duced orbital overlap in the meta and para positions, compared to 4, caused by the wider angle between the rings.

The calculated (AM1) geometry of 1 matched well with the X-ray structure as seen by the values in Figure 1. Of particular interest were the central C=C distance (1.343 (5) vs 1.36 Å (calcd)) and the C_{ipso}—C_{ipso} distance (2.65 vs 2.66 Å calcd).[4]

The toluene-like UV spectrum of 1 is explained by the X-ray structure. The orthogonal rings lacked the typical stilbene conjugation. In contrast to 3 and 4, and despite the 2.65 Å ipso–ipso separation, no appreciable bathochromic shift was observed upon comparison of 1 and 2 to suggest electronic interaction of the rings. AM1 calculations only predicted a 4-nm shift. PES would seem to be a more sensitive test for these effects. The upfield shifted aromatic resonances observed in the ^{1}H NMR spectrum of 1 were typical of 3 and 4 and are diagnostic of cofacial stilbenes.

Further work to investigate the potential for interring interactions in these systems is in progress.

Acknowledgment. Technical assistance from A. Flatow, J. McTague, and S. Roberts and financial support from the University of Toledo Faculty Research Awards and Fellowship Program, the Ohio Research Challenge Program (J.G.), the College of Arts and Science X-ray Facility, the Deutsche Forschungsgemeinschaft (Grant No. Le 288/14), and the Fonds der Chemischen Industrie (R.G.) are gratefully acknowledged.

Supplementary Material Available: Atomic positions for 1 (1 page). Ordering information is given on any current masthead page.

Base-Catalyzed Hydrogen Exchange and Estimates of the Acid Strength of Benzoyl- and (Trimethylsilyl)acetylene in Aqueous Solution. A Correlation between Acetylene pK_a Estimates and Hydroxide-Ion Catalytic Coefficients for Hydrogen Exchange

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The proton NMR chemical shift of the acetylenic hydrogen in terminal alkynes would be expected to move downfield as the acidity of this hydrogen increases. The unusually low-field value of the chemical shift for benzoylacetylene, 1, δ = 3.33 ppm,[1] thus suggests that this

$$\underset{\textbf{1}}{PhC(O)C\equiv CH} \qquad \underset{\textbf{2}}{Me_3SiC\equiv CH}$$

substance might be quite acidic. As part of our continuing interest in more strongly acidic acetylenes, we have consequently examined benzoylacetylene for the purpose of estimating its acid strength in aqueous solution. We have also examined (trimethylsilyl)acetylene, 2, in the same way, for the strong deviation it shows from a correlation of rates of hydrogen exchange of other acetylenes[2] suggests that it is fairly acidic as well.

We used a kinetic method to estimate the acidity of these acetylenes. Our method is based upon the fact that simple terminal monoacetylenes, though carbon acids, generally show normal acid behavior,[3] i.e, their uphill ionization reactions are diffusion-controlled processes in which hydron transfer is rapid and reversible and separation of the hydron-transfer products is rate determining (rd), eq 1.[4] In this circumstance, the barrier to recom-

$$RC\equiv CH + B \overset{rapid}{\rightleftharpoons} RC\equiv C^-{\cdot}HB^+ \xrightarrow{rd} RC\equiv C^- + HB^+ \tag{1}$$

bination of the hydron-transfer products can be estimated, and that can then be combined with rates of hydrogen exchange of the acetylene to provide acetylenic pK_a's.[4a] We determined the required rates of hydrogen exchange by monitoring the loss of radioactivity from tritium-labeled substrates.

Experimental Section

Materials. Benzoylacetylene[5] was made by the Friedel–Crafts benzoylation of bis(trimethylsilyl)acetylene[6] followed by fluoride-ion promoted removal of the remaining trimethylsilyl group.[7] It was labeled with tritium by exchange with tritiated water catalyzed by 2-(2,6-dimethylphenyl)-1,1,3,3-tetramethylguanidine.[8] This base was chosen as the catalyst because of its high basicity and low nucleophilicity.[9] Exchange was effected by allowing a mixture of 450 mg of benzoylacetylene and 100 μL of tritiated water (0.01 Ci g^{-1}), to which just enough dioxane had been added to achieve homogeneous solution, to stand at room temperature for 24 h. This reaction mixture was then poured into 50 mL of 1 M aqueous HCl, the resulting solution was extracted with ether, and the extract was washed with three 20-mL portions of 1 M HCl and was dried with $MgSO_4$. Removal of the ether by evaporation left a brown residue that was purified to a light yellow waxy solid by vacuum sublimation. A control experiment using D_2O in place of tritiated water showed that this procedure replaced the acetylenic proton with deuterium.

(Trimethylsilyl)acetylene (Fluka) was labeled with tritium by treating its lithium salt with tritiated water. The salt was prepared by adding 5.3 mL of a 1.4 M solution of methyl lithium in diethyl ether (Aldrich) to 1.0 mL of (trimethylsilyl)acetylene dissolved in 2.0 mL of diethyl ether. This mixture was stirred at 0 °C for 15 min, and 0.15 mL of tritiated water (0.01 Ci g^{-1}) was then added. The white precipitate of lithium hydroxide that formed was separated, the ether solution was dried with $MgSO_4$, and the labeled acetylene was separated from the ether by distillation. A parallel experiment using D_2O showed that this procedure gave (trimethylsilyl)acetylene labeled in the terminal acetylenic position.

All other materials were best available commercial grades and were used as received.

Kinetics. Rates of loss of tritium from the labeled acetylenes were measured by radiochemical assay of the substrate at appropriate time intervals. Reaction mixtures were prepared in the case of benzoylacetylene by allowing 50-mL portions of aqueous

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[7] Stang, P. J.; Fisk, T. E. *Synthesis* **1979**, 438–440.

[8] Pruszynski, P. *Can. J. Chem.* **1987**, *65*, 626–629.

[9] It was found that use of less sterically hindered, more nucleophilic, strong bases, such as the hydroxide ion, led to decomposition of benzoylacetylene accompanied by production of a deep red color; the nature of this reaction was not investigated.

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Table I. Summary of Rate Data for Detritiation of Benzoylacetylene and (Trimethylsilyl)acetylene in Aqueous Solution at 25 °C[a]

substrate	base	pK_a(BH)	buffer[b] ratio	$k_B/10^{-3}$ M^{-1} s^{-1}	$k_{HO^-}/10^3$ M^{-1} s^{-1}
PhCOC≡CT	HPO_4^{2-}	7.20[c]	1.00	18.8 ± 5.5	28.7 ± 1.0
			3.12	11.7 ± 3.7	25.4 ± 1.3
Me_3SiC≡CT	O[$(CH_2)_2$]NH	8.49[d]	1.00	2.60 ± 1.11	0.336 ± 0.014
			2.00	1.74 ± 0.75	0.351 ± 0.010

[a] Ionic strength = 0.10 M. [b] Buffer ratio = [Acid]/[Base]. [c] Grzybowski, A. K. *J. Phys. Chem.* **1958**, *62*, 555–559. [d] Hetzer, H. B.; Bates, R. G.; Robinson, R. A. *J. Phys. Chem.* **1966**, *70*, 2869–2872.

buffer solution contained in volumetric flasks to come to temperature equilibrium with a constant temperature bath operating at 25.0 ± 0.1 °C; 50 μL quantities of a tetrahydrofuran stock solution of labeled benzoylacetylene were then added, and the mixtures were shaken thoroughly to effect complete dissolution. The concentration of benzoylacetylene in these reaction mixtures was 2×10^{-4} M. Samples (5.00 mL) were taken from the reaction mixtures by volumetric pipette at measured time intervals, and the reaction was quenched by running these samples into 20-mL portions of 0.1 M HCl. The resulting solutions were extracted with 10.00 mL portions of toluene, and the toluene extracts were washed three times with 20-mL portions of 1 M HCl and were dried over $CaCl_2$; 5.00 mL aliquots of the dried solutions were then added to 15.00 mL portions of scintillation cocktail, and the final solutions were subjected to radioassay by liquid scintillation counting.

This procedure could not be used in the case of (trimethylsilyl)acetylene because the high volatility of this substrate (bp 55 °C) caused it to partition between solution and air space in the reaction flask and then escape when the flask was opened for sampling. Reaction mixtures were therefore transferred to a large syringe immediately after preparation; the syringe needle was then plugged and the whole thing was immersed in the constant temperature bath. (Trimethylsilyl)acetylene concentrations in these reaction mixtures were ca. 4×10^{-4} M. Samples were taken by expelling approximately 5.0-mL amounts into weighed flasks containing 10.00 mL of HCl for quenching and 10.00 mL of toluene for extracting the substrate. These flasks were weighed again after sampling, and the weights of the samples so obtained were used to normalize all samples in a given run to a constant value.

The kinetic data obtained by both of these techniques conformed to the first-order rate law accurately, and observed first-order rate constants, k_{obs}, were obtained by least-squares fitting to an exponential function.

Results

Rates of loss of tritium from benzoylacetylene were determined in aqueous monohydrogen phosphate buffer solutions and those of (trimethylsilyl)acetylene in morpholine buffers. Measurements were made in series of buffer solutions of varying buffer concentration but constant buffer ratio and constant ionic strength (0.10 M), and therefore constant hydroxide ion concentration. For each series, five different buffer concentrations, varying by a factor of 5, were used. The data so obtained are summarized in Table S1.[10]

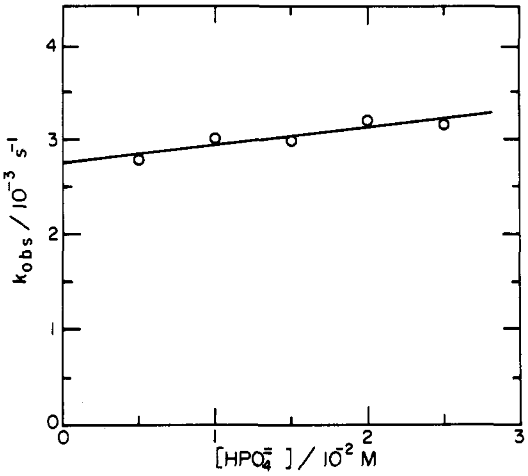

Figure 1. Buffer dilution plot showing the relationship between observed rate constants and buffer base concentration for tritium loss from benzoylacetylene catalyzed by monohydrogen phosphate ion in aqueous solution at 25 °C, ionic strength = 0.10 M.

Observed first-order rate constants determined in a given solution series increased with increasing buffer base concentration, and comparison of results obtained at different buffer ratios showed this to be due to general-base catalysis, as expected for a hydron-transfer reaction such as this. In all cases, however, the general-base catalysis was quite weak; Figure 1 illustrates this by showing a typical buffer dilution plot. The rate law that applies to this situation is given by eq 2. Least-squares analysis of

$$k_{obs} = k_{HO^-}[HO^-] + k_B[B] \tag{2}$$

the data provided general-base catalytic coefficients, k_B, as slopes of the relationship between k_{obs} and [B] and also gave the quantity $k_{HO^-}[HO^-]$ as intercepts; the latter were transformed into hydroxide-ion catalytic coefficients, k_{HO^-}, with the aid of hydroxide ion concentrations calculated from the pK_a's of the conjugate acids of the buffer bases using activity coefficients recommended by Bates.[11] The results so obtained are listed in Table I. It may be seen that catalytic coefficients determined at different buffer ratios agree within their combined statistical uncertainties. The uncertainties associated with the general-base catalytic coefficients, however, are rather high; this is an unavoidable consequence of the weakness of the general-base catalysis.

The hydroxide-ion catalytic coefficient determined here for benzoylacetylene is nicely consistent with a σ_I–ρ correlation of hydroxide-ion catalytic coefficients for detritiation of a group of 15 terminal acetylenes;[4c] the correlation predicts a value only 2.0 times lower than that observed,[12] which is within the reliability of the correlation, whose standard deviation corresponds to a factor of 2.5 in rate constant. The rate constant determined here for (trimethylsilyl)acetylene, on the other hand, misses this correlation widely: it is 100 times greater than the predicted value.[15] This is similar to, but a factor of 2 greater than, the deviation observed for (trimethylsilyl)acetylene in a previous study of acetylene detritiation using a different solvent and catalyst system.[2]

Discussion

Acetylenes that behave as normal acids[3] give Bronsted plots with unit slope for their hydrogen-exchange reac-

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(10) Supplementary material; see paragraph at the end of this paper regarding availability.

(11) Bates, R. G. *Determination of pH: Theory and Practice*; Wiley-Interscience: New York, 1973, p 49.

(12) The σ constant for PhCO needed for this prediction, $\sigma_I = 0.32$, was estimated from the relationship $\sigma_I = \sigma_m - 0.33\sigma_R$[13] using $\sigma_m = 0.36$ and $\sigma_R = 0.11$.[14]

(13) Exner, O. *Collect. Czech. Chem. Commun.* **1966**, *31*, 65–86.

(14) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119–251.

(15) The prediction was made using $\sigma_I = -0.11$ for Me_3Si.[14]

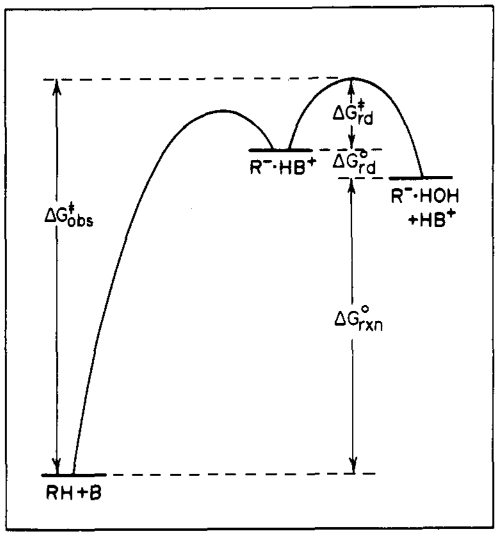

Figure 2. Free-energy profile for hydrogen exchange of a terminal acetylene behaving as a normal acid.

tions;[4a,d] buffer catalysis is consequently weak and often difficult to detect.[16] The weak general-base catalysis observed here (Figure 1) then suggests that the presently examined acetylenes were showing normal acid behavior, as expected by analogy with other terminal monoacetylenes.[4]

The free energy profile for hydrogen exchange of an acetylene functioning as a normal acid, eq 1, is shown schematically in Figure 2. Hydron transfer from the acetylene, RH, to a hydron acceptor, B, producing the hydrogen-bonded complex, $R^-{\cdot}HB^+$, does not by itself result in exchange, for in the reverse of this process the same hydrogen returns giving unexchanged acetylene; exchange is effected only after the HB^+ portion of the complex is replaced by another hydrogen-bearing species, in this case a solvent molecule to give the water-solvated carbanion $R^-{\cdot}HOH$.[4a] When the acetylene is behaving as a normal acid, this replacement step is rate determining and the hydron-transfer step is rapid and reversible, as shown in Figure 2.

In this circumstance, observed hydrogen-exchange rate constants measure the free energy difference, $\Delta G^\ddagger_{obs}$, between the initial state and the transition state of the replacement step. This quantity is also equal to the standard free energy change of the overall reaction, eq 3, ΔG°_{rxn},

$$RH + B + H_2O \rightleftharpoons R^-{\cdot}HOH + HB^+ \qquad (3)$$

plus the standard free energy change of the rate-determining step taken in the reverse direction, $-\Delta G^\circ_{rd}$, and the reaction barrier for this step in the forward direction, $\Delta G^\ddagger_{rd}$, as shown in eq 4. If the latter two quantities can

$$\Delta G^\ddagger_{obs} = \Delta G^\circ_{rxn} - \Delta G^\circ_{rd} + \Delta G^\ddagger_{rd} \qquad (4)$$

be evaluated, then they and the experimentally determined value of $\Delta G^\ddagger_{obs}$ can be transformed into $\Delta G^\ddagger_{rxn}$, and from that the equilibrium constant for the overall reaction can be calculated. Since this equilibrium constant is equal to the acid dissociation constant of the acetylene, K_a(RH), divided by the (known) acid dissociation constant of the hydron acceptor, $K_a(BH^+)$, an estimate of the acidity of the acetylene can thus be made.

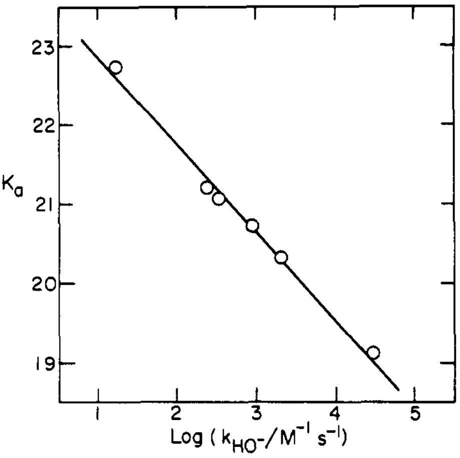

Figure 3. Relationship between acetylenic pK_a estimates and hydroxide-ion catalytic coefficients for their detritiation reactions.

The two quantities required for this calculation, ΔG°_{rd} and $\Delta G^\ddagger_{rd}$, may be evaluated in the following way. No direct information on the magnitude of barriers such as $\Delta G^\ddagger_{rd}$ appears to be available, but an estimate may be made by using known rates of dissociation of neutral amine hydrates[17] to evaluate the hydrogen-bonding interaction in $R^-{\cdot}HB^+$, $\Delta G^\ddagger_{HB}$, and then adding a Coulomb term to account for the pole–pole electrostatic interaction, E_{pp}, as in eq 5. The standard free energy change of the rate-

$$\Delta G^\ddagger_{rd} = \Delta G^\ddagger_{HB} + E_{pp} \qquad (5)$$

determining step, ΔG°_{rd}, may be estimated in an analogous way. This process trades one hydrogen bond for another, and ΔG°_{rd} should therefore contain a term allowing for any difference in hydrogen-bond strengths, $\delta\Delta G^\circ_{HB}$, plus another term for the difference between the pole–pole Coulombic interaction in $R^-{\cdot}HB^+$, E_{pp}, and the pole–dipole interaction in $R^-{\cdot}HOH$, E_{pd}; it is also necessary to include a term, $RT \ln 55$, to account for the fact that the water used to make the hydrate $R^-{\cdot}HOH$ comes from the solvent, whose concentration is 55 M. These considerations lead to eq 6, and substitution of that and eq 5 into eq 4 plus

$$\Delta G^\circ_{rd} = \delta\Delta G^\circ_{HB} + (E_{pp} - E_{pd}) - RT \ln 55 \qquad (6)$$

some rearrangement gives eq 7.

$$\Delta G^\circ_{rxn} = \Delta G^\ddagger_{obs} - E_{pd} - RT \ln 55 - \Delta G^\ddagger_{HB} + \delta\Delta G^\circ_{HB} \qquad (7)$$

It may be seen that the pole–pole Coulomb term, E_{pp}, has dropped out of this final expression and therefore need not be evaluated explicitly. Lower limits of $E_{pd} \geq 0.2$ kcal mol[18] and $-\Delta G^\ddagger_{HB} \geq 2.9$ kcal mol^{-1} have been estimated before,[4a] and $\delta\Delta G^\circ_{HB}$ may be evaluated as 1.8 kcal mol^{-1} for the benzoylacetylene system and 1.5 kcal mol^{-1} for the trimethylacetylene system using a recently determined relationship between hydrogen-bond strength and acidity of the hydrogen-bond donor.[19] These results, taken together with values of $\Delta G^\ddagger_{obs}$ calculated from the general base catalytic coefficients for the detritiation reactions determined here,[20] then lead to the upper limits p$K_a \leq 19.1$

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[17] Grunwald, E.; Ralph, E. K. *J. Am. Chem. Soc.* **1967**, *89*, 4405–4411; *Acc. Chem. Res.* **1971**, *4*, 107–113.

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[19] Stahl, N.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 4196–4205.

[20] Since hydrogen is not being transferred in the rate-determining step of these detritiation reactions, isotope effects will be small and rate constants for tritium exchange may be taken as reasonable approximations of those for any hydron exchange.

Table II. Estimates of Upper Limits of pK_a's for Some Acetylenes in Aqueous Solution at 25 °C

acetylene	≤pK_a	acetylene	≤pK_a
$CF_3C\equiv CH$	18.5[a]	$CH\equiv CH$	21.7[a]
$CH_3OCOC\equiv CH$	18.8[a]	$CH_3(CH_2)_2CH(OH)C\equiv CH$	21.9[a]
$C_6H_5COC\equiv CH$	19.1[b]	$(CH_3)_3CC\equiv CH$	22.2[a]
$CH_3(CH_2)_2COC\equiv CH$	20.3[a]	$CH_3CH_2C\equiv CH$	22.5[a]
$C_6H_5{}^+(CH_3)_2C_2C\equiv CH$	20.3[b]	$CH_3(CH_2)_2C\equiv CH$	22.5[a]
$4\text{-}NO_2C_6H_4C\equiv CH$	20.7[b]	$CH_3(CH_2)_3C\equiv CH$	22.5[a]
$(CH_3)_3SiC\equiv CH$	21.1[b]	$CH_3C\equiv CH$	22.7[a]
$CH_2FC\equiv CH$	21.1[a]	$CH_3(CH_2)_5C\equiv CH$	22.7[b]
$C_6H_5C\equiv CH$	21.2[b]		

[a] Obtained using the correlation of Figure 3. [b] Obtained via eq 7.

for benzoylacetylene and pK_a ≤ 21.1 for (trimethylsilyl)acetylene.

General-base catalytic coefficients for the detritiation of three other acetylenes in aqueous solution are available,[4d] and these, when treated as described above for benzoyl- and (trimethylsilyl)acetylene, give the estimates pK_a ≤ 20.3 for [(phenyldimethylamonio)methyl]acetylene, pK_a ≤ 20.7 for (4-nitrophenyl)acetylene, and pK_a ≤ 22.7 for *n*-hexylacetylene. An estimate made in the same way is also available for phenylacetylene, pK_a ≤ 21.2.[4a,21]

These six pK_a estimates were found to correlate well with hydroxide-ion catalytic coefficients for detritiation of these acetylenes. The relationship is shown in Figure 3; least-squares analysis gives pK_a = 23.98 ± 0.13 – (1.114 ± 0.045) log (k_{HO^-}/M^{-1} s^{-1}). On the assumption that this correlation applies also to other terminal acetylenes whose hydroxide ion catalytic coefficients fall into the range encompassed, upper limits of pK_a's for other acetylenes for which such catalytic coefficients are available[4c] may be calculated. The results so obtained are listed in Table II, together with the pK_a estimates upon which this correlation is based.

It may be seen that, on the basis of these estimates, benzoylacetylene is a fairly strongly acidic acetylene: of the entries in Table II, only (trifluoromethyl)acetylene and carbomethoxyacetylene appear to be stronger. The three acetylenes of Table II with carbonyl groups attached directly to acetylenic carbon, moreover, fall in a sensible order, with acidity increasing in accord to the electron-withdrawing ability of the substituent attached to the other side of the carbonyl group.

(Trimethylsilyl)acetylene appears to be a notably acidic substance as well. Silicon is less electronegative than either carbon or hydrogen,[22] and, as has been pointed out before,[2] (trimethylsilyl)acetylene might therefore be expected to be less acidic than either *tert*-butylacetylene or acetylene itself. The estimates of Table II indicate otherwise.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada and the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work at the University of Toronto and to the National Cancer Institute of the National Institutes of Health for financial support under Grant Number 2ROCA16903 at the University of Utah.

Supplementary Material Available: Table S1 of rate data (2 pages). Ordering information is given on any current masthead page.

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(21) The original estimate, pK_a ≤ 20.0,[4a] did not take into account the difference in hydrogen-bond strength, $\delta\Delta G°_{HB}$; when this is included that estimate rises to pK_a ≤ 21.2.

(22) Colvin, E. *Silicon in Organic Synthesis*; Butterworths: Toronto, 1981; p 5.

A Novel Friedel–Crafts Reaction: Synthesis of 4-Phenylnaphthalen-1-ols

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Gossypol (1, Chart I), a complicated dimer of sesquiterpene with multiple biological activities, was isolated from certain species of the cotton plant. The chemical structure was first proposed by Adams[1] in 1938 and was confirmed by total synthesis in 1958.[2] Venuti[3] completed a formal total synthesis of gossypol. Manmade et al.[4] reported the synthesis of some O-methylated hemigossypol derivatives, which exhibited in vitro spermicidal activity as effective as that of gossypol. Meltzer et al.[5] converted gossypol into the 5,5′-dideisopropyl-5,5′-diethyl analogue.

During the course of our studies on the synthesis of gossypol analogues, we discovered a novel Friedel–Crafts reaction leading to the synthesis of 1-phenylnaphthalenes. We attempted to synthesize derivatives of 1,4-diphenylbutane-1,4-diol 2 (Chart I), which may be considered the simplest analogue of gossypol, lacking both the B rings, by reaction of veratrole (**3b**) with succinyl chloride.

In 1955 Buchta et al.[6] obtained lactone **5a** in 13–16% yield from the Friedel–Crafts reaction of anisole (**3a**) with succinyl chloride (4) at low temperature (between –10 and –5 °C) using carbon disulfide as the solvent, while at higher temperature (60 °C), both lactone **5a** (13%) and diketone **6a** (18–21%) were obtained. It was shown that succinyl chloride exists in acyclic and cyclic forms (**4a and 4b**), the former prevailing at low temperature. It is interesting to note that, after repeating the Buchta reaction,[6] we isolated, in addition to **5a** (33%), diketone **6e** (8%) and traces of its isomer **6f** (2%) in CS_2 as well as in dichloroethane ($ClCH_2CH_2Cl$) at –5 °C. This reaction was then applied to the construction of **2**. We found that the Friedel–Crafts reaction of veratrole (**3b**) with succinyl chloride at 60 °C using $ClCH_2CH_2Cl$ as the solvent afforded diketone **6b** albeit in a very low yield (0.6%). The same reaction at low temperature (–10 to –5 °C) gave lactone **5b** (Scheme I) in 23% yield as the major product.

Attempts to remove the methyl functions from the phenyl moiety of **5b** by prolonged treatment (overnight) with boron tribromide (BBr_3) caused an intramolecular Friedel–Crafts acylation, giving 4-phenylnaphthalen-1-ol (**7b**, $R_1 = R_2$ = OH) in 53% yield, Scheme II). After brief treatment of **5b** with BBr_3, a small amount of the de-O-methylated compound 8 was obtained. There are several approaches to the synthesis of α-phenylnaphthalenes.[7-9] To our best knowledge, there is little literature that deals with the synthesis of 4-phenylnaphthalen-1-ol derivatives. We, therefore, studied our new reaction for the synthesis

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