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Rearrangement Reactions of (Hydroxyphenyl)carbenes

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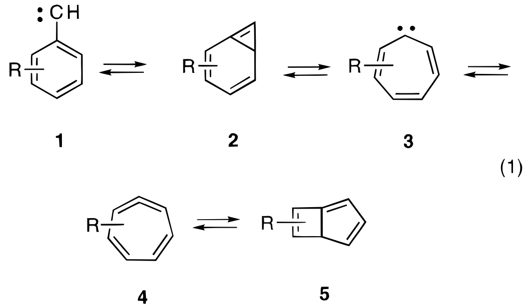
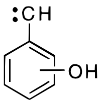
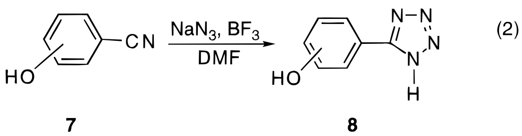
The phenylcarbene isomerization system **1**−**5** (eq 1) leads to some of the most extensive rearrangements known to organic chemistry.[1] However, other than for aryl, alkyl, and substituted alkyl groups, little is known of the effects of substituents on the rearrangements of arylcarbenes.[1] The intramolecular behaviors of various (hydroxyphenyl)carbenes **6** at elevated temperatures in the gas phase are now reported.





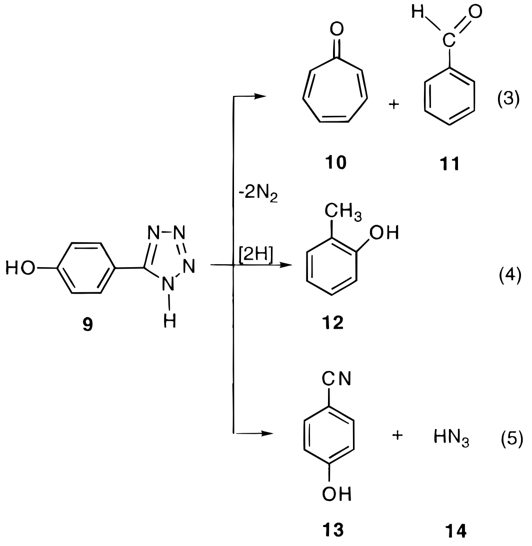
6

Carbenes may be generated by thermal decompositions of 5-substituted tetrazoles.[2] Of initial interest for study of **6** are 5-(hydroxyphenyl)tetrazoles **8** as now prepared advantageously (eq 2, 95−60%; see Experimental Section) from cyanophenols **7**, sodium azide, and boron trifluoride/ethyl ether in refluxing dimethylformamide.



7 **8**

Flash vacuum thermolyses of gaseous 5-(4-hydroxyphenyl)tetrazole (**9**, eqs 3−5) in various quartz-packed flow tubes at 620−650 °C/0.1−1.8 Torr are found to give in the indicated yields: tropone (**10**, 23−40%), benzaldehyde (**11**, 5−6%), and *o*-cresol (**12**, 5−8%) along with 4-cyanophenol (**13**, 30−53%), hydrogen azide (**14**), nitrogen, and other products.[3,4] Similarly, 5-(3-hydroxyphenyl)tetrazole (**15**, eqs 6−8) converts at 650−800 °C/0.1−1.5 Torr to **10** (1−5%), **12** (1%), 3-cyanophenol (**16**, 50−84%), **14**, nitrogen, and nonvolatiles.[3] At 650−710 °C/0.1−2.0 Torr 5-(2-hydroxyphenyl)tetrazole (**17**, eqs 9−11) collapses mainly to 2-cyanophenol (**18**, 60−90%) and **14**, **10**, **12**, phenol, and other volatiles are trace products (~1% each). The principal flash vacuum pyrolytic reactions of **9**, **15**, and **17** conducted as above are 1,3-dipolar reversions to **13**, **16**, and **18**, respectively, and to **14**. However, the processes of present interest, their reaction mechanisms, and their development are decompositions of **9**, **15**, and **17** to **10, 11**, and **12** as now discussed.



Thermolysis of a (hydroxyphenyl)tetrazole (**8**) is expected to generate the corresponding (hydroxyphenyl)carbene (**6**).[2] Of significance in the decompositions of **9** is that (4-hydroxyphenyl)carbene (**19**) appears to isomerize to (3-hydroxyphenyl)carbene (**21**) which converts to hydroxy(phenyl)carbene (**25**) via (2-hydroxyphenyl)car-

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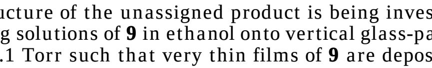
(1) (a) Joines, R. C.; Turna, A. B.; Jones, W. M. *Tetrahedron* **1969**, *91*, 7754. Schissel, P.; Kent, M. E.; McAdoo, D. J.; Hedaya, E. *J. Am. Chem. Soc.* **1970**, *92*, 2147. (c) Crow, W. D.; Wentrup, C. *Chem. Commun.* **1969**, *1387*. (d) Baron, W. J.; Jones, M., Jr.; Gaspar, P. P. *J. Am. Chem. Soc.* **1970**, *92*, 4739. (e) Brown, W. T.; Jones, W. J. *J. Org. Chem.* **1979**, *44*, 3090. (f) Vander Stouw, G. G.; Kraska, A. P.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 1655. (g) Tomioka, H.; Takesuji, K. *J. Org. Chem.* **1993**, *58*, 4196. (h) For an excellent summary of the products and various mechanisms of benzylidene rearrangements, see: Gasper, P. P.; Hsu, J.-P; Chari, S.; Jones, M., Jr. *Tetrahedron* **1985**, *41*, 1479.

(2) (a) Wentrup, C. *Tetrahedron* **1974**, *30*, 1301. (b) Wentrup, C. *J. Am. Chem. Soc.* **1976**, *98*, 1258.

(3) A. D. Golden and M. Jones, Jr., Princeton University, Princeton, NJ, have found that thermal carbenic decompositions of **9** and **15** under conditions and in equipment different from that of the present study yield phenol, tropone (**10**), and *o*-cresol (**12**). Upon learning that **12** is formed in major amounts in their experiments, we have reopened study of the behavior of **27**. We thank Professor Jones for informing us of the results from his laboratory.

(4) (a) Phenol (3−4%), benzoin, a solid having a molecular formula of $C_{14}H_{12}O_2$,[4b] and products of higher molecular weight are also formed in the present thermolyses of **9**. The phenol obtained does not result from loss of carbon monoxide from 4-hydroxybenzaldehyde possibly produced by reaction of **19** with oxygen always present during a flash vacuum pyrolysis experiment. Of particular interest is that phenol may be formed from **9** by hydrogen migration and *ipso* loss of carbon and nitrogen shown below.



(b) The structure of the unassigned product is being investigated. (c) On dropping solutions of **9** in ethanol onto vertical glass-packed tubes at 650 °C/0.1 Torr such that very thin films of **9** are deposited on the glass surfaces, thermolyses have been found to give **10** in up to 42% yields on small-scale along with phenol (3%), **12** (2%), and **13** (53%).

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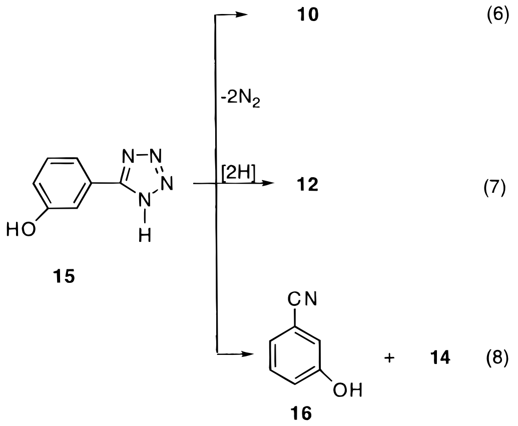

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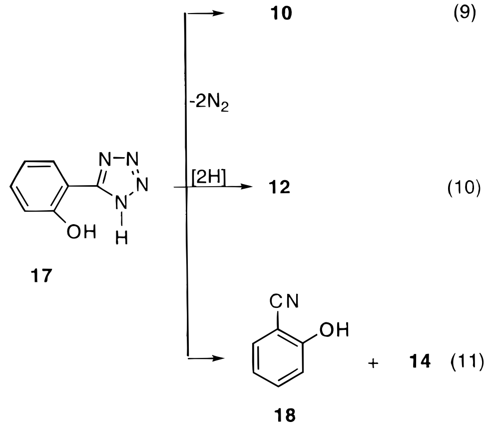

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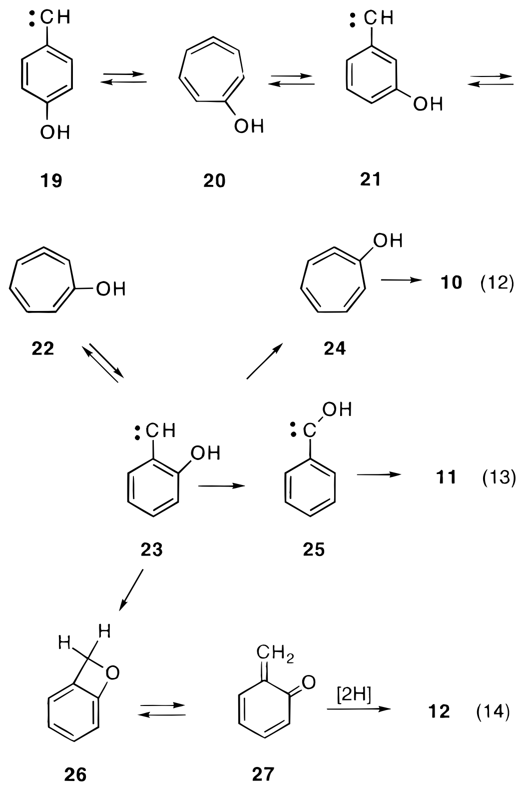
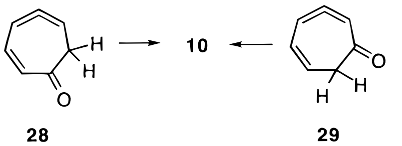
18

bene (**23**) by carbon-skeleton rearrangement processes as summarized in eq 13. The hydroxycycloheptatetraenes



presumed, **20, 22,** and **24,**[5] may be formed concertedly from **19**, **21**, and **23** or by rearrangements of their corresponding hydroxy[3.2.0]bicyclo-1,3,6-heptatriene (**2**, R = OH) and/or their hydroxy-2,4,6-cycloheptatrienylidene (**3**, R = OH) precursors. Hydrogen rearrangements in **24** and **25** then yield **10** (eq 12) and **11** (eq 13). Alternate thermodynamically-favorable routes to **10** from **19** are ketonizations of **6**, **20,** and **21** to cycloheptatrienones **28** and **29**, respectively, and then hydrogen migrations (eq 15).[6]



28 **29**

o-Cresol (**12**), as obtained from **9** (eq 4), possibly arises sequentially from **19** by multiple rearrangements to give **21** and then **23** (eq 13), ring-closure of **23** to benzooxetene (**26**, eq 14), and then formation and reduction of *o*-quinomethide (**27**, eq 14). The conversions of **15** and **17** to **27** are consistent with the proposed mechanism. Benzooxetene (**26**) is as yet unknown because of its ready isomerization to **27**. *o*-Quinomethide (**27**) has been isolated previously at −195 °C [7a] but trimerizes and tetramerizes rapidly on warming to chroman derivatives.[7b] In the present decompositions of **9**, **15**, and **17**, the source of the hydrogen for reduction of **27** to **12** (eq 14) has not been established. Among the likely routes for conversion of **9** to **12** are (1) addition of **9** or/and **13** to **27** and homolytic decomposition(s) of the 1,4-adducts to the *o*-cresoxy radical which abstracts hydrogen from **9**, **13**, **14**, or other sources in the reaction environment and (2) reduction by **9** and/or **14**. Similar sequences may be envisaged for conversions of **15** and **17** to **12**. Though as yet not understood, the ability of **27** to effect hydrogen abstraction to give **12** has been previously reported in thermolysis of chroman[7c] and photolysis of *trans*-2-cinnamylphenol.[7d] The details in the conversion(s) of **27** to **12** in appropriate thermolyses of **9**, **15**, and **17** are being further studied.[8]

Although the mechanisms of thermal decompositions of **6** are of interest, the method is of limited value for preparing tropones. Efforts are being made to develop other (hydroxyphenyl)carbene rearrangement methods for practical synthesis of **10**.[9] 4-Hydroxy-(α-trimethylsilyl)benzyl methyl ether (**34**), a readily handlable liquid prepared from 4-acetoxybenzyl acetate (**30**) as summarized in eq 16, is found to pyrolyze in preparative quantities in quartz flow chambers at 720 °C/3.5 Torr via **19** to give **10** (56−60%) and **11** (6%) as the major

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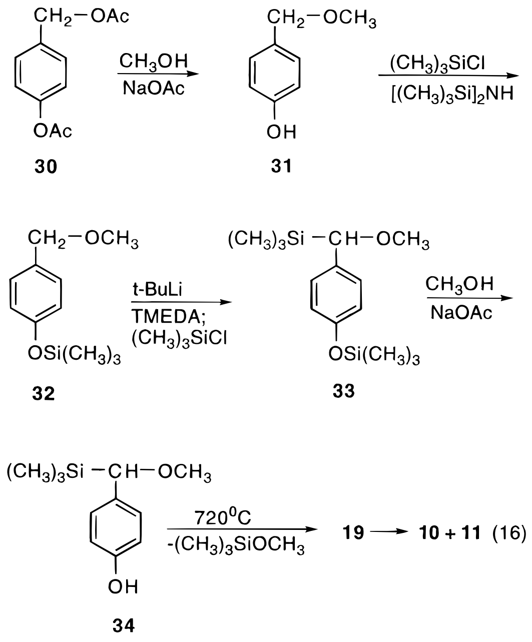
(5) (a) Various calculations have led to the conclusion that nonplanar 1,2,4,6-cycloheptatetraene is more stable than planar 1,2,4,6-cycloheptatetraene and 2,4,6-cycloheptatrienylidene.[5b−e] (b) Tyner, R. L.; Jones, W. M.; Ohrn, Y.; Sabin, J. R. *J. Am. Chem. Soc.* **1974**, *96*, 3765. (c) Wentrup, C.; Major, C.; Fleiter, R. *Helv. Chim Acta* **1972**, *55*, 2628. (d) Dewar, M. J. S.; Landman, D. *J. Am. Chem. Soc.* **1977**, *99*, 6179. (e) Radom, L.; Schaefer, H. F., III; Vincent, M. A. *Nouv. J. Chem.* **1980**, *4*, 411. (f) It is not yet clear whether there will be significant differences in the behaviors of hydroxy-2,4,6-heptatrienylidenes (**3**, R = OH) and their corresponding hydroxy-1,2,4,6-cycloheptatetraenes (**4**, R = OH).

(6) (a) Cycloheptatrienone **30** is more conjugated and thus may be more stable than is **29**. (b) Further, **20**−**22**, **28**, and **29** will be quite acidic at 600−800 °C and possibly isomerize to **10** by tautomeric processes.

(7) (a) McIntosh, C. L.; Chapman, O. L. *J. Chem. Soc., Chem. Commun.* **1971**, 771. (b) Gardner, P. D.; Sarrafizadeh, R.; Brandon, R. L. *J. Am. Chem. Soc.* **1959**, *81*, 5515. (c) Paul, G. C.; Gajewski, J. J. *J. Org. Chem.* **1993**, *58*, 5060. (d) Jimenez, M. S.; Marquez, F.; Miranda, M. A.; Tormes, R. *J. Org. Chem.* **1994**, *59* 197.

(8) Further references to the behavior of **27** have been summarized by Paul and Gajewski.[7c]

volatile products in the indicated yields. The method is much cleaner than pyrolysis of **8** and is being extended to practical synthesis of analogs and derivatives of **10**. Finally, the mechanistic principles in the thermal conversions of **34** to **10** and **11** are identical with those found for **9**.



Experimental Section

Melting points were determined in capillaries and are uncorrected. The ^{1}H NMR of all compounds of the present study are reported on the δ scale in parts per million from tetramethylsilane in CDCl$_3$. Elemental analyses were conducted by Micro Analyses, Wilmington, DE. All reagents and solvents were dried and purified, and subsequent reactions were conducted under argon when deemed necessary.

5-(2-Hydroxyphenyl)tetrazole (17). To 2-cyanophenol (**18**, 0.6 g, 5 mmol) and sodium azide (0.54 g, 8 mmol) in anhydrous dimethylformamide (15 mL) under argon was added boron trifluoride (0.10 g, 1.60 mmol) in ethyl ether (1.2 mL). The mixture was refluxed 24 h, concentrated under reduced pressure, cooled, diluted with water, neutralized, and filtered to separate the **17** that precipitated. The filtrate was diluted with water (5 mL). Acidification with concentrated hydrochloric acid to pH 2, storage (24 h), and separation gave additional **17**. The mother liquor, after vacuum concentration, addition of ethanol to precipitate the sodium chloride and excess sodium azide, evaporation to dryness, addition of water (5 mL) and dilute hydrochloric acid, and storage at 0−5 °C, yielded additional **17**. After crystallization from water, the combined **17** (0.72 g, 89%) melted at 225−226 °C, lit.[10] mp 221−222 °C: ^{1}H NMR (500 MHz, CD$_3$COCD$_3$) δ 3.0 (br, 1H, OH variable), 7.09 (dd, 1H, Ph-H$_4$), 7.14 (d, 1H, Ph-H$_3$), 7.47 (dd, 1H, Ph-H$_5$), 8.12 (d, 1H, Ph-H$_6$), 10.6 (br, 1H, NH); MS 162, 134, 119, 105, 91, 78, 64, 51; exact mass for C$_7$H$_6$N$_4$O, m/e (calcd) 162.0542, m/e (obsd) 162.0541. *Anal.* Calcd for C$_7$H$_6$N$_4$O: N, 34.55. Found: N, 34.96.

5-(3-Hydroxyphenyl)tetrazole (15). Reaction of 3-cyanophenol (**16**), sodium azide, and boron trifluoride etherate as for **17** yielded **15** (0.72 g, 88%): lit.[11] mp 214−216 °C[11]; ^{1}H NMR (500 MHz, CD$_3$COCD$_3$) δ 3.0 (br, 1H, OH variable), 7.05 (dd, 1H, Ph-H), 7.4 (dd, 1H, Ph-H), 7.56−7.61 (m, 2H, Ph-H), 9.1 (br, 1H, Ph-H), 15.7 (br, 1H, NH); MS 162, 134, 119, 107, 91, 79, 65; exact mass for C$_7$H$_6$N$_4$O, m/e (calcd) 162.0542, m/e (obsd) 162.0555. *Anal.* Calcd for C$_7$H$_6$N$_4$O: N, 34.55. Found: N, 34.22.

5-(4-Hydroxyphenyl)tetrazole (9). 4-Cyanophenol (**13**), sodium azide, and boron trifluoride etherate as for **17** gave **9** (0.44 g, 54%): mp 234−238 °C, lit.[10b,12] mp[12] 239−241 °C; ^{1}H NMR (500 MHz, CD$_3$COCD$_3$) δ 2.95 (br, 1H, NH), 7.02 and 7.95 (AB q, 4H, $J_{AB} = 11.5$ Hz), 10.1 (br, 1H, OH); MS 162, 134, 119, 107, 91, 79, 69, 65, 51; exact mass for C$_7$H$_6$N$_4$O, m/e (calcd) 162.0542, m/e (obsd) 162.0538. *Anal.* Calcd for C$_7$H$_6$N$_4$O: N, 34.55. Found: N, 34.39.

Pyrolysis of 9. The products of volatization of **9** (320 mg, 2 mmol) through a packed quartz tube (3 × 35 cm) at 1.8 mmHg at 620 °C were trapped at −78 °C. Addition of hexane (50 mL) to the pyrolysate and filtration gave 4-cyanophenol (**13**, 71 mg, 0.6 mmol, 30%), identified by comparison with an authentic sample. The filtrate was concentrated under reduced pressure at room temperature. Gas chromatographic analysis (7.5% QF-1 Chromosorb, 10 in. × 1/4 in. column, 140 °C) of the concentrate revealed the presence of benzaldehyde (**11**, ~6%), tropone (**10**), and *o*-cresol (**12**).

The concentrated solution was flash column-chromatographed on silica gel using 1:1 methylene chloride:hexane (400 mL), 3:1 methylene chloride:ethyl acetate (500 mL), and 1:1 methylene chloride:ethyl acetate (300 mL) as eluents. Separation and/or analyses of the products yielded: (1) **11** (10 mg, 0.096 mmol, 5%), identified by its IR absorption and conversion to authentic benzaldehyde (2,4-dinitrophenyl)hydrazone, (2) **10** (49 mg, 0.46 mmol, 23%), assigned by comparison of its R$_f$ value and IR absorption with an authentic sample, (3) **12** (5−8%) as identified chromatographically by comparison with an authentic sample, and (4) an unidentified red product (C$_{14}$H$_{12}$O$_2$, 120 mg) which is homogeneous by thin layer chromatography, has hydroxyl (OH, 3400 cm^{-1}) and weak carbon−carbon double bond IR absorptions, changes to dark brown with decomposition on heating, thin layer chromatography, or crystallization from ethanol, and exhibits ^{1}H NMR (CD$_3$COCD$_3$) at δ 3.2 (br s), 6.95, and 8.22−8.45 (br).[4]

Pyrolysis of 15. Thermolysis of **15** at 800 °C/1.5 Torr and product isolation as described for **9** yielded **10** (4−5%) and 3-cyanophenol (**16**, >50%) along with initial **15** (>25%) and involatile products. Similar results were obtained on volatization of **15** through glass-packed tubes at different temperature and pressures. On dropping solid **15** into vertical pyrolysis tubes at 650 °C/0.1 Torr, **10** (1%), **12** (1%), and phenol (1%) along with **16** (84%) were obtained.

Pyrolysis of 17. Flash vacuum decompositions of **17** at 650−710 °C at 1.5−2.0 Torr as for **9** gave **10** (~1%), **12** (~1%), 2-cyanophenol (**18**, 49−75%), phenol (~1%), and intractables along with **17** (up to 25% recovery). Such experiments were conducted at various temperatures and contact times. The principal reaction was always decomposition of **17** to **14** and **18**.

4-Acetoxybenzyl Acetate (30). Triethylamine (3 mL) was added to a solution of 4-hydroxybenzyl alcohol (1.24 g, 11.5 mmol), acetic anhydride (4.1 mL, 44 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 100 mg) in methylene chloride (50 mL). The mixture was stirred for 2.5 h, extracted with water, hydrochloric acid (2.4 N), and saturated aqueous sodium bicarbonate, and then dried over anhydrous potassium carbonate. Concentration of the extract, filtration through silica gel, elution with ethyl acetate:hexane (1:3), and evaporation of the eluents yielded **30** (1.95 g, 95%):[12] ^{1}H NMR (CDCl$_3$) δ 1.9 (s, 3H), 2.13 (s, 3H), 4.23 (s, 2H), 6.8−7.2 (AB q, 4H); IR (KBr, cm^{-1}) 1760, 1740 (>C=O); MS$^+$ calcd 208, MS$^+$ found 208.[13]

4-Hydroxybenzyl Methyl Ether (31). A mixture of **30** (14.9 g, 0.077 mol; prepared as above), anhydrous methanol (200 mL), and sodium acetate (5.7 g, 0.07 mol) was refluxed under argon for 3 days and then cooled. Concentration of the mixture, addition of water, neutralization with sodium bicarbonate,

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(9) Slow addition of the dry sodium salt of 4-hydroxybenzaldehyde (*p*-toluenesulfonyl)hydrazone to a vertical glass-packed column at 800 °C/0.1 Torr results in formation of phenol (49%), **10** (4−5%), **12** (4%), and less volatile products. The dry sodium salt of 2-hydroxybenzaldehyde (*p*-toluenesulfonyl)hydrazone at 650 °C/0.1 Torr yields phenol (39%), **10** (~1%), **12** (9%), and high molecular weight derivatives. These systems are based on generation of and decomposition diazo(4-hydroxyphenyl)methane and diazo(2-hydroxyphenyl)methane and are of interest because of formation of phenol rather than **10** and **12**.

(10) (a) Brower-Van Straaten, B.; Solinger, D.; Vande Westeringh, C.; Veldstra, H. *Recl. Trav. Chim.* **1958**, *77*, 1129. (b) Kaczmarek, J.; Smagowski, H.; Grzonka, Z. *J. Chem. Soc., Perkin Trans. 2* **1979**, 12, 1670.

(11) Carboni, B. Ger. Offen. DE 3, 427, 606, Feb 16, 1985.

(12) Antonowa, A.; Hauptmann, S. *Z. Chem.* **1976**, *16*(1), 17.

(13) Culbertson, H. M.; Woodbrey, J. C. *Anal. Chem.* **37**, *8*, 1034.

extraction with methylene chloride, distillation of the dried (Na_2SO_4) extract, and solidification of the distillate yielded **31** (8.9 g, 92%): mp 81−83 °C; lit.[14] mp 82−83 °C.

Methyl 4-(Trimethylsiloxy)benzyl Ether (32). A solution of **31** (2.76 g, 20 mmol), hexamethyldisilazane (4.2 mL, 20 mmol), and concentrated sulfuric acid (2 drops) was refluxed 4 h under nitrogen and cooled. The mixture, after addition of water and extraction with methylene chloride, was dried ($MgSO_4$) and concentrated. Kugelrohr distillation (80−85 °C, 4 mm) of the concentrate (4.15 g, 98%) yielded **32** as a colorless liquid: ^1H NMR (CCl_4) δ 0.01 (s, 9H), 3.3 (s, 3H), 4.31 (s, 2H), 6.74−7.16 (AB q, 4H); exact mass for $C_{11}H_{18}O_2Si$, *m/e* (calcd) 210.1076, *m/e* (obsd) 210.1072.

4-Hydroxy-α-(trimethylsilyl)benzyl Methyl Ether (34). *tert*-Butyllithium (3.8 g, 0.06 mol) in hexane was added to a solution of **32** (11.58 g, 0.055 mol) and tetramethylethylenediamine (9.7 g, 0.066 mol) in anhydrous ethyl ether (150 mL) at −78 °C. The green-yellow solution obtained was stirred at −78 °C for 45 min, and trimethylsilyl chloride (8.9 g, 0.08 mol) was added. After the mixture had been stirred at 0 °C for 14 h, water (50 mL) was added and the organic layer was separated, washed with water (3 × 50 mL) and a saturated sodium chloride solution (50 mL), and dried over magnesium sulfate. Removal of the solvent gave 4-(trimethylsiloxy-α-trimethylsilyl)benzyl methyl ether (**33**, 11.0 g, 71%) as a yellow oil usable without further purification.

A mixture of **33** (9.05 g, 0.032 mmol) and sodium acetate (4.5 g, 55 mol) in anhydrous methanol (50 mL) was stirred at room temperature for 12 h under argon, concentrated at reduced pressure, and cooled to give **34** (5.05 g, 75%) as a white solid: mp 88−91 °C; ^1H NMR ($CDCl_3$) δ 0.01 (s, 9H), 3.33 (s, 3H), 3.9 (s, 1H), 6.8−7.2 (AB q, 4H); MS 195, 179, 167, 151, 137, 120, 73; exact mass for $C_{11}H_{18}O_2S$, *m/e* (calcd) 210.1076, *m/e* (obsd) 210.1071.

Pyrolysis of 34. 4-Hydroxy-α-trimethylsilyl)benzyl methyl ether (**34**, 420 mg, 2 mmol) was volatilized at 740 °C/3.0−3.5 Torr through a packed quartz tube (3.5 × 30 cm) flushed with argon. The pyrolysate was trapped at −195 °C. While the vacuum system was being disconnected, the pyrolysate was blanketed with argon and hexanes (25 mL) were added. The mixture was concentrated under reduced pressure at room temperature and passed rapidly through a pad (2 in. × 2 in.) of silica gel using chloroform:hexanes (1:1) as eluent (100 mL). The pad was washed with ethyl acetate:methylene chloride (60:40). The chloroform:hexane fraction (QF-1 column at 100 °C) contained benzaldahyde (**11**, 12 mg, 6%). Tropone (**10**, 119 mg, 56%) was isolated upon concentration of the ethyl acetate:methylene chloride washings. The **10** obtained was identical (GC, MS, and IR) to an authentic sample. The pyrolysis can be scaled up satisfactorily.

Acknowledgment. We thank the National Science Foundation for support of this research.

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[14] Hayashi, H.; Oka, S. *Bull Inst. Chem. Res. Kyoto Univ.* **1974**, *52*(3), 514.