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SELENIUM REAGENT IN THE SYNTHESIS OF NAPHTHO[2,3-*b*]FURAN-4,9-DIONES

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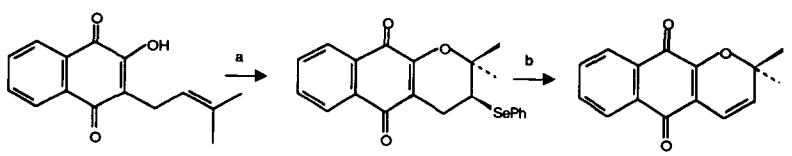
Summary- Phenylselenoetherification was used to synthezise naphtho[2,3-*b*]furan-4,9-diones and naphtho[2,3-b]pyran-5,10-diones from 2-hydroxynaphthoquinones.

Naphthoquinones and naphtho[2,3-*b*]furan-4,9-diones are plant metabolites found to be responsible for the pharmacological activities, antitumoral, antibacterial, antifungal and immunostimulating effects of various bark and wood extracts.[1]

The phenylselenoetherification is a highly efficient cyclisation process for the synthesis of O- and S-heterocycles, starting from unsaturated hydroxy- or thio- compounds and benzeneselenenyl halides.[2] The hydroxy compounds could be an alcohol or a phenol. We used this reaction for the synthesis of naphtho[2,3-*b*]furan-4,9-diones and naphtho[2,3-*b*]pyran--5,10-diones starting from 2-hydroxy-naphthoquinones.

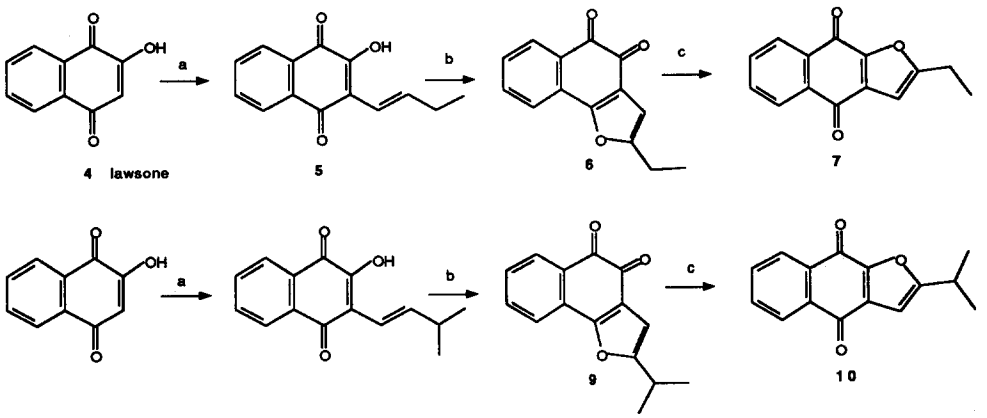
Thus, when lapachol [3] **1** was treated with benzeneselenenyl chloride the selenide **2** [4] was formed and gave xyloidone **3** in 60% yield [5,6] classically upon treatment with hydrogen peroxide by thermal *syn* elimination of the selenoxide.[2]



1 lapachol 2 3

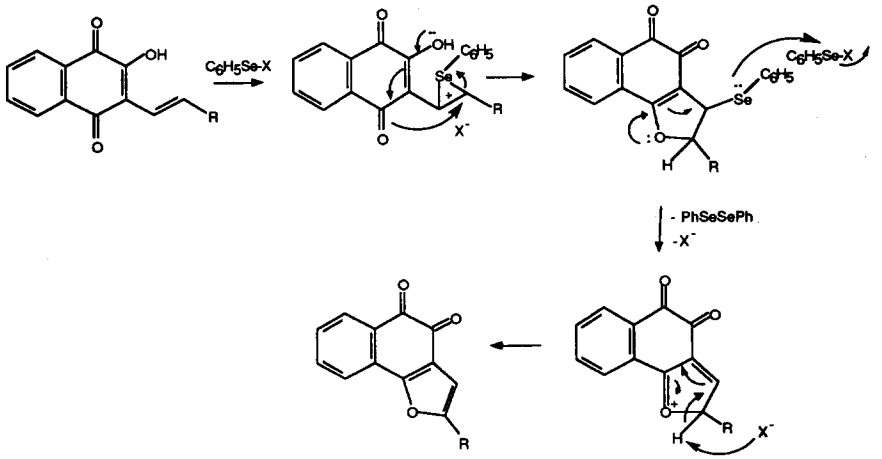
a- **1**, 1 eq., C_6H_5SeCl 1.1 eq., CH_2Cl_2, -78°C, 1 h then r.t, 75%. b- **2**, 1 eq., CH_2Cl_2, H_2O_2 30% 1 eq., r.t., 2 h, silicagel chromatography , 60%.

However, when derivative **5** [7] or isolapachol **8** [8], prepared from lawsone **4** according to Hooker's procedure,[9] was treated under the same conditions, the reaction was incomplete and required 2 equivalents of benzeneselelenyl chloride to go to completion, giving the naphtho[1,2-*b*]furan-4,5-diones **6** [10] or **9** [11], respectively, in 75% yield and dibenzenediselenide .



a- 4, 1 eq., *n*-butyraldehyde or *iso*-valeraldehyde, 10 eq., acetic acid, HCl, 80°, 2 h, 60%. **b-** 5 or 8, 1 eq., C_6H_5Cl, 2 eq., CH_2Cl_2, -78°, 1 h, then r.t., silica gel chromatography, 75%. **c-** 6 or 9, aqueous H_2SO_4 30%, reflux, 30 min, 82%.

The intermediate selenide was not isolated. A nucleophilic displacement reaction at Se (II) with the participation of the oxygen atom of the dihydrofuran ring may be invoked to explain this process (scheme 1).[11]



Scheme 1

Such a nucleophilic displacement at Se (II) was used by Schmid and Garratt to explain the formation of dibenzenediselenide when benzeneselenyl chloride was reacted with 2-chloroalkyl phenyl selenides [11] and could account for the formation of dibenzenediselenide and bromoacetophenone which was observed when benzeneselenyl chloride and acetophenone reacted together under certain conditions.[12]

The orthoquinones **6** and **9** could be isomerized with acid [13] to lead to the corresponding naphtho[2,3-*b*]furan-4,9-diones **7** [14] and **10** [15], respectively.

Hence, this selenoetherification reaction could be a convenient alternative method for the synthesis of these furanonaphthoquinones beside the previously published ones.[16]

References and Notes

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3 Isolated from *Tabebuia* sp., Bignoniaceæ.

4 $C_{21}H_{18}O_3Se$, mp 116°C; MS EI: M^+ 398 and 396, m/z 241 (M-SePh), 199; ^1H NMR ($CDCl_3$) 200 MHz; δ ppm 1.48 (3H, *s*, CH3), 1.63 (3H, *s*, CH3), 2.73 and 3.10 (ABX, J_{AB}=19 Hz, J_{AX}=9 Hz, J_{BX}=5 Hz, CH2-9), 3.35 (1H, *dd*, J=9 Hz, J'=5, H-8), 7.26 (2H, *m*, Ar), 7.60 (5H, *m*, Ar), 8.03 (2H, *m*, Ar).

5 $C_{15}H_{12}O_3$, mp 141°C; MS EI: M^+ 240, m/z 225, 212, 197, 141. ^1H NMR 200 MHz, $CDCl_3$: δ ppm 1.55 (6H, *s*, CH3), 5.73 and 6.66 (2H, AB, J=10 Hz, H-8 and H-9), 7.70 (2H, *m*, Ar), 8?08 (2H, *m*, Ar).

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7 $C_{14}H_{12}O_3$, mp 105°C; MS EI: M^+ 228, m/z 213, 189; ^1H NMR ($CDCl_3$) 200 MHz: δ ppm 1.23 (3H, *t*, J=7 Hz, CH_3-4'), 2.33 (2H, *q*, J=7 Hz, CH_2-3') 6.63 (1H, ABX2, J_{AB}=16 Hz, J_{AX}=1 Hz, H-1'), 7.13 (1H, ABX2, J_{AB}+16 Hz, J_{BX}=7 Hz, H-2'), 7.73 (2H, *td*, J=7.5 Hz, J'= 2 Hz, H-6 and H-7), 8.10 (2H, *dd*, J=7.5 Hz, J'=2 Hz, H-5 and H-8).

8 $C_{15}H_{14}O_3$, mp 119°C; MS EI: M+ 242, m/z 227, 199; ^1H NMR ($CDCl_3$) 200 MHz: δ ppm 1.13 (6H, *d*, J=7 Hz, CH_3), 2.55 (1H, *septuplet*, J=7 Hz, H3'), 6.67 and 7.06 (2H, ABX, J_{AB}=16 Hz, J_{AX}=7 Hz, J_{BX}=1 Hz, H1' and H-2'), 7.73 (2H, *td*, J=7 Hz, J'=2 Hz, H-6 and H-7), 8.08 and 8.13 (2H, 2 *dd*, J=7 Hz, J'=2 Hz, H-5 and H-8).

9 Hooker, S.C. *J. Amer. Chem. Soc.* **1936**, *58*, 1163.

10 $C_{14}H_{10}O_3$, mp 140-142°C; MS EI: M^+ 226, m/z 197, 182; ^1H NMR ($CDCl_3$) 200 MHz: δ ppm 1.31 (3H; *t*, J=7 Hz, CH_2-$\underline{CH_3}$), 2.76 (2H, *q*, J=7 Hz, $\underline{CH_2}$-CH_3), 6.46 (1H, *s*, H-3), 7.43 (1H, *td*, J=7 Hz, J'=2 Hz, H-7) 7.66 (2H, *m*, H-8 and H-9) 8.06 (1H, *d*, J=7 Hz, H-6).
$C_{15}H_{12}O_3$, mp 92-94°; MS EI: M^+ 240, m/z 227, 212, 197; ^1H NMR ($CDCl_3$) 200 MHz: δ ppm 1.33 6H, d, J=7 Hz, CH3), 3.03 (1H, *septuplet*, J=7 Hz, H-1'), 6.46 (1H, s, H-3), 7.43 (1H, m, H-7), 7.66 (2H, m, H-8 and H-9), 8.02 (1H, d, J=7 Hz, H-6)

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14 $C_{14}H_{10}O_3$, mp 138-140°C; MS EI: M^+ 226, m/z 211, 183; ^1H NMR 200 MHz, CDCl3: δ ppm 1.36 (3H, *t*, J=7 Hz, CH_2-$\underline{CH_3}$), 2.86 (2H, *q*, J=7 Hz, $\underline{CH_2}$-CH_3), 6.63 (1H, *s*, H-3), 7.76 (2H, *m*, H-7 and H-8), 8.20 (2H, *m*, H-6 and H-9).

15 $C_{15}H_{12}O_3$, mp 96-98°C; MS EI: M^+ 240, m/z 225, 197, 149; ^1H NMR 200 MHz $CDCl_3$: δ ppm 1.38 (6H, *d*, J=7 Hz, CH3), 3.15 (1H, *septuplet*, J=7 Hz, H-1'), 6.63 (1H, *s*, H-3), 7.73 (2H, *m*, H-7 and H-8), 8.20 (2H, *m*, H-6 and H-9).

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