The synthesis of 2,3,5-trisubstituted phenols

Alan R. Katritzky,* Yu Ji, Dmytro O. Tymoshenko, Yunfeng Fang, and Keisha-Gay Hylton

Center for Heterocyclic Compounds, University of Florida, Department of Chemistry, Gainesville, Florida 32611-7200, USA
E-mail: Katritzky@chem.ufl.edu

Dedicated to Prof. Alfred Hassner on the occasion of his 70th birthday

(received 18 Jan 01; accepted 28 Oct 01; published on the web 05 Nov 01)

Abstract

Synthetic route to 2,3,5-trisubstituted phenols based on two-step [1+2+3] construction of the phenol backbone from 1-[(trimethylsilyl)methyl]-1*H*-1,2,3-benzotriazole, aliphatic or arylacetic acid chlorides and chalcones or α,β-unsaturated-γ-diketones was developed. 2,3,5-Trisubstituted phenols **8**, **9a-e**, **10a-d**, **12a-e** were successfully synthesized.

Keywords: 2,3,5-Trisubstituted phenols, 1-[(trimethylsilyl)methyl]-1*H*-1,2,3-benzotriazole, chalcones, α,β-unsaturated-γ-diketones

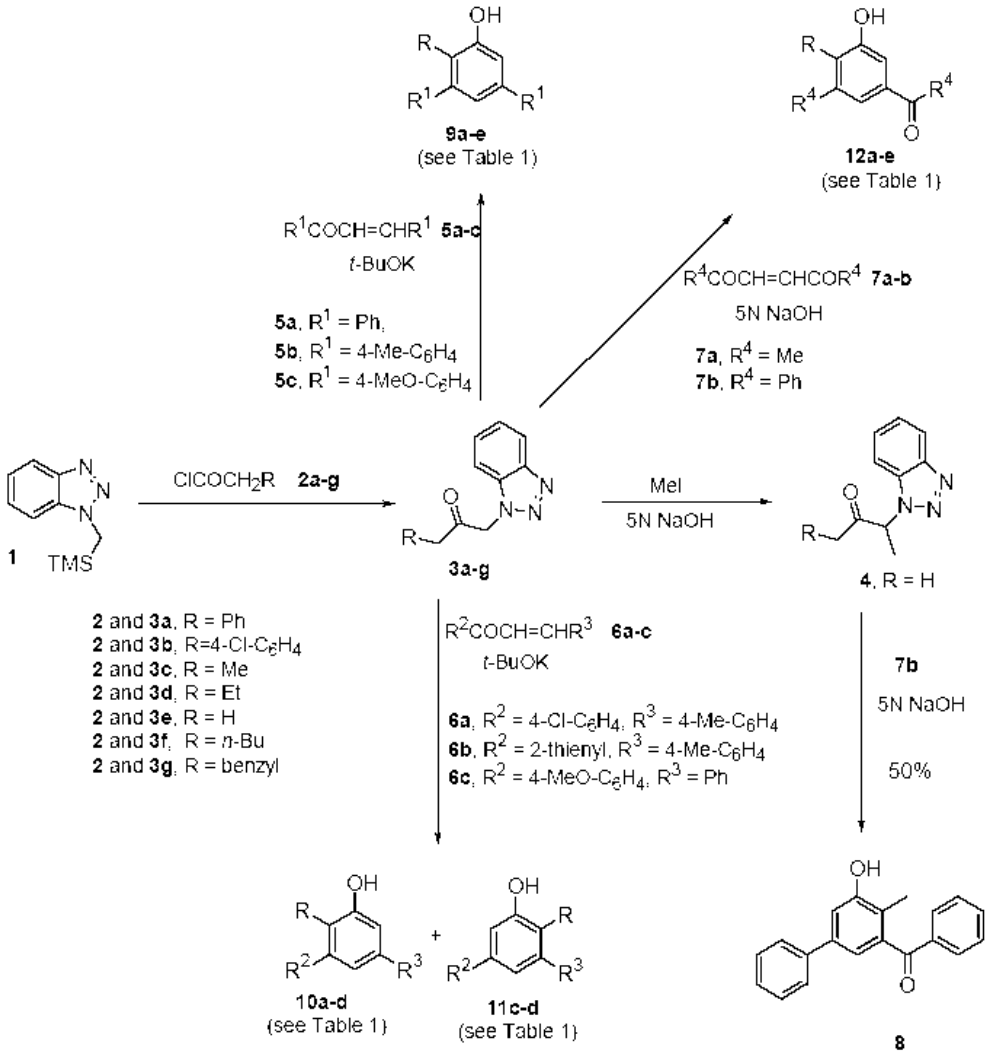
Introduction

ortho-Aryl-substituted phenols are important ligands used in organometallic chemistry to increase the stereo-, regio-and chemo-selectivity of catalytic processes.[1a-d] Phenols are also valuable precursors, e.g. for oxidation[2a-d] into polysubstituted quinones which are potent biocides.[3a-d]

Synthetic strategies used for the preparation of 2,3,5-polysubstituted phenols include the following multistep sequences: (i) from pyrylium salts and nitromethane[4] and (ii) by base-catalyzed reactions of pre-formed ethynyl ketones with benzyl ketones.[5]

Our recent study of [3+3] annulation reactions of 1-(benzotriazol-1-yl)propan-2-one with chalcones[6] gave an access to 3,5-diarylphenols advantageous as compared to the previously reported aromatization of cyclohexenones[7a,b] and Michael addition/aldol condensation of 1-(2-oxopropyl)pyridiniums salts with chalcones.[8] No general method has previously been described for the preparation of *meta*-acylphenols, few of which are known.[9a-c] We have now generalized our previous approach[6] to obtain 2,3,5-trisubstituted phenols **9a-e**, **10a-d** and **11c-d** *via* stepwise [1+2+3] formation of the phenol backbone from "aliphatic" building blocks (Scheme 1). Our

sequence affords 1-(benzotriazol-1-yl)-2-ones **3a-g** in high yields from the one-carbon synthon 1-[(trimethylsilyl)methyl]-1*H*-1,2,3-benzotriazole (**1**)[10] by heating neat with aliphatic or arylacetic acid chlorides **2a-g**. Compared to the previous preparation of **3** from α-haloketones[6], the new approach broadened the variety of available intermediates **3**. Thus, compound **3e** on treatment with MeI and 5 M NaOH in acetonitrile affords compound **4**. Compounds **3a-g** and **4** react with α, β- unsaturated ketones to form tri-substituted phenols **12a-e** and **8** with points of diversity at the 2, 3, and 5 positions (Scheme 1).



Scheme 1

Results and Discussion

The reactions of the intermediates **3a-g** or **4** and α,β-unsaturated ketones are discussed in several separate subsections according to the proposed reaction mechanisms reported earlier.[6]

(i) The reactions of intermediates 3a-c with the symmetrical chalcones 5a,b or c. Treatment of the mixture of each intermediate **3a-c** and the appropriate chalcone **5a, b** or **c** in *n*-butanol with 2 equiv. of potassium *tert*-butoxide and refluxing for 48 h gave 2,3,5-trisubstituted phenols **9a-e** in good yields (Table 1). The structures of **9a-e** were assigned by their ^{1}H NMR and ^{13}C NMR spectra: only one new set of signals was found.

In the ^{1}H NMR of **9a**, the three singlets at 2.07 ppm, 2.26 ppm and 2.30 ppm were assigned to the three methyl groups of **9a**; in the ^{13}C NMR of **9a**, the signals of these groups appear at 12.8 ppm, 21.0 ppm and 21.1 ppm. In the ^{1}H NMR and ^{13}C NMR spectra of the phenols **9b-e**, we have also found only one set of proton and carbon signals in each case, this confirming that the sequence afforded a single product. There are some differences in the acidity of the active methylenes alpha to the carbonyl in the intermediates **3a-c**, depending on whether R is an aliphatic group or an aromatic group, but that had no affect on the reactions of symmetrical chalcones **5a,b,c**, which gave only one final product.

(ii) The reactions of intermediates 3a, c, or d with unsymmetrical chalcones 6a,b, or c. When the intermediates **3a**,**c** or **d** reacted with the chalcones **6a-c** under the same conditions as used for the preparation of **9a-e**, the results obtained varied as follows.

a) The reaction of the intermediate **3c** or **3d** with chalcone **6c** afforded 2,3,5-trisubstituted phenols **10a** and **10b**, respectively. Structures **10a,b** were assigned by their ^{1}H NMR and ^{13}C NMR spectra; only one new set of signals could be observed. In the ^{1}H NMR spectrum of **10a**, the singlet at 2.20 ppm was assigned to the methyl group of **10a**; in the ^{13}C NMR of **10a**, the signal at 21.0 ppm was assigned to the same group. In the ^{1}H NMR of **10b**, the triplet at 1.06 ppm and the quartet at 2.61 ppm were assigned to the ethyl group of **10b**; in the ^{13}C NMR of **10b**, the signals of this group appear at 14.4 ppm and 21.0 ppm. According to our previous mechanistic study[6], if substituent R in a compound **3** is aliphatic, the pronounced difference in reactivities of the two methylenes alpha to the carbonyl, caused by the strong electron-withdrawing ability of the benzotriazole group, results in the regiospecificity of these reactions.

b) The reactions of the intermediate **3a** with chalcones **6a** or **6b** gave inseparable mixtures of regioisomers **10c/11c** and **10d**/**11d**, respectively. In the ^{1}H NMR spectra of each of these mixtures, two singlets were found near 2.00 ppm, which were assigned to the methyl groups. The ratio of compound **10c** to **11c** is 4:1, while the ratio of compound **10d** to **11d** is 1.6:1 according to the peak areas of the methyl groups in the ^{1}H NMR spectra. Two sets of signals could also be found in the ^{13}C NMR spectra: at 21.7 ppm and 21.0 ppm for the mixture of **10c** and **11c**, at 20.9 ppm and 21.0 ppm for the mixture of **10d** and **11d**. These observed ratios for **10c**,**d** and **11c**,**d** can be explained according to the high reactivity of the benzylic protons of **3a**, which react via a 1,4-addition pathway with chalcones **6a** or **6b**. Thus, for **3a** with R equal to phenyl, the regioselectivity of the reaction decreased and two regioisomers were obtained.

(iii) The reaction of intermediate 4 with α,β-unsaturated-γ-diketone 7b. Treatment of the intermediate **4** with α,β-unsaturated-γ-diketone **7b** in acetonitrile in the presence of 5 N NaOH at room temperature overnight gave 2,3,5-trisubstituted phenol **8** in 50% yield (Table 1). In the ^{1}H NMR spectrum of the product, only one singlet at about 2.00 ppm could be found, which was

assigned to the methyl group of the phenol **8**. In the ^{13}C NMR spectrum, there is also only one signal at 12.9 ppm and it was assigned to the same group. As in this case R is an aliphatic group, there is a large difference between reactivities of the two positions alpha to the carbonyl group in the intermediate **4**. Thus, this reaction is regiospecific, and only one product **8** was obtained. However, one point is noteworthy: the reaction of α,β-unsaturated diketone with α-substituted α-benzotriazolylmethyl ketones is very sensitive to the size of the α-substituent. For example, the yield of the compound **8** in this reaction (50%) is significantly lower than the yield of the analogous 2-unsubstituted product **12b** (90%) (Table 1). When 3-(1*H*-1,2,3-benzotriazol-1-yl)-2-pentanone **3d** bearing the ethyl group in the α-position reacted with the compound **7b**, the only result was a complex reaction mixture, which contained less than 10% of the desired product according to GC/MS.

(iv) The reactions of intermediates 3c,e,f,g with α,β–unsaturated-γ-diketones 7a,**b**. The reactions of α-benzotriazolylmethyl ketones **3c**,**e**,**f,g**, with α,β-unsaturated-γdiketones **7a** or **7b** in acetonitrile in the presence of 5N NaOH gave 2,3,5-trisubstituted phenols **12a-e** in yields of 33%-90%. The ^{1}H NMR spectra of **12a-e** each showed only one set of signals for the appropriate protons. For example, in the ^{1}H NMR spectrum of product the **12a**, two singlets at 2.34 ppm and 2.57 ppm were assigned for the two methyl groups. In the ^{13}C NMR of **12a**, the signals of these groups appear at 10 ppm − 60 ppm. This demonstrated that this reaction sequence gives only one product.

Each of the two carbonyl groups present in α,β-unsaturated-γ-diketones **7a**,**b** could be involved in a 1,4 conjugated addition. However, because both α,β-unsaturated-γ-di-ketones **7a**,**b** are symmetrical and R in compounds **3c**,**e**,**f**,**g** are aliphatic, thus providing a marked reactivity differences between two methylene groups α to the carbonyl group in the intermediates **3c,e,f,g**, these reactions are regiospecific.

These reactions can be further divided into two classes according to the R^4 substituent: i) when R^4 is a methyl group, the α,β-unsaturated-γ-diketone **7a** reacted with the intermediate **3e** to give the product **12a** in 33% yield; the low yield perhaps could be explained by the low stability of **7a** under basic conditions; ii) when R^4 is a phenyl group, the reaction of α,β-unsaturated-γ-diketone **7b** with intermediates **3c,e,f,g** gave the products **12b-e** respectively, with excellent yields for **12b,c** (R = H or Me) and moderate yields for **12d,e** (R = *n*-Bu or benzyl) (Table 1).

These results demonstrate the effect of the R substituent: increasing bulk of the R group decreases product yield. Sodium hydroxide as a base in this reaction of **3** with **7** is preferable to potassium *tert*-butoxide. Being a strong enough base to complete the reaction successfully, sodium hydroxide does not cause the formation of byproducts, which could arise from the subsequent reactions of the acyl group in the products **12**. On the other hand, the preparation of compound **12b** using potassium *tert*-butoxide as a base afforded it only in 30% yield. However, the reactions of **3** with less reactive chalcones (discussed above) require stronger base, and in this case potassium *tert*-butoxide is preferable. (Scheme 2)

Table 1. Preparation of 2,3,5-trisubstituted phenols **9a-e**, **10a-d**, **11c-d** and **12a-e**

Phenols	R	R^1	R^2	R^3	R^4	Yield %
9a	Me	4-Me-C_6H_4	—	—	—	48
9b	Ph	Ph	—	—	—	89
9c	Ph	4-Me-C_6H_4	—	—	—	43
9d	Ph	4-MeO-C_6H_4	—	—	—	86
9e	4-Cl-C_6H_4	4-Me-C_6H_4	—	—	—	43
10a	Me	—	4-MeO-C_6H_4	Ph	—	50
10b	Et	—	4-MeO-C_6H_4	Ph	—	65
10c+11c	Ph	—	4-Cl-C_6H_4	4-Me-C_6H_4	—	49
10d+11d	Ph	—	2-thienyl	4-Me-C_6H_4	—	49
12a	H	—	—	—	Me	33
12b	H	—	—	—	Ph	90
12c	Me	—	—	—	Ph	84
12d	*n*-Bu	—	—	—	Ph	62
12e	benzyl	—	—	—	Ph	40

In summary, a novel synthetic route to 2,3,5-trisubstituted phenols was developed based on the two-step [1+2+3] construction of the phenol backbone from 1-[(trimethylsilyl)methyl]-1*H*-1,2,3-benzotriazole, an aliphatic or arylacetyl acid chloride and a chalcones or α,β-unsaturated-γ-diketone.

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ or DMSO-d^6 with TMS as the internal standard for ^1H (300 MHz) or a solvent as the internal standard for ^{13}C (75 MHz). Microanalyses were performed on a Carlo Erba -1106 elemental analyzer. Benzene and toluene were dried over molecular sieves. Column chromatography was conducted with silica gel 200−425 mesh.
Trimethylsilylmethylbenzotriazole **1** was synthesized according to the procedure already reported.[10] Compound **3e** was prepared according to the reported procedure[6]. Compounds **3f** and **3g** were prepared according to the reported procedure[11].

General procedure for the preparation of α-(benzotriazol-1-yl)alkyl ketones (3)
1-[(Trimethylsilyl)methyl]-1*H*-1,2,3-benzotriazole (**1**) (2.05 g, 10 mmol) was dissolved in the corresponding acyl chloride (10 mmol) at 40-50 °C. After 10−20 s the evolution of chlorotrimethylsilane was observed and the mixture began to solidify. The solid obtained was triturated with ether, filtered off and recrystallized from benzene/hexanes to afford an analytically pure sample.

1-(Benzotriazol-1-yl)-3-phenylacetone (3a). White prisms (chloroform/ hexanes), mp 112−113 °C (66%); ^{1}H NMR δ 3.78 (s, 2H), 5.43 (s, 2H), 7.13−7.18 (m, 3H), 7.26−7.41 (m, 5H), 8.05 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR δ 47.2, 55.3, 109.0, 119.9, 124.0, 127.6, 127.8, 129.0, 129.2, 132.1, 133.3, 145.8, 199.5. Anal. Calcd for $C_{15}H_{13}N_3O$: N, 16.73. Found: N, 16.69.

1-(Benzotriazol-1-yl)-3-(4-chlorophenyl)acetone (3b). White prisms (ether), mp 112113 °C (75%); ^{1}H NMR δ 3.75 (s, 2H), 5.45 (s, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.18−7.30 (m, 3H), 7.36−7.52 (m, 2H), 8.08 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR δ 46.3, 55.6, 108.8, 120.2, 124.2, 128.0, 129.1, 130.3, 130.5, 133.4, 133.7, 145.9, 199.3. Anal. Calcd for $C_{15}H_{12}ClN_3O$: N, 14.71. Found: N, 14.65.

1-(Benzotriazol-1-yl)-2-butanone (3c). White prisms (chloroform/ hexanes), mp 109110°C (68%); ^{1}H NMR δ 1.09 (t, *J* = 7.2 Hz, 3H), 2.48 (q, *J* = 7.2 Hz, 2H), 5.44 (s, 2H), 7.36−7.42 (m, 2H), 7.47−7.53 (m, 1H), 8.08 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR δ 7.1, 33.1, 56.0, 109.1, 120.1, 124.1, 127.9, 133.4, 145.8, 202.7. Anal. Calcd for $C_{10}H_{11}N_3O$: N, 22.21. Found: N, 22.10.

1-(Benzotriazol-1-yl)-2-pentanone (3d). White prisms (chloroform/ hexanes), mp 106-107 °C (85%); ^{1}H NMR δ 0.71 (t, *J* = 7.4 Hz, 3H), 1.41−1.48 (m, 2H), 2.26 (t, *J* = 7.2 Hz, 2H), 5.23 (s, 2H), 7.16−7.21 (m, 2H), 7.26−7.31 (m, 1H), 7.87 (d, *J* = 8.6 Hz, 1H);^{13}C NMR δ 13.4, 16.6, 41.6, 56.2, 109.1, 120.0, 124.0, 127.8, 133.3, 145.7, 202.1. Anal. Calcd for $C_{11}H_{13}N_3O$: N, 20.68. Found: N, 20.76.

General procedure for the preparation of 2,3,5-trisubstituted phenols 9a-e, 10a-d and 11c-d

α-(Benzotriazol-1-yl)alkyl ketones **3**, potassium *tert*-butoxide (2 equiv) and the corresponding chalcones (1 equiv) were refluxed in *n*-butanol for 48 h. The resulting mixture was acidified, extracted with ethyl acetate (2 × 15 mL), washed with brine and purified by column chromatography.

2-Methyl-3,5-bis(4-methylphenyl)phenol (9a). Reddish oil (hexanes/ethyl acetate, 4:1), (48%); ^{1}H NMR δ 2.10 (s, 3H), 2.29 (s, 3H), 2.33 (s, 3H), 4.94 (s, 1H), 6.93 (s, 1H), 7.00 (s, 1H), 7.12−7.16 (m, 6H), 7.39 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR δ 12.9, 21.1, 21.2, 112.1, 120.4, 121.2, 126.7, 128.8, 129.2, 129.4, 136.6, 137.0, 137.7, 138.7, 139.3, 143.9, 154.3. HRMS. Calcd for $C_{21}H_{21}O$ (M+1): 289.1592. Found: 289.1590.

2,3,5-Triphenylphenol (9b). Reddish orange plates (hexanes/ethyl acetate, 5:1), mp 152.1−153.8 °C (89%), (lit.[4] mp 162−163 °C); ^{1}H NMR δ 5.22 (s, 1H), 7.05−7.40 (m, 15H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR δ 113.0, 116.5, 121.3, 126.5, 127.1, 127.6, 127.7, 127.8, 128.8, 129.1, 129.6, 130.9, 134.8, 140.4, 141.9, 142.6, 153.2, 154.5. HRMS. Calcd for $C_{24}H_{18}O$: 322.1358. Found: 322.1387.

3,5-bis(4-Methylphenyl)-2-phenylphenol (9c). Reddish orange plates (hexanes/ethyl acetate, 4:1), mp 156.5−157.9 °C (43%); ^{1}H NMR δ 2.50 (s, 3H), 2.60 (s, 3H), 5.25 (s, 1H), 7.10−7.80 (m, 15H); ^{13}C NMR δ 21.1, 21.1, 112.5, 121.1, 125.4, 126.9, 127.7, 128.4, 129.1, 129.5, 130.9, 135.0, 136.1, 137.4, 137.6, 138.1, 141.8, 142.4, 153.2. HRMS. Calcd for $C_{26}H_{22}O$: 350.1671. Found: 350.1677.

3,5-Bis(4-methoxyphenyl)-2-phenylphenol (9d). yellow oil (hexanes/ethyl acetate, 4:1), (86%); ^{1}H NMR δ 3.63 (s, 3H), 3.74 (s, 3H), 5.14 (s, 1H), 6.60 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 7.00-7.26 (m, 7H), 7.49 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 55.1, 55.3, 112.1, 113.1, 114.2, 120.8, 125.1, 127.6, 128.0, 129.1, 130.7, 130.9, 132.9, 133.5, 135.1, 141.4, 142.1, 153.2, 158.2, 159.3; HRMS. Calcd for $C_{26}H_{22}O_3$: 382.1569. Found: 382.1577.

2-(4-Chlorophenyl)-3,5-bis(4-methylphenyl)phenol (9e). reddish orange plates (hexanes/ethyl acetate, 4:1), mp 173.5−175.8 °C (42%); ^{1}H NMR δ 2.50 (s, 3H), 2.60 (s, 3H), 5.25 (s, 1H), 7.16 (s, 4H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.38−7.52 (m, 6H), 7.74 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ 21.1, 21.1, 112.7, 121.3, 124.2, 126.9, 128.6, 129.2, 129.5, 129.5, 132.3, 133.7, 136.4, 137.4, 137.5, 137.8, 142.0, 142.6, 153.1, 207.0. HRMS. Calcd for $C_{26}H_{21}ClO$: 384.1281 Found: 384.1276.

3-(4-Methoxyphenyl)-2-methyl-5-phenylphenol (10a). yellow oil (hexanes/ethyl acetate, 4:1), (50%); ^{1}H NMR δ 2.20 (s, 3H), 3.82 (s, 3H), 5.28 (s, 1H), 6.96 (d, *J* = 8.2 Hz, 2H), 7.03 (d, *J* = 1.8 Hz, 1H), 7.10 (d, *J* = 1.8 Hz, 1H), 7.23−7.33 (m, 3H), 7.39 (t, J = 8.7 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 12.9, 55.3, 112.2, 113.5, 113.7, 121.4, 126.9, 127.2, 128.7, 130.7, 134.1, 139.3, 140.6, 143.6, 154.4, 158.6. HRMS. Calcd for $C_{20}H_{18}O_2$: 290.1385. Found: 290.1332.

3-(4-Methoxyphenyl)-2-ethyl-5-phenylphenol (10b). yellow oil (65%); ^{1}H NMR δ 1.06 (t, *J* = 4.5 Hz, 3H), 2.61 (q, *J* = 4.5 Hz, 2H), 3.90 (s, 3H), 5.00 (s, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 1.8 Hz, 1H), 7.05 (d, *J* = 1.8 Hz, 1H), 7.24−7.34 (m, 3H), 7.36−7.44 (m, 2H), 7.54−7.60 (m, 2H); ^{13}C NMR δ 14.4, 20.2, 55.3, 112.7, 113.4, 121.7, 126.9, 127.2, 127.4, 128.7, 130.1, 134.2, 139.3, 140.5, 143.5, 154.1, 158.6. HRMS. Calcd for $C_{21}H_{20}O_2$: 304.1542. Found: 304.1545.

Mixture of 3-(4-Chlorophenyl)-5-(4-methylphenyl)-2-phenylphenol (10c) and 5-(4-chlorophenyl)-3-(4-methylphenyl)-2-phenylphenol (11c). Molar ratio **10c**:**11c** = 4:1. Colorless oil (hexanes/ethyl acetate, 5:1) (49%); ^{1}H NMR (**10c**) δ 2.27 (s, 3H), 5.10 (b.s, 1H), 6.85−6.93 (m, 2H), 6.99−7.28 (m, 11H), 7.43 (d, *J* = 7.9 Hz, 2H); (**11c**) δ2.14 (s, 3H), 5.10 (b.s, 1H), 6.85−6.93 (m, 2H), 6.99−7.28 (m, 11H), 7.43 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR (Superposition of **10c** and **11c**) δ 21.0, 21.1, 112.6, 113.1, 120.8, 121.0, 125.4, 126.0, 126.8, 127.7, 127.9, 128.2, 128.4, 128.7, 128.9, 129.1, 129.2, 129.4, 129.5, 130.9, 132.5, 133.6, 134.6, 134.8, 136.2, 137.3, 137.5, 137.9, 138.9, 139.5, 140.4, 141.2, 141.9, 142.7, 153.3; Anal. Calcd for $C_{25}H_{19}ClO$: C, 80.96. H, 5.17. Found: C, 81.16; H, 5.47.

Mixture of 5-(4-Methylphenyl)-2-phenyl-3-(2-thienyl)phenol (10d) and 3-(4-methyl phenyl)-2-phenyl-5-(2-thienyl)phenol (11d). Molar ratio **10d**:**11d** = 1.6:1. Colorless oil (hexanes/ethyl acetate, 5:1) (69%); ^{1}H NMR (**10d**) δ 2.23 (s, 3H), 5.00 (s, 1H), 6.52 (d, *J* = 3.6 Hz, 1H), 6.64 (t, *J* = 5.0 Hz, 1H), 6.79−6.95 (m, 2H), 7.00 (d, *J* = 6.7 Hz, 1H), 7.04−7.14 (m, 5H), 7.18−7.25 (m, 2H), 7.28 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 1H); (**11d**) δ2.10 (s, 3H), 5.11 (s, 1H), 6.79−6.95 (m, 2H), 7.00 (d, *J* = 6.7 Hz, 1H), 7.04−7.14 (m, 5H), 7.18−7.25 (m, 3H), 7.28 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (Superposition of **10d** and **11d**) δ 20.9, 21.0, 111.5, 113.1, 120.1, 120.8, 123.4, 124.9, 125.2, 125.5, 125.9, 126.6, 126.8, 126.8, 127.6, 127.9, 128.3, 128.4, 129.0, 129.2, 129.4, 129.4, 130.8, 130.9, 134.6, 134.7, 134.8, 136.2, 137.2, 137.4, 137.7, 141.9, 142.6, 142.7, 143.6, 153.2, 153.5. Anal. Calcd for $C_{23}H_{18}OS$: C, 80.66; H, 5.31. Found: C, 80.66; H, 5.28.

Preparation of 3-(1*H*-1,2,3-benzotriazol-1-yl)-2-butanone (4). To a solution of 1-(1*H*-1,2,3-benzotriazol-1-yl)propan-2-one (1 equiv) and MeI (1.5 equiv) in acetonitrile, aqueous 5 M NaOH (3 equiv) was added, and the reaction mixture was stirred at room temperature for 12 h. Then acetonitrile was removed in *vacuo*, and the oil residue was purified by column chromatography (hexanes/ethyl acetate, 10:1) to afford the pure sample **4** (85%) as a yellow oil: ^{1}H NMR δ 1.93 (d, *J* = 7.5 Hz, 3H), 2.04 (s, 3H), 5.62 (q, *J* = 7.2 Hz, 1H), 7.35−7.54 (m, 3H), 8.10(d, *J* = 8.4 Hz, 1H); ^{13}C NMR δ 15.3, 26.2, 63.3, 109.4, 120.4, 124.1, 127.7, 132.3, 146.0, 202.9. Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.15; H, 6.16; N, 22.33.

General procedure for the preparation of *meta*-acylphenols 12a-e and 8

To a solution of α-(benzotriazol-1-yl)ketone (1 equiv) and the corresponding 2,5-diketone (1 equiv) in acetonitrile, aqueous 5 M NaOH (3 equiv) was added. The reaction mixture was stirred at room temperature for 12 h. Acetonitrile was removed in *vacuo*, and the oil residue was purified by column chromatography to afford the pure sample.

1-(3-Hydroxy-5-methylphenyl)-1-ethanone (12a). Yellow plates (hexanes /ethyl acetate, 5:1), mp 122−123 °C (33%), (lit.[9c] mp 122−123 °C); ^{1}H NMR δ 2.34 (s, 3H), 2.57 (s, 3H), 6.93 (s, 1H), 7.32 (s, 2H); ^{13}C NMR δ 21.5, 27.0, 112.3, 121.7, 121.9, 138.4, 140.3, 156.5, 199.8.

(5-Hydroxy[1,1'-diphenyl]-3-yl)(phenyl)methanone (12b). Yellow plates (hexanes /ethyl acetate, 5:1), mp 76−77 °C (90%); ^{1}H NMR δ 7.25−7.53 (m, 11H), 7.89 (d, *J* = 7.2 Hz, 2H), 7.94 (b.s, 1H); ^{13}C NMR δ 116.0, 119.0, 121.4, 127.2, 128.0, 128.5, 129.0, 130.4, 133.1, 137.2, 139.1, 139.8, 143.0, 156.8, 198.2. Anal. Calcd for $C_{19}H_{14}O$: C, 83.19; H, 5.14. Found: C, 82.98; H, 5.48.

(5-Hydroxy-6-methyl[1,1'-biphenyl]-3-yl)(phenyl)methanone(12c). Yellow plates (hexanes /ethyl acetate, 5:1), mp 92−94 °C (84%); ^{1}H NMR δ 2.23 (s, 3H) 7.21 (s, 1H), 7.26−7.41 (m, 7H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.58 (s, 2H), 7.79 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR δ 13.9, 115.1, 124.8, 127.3, 128.3, 128.4, 128.8, 129.4, 130.3, 132.7, 135.3, 137.7, 141.1, 143.5, 155.2, 197.8. Anal. Calcd for $C_{20}H_{16}O$: C, 83.31; H, 5.59. Found: C, 83.00; H, 5.72.

(6-Butyl-5-hydroxy[1,1'-diphenyl]-3-yl)(phenyl)methanone (12d). Orange plates (hexanes/ethyl acetate, 5:1), mp 64−66 °C (62%); ^{1}H NMR δ 0.78 (t, *J* = 7.3 Hz, 3H), 1.29−1.18 (m, 2H), 1.54−1.43 (m, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 6.27 (s, 1H), 7.19 (s, 1H), 7.61−7.25 (m, 9H), 7.82 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR δ 13.9, 23.0, 27.3, 31.9, 115.5, 125.2, 127.4, 128.3, 128.5, 129.3, 130.3, 132.6, 133.4, 135.5, 137.8, 141.3, 143.6, 154.7, 197.0. HRMS. Calcd for $C_{23}H_{22}O_2$: 330.1620. Found: 330.1573.

(6-Benzyl-5-hydroxy[1,1'-diphenyl]-3-yl)(phenyl)methanone (12e). Orange plates (hexanes/ethyl acetate, 5:1), mp 86−88 °C (40%); ^{1}H NMR δ 4.07 (s, 2H), 5.35 (b.s, 1H), 7.07 (d, *J* = 6.9 Hz, 2H), 7.14−7.28 (m, 6H), 7.32−7.36 (m, 4H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR δ 33.3, 116.2, 125.1, 126.6, 127.6, 128.4, 128.4, 128.5, 128.8, 129.3, 129.8, 130.2, 132.6, 136.8, 137.8, 139.7, 140.7, 144.4, 154.8, 196.4. HRMS. Calcd for $C_{26}H_{20}O_2$: 364.1443. Found: 364.1463.

(5-Hydroxy-4-methyl[1,1'-biphenyl]-3-yl)(phenyl)methanone (8). Yellow plates (hexanes/ethyl acetate, 5:1), mp 95−97 °C (50%). ^{1}H NMR δ 2.18 (s, 3H), 6.28 (s, 1H), 7.09 (d, *J* = 1.2 Hz, 1H), 7.15 (d, *J* = 1.2 Hz, 1H), 7.23−7.36 (m, 3H), 7.47−7.41 (m, 4H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR δ 12.9, 115.6, 119.1, 121.9, 127.0, 127.7, 128.8, 128.9, 130.5, 133.8, 137.5, 139.7, 140.0, 141.0, 155.1, 199.4. Anal. Calcd for $C_{20}H_{16}O$: C, 83.31; H, 5.59. Found: C, 83.40; H, 5.36.

References

1. (a) Saito, S.; Yamamoto, H. *Chem. Commun.* **1997**, 1585. (b) Thorn, M. G.; Vilardo, J. S.; Fanwick, P. E.; Rothwell, I. P. *Chem. Commun.* **1998**, 2427. (c) Vilardo, J. S.; Thorn, M. G.; Fanwick, P. E.; Rothwell, I. P. *Chem. Commun.* **1998**, 2425. (d) Saito, S.; Kano, T.; Hatanaka, K.; Yamamoto, H. *J. Org. Chem.* **1997**, *62*, 5651.
2. (a) Letcher, R. M.; Wong, M.-C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3035. (b) Bubb, W. A.; Sternhell, S. *Tetrahedron Lett.* **1970**, 4499. (c) McKillop, A.; Perry, D. H.; Edwards, M.; Antus, S.; Farkas, L.; Nogradi, M.; Taylor, E. C. *J. Org. Chem.* **1976**, *41*, 282. (d) Majetich, G.; Zhang, Y. *J. Am. Chem. Soc.* **1994**, *116*, 4979.
3. (a) Bergeron, D.; Brassard, P. *Heterocycles* **1992**, *34*, 1835. (b) Brimble, M. A.; Phythian, S. J. *Tetrahedron Lett.* **1993**, *34*, 5813. (c) Magnus, P.; Eisenbeis, S. A.; Magnus, N. A. *J. Chem. Soc., Chem. Commun.* **1994**, 1545. (d) Nicolaou, K. C.; Gross, J. L.; Kerr, M. A.; Lemus, R. H.; Ikeda, K.; Ohe, K. *Angew. Chem., Int. Ed.* **1994**, *33*, 781.
4. Von Dimroth, K.; Laubert, G.; Blöcher, K. H. *Liebigs Ann. Chem.* **1972**, *765*, 133.
5. Ried, W.; König, E. *Liebigs Ann. Chem.* **1972**, *757*, 153.
6. Katritzky, A. R.; Belyakov, S. A.; Henderson S. A. *J. Org. Chem.* **1997**, *62*, 8215.
7. (a) Downes, A. M.; Gill, N. S.; Lions, F. *J. Am. Chem. Soc.* **1950**, *72*, 3464. (b) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, *84*, 4527.
8. Eichinger, K.; Nussbaumer, P.; Balkan, S.; Schulz, G. *Synthesis* **1987**, 1061.
9. (a) Da Re, P.; Cimatoribus, L. *J. Org. Chem.* **1961**, *26*, 3650. (b) Kloetzel, M. C.; Dayton, R. P.; Herzog, H. L. *J. Am. Chem. Soc.* **1950**, *72*, 273. (c) Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939.
10. Katritzky, A. R.; Lam, J. N. *Heteroatom. Chem.* **1990**, *1*, 21.
11. Katritzky, A. R.; Wang, J.; Karodia, N.; Li, J. *J. Org. Chem*. **1997**, *62*, 4142.