**3,5,6-Trimethyl-2-methylene-4-oxahept-6-enoic Acid (5).** Following the general procedure, from the reaction of 300 mg (2.6 mmol) of **3a** and 1.82 g (26 mmol) of 2-methyl-2-butene was obtained 390 mg (82%) of **5** as colorless oil: bp 120–125 °C (0.08 torr); IR (film) 3420, 3001, 2952, 1702, 1639, 1441, 1378, 1282, 1096, 971, 909 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.22 (d, $J$ = 6.4 Hz, 3 H), 1.27 (d, $J$ = 7.2 Hz, 3 H), 1.62 (s, 3 H), 3.93 (q, $J$ = 7.2 Hz, 1 H), 4.31 (q, $J$ = 6.4 Hz, 1 H), 4.78 (s, 1 H), 4.88 (s, 1 H), 6.02 (s, 1 H), 6.35 (s, 1 H), 11.16 (s, 1 H, COO*H*); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 17.07 (q), 20.03 (q), 21.23 (q), 70.24 (d), 77.28 (d), 111.95 (t), 126.60 (t), 143.46 (s), 146.46 (s), 171.71 (s). Anal. Calcd for $C_{10}H_{16}O_3$ (184.2): C, 65.22; H, 8.69. Found: C, 65.39; H, 8.78.

**Reaction of 3a with 2,5-Dimethyl-2,4-hexadiene.** Following the general procedure, from the reaction of 300 mg (2.6 mmol) of **3a** with a fivefold excess of 2,5-dimethyl-2,4-hexadiene was isolated by Kugelrohr distillation at 158–170 °C (0.1 torr) 410 mg (70%) of colorless oil consisting of a 28:72 mixture of **6** and **7**. Separation by means of preparative HPLC afforded from a 100-mg mixture 21 mg of **6** ($t_r$ 3.7 min) and 52 mg of **7** ($t_r$ 5.6 min), using 92:8 petroleum ether (40–80)–ethyl acetate as eluant.

**2,2,7-Trimethyl-3-(2-methyl-1-propenyl)-6-methylene-1,4-dioxacycloheptan-5-one (6a)**: IR (film) 2991, 2938, 2860, 1726, 1450, 1388, 1267, 1168, 1088, 1052, 981 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.04 (s, 3 H, 2-$CH_3$), 1.26 (s, 3 H, 2-$CH_3$), 1.32 (d, $J$ = 5.9 Hz, 3 H, 7-$CH_3$), 1.62 (d, $J$ = 1.9 Hz, 3 H, propenyl $CH_3$), 1.70 (d, $J$ = 1.3 Hz, 3 H, propenyl $CH_3$), 4.34 (dq, $^3J$ = 5.9 Hz, $^4J$ = 1.1 Hz, 1 H, 7-H), 4.87 (d, $^3J$ = 9.6 Hz, 1 H, 3-H), 5.18 (dqq, $^3J$ = 9.6 Hz, $^4J$ = 1.9 and 1.3 Hz, 1 H, propenyl H), 5.68 (d, $^4J$ = 1.1 Hz; 1 H, methylene H), 5.92 (s, 1 H, methylene H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 17.56 (q) 18.93 (q), 25.85 (q), 27.08 (q), 29.78 (q), 64.54 (d), 77.59 (s), 84.20 (d), 120.59 (d), 122.46 (t), 138.53 (s), 145.46 (s), 169.65 (s); MS (70 eV); $m/e$ (relative intensity) 222 ($M^+$ – 2, 0.1), 193 (3), 150 (15), 107 (24), 95 (17), 91 (18), 43 (100). Anal. Calcd for $C_{13}H_{20}O_3$ (224.1): C, 69.61; H, 8.99. Found: C, 69.38; H, 9.21.

**2,6,6-Trimethyl-7-(2-methyl-1-propenyl)-3-methylene-1,5,8-trioxaspiro[3.4]octane (7a)**: IR (film) 2996, 2938, 1.8 1600, 1552, 1448, 1372, 1281, 1182, 1088, 1040, 982 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.08 (s, 3 H, 6-$CH_3$), 1.16 (s, 3 H, 6-$CH_3$), 1.31 (d, $J$ = 6.3 Hz, 3 H, 2-$CH_3$), 1.63 (d, $J$ = 1.4 Hz, 3 H, propenyl $CH_3$), 1.72 (d, $J$ = 1.4 Hz, 3 H, propenyl $CH_3$), 4.54 (ddq, $^3J$ = 6.3 Hz, $^4J$ = 1.8 and 2.9 Hz, 1 H, 2-H), 4.97 (d, $^3J$ = 8.8 Hz, 1 H, 7-H), 5.23 (ddd, $^3J$ = 8.8 Hz, $^4J$ = 1.4 and 1.2 Hz, 1 H, propenyl H), 5.35 (d, $^4J$ = 1.8 Hz, 1 H, methylene H), 5.79 (d, $^4J$ = 2.9 Hz, 1 H, methylene H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 19.19 (q), 20.75 (q), 22.32 (q), 23.78 (q), 25.97 (q), 65.76 (d), 77.40 (s), 77.79 (d), 119.14 (d), 120.11 (s), 120.18 (t), 139.61 (s), 149.70 (s); MS (70 eV), $m/e$ (relative intensity) 224 ($M^+$, 0.5), 163 (20), 121 (14), 95 (23), 55 (24), 43 (100), 41 (32). Anal. Calcd for $C_{13}H_{20}O_3$ (224.1): C, 69.61; H, 8.99. Found: C, 69.85; H, 9.14.

**Acknowledgment.** We thank the Deutsche Forschungsgemeinschaft (Sonderforschungsberich 172, "Molekulare Mechanismen kanzerogener Primärveränderungen"), the Stiftung Volkswagen, the Frith Thyssen Stiftung, and the Fonds der Chemischen Industrie for the generous financial support. The technical assistance by Petra Seufert and spectral services by Dr. G. Lange (MS) and Dr. D. Scheutzow (NMR) is gratefully appreciated.

## C-Prenylation of Phenols Promoted by Aluminum Oxide Surfaces

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C-Alkenylation of phenols are traditionally carried out in acidic[1] or basic media.[2-4] Other processes, such as those utilizing unusual Friedel–Crafts conditions,[5] platinum catalysis,[6] and silicon chemistry[7] were developed more recently. Attempts to C-alkylate phenols containing strongly electron-withdrawing substituents with allylic halides have met with only limited success.[5] These reactions produced mainly *O*-alkylated phenols and only very minor amounts of the C-alkylated isomers.

A large number of natural products of mixed acetate–mevalonate origin contain prenyl substituents and in connection with a synthetic project in this area we had occasion to examine the prenylation of phenols containing electron-withdrawing appendages and found that C-alkylation with either prenyl chloride or bromide can be accomplished with acceptable yields, in two-phase systems. The solid phases examined consisted of a mixture of aluminum oxide and barium oxide or simply commercial aluminum oxide used for thin-layer chromatography. The reactions were found to proceed slowly at room temperature, and the conditions are sufficiently mild that even the sensitive phenol **15** could be prenylated in satisfactory yield. No $\alpha,\alpha$-dimethallyl-substituted phenols were detected, and in three cases minor amounts of isomeric, C-substituted $\gamma,\gamma$-dimethallyl derivatives were formed. Two of these are derived from cyclohexadienone intermediates not containing the $\beta$-hydroxy $\alpha,\beta$-unsaturated aldehyde chelate and the third from an intermediate with disrupted $\alpha$-pyrone ring. We have prepared nine dimethallyl-substituted phenols employing this method and the results are summarized in Table I. The solid phases can be reused provided solvents have been removed by heating in vacuo at approximately 80 °C. Raising the temperature of the reaction medium caused darkening of the solutions and yields were lower.

### Experimental Section

The following spectrometers were used: IR, Perkin-Elmer 397; NMR, Varian T-60, JEOL FXQ, Bruker wm 250; UV, Hitachi Perkin-Elmer 200; MS, Varian MAT-44, Finnigan MAT 8200. Melting points were determined on a Reichert hot stage microscope and are uncorrected.

**Method A.** The phenol (1.0 mmol) in 5 mL of THF was added to a slurry of 5–10 g of $Al_2O_3$ (basic, or neutral Type T or E for thin layer chromatography, Merck) in ether. The solvent was evaporated and 1–5 equiv of the allylic halide in ether–hexane (30–100%) or $CH_2Cl_2$ was added. After stirring for 1–5 days, $Al_2O_3$ was filtered off and washed with 1% HOAc–EtOAc. The combined organic layer was evaporated and the product purified by chromatography or crystallization.

**Method B.** The phenol (1.0 mmol) in 5 mL of THF was added to a slurry of 30% $BaO$–$Al_2O_3$ (3–5 equiv by weight as a fine powder (10 $\mu$m) in dry ether. The solvent was evaporated and 1–5 equiv of the allylic halide in ether–hexane (30–100%) or $CH_2Cl_2$ was added. After 1–6 days the solid was filtered off and washed with 1% HOAc–EtOAc. The combined organic layers were evaporated and purified by chromatography or crystallization.

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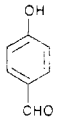
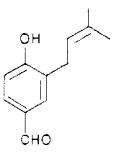
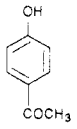
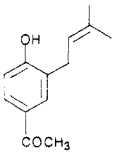
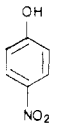
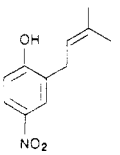
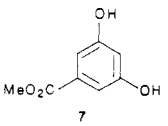
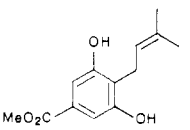
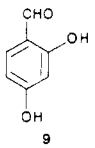
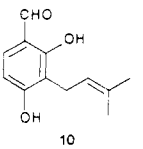
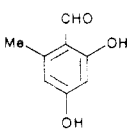
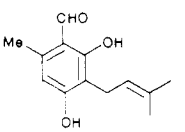
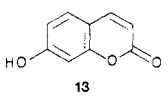
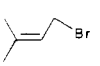
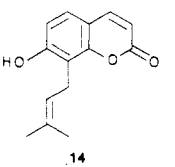
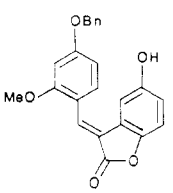
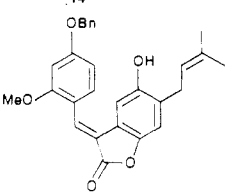
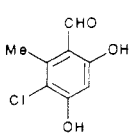
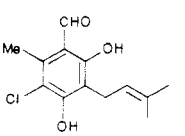
0022-3263/86/1951-4481$01.50/0 

**Table I**

| phenol | allylic halide | allylphenol | yield (%) | lit. yield (%) | C/O ratio (method) | time (days) (solvent) |
|---|---|---|---|---|---|---|
|  1 |  |  2 | 35 | <10[8] | 1:1 (B) | 6 (I) |
|  3 |  |  4 | 39 | 15[9] | 3:1 (B) | 6 (I) |
|  5 |  |  6 | 32 | 0 | 3:2 (B) | 7 (II) |
|  7 |  |  8 | 21 | | 1:1 (A) | 3 (II) |
|  9 |  |  10 | 25[a] | 10[8] | 1:1 (A) | 3 (II) |
|  11 |  |  12 | 38[a] | | 1:5 (B) | 5 (I) |
|  13 |  |  14 | 29[a] | | 1:1 (A) | 5 (I) |
|  15 |  |  16 | 58[b] | | 3:2 (A) | 3 (III) |
|  17 |  |  18 | 42 | [c] | 1:2 (B) | 4 (IV) |

[a] Very minor amounts of an isomeric C-prenylated product were isolated. [b] Only this reaction was optimized. [c] Reference 11.

Solvent systems: I, ether–hexane (1:1); II, ether; III, dichloromethane; IV, ether–hexane (1:3).

**Physical Properties of the New Prenylated Phenols. 4-Hydroxy-3-(3-methyl-2-butenyl)nitrobenzene (6)**: method B; white needles, mp 71 °C (from ether–hexane); UV max (MeOH) 410, 425 (sh) 266, 234 (sh); IR ($CH_2Cl_2$) 3560, 3400, 2950, 2910, 1585, 1520, 1340 $cm^{-1}$; NMR ($CDCl_3$, 60 MHz) $\delta$ 1.73 (br, s, 6), 3.35 (d, 1, $J$ = 7.0 Hz), 5.22 (br, t, 1, $J$ = 7.0 Hz), 6.43 (s, 1, OH), 6.75 (d, 1, $J$ = 10.0 Hz), 7.90 (m, 2); mass spectrum, $m/e$ (relative intensity) 207 ($M^+$, 18), 192 (10), 177 (18), 175 (23).

**4,5-Dihydroxy-4-(3-methyl-2-butenyl)benzoic acid methyl ester (8)**: method A; white needles, mp 139 °C (from ether–hexane); UV max (MeOH) 263, 308; IR ($CH_2Cl_2$) 3680, 3570, 2950, 1720, 1590, 1440 $cm^{-1}$; NMR (acetone-$d_6$, 250 MHz) $\delta$ 1.63 (s, 3), 1.78 (s, 3), 1.95 (m, 2, OH), 3.40 (d, 2, $J$ = 10.5 Hz), 3.81 (s, 3), 4.28 (br, t, 1, $J$ = 10.5 Hz), 7.10 (s, 2); mass spectrum, $m/e$ (relative

intensity) 236 ($M^+$, 46), 220 (14), 205 (14).

**2,4-Dihydroxy-6-methyl-3-(3-methyl-2-butenyl)benzaldehyde (12)**: method B; colorless needles, mp 148 °C (from ether–hexane); UV max (MeOH) 238, 250, 338; IR ($CH_2Cl_2$) 3550, 3300, 3960, 3920, 1620 $cm^{-1}$; NMR ($CD_2Cl_2$, 250 MHz) $\delta$ 1.75 (d, 3, $J$ = 1.5 Hz), 1.82 (s, 3), 2.45 (s, 3), 3.35 (d, 2, $J$ = 7.5 Hz), 5.27 (dt, 1, $J$ = 1.5 Hz), 6.20 (s, 1), 6.33 (s, 1, OH), 10.04 (s, 1), 12.66 (s, 1, OH); mass spectrum, $m/e$ (relative intensity) 220 ($M^+$, 56), 205 (28), 177 (27), 166 (10), 165 (100), 163 (18), 136 (11); high-resolution mass spectrum calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1098.

**3-[[4-(Benzyloxy)-2-methoxyphenyl]methylene]-5-hydroxy-6-(3-methyl-2-butenyl)-2(3*H*)-benzofuranone (16)**: method A; yellow needles mp 113 °C (from ether–hexane); UV max (MeOH); IR ($CH_2Cl_2$) 3550, 3025, 2925, 1760 (sh), 1600 $cm^{-1}$; NMR ($CDCl_3$, 250 MHz) $\delta$ 1.76 (s, 3), 1.78 (s, 3), 3.35 (d, 1, $J$ = 6.8 Hz), 3.84 (s, 2.4), 3.88 (s, 0.6), 4.99 (s, 0.8), 5.05 (s, 0.2), 5.13 (s, 0.2), 5.25 (br, t, 1 $J$ = 6.8 Hz), 6.57 (br, s, 0.2), 6.60 (br, s, 0.8), 6.64 (d, 1, $J$ = 8.0 Hz), 6.87 (s, 0.2), 6.90 (s, 0.8), 7.00 (s, 0.2), 7.16 (s, 0.8), 7.70 (d, 0.8, $J$ = 8.0 Hz), 7.82 (d, 0.2, $J$ = 8.0 Hz), 7.94 (s, 1); mass spectrum, $m/e$ (relative intensity) 442 ($M^+$, 45), 387 (5), 351 (12), 91 (100); high-resolution mass spectrum calcd for $C_{28}H_{26}O_5$ 442.1778, found 442.1785.

**5-Chloro-2,4-dihydroxy-6-methyl-3-(3-methyl-2-butenyl)benzaldehyde (18)**: method B: colorless needles, mp 150 °C (from ether–hexane), UV max (MeOH) 263, 350; IR ($CH_2Cl_2$) 3675, 3500, 3100, 2925, 1618; NMR ($CDCl_3$, 250 MHz) $\delta$ 1.60 (s, 3), 1.80 (s, 3), 2.61 (s, 3), 3.42 (d, 2, $J$ = 7.0 Hz), 5.24 (br, t, 1, $J$ = 7.0 Hz), 6.45 (s, 1), 10.19 (s, 1), 12.71 (s, 1); mass spectrum, $m/e$ (relative intensity) 254 ($M^+$, 13), 239 (22), 213 (5), 210 (16), 201 (32), 199 (100); high-resolution mass spectrum calcd for $C_{13}H_{15}ClO_3$ 254.0709, found 254.0709.

**Acknowledgment.** This work was supported by a National Research Service Award (No. 2T32CA09112) from the Naional Cancer Institute, DHEW, the National Institutes of Health (Grant GM 09868), and Hoffmann-La Roche Inc. High-resolution mass spectra were provided by the facility, supported by the National Institutes of Health (Grant RR 00317) (Principle Investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resources.

## Chemistry of the Adducts of *N,N'*-Diphenylformamidine with Oxalyl Chloride and Phosgene

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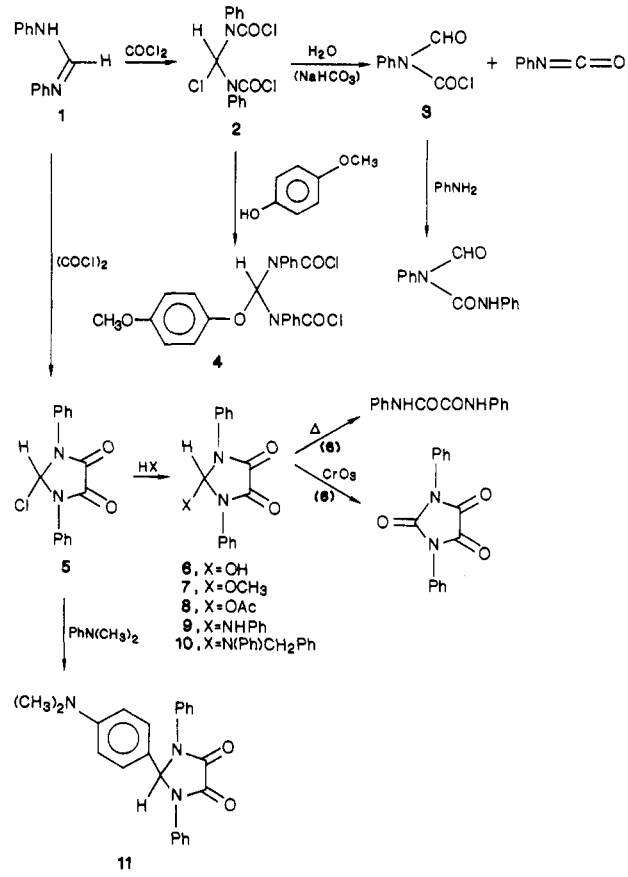
Reactions of N-substituted carboxylic acid amides with acylating agents such as acyl halides, phosphoryl chloride, thionyl chloride, and phosgene have been investigated in detail; the adduct formation between N,N-disubstituted formamides and $POCl_3$ has become the basis of the widely used Vilsmeyer–Haack synthesis of aldehydes.[1] Only few reactions involving substrates containing a C=N bond and acylating agents have been reported.[2] Heterocumulenes such as isocyanates, isothiocyanates, and carbodiimides have been shown to form a variety of adducts by reacting with phosgene or oxalyl chloride at the CN double bond of the N=C=X system.[3,4] We have now extended our investigations to include systems having a heteroatom conjugated to a CN double bond, and we chose *N,N'*-diphenylformamidine (1) as a candidate. The amidine 1 was reacted with both phosgene and oxalyl chloride in the hope of arriving at products or adducts useful in the synthesis of heterocyclic systems.

Scheme I




On adding 1 to a solution of excess phosgene in chlorobenzene at 0 °C and heating the resulting suspension to 70–75 °C with excess phosgene, a colorless product was formed in high yield that was identified as bis[(chlorocarbonyl)anilino]chloromethane (2). The $^{13}C$ NMR spectrum of 2 shows a signal at 80.6 ppm that was assigned to the central carbon atom. The bis(carbamoyl chloride) 2 was readily hydrolyzed under mild basic conditions to yield *N*-phenyl-*N*-formylcarbamoyl chloride (3) together with phenyl isocyanate.[5] This mode of hydrolysis, where presumably the chlorine on the central carbon of 2 is replaced by hydroxide followed by cleavage to 3, HCl, and phenyl isocyanate, shows that the chlorine on the central carbon is actually more labile than the carbamoyl chloride groups of 2. Compound 3 is thermally decomposed to

(1) For a review see: Jutz, C. In *Iminium Salts in Organic Chemistry*; Böhme, H., Viehe, H. G., Eds.; Wiley-Interscience: New York, 1976; p 225.

(2) Böhme, H.; Hartke, K. *Chem. Ber.* **1963**, *96*, 600. Böhme, H.; Ebel, S.; Hartke, K. *Ibid.* **1965**, *98*, 1463. Bose, A. K.; Spiegelman, G.; Manhas, M. S. *Tetrahedron Lett.* **1971**, 3167. See also: Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.

(3) Ulrich, H.; Sayigh, A. A. R. *J. Org. Chem.* **1965**, *30*, 2781. Stachel, H. D. *Angew. Chem.* **1959**, *71*, 246.

(4) Richter, R.; Stuber, F. A.; Tucker, B. *J. Org. Chem.* **1984**, *49*, 3675. Richter, R.; Barsa, E. A. *J. Org. Chem.* **1986**, *51*, 417.

(5) Compound 3 is hydrolyzed further under these conditions, thus reducing the isolated yield of 3. The major products from the hydrolysis of 3 appear to be formanilide and unexpectedly *N*-formyl-*N,N'*-diphenylurea with a small amount of *N,N'*-diphenylurea.

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