chile, Valdivia, February 1979; b) Part V of this series: J. Santos, D. Schalscha and J. Valderrama, An. Quím. 74, 827 (1978).
2. C.H. Eugster and P. Bosshard, Helv. Chim. Acta, 46, 815 (1963).
3. C.H. Eugster and P. Kuser, Chimia, 18, 358 (1964).
4. C.H. Eugster and S.E. Fumagalli, Helv. Chim. Acta 54, 959 (1971).
5. F. Fariña and J. Valderrama, Synthesis, 315 (1971).
6. F. Fariña and J. Valderrama, An. Quím., 70, 258 (1974).
7. F. Fariña and J. Valderrama, An. Quím., 72, 902 (1976).
8. J. Valderrama and J.C. Vega, An. Quím., 73, 1212 (1977).
9. a) All new compounds gave satisfactory data in elemental analysis; b) All ^{1}H-NMR spectra were run in a VARIAN XL-100 Spectrometer using $CDCl_3$ as solvent and TMS as internal standard.
10. All juglones were purified by column chromatography on silica gel and the yield are based on the pure products. No further attemps were made in order to improve the yields.
11. K. Torssell, Acta Chem. Scand. B 30, 353 (1976).
12. F.M. Dean, P.G. Jones, R.B. Morton, and P. Sidisunthorn, J. Chem. Soc., 411 (1964).
13. M.P. Mertes, L.J. Powers, and E. Shefter, Chem. Commun., 620 (1970).
14. M.P. Mertes, L.J. Powers, and E. Shefter, J. Org. Chem., 36, 1805 (1971).
15. L.H. Zalkow and M. Thosal, Chem. Commun., 922 (1967).
16. L.H. Zalkow and M. Thosal, J. Org. Chem., 34, 1646 (1969).
17. R.H. Thomson, J. Chem. Soc., 1737 (1950).

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