analytical sample of **20**: mp 245–248 °C; $[\alpha]^{22}_D$ +27.4 (*c* 0.5, $Me_2SO$); $^1H$ NMR ($Me_2SO$-$d_6$) δ 3.39–3.64 (m, 2), 3.77–4.14 (m, 3), 4.90 (d, 1, *J* = 5.4 Hz, H-1′), 4.70–5.50 (br, 3 H), 8.15 (s, 1, H-6); $^{13}C$ NMR ($Me_2SO$-$d_6$) δ 61.7, 71.4, 77.0, 82.5, 85.2, 137.8, 146.7, 155.78, 161.4, 169.4; IR $cm^{-1}$ 1770, 1570; UV $\lambda_{max}$ (pH 1) 282 nm (ε 4857), 261 (ε 5714), 254 (ε 5514), 215 (ε 14857), $\lambda_{max}$ (pH 11) 289 (ε 5485), 263 (ε 5700), 257 (ε 5914), 225 (ε 11457); MS, *m/e* 285, 249, 232, 220, 196, 182; TLC (solvent E) $R_f$ 0.26. Anal. Calcd for $C_{10}H_{11}N_3O_5S$: C, 42.10; H, 3.89; N, 14.73; S, 11.24. Found: C, 42.08; H, 4.07; N, 14.52; S, 11.04.

**2-(β-D-Ribofuranosyl)selenazolo[5,4-*d*]pyrimidin-4-(5*H*)-one (21).** The same procedure used to prepare **20** was also used to prepare **21**. Thus 5-amino-2-(β-D-ribofuranosyl)selenazole-4-carboxamide (**13**) (1.0 g, 3.1 mmol) yielded 720 mg (69%) of **21**: mp 232–235 °C; $[\alpha]^{22}_D$ +20.0 (*c* 0.5, $Me_2SO$); $^1H$ NMR ($Me_2SO$-$d_6$) δ 3.50–3.65 (m, 2), 3.82–4.12 (m, 3), 4.84 (d, 1, *J* = 4.5, H-1′), 8.15 (s, 1, H-6); $^{13}C$ NMR ($Me_2SO$-$d_6$) δ 61.7, 71.5, 77.3, 84.8, 85.2, 140.7, 145.7, 156.3, 167.7, 177.7; IR $cm^{-1}$ 1675; UV $\lambda_{max}$ (pH 1) nm 290 (ε 5769), 258 (sh, ε 4192), 233 (ε 18077), $\lambda_{max}$ (pH 11) 295 (ε 6538), 263 (sh, ε 5000), 238 (ε 14115); MS, *m/e* ($^{80}Se$) 333, 297, 280, 268, 244, 230; TLC (solvent E) $R_f$ 0.26. Anal. Calcd for $C_{13}H_{11}N_3O_5Se \cdot {}^1/_2H_2O$: C, 35.20; H, 3.55; N, 12.32. Found: C, 35.57; H, 3.54, N, 12.17.

**4-Amino-2-(β-D-ribofuranosyl)thiazolo[5,4-*d*]pyrimidine (22).** To a solution of 5-amino-4-cyano-2-(β-D-ribofuranosyl)-thiazole (**12**) (150 mg, 0.58 mmol) in ethoxyethanol (10 mL) was added formamidine acetate (200 mg, 1.92 mmol) and the mixture was refluxed for 30 min. The solution was allowed to cool to room temperature followed by evaporation in vacuo. The residue spontaneously crystallized. The product purified by recrystallization from absolute ethanol (2x) to give 124 mg (75%) of **22**: mp 208–211 °C; $[\alpha]^{22}_D$ +73.2 (*c* 0.5, $Me_2SO$); $^1H$ NMR ($Me_2SO$-$d_6$) δ 3.52–3.68 (m, 2), 3.88–4.44 (m, 3), 4.91 (t, 1, *J* = 5.4 Hz), 5.0 (d, 1, *J* = 6.3 Hz, H-1′), 5.06–5.12 (m, 1), 5.42 (d, 1, *J* = 5.4 Hz), 7.65 (br s, 2, $NH_2$), 8.29 (s, 1, H-6); $^{13}C$ NMR ($Me_2SO$-$d_6$) δ 61.7, 71.4, 77.0, 82.6, 85.6, 129.7, 154.2, 156.9, 162.2, 168.7; IR $cm^{-1}$ 1570; UV $\lambda_{max}$ (pH 1) 268 nm (ε 11857), 222 (ε 21714), $\lambda_{max}$ (pH 11) 290 (sh, ε 5571), 265 (ε 9857), 226 (ε 14857); MS, *m/e* 284, 195, 181; TLC (solvent E) $R_f$ 0.38. Anal. Calcd for $C_{10}H_{12}N_4O_4S$: C, 42.25; H, 4.25; N, 19.71; S, 11.28. Found: C, 42.22; H, 4.46; N, 19.44; S, 11.18.

**2-(β-D-Ribofuranosyl)thiazolo[5,4-*d*][1,2,3]triazin-7-(6*H*)-one (23).** To a cold (−22 °C, $CCl_4$/dry ice slush bath) stirred solution of 5-amino-2-(β-D-ribofuranosyl)thiazole-4-carboxamide (**10**) (300 mg, 1.09 mmol) in 6 N aqueous hydrochloric acid (5.5 mL) was added sodium nitrite (230 mg, 3.27 mmol) dissolved in water (2 mL). After 30 min the solution was made slightly basic (pH 8) by addition of cold concentrated ammonium hydroxide (2.18 mL). After silica gel (60–200 mesh, 1 g) had been added the red solution was evaporated in vacuo. The dry powder was added to the top of a 24 mm × 175 mm silica gel column and the column was eluted with solvent E. Evaporation of the product fractions yielded 200 mg (65%) of **23** as a crystalline solid: mp 178 °C dec with gas evolution; $^1H$ NMR ($Me_2SO$-$d_6$) δ 3.48–3.68 (m, 2), 3.86–4.23 (m, 3 H), 5.05 (d, 1, *J* = 4.5, H-1′), exchangeable protons were observed as broad undefined absorptions; $^{13}C$ NMR ($D_2O$) δ 61.5, 71.4, 77.1, 82.6, 85.1, 139.1, 152.9, 156.3, 177.4; IR $cm^{-1}$ 1700; UV $\lambda_{max}$ (pH 1) 295 nm (ε 5507), 223 (ε 13590), $\lambda_{max}$ (pH 11) 310 (ε 6795), 258 (ε 4220), 230 (ε 12088); MS, *m/e* 286, 257, 243, 204, 197, 185, 171, 149, 129, 97, 69; TLC (solvent E) $R_f$ 0.51. Anal. Calcd for $C_9H_{10}N_4O_5S$: C, 37.76; H, 3.52; N, 19.57; S, 11.20. Found: C, 37.81; H, 3.72; N, 19.31; S, 11.46.

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**Registry No.** **1**, 60084-10-8; **2**, 83705-13-9; **3**, 95936-45-1; **4**, 95936-46-2; **5**, 62404-62-0; **7**, 6719-21-7; **8**, 32683-02-6; **9**, 5098-14-6; **10**, 95936-47-3; **11**, 95936-48-4; **12**, 95936-49-5; **13**, 95936-50-8; **14**, 95936-51-9; **16**, 13433-00-6; **17**, 95936-52-0; **18**, 95936-53-1; **19**, 95936-54-2; **20**, 95936-55-3; **21**, 95936-56-4; **22**, 95936-57-5; **23**, 95936-58-6; ethyl 2-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-thiazole-4-carboxylate, 60084-09-5; ethyl 2-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)selenazole-4-carboxylate, 83705-11-7; triethyl orthoformate, 122-51-0; formamidine acetate, 3473-63-0.

# *Notes*

## Hydrogen–Deuterium Exchange of Weak Carbon Acids under Phase-Transfer Catalysis Conditions

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Phase-transfer catalysis (PTC) enables the chemist to maintain a concentration of substances from an aqueous reservoir in an organic phase which contains an organic substrate.[1] The mechanism of this process has been the subject of much discussion[1c] and study.[1a] An extraction mechanism has been considered by Starks in which the nucleophile is extracted from the aqueous reservoir into the organic phase with the aid of a quaternary ammonium or phosphonium ion (quat).[2-4] Makosza proposed an alternative mechanism for alkylation and carbene addition in which proton abstraction by the hydroxide ion occurs in the interface.[5,6] In the latter case, the quat has the role of removing the resulting organic anion from the interface into the bulk organic phase for subsequent reaction. The critical component of PTC reactions is the catalyst, and it has recently been shown that the choice of this parameter may lead to favorable results.[7] Hydroxide ion initiated reactions performed under PTC conditions provide unique advantages in the laboratory and industry due to the employment of an aqueous base instead of the classical alkoxides and hydrides in strictly dry media.

Proton exchange in compounds of low acidity is often difficult in a practical method because of high kinetic barriers associated with removal of the hydrogen. Toluene and toluene derivatives were shown by Streitwieser to

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undergo slow H/D exchange processes.[8] We now report a general method based on our previous studies on PTC/$OH^-$ systems[7] for exchanging very weak carbon acid protons under readily obtainable conditions.

## Results and Discussion

Until very recently, only compounds as acidic as fluorene ($pK_a$ = 23)[9] underwent PTC reactions under conditions which favor the interfacial mechanism.[5,10] It seemed, therefore, that fluorene represents a compound of the lowest limit of acidity suitable for such a reaction. This behavior of an interfacial mode can be rationalized by the thermodynamic parameters of the following process.[11]:

$$2NaOH + H^+ \rightleftharpoons Na^+ + NaOH{\cdot}H_2O \qquad K = 10^{23}$$

Thus, an acid of a $pK_a$ value up to 23 should react with solid NaOH to give the sodium salt. The empirical limit for exchange on a practical time scale is therefore represented by the fluorene molecule ($pK_a$ = 23). On the other hand, we have recently reported that very weak carbon acids ($pK_a$ = 34)[12] do undergo rapid reactions operative under PTC/$OH^-$ conditions. We rationalized this expansion of the acidity range of compounds capable of undergoing this process by assuming that the reaction occurs via an extraction mechanism. We have shown that the hydroxide ion can be extracted into the organic phase with the appropriate catalyst under PTC conditions.[7b] This process affords an increased basicity of the hydroxide ion, relative to that of the hydroxide ion acting at the interface, and hence enables the abstraction of a proton from compounds of very low acidity. The intrinsic basicity of the relatively unsolvated hydroxide ion is much greater than that which can be achieved in a solvent such as water or alcohol.[11] This property could be employed for H/D exchange studies as well as for many deuterated compounds. The increased basicity of the $OH^-$ or $OD^-$ ions is obtained by the employment of an organophilic catalyst, a hydrophilic counterion (to avoid catalyst poisoning), and very high concentrations of the aqueous base. In an ideal system the extracted $OD^-$ ion is followed by just a few molecules of $D_2O$ as the NaOD pasty solution acts as a dessicant which "dries" the ion pair. This high base concentration should also promote the base into the organic layer due to salting-out and the Le Chatellier principle. The system of choice appears to be tetrabutylammonium hydrogen sulfate ((TBA)$HSO_4$) and 63% of NaOD in $D_2O$.

We are interested in determining the lowest limit of acidity of a compound that can still exchange its protons rapidly. We assumed that the extension of the acidity range to substrates of very low acidity can be materialized by applying conditions which favor the extraction mechanism (high base concentrations, lypophilic ammonium ions, and hydrophilic counteranions).

Unless otherwise stated, we apply Streitwieser's $pK_a$ scale in order to assess the acidity of the substrates. The H/D exchange reaction has been previously carried out under PTC/$OD^-$ conditions;[2,13-16] however, the least acidic compound on which this reaction was employed is thiazole[15] ($pK_a$ = 29.5).[17] Previously we reported the extension of this limit to $pK_a$ = 34.[18] We note that although toluene ($pK_a$ = 41)[19] does not undergo any rapid exchange reaction, the following substrates do: xanthene ($pK_a$ = 27),[20] 10,11-dibenzo[*a*,*d*]cycloheptadiene ($pK_a$ = 31.2),[19] 1,2,3,4-tetrafluorobenzene ($pK_a$ = 31.5),[21] triphenylmethane ($pK_a$ = 31.4),[19] diphenylmethane ($pK_a$ = 33.4),[19] and allylbenzene ($pK_a$ = 34).[22] Toluene seems therefore to represent the extreme limit of low acidity for this reaction even under extractive PTC conditions. Here we report the H/D exchange reaction of substrates in the $pK_a$ range 34–41. In order to place toluene within this range, several substituted toluenes with electron-withdrawing groups were studied.

**Table I. Proton-Deuterium Exchange in Substituted Toluenes[a]**

| | substituent | | | | |
|---|---|---|---|---|---|
| position | F | Cl | Br | I | $NO_2$ |
| ortho | 4 | 44 | 62 | *b* | 80 |
| meta | 12 | 39 | 46 | 42 | 0 |
| para | 0 | 5 | 11 | 16 | 40[c] |

[a] One run (hexane), percentage of exchanged methyl group protons of the isolated compound as estimated by $^1H$ NMR. For liquid substrates used in neat form an increase of 5–10% was obtained (see Experimental Section). [b] Not studied. [c] This compound is rather insoluble in hexane, and therefor 1 mL of solvent was added.

The hydrogen–deuterium exchange of the substituted toluenes (Table I) shows the following trend. chloro-, bromo-, and iodotoluene afford relatively good yields (39–62%) when substituted in the ortho or meta position; however, para substitution affords lower yields (5–16%). *o*– or *m*–Fluorotoluene afford deuterium exchange in low yields (4% and 12%, respectively), whereas no exchange was detected with *p*-fluorotoluene. The fact that *m*-fluorotoluene exchanges to a higher degree is in accord with Streitwieser's reported studies of lithium cyclohexylamide in cyclohexylamine.[8] *o*-Nitrotoluene affords 80% H/D exchange of the methyl group, while *p*-nitrotoluene gave 40% and the meta isomer did not afford any exchange product.

An exchange experiment carried out on 2,4-dichlorotoluene afforded 42% of the deuterated compound. This observation emphasizes the small contribution of the *p*-chloro substituent to the enhancement of the substrate acidity. As a practical method for the preparation of compounds with a high degree of deuteration one can repeat the exchange procedure. In this manner repetition of the H/D exchange of, for example, *o*-bromotoluene enhanced the degree of exchange from 62% to 81%.

The greater H/D exchange of *m*-fluorotoluene is consistent with Klein's hypothesis[23] that two groups in the

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meta position to each other are stabilized relative to the ortho and particularly to para isomers when the substituents carry interacting lone pairs with the aromatic ring. This stabilization is caused by a polarization which results in a charge alternation around the ring by donor–acceptor interactions. The results of both the fluorine and the nitro-substituted toluenes agree with this hypothesis since the nitro group is an acceptor that stabilizes the system in the ortho and para positions. The results in Table I reflect two effects, one of them is the effect discussed above and the other one is a field effect exerted by the electronegative substituent. The sequence of the reactivities of halogen–substituted toluene seems to follow the size of the halogen atom and its ability to disperse the charge withdrawn by the inductive effect.

The degree of exchange was deduced from the decrease in the respective resonance area of the proton spectrum relative to an internal standard which does not undergo such a process (aromatic protons or hexamethylbenzene). The position of the exchanged hydrogen and the degree of exchange of the methyl protons were also elucidated from proton-decoupled $^{13}C$ NMR spectra. The $^{1}J_{C-D}$ (as well as $^{2}J_{H-D}$) coupling pattern allowed for the assignment of the particular carbon atom which has undergone the process and the degree of exchange of its protons. The $^{1}H$ NMR spectrum of the substituted toluenes shows a mixture of starting material as well as mono- and dideuterated products, as deduced from patterns composed of a triplet and quintuplet shifted to high field. Additional support to the exchange process is given by mass spectroscopy. Electron-impact spectra obtained on a GC/MS spectrometer showed evidence for the existence of deuterated molecules in representative cases.

The proton–deuterium exchange process was also carried out on aromatic halogen derivatives which have more than one methyl group. The introduction of an additional methyl group is expected to decrease the degree of the exchange. Reaction of neat 2-bromo-1,3-dimethylbenzene (1) (2-bromo-*m*-xylene) showed 45% deuterium exchange. The $^{1}H$ NMR spectrum shows a complex pattern of the methyl resonance at 2.36 ppm which is composed of a triplet and a quintuplet ($J = 2 \pm 0.3$ Hz) shifted to high field, thus pointing at a mixture of singly and doubly deuterated methyl groups. In the $^{13}C$ NMR spectrum, the methyl singlet of 1 at 23.52 ppm is split in the exchanged molecule to an unsymmetrical pattern composed of five lines ($J = 19.3 \pm 1.6$ Hz), thus exhibiting that more than one hydrogen atom of the methyl group has been exchanged. However, reaction under the standard conditions (hexane solution) afforded only 14% of the deuterated product. Neat 1-bromo-2,4-dimethylbenzene (2) gave an overall exchange of 36%. The *o*-methyl group is deuterated to a higher extent relative to the para position (59% and 13%, respectively). The *o*- and the *p*-methyl singlets of 2 (2.31 ppm and 2.23 ppm, respectively) show a pattern composed of a triplet and a quintuplet ($J = 2 \pm 0.3$ Hz) shifted to a high field. In the $^{13}C$ NMR spectrum, the *o*-methyl group appears as a superposition of a triplet and a quintuplet while the *p*-methyl appears as a triplet ($J = 19.3 \pm 1.6$ Hz). Here again, when the reaction is carried out in hexane solution at the standard conditions, the yield decreased significantly (11% total exchange, 16% at the ortho position and 5% at the para position).

Neat 1-bromo-2,4,6-trimethylbenzene (3) afforded only 13% of total exchange of the methyl group hydrogen atoms. In the $^{13}C$ NMR spectrum, only the *o*-methyl group ($\delta = 23.36$ ppm) shows a split pattern ($J = 19.3 \pm 1.6$ Hz), thus showing that the *p*-methyl group did not undergo an exchange process. Reaction in hexane afforded only the starting materials. The introduction of an additional methyl group to the aromatic ring decreases the acidity to a greater extent. Therefore, 1-iodo-2,3,5,6-tetramethylbenzene (4) (iododurene) did not show any H/D exchange.

## Conclusion

A practical method for H/D exchange is obtained via extractive hydroxide ion initiated phase-transfer catalysis. The reaction of $NaOD/D_2O$ system allows the easy production of compounds that otherwise would require very strong bases and aprotic solvents. The strong basicity of $OD^-$ anion is attributable to its relative freedom from water molecules when $OD^-$ is extracted into the depth of the organic layer.

## Experimental Section

**Materials.** Substituted toluenes, 2-bromo-1,3-dimethylbenzene, and 1-bromo-2,4,6-trimethylbenzene were prepared by standard procedures according to the literature.[24] The catalyst tetrabutylammonium hydrogen sulfate ($(TBA)HSO_4$) was purchased from Sigma Chemical Co. Sodium deuteroxide (NaOD) was prepared by a careful addition of sodium metal to $D_2O$ under nitrogen atmosphere. Toward the end of the reaction heating is required. The pasty $NaOD/D_2O$ solution was titrated with standard solution of HCl to show that the solution contained 63% w/w of NaOD.

**NMR Spectra.** The NMR spectra were recorded on a Bruker WH-300 pulsed FT spectrometer operating at 300.133 and 75.46 MHz for $^{1}H$ and $^{13}C$, respectively. The field/frequency stabilizations were maintained by locking to the solvent ($CDCl_3$) deuterium. The free induction decay signals were digitized and accumulated on an Aspect-2000 computer (32K). The estimation of the degree of exchange was obtained from the relative band areas before and after the process. In the substituted toluenes, the aromatic protons served as an internal standard. In other cases hexamethylbenzene (Fluka) served as internal standard.

**H/D Exchange Experiments. General Procedure.** Unless otherwise stated, reactions were carried out in a standard reaction vial (35 mm high and 21 mm diameter) with strong magnetic stirring. The stirring bar was Teflon coated (10 mm long and 3 mm diameter). In a typical reaction 3 mmol of substrate were added to 0.5 mL of hexane, 0.6 mmol of catalyst (20 mol %), and 1.1 g of the solidous solution of NaOD. The reaction mixture was stirred at room temperature for 20 h, followed by three extractions with methylene chloride. The combined extracts were washed with water, dried with $MgSO_4$, and filtered and the filtrate was chromatographed on a short column (10 × 1 cm of Florisil) and evaporated to dryness under vacuum. These operations afforded a solution which is free from catalyst and its decomposition products.

**Reaction of 2-Bromo-1,3-dimethylbenzene (2-Bromo-*m*-xylene, 1).** Into the standard vial were added 0.785 g (4.24 mmol) of 1, 0.574 g (1.69 mmol, 40 mol %) of $(TBA)HSO_4$, and 2.55 g of $NaOD/D_2O$. The reaction mixture was stirred magnetically for 19 h at room temperature. The workup was carried out according to the standard procedure. In addition, the reaction was carried out also in a solvent under the previously described conditions: $^{1}H$ NMR $\delta$ 7.00 (m, aromatic), 2.35 (superimposed, s, t, q, $J_{H-D} = 2$ Hz); $^{13}C$ NMR $\delta$ 137.96 (s), 127.42 (s), 126.40 (s), 22.99 (superimposed s, t, q, $J_{C-D} = 19.3$ Hz).

**Reaction of 1-Bromo-2,4-dimethylbenzene (2).** A mixture of 0.827 g (4.47 mmol) of 2, 0.61 g (1.8 mmol, 40 mol %) of $(TBA)HSO_4$, and 2.86 g of $NaOD/D_2O$ was stirred at room temperature with a magnetic stirrer in the standard vial for 23 h. The standard workup procedure was applied. In addition, this reaction

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was also carried out in a solvent: $^1$H NMR $\delta_A$ 7.35 ($J_{AB}$ = 8.2 Hz), $\delta_B$ 6.8 ($J_{AB}$ = 8.2 Hz, $J_2$ = 1.96 Hz), 7.00 (d, $J$ = 19.6 Hz), 2.27 (superimposed, s, t, q, $J$ = 2 Hz), 2.2 (s), 2.19 (t, $J$ = 2 Hz); $^{13}$C NMR $\delta$ 137.19 (s), 136.81 (s), 131.89 (s), 131.49 (s), 127.96 (s), 121.42 (s), 21.91 (superimposed s, t, q), 20.50 (superimposed s, t, $J$ = 19.3 Hz).

**Reaction of 1-Bromo-2,4,6-trimethylbenzene (2-Bromomesitylene, 3).** A mixture of 0.769 g (3.86 mmol) of **3**, 0.525 g (1.54 mmol, 40 mol %) of (TBA)$HSO_4$, and 3.370 g of NaOD/$D_2O$ was stirred magnetically in the standard vial for 23 h at room temperature. The standard workup procedure was applied. The same reaction was also carried out in a solvent: $^1$H NMR $\delta$ 6.76 (s), 2.29 (s), 2.15 (s); $^{13}$C NMR $\delta$ 137.57 (s), 135.93 (s), 128.85 (s), 124.06 (s), 23.08 (superimposed s, t, $J$ = 19.3 Hz), 20.38 (s).

**Reaction of 1-Iodo-2,3,5,6-tetramethylbenzene (1-Iododurene, 4).** A mixture of 0.515 g (1.98 mmol) of **4**, 0.28 g (0.82 mmol, 41 mol %) of (TBA)$HSO_4$ and 2.54 g of NaOD/$D_2O$ in 3 mL of hexane was magnetically stirred for 23 h at room temperature. The reaction mixture was worked up in diethyl ether: $^1$H NMR $\delta$ 6.86 (s), 2.42 (s), 2.28 (s).

**Mass Spectroscopy.** Electron-impact mass spectra of the following deuterated compounds were recorded on a Finnigan GC MS.

*o*-Bromotoluene: *m/e* 170 (M), 171 (M + 1), 172 (M + 2), 173 (M + 3), 174 (M + 4), 175 (M + 5).

*o*-Chlorotoluene: *m/e* 126 (M), 127 (M + 1), 128 (M + 2), 129 (M + 3), 130 (M + 4).

*m*-Iodotoluene: *m/e* 218 (M), 219 (M + 1), 220 (M + 2), 221 (M + 3), 222 (M + 4).

*m*-Bromotoluene: *m/e* 170 (M), 171 (M + 1), 172 (M + 2), 173 (M + 3), 174 (M + 4), 175 (M + 5).

*p*-Chlorotoluene: *m/e* 126 (M), 127 (M + 1), 128 (M + 2).

*p*-Bromotoluene: *m/e* 170 (M), 171 (M + 1), 172 (M + 2), 173 (M + 3).

2-Bromo-1,3-dimethylbenzene: *m/e* 107, 184 (M), 185 (M + 1), 186 (M + 2), 187 (M + 3), 188 (M + 4), 189 (M + 5), 190 (M + 6).

1-Bromo-2,4-dimethylbenzene: *m/e* 107, 184 (M), 185 (M + 1), 186 (M + 2), 187 (M + 3), 188 (M + 4), 189 (M + 5).

1-Bromo-2,4,6-trimethylbenzene: *m/e* 119, 198 (M), 199 (M + 1), 200 (M + 2), 201 (M + 3), 202 (M + 4), 203 (M + 5).

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**Registry No.** 1, 576-22-7; 2, 583-70-0; 3, 576-83-0; 4, 2100-25-6; (TBA)$HSO_4$, 32503-27-8; *o*-fluorotoluene, 95-52-3; *o*-chlorotoluene, 95-49-8; *o*-bromotoluene, 95-46-5; *o*-nitrotoluene, 88-72-2; *m*-fluorotoluene, 352-70-5; *m*-chlorotoluene, 108-41-8; *m*-bromotoluene, 591-17-3; *m*-iodotoluene, 625-95-6; *p*-chlorotoluene, 106-43-4; *p*-bromotoluene, 106-38-7; *p*-iodotoluene, 624-31-7; *p*-nitrotoluene, 99-99-0.

## Magnesium in Methanol: Substitute for Sodium Amalgam in Desulfonylation Reactions

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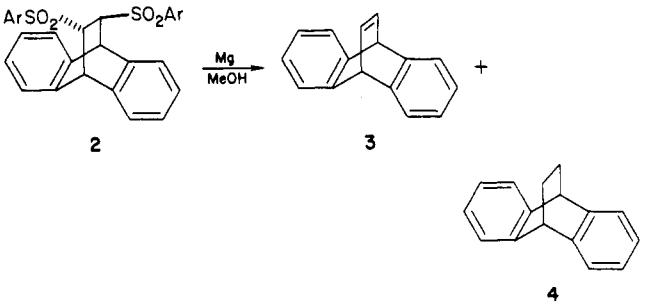
Synthetic equivalents of acetylene in the Diels–Alder reaction are of special utility in view of the low reactivity of acetylene itself toward most dienes. Recently[1] *cis*- and *trans*-1,2-bis(phenylsulfonyl)ethylenes (1, Ar = $C_6H_5$) have

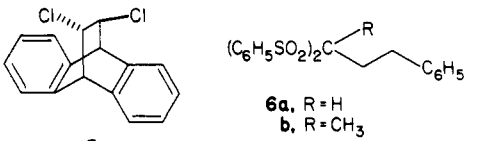
$$ArSO_2CH{=}CHSO_2Ar$$
**1**

been recommended for this purpose, with eventual reductive elimination of the activating sulfone functions by treatment with sodium amalgam. In connection with a study of some general routes to substituted derivatives of ethenoanthracene **3**, we examined the utility of *cis*- and




**2** **3** **4**

*trans*-**1** (Ar = *p*-$CH_3C_6H_4$) in this system. In the initial Diels–Alder reaction *trans*-**1** proved far more reactive than the corresponding cis isomer[2] and was therefore used exclusively in this study. Not wishing to be faced, in expectation of eventual large-scale work, with the tedious handling of massive quantities of toxic metallic mercury, we devised a simple method of desulfonylation involving treatment of the appropriate bis(sulfone) with an excess of magnesium in methanol at 50 °C for several hours. Under these conditions adduct **2** gave **3** in 62% yield accompanied by 21% of the corresponding dihydro derivative **4**. For comparison, under the same conditions the analogous dichloro compound **5** gave only 27% of **3**.




**5** **6a**, R = H; **b**, R = $CH_3$

The simplicity of this technique encouraged us to extend it to 1,1-bis(sulfones) as well as simple monosulfones. Application to **6a** and **6b** gave the expected hydrocarbons *n*-propylbenzene and *n*-butylbenzene in yields of 84% and 81%, respectively. Phenyl β-phenethyl sulfone gave ethylbenzene in 68% yield. The fate of the sulfonyl residues was not determined in any of these conversions. The magnesium turnings used in this study were activated by treatment with dilute hydrochloric acid. Turnings activated in this way were especially reactive in the Grignard reaction as well as these desulfonylation processes.

### Experimental Section[3]

**(*Z*)-1,2-Bis[(4-methylphenyl)sulfonyl]ethene.** Obtained by oxidation of the corresponding bis(thio ether) by the method of Truce and McManimie.[4] The precursor was most simply prepared from vinylidene chloride by the technique of Truce and Boudakian[5] except that refluxing the *p*-toluenethiol for a 4-day period with lithium isopropoxide in isopropyl alcohol took the place of the sealed tube reaction. The sulfone was obtained in an overall yield of 40%: mp 152–153 °C (lit.[4] mp 149 °C); $^1$H

(1) For recent references and citations to earlier examples, see: (a) DeLucchi, O.; Lucchini, V.; Pasquato, L.; Modena, G. *J. Org. Chem.* **1984**, *49*, 596. (b) DeLucci, O.; Modena, G. *Tetrahedron* **1984**, *40*, 2585.

(2) The greater reactivity of *trans*-**1** over *cis*-**1** has been previously noted. See: Sauer, J.; Wiest, H.; Mielert, A. *Chem. Ber.* **1964**, *97*, 3183.

(3) Melting points and boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer 237B instrument and NMR spectra on Varian A-60 and Perkin-Elmer R12 instruments with $Me_4Si$ as internal standard. Elemental analyses were carried out by the University of Massachusetts Microanalytical Laboratory under the direction of Greg Dabkowski. Thin-layer chromatography was performed on aluminum-backed Merck silica gel 60 F254 plates using the solvents specified.

(4) Truce, W. E.; McManimie, R. J. *J. Am. Chem. Soc.* **1953**, *75*, 1672.

(5) Truce, W. E.; Boudakian, M. M. *J. Am. Chem. Soc.* **1956**, *78*, 2750.

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