NOTES

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The Reaction of Phenolic Compounds with Isoprenoids. VIII.1) The *o*-Isoprenylation of Phenols in the Presence of Metallic Sodium

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Synopsis. Phenols (phenol, hydroquinone, resorcinol, and *o*-cresol) reacted with prenyl halides (3-methyl-2-buteny chloride and geranyl chloride) in the presence of an alkali metal (Na) in ether. In these reactions, phenols with the corresponding prenyl group at the ortho position were obtained selectively.

Claisen *et al.* have reported that, in general, the amount of C-alkylation can be greatly increased by the alkylation of sodium phenolates in benzene.2) In a previous paper, we ourselves reported that phenol reacted with 3-methyl-2-butenyl chloride in the presence of metallic sodium in ether and that *o*-(3-methyl-2-butenyl)phenol (**1**) was thus isolated selectively (98%). In this paper, the studies of this reaction will be reported in detail.

In the reaction of phenol with geranyl chloride, *o*-geranylphenol (**2**) was also obtained in a high yield (90%) in a reaction similar to that in the case of 3-methyl-2-butenyl chloride. *o*-Cresol reacted with 3-methyl-2-butenyl chloride in the same manner, and 2-methyl-6-(3-methyl-2-butenyl)phenol (**3**) was obtained in a 76% yield. A similar reaction of hydroquinone with 3-methyl-2-butenyl chloride afforded 4-hydroxy-2-(3-methyl-2-butenyl)phenol (**4**) in a 66% yield. In the case of resorcinol, 3-hydroxy-4-(3-methyl-2-butenyl)-phenol (**5**) and 3-hydroxy-2-(3-methyl-2-butenyl)phenol (**6**) were obtained in 16 and 27% yields respectively. In this case, though the structures were not determined, the di- and tri-isoprenylated compounds were confirmed by GC-MS (GLC peaks showing molecular ion peaks at *m*/*e* 246 and 414 were observed).

From these results, metallic sodium in an aprotic solvent was found to be useful in obtaining selectively phenols with an acyclic isoprenyl group at the ortho position, while the Friedel-Crafts alkylation did not give such phenols mainly.3)

Experimental

The Reaction of Phenols with Allylic Chloride. To an ethereal solution (50 ml) of phenol (0.05 mol), metallic sodium (0.2 mol) was added. After the mixture had been stirred for 0.5—1.5 h, an allylic chloride (0.05 mol) was added slowly; then the mixture was refluxed for 10 h. After the unreacted metallic sodium had been taken out, the solution was acidified with 0.1M aq HCl (20 ml) and extracted with ether. The ethereal solution was treated with 5% aq NaOH to remove the unreacted phenol, and then washed with water and dried over anhydrous sodium sulfate. After the removal of the solvent by distillation under reduced pressure, the products were obtained. The structures of the products were identified by means of the IR, NMR, and mass spectra. These IR and NMR spectral data agreed with the previously reported data.

*2-Geranylphenol (**2**).*4) IR (cm^{-1}): 3400, 1925, 1890, 1780, 1210, 840, 750. NMR (δ, CCl_4): 1.57(s, 3,$-CH_3$), 1.65 (s, 3, $-CH_3$), 1.69 (s, 3, $-CH_3$), 2.00 (m, 4), 3.25 (d, 2, J=7.0 Hz, $-CH_2-$), 5.10 (s, 1, $-OH$), 5.25 (t, 2, J=7.0 Hz, $=CH-$), 6.50—7.10 (m, 4, aromatic protons). Mass (*m*/*e*): 230 (M^+).

*2-Methyl-6-(3-methyl-2-butenyl)phenol (**3**.*5)*)* IR (cm^{-1}): 3500, 1910, 1780, 845, 760, 740. NMR (δ,CCl_4): 1.72 (s, 6, $=C(CH_3)_2$), 2.10 (s, 3, $-CH_3$), 2.00 (m, 4), 3.25 (d, 2, J= 7.0 Hz, $-CH_2-$), 5.10 (s, 1, $-OH$), 5.25 (t, 2, J=7.0 Hz, $=CH-$), 6.50—7.10 (m, 4, aromatic protons). Mass (*m*/*e*): 176 (M^+), 161 (M^+-15), 121 (M^+-55).

*4-Hydroxy-2-(3-methyl-2-butenyl)phenol (**4**).* mp 99—100 °C (colorless plates, lit,6) mp 102°C). IR (cm^{-1}): 3500, 1895, 1815 1780, 840, 810. NMR (δ, CD_3OD): 1.67 (s, 6, $=C(CH_3)_2$), 3.15 (d, 2, J=7.0 Hz, $-CH_2-$), 5.10 (t, 1, J=7.0 Hz, $=CH-$), 6.25—6.70 (m, 3, aromatic protons). MS (*m*/*e*): 178 (M^+), 123 (M^+), 123 ($M^+ -55$).

*3-Hydroxy-2-(3-methyl-2-butenyl)phenol (**5**).*7) IR (cm^{-1}): 3500, 1655, 1200, 840, 800. NMR (δ, CCl_4): 1.74 (s, 3, $-CH_3$), 1.79 (s, 3, $-CH_3$), 3.32 (d, 2, J=7.0 Hz, $-CH_2-$), 5.20(m, 3), 6.10—6.60 (m, 3, aromatic protons). MS (*m*/*e*): 178 (M^+), 163 ($M^+ -15$), 123 ($M^+ -55$).

*3-Hydroxy-2-(3-methyl-2-butenyl)phenol (**6**).*7) IR (cm^{-1}): 3400, 1645, 1220, 835, 785, 775. NMR (δ, CCl_4): 1.66 (s, 3, $-CH_3$), 1.72 (s, 3, $-CH_3$), 3.09 (d, 2, J=7.0 Hz, $-CH_2-$), 4.85 (s, 2, $-OH$), 5.13 (t, 1, J=7.0 Hz, $=CH-$), 6.15—6.80 (m, 3, aromatic protons). MS (*m*/*e*): 178 (M^+), 163 (M^+-15), 123 (M^+-55).

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