tography of the crude material (silica gel; 6:1 hexane–ether) gave the pure hydroxy ester in 67% yield: ^{1}H NMR δ 7.40–7.25 (m, 5 H), 5.16 (s, 2 H), 3.62 (t, 2 H), 2.38 (t, 2 H), 1.75–1.50 (m, 4 H), 1.30 (m, 10 H).

Diethyl Fumarate. Reduction of diethyl fumarate ozonide with 3.5 equiv of BH_3–DMS afforded ethyl glycolate (≥98 mol %) in 75% yield. No attempt was made to further purify this compound: ^{1}H NMR δ 4.25 (q, J = 7 Hz, 2 H), 4.17 (s, 2 H), 3.00 (br s, 1 H), 1.33 (t, J = 7 Hz, 3 H).

Methyl Oleate. Ozonolysis of methyl oleate and reduction of the ozonide with 4.0 equiv of BH_3–DMS gave a 1:1 mixture of 1-nonanol and methyl 10-hydroxydecanoate (≤2 mol % contaminants) in 96% yield.

Anethole. Ozonolysis of this compound and reduction of the ozonide with 4.0 equiv of BH_3–DMS gave a quantitative yield of crude *p*-methoxybenzyl alcohol. Column chromatography (silica gel; 19:1 hexane–ether) afforded 78% of the pure alcohol:[12] ^{1}H NMR δ 7.31 (d, J = 9 Hz, 2 H), 6.89 (d, J = 9 Hz, 2 H), 4.63 (s, 2 H), 3.83 (s, 3 H), 1.68 (s, 1 H).

***trans*-Stilbene.** Reduction of *trans*-stilbene ozonide with 4.0 equiv of BH_3–DMS gave pure (100 mol %) benzyl alcohol[12] in 90% yield: ^{1}H NMR δ 7.38–7.28 (m, 5 H), 4.70 (s, 2 H), 1.73 (s, 1 H).

Cyclohexene. Reduction of cyclohexene ozonide with 4.0 equiv of BH_3–DMS afforded 1,6-hexanediol (97 mol %; mp 39–41 °C) in 95% yield. Recrystallization of the crude material from ether afforded 1,6-hexanediol,[3d] mp 42.0–43.0 °C, in 81% yield: ^{1}H NMR δ 3.66 (t, J = 6.3 Hz, 4 H), 1.65 (s, 2 H), 1.63–1.51 (m, 4 H), 1.48–1.33 (m, 4 H).

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Registry No. 1, 143-08-8; 2, 20525-37-5; 3, 124-19-6; 4, 2640-94-0; 5, 96620-40-5; 6, 112-47-0; 7, 14811-73-5; BH_3-DMS, 13292-87-0; *p*-anisyl alcohol, 105-13-5; benzyl alcohol, 100-51-6; benzyl 10-hydroxydecanoate, 67853-00-3; ethyl glycolate, 623-50-7; 1,6-hexanediol, 629-11-8; 1-decene, 872-05-9; methyl 10-undecenoate, 111-81-9; methyl oleate, 112-62-9; anethole, 104-46-1; *trans*-stilbene, 103-30-0; benzyl 10-undecenoate, 106262-52-6; diethyl fumarate, 623-91-6; cyclohexene, 110-83-8.

Facile Synthesis of Trifluoro- and Hexafluoroisopropyl Halides

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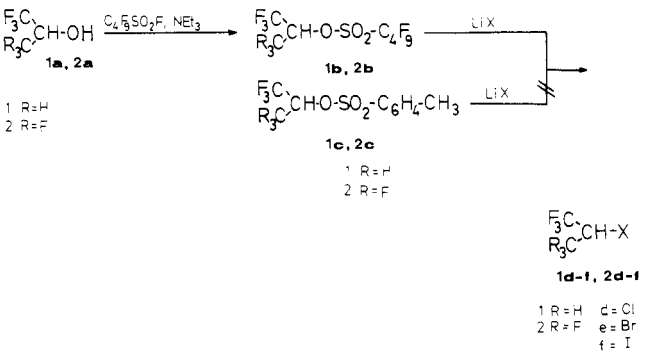
We report here about a facile synthesis of trifluoro- and hexafluoroisopropyl halides **1d–f** and **2d–f** by a simple nucleophilic substitution at the secondary carbon atom of the corresponding nonafluorobutanesulfonates (nonaflates) **1b** and **2b**.

The methods reported hitherto for the synthesis of tri- and hexafluoroisopropyl chlorides, bromides, and iodides **1d–f** and **2d–f** are summarized briefly. The general application of these methods in common laboratories is limited owing to the expenditure of the reaction conditions, the toxicity of the chemicals used, or the difficult accessibility of the starting materials.

A method for preparing **1d–f** and **2d–f** is, e.g., the direct halogenation of 1,1,1-trifluoropropane to give the halides **1d,e**, formed as a mixture of mono- and dihalotrifluoropropanes, which is difficult to separate.[1-6] **1d** is also



synthesized by treating 1,1,1,2-tetrachloropropane with HF and HgO.[2,7] **1d** and **1e** are prepared[8,9] from α-chloro(or α-bromo)propionic acid and SF_4. 1,1,1-Trifluoroisopropyl iodide (**1f**) has not been described yet. Chlorination, bromination, or iodation of the potassium salt of the hexafluoroisobutyric acid[10] yields the 1,1,1,3,3,3-hexafluoroisopropyl halides **2d–f** in good yields. The acid, however, is not commercially available and requires the application of the toxic octafluoroisobutene.[11] (Basic cleavage of an α-halohexafluoroisopropyl pentafluoroethyl ketone[12,13] and treatment of the α-bromohexafluoroisobutyramide with KCN[14] is a tedious synthetic route due to the difficult preparation of the educts). A direct synthesis of **2d,e** from 1,1,1,3,3,3-hexafluoro-2-propanol (**2a**) and phosphorus pentachloride,[15] phosphorus tribromide/bromine,[15] or dibromotriphenylphosphorane[16] respectively yields the products impure and in small quantities. **2d** is produced as one of four differently substituted chlorofluoropropanes,[17,18] from 3,3,3-trifluoro-1,1,2-trichloropropene and HF in the presence of $SbCl_5$; **2d** is formed by reacting 1,1,3,3,3-pentafluoro-2-chloropropene with KF in formamide.[19] (After HCl elimination, heptachloropropane reacts with KF to give the same product[20]). **2e** is obtained by the reaction of bromomalonic

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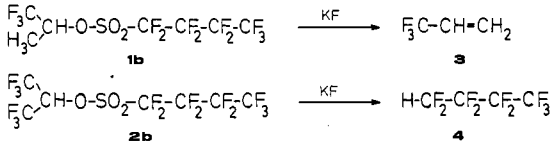
acid with SF_4[21] or by direct bromination of 1,1,1,3,3,3-hexafluoropropane[6] or bis(hexafluoroisopropyl)mercury.[22,23]

The reaction of the nonflates **1b** and **2b** with either LiCl, LiBr, or LiI respectively under the reaction conditions given in the Experimental Section yields the corresponding halides **1d–f** and **2d–f** almost quantitatively. After completion of the reaction, the formed halides are distilled off directly from the reaction mixture through a Spaltrohr column. Thereby they are isolated virtually without impurities.

The best polar solvent we found is acetylacetone. When DMSO is used, the formation of **1d–f** and **2d–f** is accompanied by the evolution of major amounts of dimethyl sulfide.

Attempts to prepare the corresponding halides **1d–f** and **2d–f** by reacting the tosylates **1c** and **2c** with LiCl, LiBr, and LiI respectively in a polar medium afforded the halides either in very low yields or not at all. For example, 1,1,1-trifluoroisopropyl tosylate (**1c**) reacted with sodium iodide in acetylacetone under reflux for 20 h to give only traces of 1,1,1-trifluoroisopropyl iodide (**1f**). The corresponding nonaflate **1b**, however, was completely converted already at room temperature. 1,1,1,3,3,3-Hexafluoroisopropyl tosylate (**2c**), upon heating to 140 °C in acetylacetone, did not react with sodium iodide and was reisolated without decomposition.

The nonaflates **1b** and **2b** are easily prepared in high yields by reaction of trifluoro-2-propanol **1a** and hexafluoro-2-propanol **2a** respectively with nonafluorobutanesulfonyl fluoride and triethylamine in dichloromethane. Both nonaflates are remarkably stable; they are purified by distillation.



1b **3** **2b** **4**

The corresponding fluoroisopropyl fluorides could not be prepared by treatment of the trifluoro- and hexafluoroisopropyl nonaflates **1b** and **2b** with, e.g., KF under the same conditions. When **1b** is treated with KF, mainly 3,3,3-trifluoropropene (**3**) is obtained by an elimination reaction. Under the same conditions, hexafluoroisopropyl nonaflate **2b** is cleaved at the carbon–sulfur bond to give 1-hydryl-*F*-butane (**4**).

Experimental Section

1,1,1-Trifluoro-2-propanol (**1a**) is commercially available from Ventron GmbH (Alpha) or is easily prepared according to the published procedure of Nad et al.,[25] followed by spinning-band distillation. 1,1,1,3,3,3-Hexafluoro-2-propanol (**2a**) was purchased from Fluka AG. We thank Bayer AG for the generous gift of nonafluorobutanesulfonyl fluoride. Nonafluorobutanesulfonyl fluoride [also purchasable from Ventron GmbH (PCR Inc.)] and acetylacetone were purified by simple distillation. The inorganic salts were dried at 180 °C/0.1 mbar for 12 h.

1,1,1-Trifluoroisopropyl Nonaflate (1b). A stirred solution of 1,1,1-trifluoro-2-propanol (**1a**) (13.7 g, 120 mmol) in 40 mL of absolute dichloromethane is cooled to −40 °C under an N_2 atmosphere, and triethylamine (12.1 g, 120 mmol) is added through a syringe. After the addition of nonafluorobutanesulfonyl fluoride (49.8 g, 165 mmol) through a dropping funnel, the reaction mixture is allowed to warm to room temperature and is stirred overnight. The layers are separated, the dichloromethane phase is washed with a small amount of nonafluorobutanesulfonyl fluoride, and the nonafluorobutanesulfonyl fluoride of the combined phases is removed at room temperature under aspirator pressure by using a rotary evaporator. Distillation of the residue under reduced pressure yields 41.8 g (88%) of pure **1b** (Table I).

1,1,1-Trifluoroisopropyl Tosylate (1c). 1,1,1-Trifluoro-2-propanol (**1a**) (5.7 g, 50 mmol) and benzyltriethylammonium chloride (0.5 g, 2.2 mmol) are added to a 1:1 emulsion of toluene and 30% aqueous sodium hyroxide. Toluenesulfonyl chloride (9.6 g, 50 mmol), dissolved in toluene, is introduced dropwise with vigorous stirring. After 3 days, the organic layer is separated and neutralized, and toluene is removed by rotary evaporation. Distillation of the crude product under reduced pressure affords the pure tosylate (11.6 g, 86%). Formation of **1c** is accelerated by the phase-transfer catalyst.[26]

1,1,1-Trifluoroisopropyl Chloride (1d). A mixture of 1,1,1-trifluoroisopropyl nonaflate (**1b**) (11.9 g, 30 mmol) and excess lithium chloride (5.1 g, 120 mmol) in acetylacetone (100 mL) is placed in a round-bottomed flask equipped with a reflux condenser cooled to −20 °C. After heating under reflux for 16 h, the formed halide is distilled off directly from the reaction mixture through a Spaltrohr column into a flask cooled in a dry ice–acetone bath: complete conversion; yield of pure isolated **1d**, 3.3 g, 83%.

1,1,1-Trifluoroisopropyl Bromide (1e). A mixture of 1,1,1-trifluoroisopropyl nonaflate (**1b**) (11.9 g, 30 mmol) and lithium bromide (10.4 g, 120 mmol) in acetylacetone (100 mL) is stirred at room temperature for $2^1/_2$ days (complete conversion), followed by the usual Spaltrohr distillation (yield 4.8 g, 90%).

1,1,1-Trifluoroisopropyl Iodide (1f). To 1,1,1-trifluoroisopropyl nonaflate (**1b**) (11.9 g, 30 mmol) in acetylacetone (100 mL) is added sodium iodide (18.0 g, 120 mmol), and the reaction mixture is stirred at room temperature for $2^1/_2$ days (complete conversion). Spaltrohr distillation gives pure **1f** (6.2 g, 92%).

1,1,1,3,3,3-Hexafluoroisopropyl nonaflate (2b) is prepared from 1,1,1,3,3,3-hexafluoro-2-propanol (**2a**) as described for **1b**, to give **2b** in 83% yield.

1,1,1,3,3,3-Hexafluoroisopropyl tosylate (2c) is prepared from **2a** similarly to 1c: yield 66%.

1,1,1,3,3,3-Hexafluoroisopropyl Chloride (2d). Hexafluoroisopropyl nonaflate (**2b**), 12-crown-4, and lithium chloride (molar ratio 5:1:20) are reacted in acetylacetone at 130 °C for 16 h, using equipment similar to that employed to prepare **1d**: complete conversion; yield of pure **2d** after distillation 78%.

1,1,1,3,3,3-Hexafluoroisopropyl bromide (2e) is obtained by reacting 1,1,1,3,3,3-hexafluoroisopropyl nonaflate (**2b**), 12-crown-4, and lithium bromide (molar ratio 5:1:20) in acetylacetone at 130 °C for 20 h, using equipment as described for the preparation of **1d** (complete conversion). Spaltrohr distillation affords pure **2e** (yield 81%).

1,1,1,3,3,3-Hexafluoroisopropyl iodide (2f) is obtained in 88% yield from 1,1,1,3,3,3-hexafluoroisopropyl nonaflate (**2b**) and sodium iodide (molar ratio 1:4) in acetylacetone by heating the mixture at 110 °C for 16 h (complete conversion), followed by Spaltrohr distillation.

3,3,3-Trifluoropropene (3). A flask containing acetylacetone is charged with 1,1,1-trifluoroisopropyl nonaflate (**1b**), 18-crown-6, and potassium fluoride (molar ratio 5:1:20). The product formed by heating the mixture at 100–140 °C for 2–4 h is distilled directly during the reaction through a condenser cooled to −10 °C into a dry ice–acetone trap (yield 80%).

1-Hydryl-*F*-butane (4) is formed in 60–70% yield from 1,1,1,3,3,3-hexafluoroisopropyl nonaflate (**2b**) by the same procedure as described for **3**.

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Table I. Properties and Spectral Data of the Prepared Compounds[a] 1–4

no.	formula	bp,[b] °C (mbar)	IR,[c] cm^{-1}	^1H NMR ($CDCl_3$):[d] δ; J, Hz	^{13}C NMR ($CDCl_3$):[d] δ; J, Hz	^{19}F NMR ($CDCl_3/CCl_3F$):[e] δ; J, Hz	MS:[f] M^+, EI, 70 eV, 200 °C
1b	$C_7H_4F_{12}O_3S$	61.5–62.0 (30)	3002, 1464–1012, 946, 878, 798, 739, 702, 653	1.63 (d, 3 H, J = 6.7), 5.12 (sept, 1 H, J = 6.1)	13.9 (s, CH_3), 79.5 (q, J = 36, CH), 94.3–136.7 (m, C_4F_9), 122.6 (q, J = 279, CF_3)	–126.4, –121.4, –111.0 (3 m, 3 × 2 F), –81.3 (t, 3 F, J = 9.9), – 79.5 (ps, 3 F)	396[g]
1c	$C_{10}H_{11}F_3O_3S$	156.5–157.0 (30)	3066–2928, 1598, 1494, 1458–1021, 940, 824, 793, 706, 686, 662	1.42 (d, 3 H, J = 6.6), 2.42 (s, 3 H), 4.81 (sept, 1 H, J = 6.3), 7.34 (d, 2 H, J = 8.4), 7.77 (d, 2 H, J = 8.4)	14.2 (s, $CHCH_3$), 21.3 (s, $C_6H_4CH_3$), 73.1 (q, J = 35, CH), 122.9 (q, J = 280, CF_3), 127.8, 129.9, 132.9, 145.6 (4 s, C_6H_4)	–63.6 (d, J = 5.9)	268
1d	$C_3H_4ClF_3$	30[7]	3014, 3006, 1460–991, 824, 739, 652	1.63 (d, 3 H, J = 6.9), 4.20 (sept, 1 H, J = 6.7)	17.6 (s, CH_3), 52.5 (q, J = 35, CH), 124.6 (q, J = 277, CF_3)	–65.5 (d, J = 6.4)	134, 132
1e	$C_3H_4BrF_3$	48.4–49[6]	3007, 3002, 1458–982, 687, 665	1.77 (d, 3 H, J = 7.0), 4.18 (sept, 1 H, J = 7.0)	18.6 (s, CH_3), 40.6 (q, J = 34, CH), 124.4 (q, J = 276, CF_3)	–67.6 (d, J = 6.8)	178, 176
1f	$C_3H_4F_3I$	73.7–73.9 (980)	2989, 2941, 1452–974, 649	1.94 (d, 3 H, J = 7.1), 4.16 (sept, 1 H, J = 7.5)	13.9 (q, J = 33, CH), 21.2 (d, CH_3), 124.8 (q, J = 276, CF_3)	–70.8 (d, J = 7.8)	224
2b	$C_7HF_{15}O_3S$	46.5–47.5 (30)	2984, 1443–1011, 908, 878, 847, 822, 796, 746, 732, 702, 691, 653	5.29 (sept, J = 5.2)	74.9 (sept, J = 37, CH), 94.3–138.1 (m, C_4F_9), 119.2, 119.3 (2 q, J = 282, 2 × CF_3)	–126.4, –121.1, –109.1 (3 m, 3 × 2 F), –81.4 (t, 3 F, J = 9.6), –73.6 (d, 6 F, J = 4.4)	283 ($C_4F_9SO_2^+$)
2c	$C_{10}H_8F_6O_3S$	133.5–134.0 (30); mp 41–42	3065, 2968, 1598, 1452–1072, 1021, 908, 888, 820, 800, 739, 708, 697, 674	2.45 (s, 3 H), 5.25 (sept, 1 H, J = 5.7), 7.37 (d, 2 H, J = 8.5), 7.80 (d, 2 H, J = 8.5)	21.0 (s, CH_3), 72.0 (sept, J = 36, CH), 120.1, 120.2 (2 q, J = 283, 2 × CF_3), 128.1, 130.2, 132.0, 146.9 (4 s, C_6H_4)	–68.9 (d, J = 5.6)	322
2d	C_3HClF_6	14–16[10]	2996, 1362–1115, 903, 822, 728, 679	4.52 (sept, J = 5.9)	54.8 (sept, J = 36, CH), 121.1, 121.2 (2 q, J = 281, 2 × CF_3)	–71.0 (d, J = 5.8)	188, 186
2e	C_3HBrF_6	32.5–33[10]	3005, 1359–1113, 892, 875, 784, 725, 677	4.50 (sept, J = 6.3)	41.9 (sept, J = 35, CH), 121.3, 121.4 (2 q, J = 280, 2 × CF_3)	–67.6 (d, J = 6.9)	232, 230
2f	C_3HF_6I	58[10]	2994, 1464–1097, 948, 861, 742, 720, 671	4.68 (sept, J = 7.1)	15.4 (sept, J = 34, CH), 121.9, 122.1 (2 q, J = 278, 2 × CF_3)	–65.2 (d, J = 7.0)	278
3	$C_3H_3F_3$	–22[4]	1437, 1294, 1285, 1172, 1023, 980, 964	5.54–6.24 (m)	123.1 (q, J = 269, CF_3), 123.2 (q, J = 7, CH_2), 126.6 (q, J = 35, CH)	–67.0 (d, J = 4.2)	96[h]
4	C_4HF_9	14[24]	3006, 1373–1088, 1035, 1002, 972, 922, 818, 744, 668	6.02 (tt, J = 51.8 + 5.0)	105.1–112.7 (m, 2 × CF_2), 107.7 (tt, J = 254 + 32, CF_2H), 117.3 (qt, J = 287 + 33, CF_3)[e]	–138.2 (dm, 2 F, J = 49.4), –131.0, –128.6 (2 m, 2 × 2 F), –82.1 (t, 3 F, J = 8.8)	219[h] ($C_4F_9^+$)

[a] Satisfactory analytical data (±0.1 for C, H) were obtained for the new compound **1f**. **1b** and **2b** only gave satisfactory H (±0.0%), F (±0.4%), and S (±0.2%) analysis (C = –2.5%). [b] In each case for which the boiling point agrees with the published value, the pertinent literature is cited. The boiling points of **3** and **4** have not been reexamined. [c] Recorded on a Perkin-Elmer 398 infrared spectrophotometer [**1b,c**, **2b,c** (liquid film)] and a Bruker IFS 48 instrument [**1d–f**, **2d–f**, **3**, **4** (gas)]. [d] Obtained on a Bruker WH 90 instrument (90 MHz for ^1H, 22.63 MHz for ^{13}C), unless otherwise stated. [e] Obtained on a Bruker WM 400 instrument (100 MHz for ^{13}C, 376.31 MHz for ^{19}F). [f] Taken on a Varian MAT 711 instrument. [g] M^+ peak was observed in an extremely low intensity. [h] GC/MS analysis was done on a Hewlett-Packard 5890A/MSD 5970 instrument.

Registry No. **1a**, 374-01-6; **1b**, 118334-94-4; **1c**, 6189-13-5; **1d**, 421-47-6; **1e**, 421-46-5; **1f**, 118334-95-5; **2a**, 920-66-1; **2b**, 118334-96-6; **2c**, 67674-48-0; **2d**, 431-87-8; **2e**, 2252-79-1; **2f**, 4141-91-7; **3**, 677-21-4; **4**, 375-17-7; $C_4F_9SO_2F$, 375-72-4; toluenesulfonyl chloride, 98-59-9.

Synthesis of Substituted Benzocyclobutenediones

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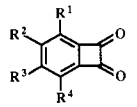
Introduction

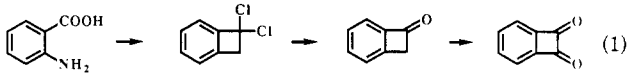
Benzocyclobutenediones **1** are proving to be useful intermediates for the controlled synthesis of complex organics.[2] Although a number of methods describing synthetic approaches to substituted and unsubstituted benzocyclobutenediones have been published,[2a,3] none to date allow the general synthesis of substituted benzocyclobutenediones in a simple, straightforward fashion. Our interest in the organic and organometallic chemistry of cyclobutenediones and benzocyclobutenediones[2h-n,v,w,4] mandated that we find a practical method for the construction of these strained-ring compounds. We recently disclosed, in detail, our procedures used for the synthesis of substituted cyclobutenediones,[5] and we now describe a simple preparation of substituted benzocyclobutenediones.



1

Results and Discussion

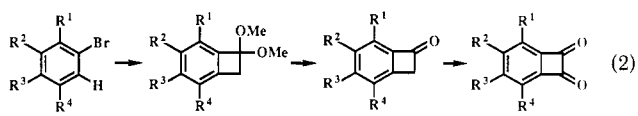
We have previously described a very practical route to the parent benzocyclobutenedione **1**, R^1–R^4 = H, that proceeded by the double benzylic bromination of benzocyclobutenone with *N*-bromosuccinimide (NBS) followed by acid-catalyzed hydrolysis of the geminal dibromo group.[3j,m] Benzocyclobutenone (**2**) was readily available from anthranilic acid by routine conversion to benzyne and trapping with vinylidene chloride followed by hydrolysis of the geminal dichloride (eq 1).[6] Utilization of this



(1)

2

synthetic sequence for the preparation of substituted benzocyclobutenediones was not considered practical because it required the synthesis of substituted anthranilic acids, a task that would diminish the convenience of the chemistry.[7] However, Stevens and Bisacchi had shown that 1,1-dimethoxyethylene participated in a [2 + 2] reaction with benzynes generated by the $NaNH_2$-induced dehydrobromination of bromobenzenes **3**, and after hydrolysis of the intermediate benzocyclobutenone ketals **4**, moderate to very good yields of substituted benzocyclobutenones **5** were obtained.[8] We simply repeated and extended the Stevens and Bisacchi chemistry and then introduced the α-diketone moiety of the benzocyclobutenone through the NBS route mentioned above. This chemistry provided a simple and straightforward method for the synthesis of substituted benzocyclobutenediones **1** (eq 2).



(2)

3 **4** **5** **1**

During the 1,1-dimethoxyethylene trapping of benzyne generated by dehydrohalogenation of bromobenzenes with $NaNH_2$, Stevens and Bisacchi observed an unexplained induction period to the reaction that could vary from 0.5 to several hours, even within multiple runs of the same system. In our early attempts to repeat some of the results of Stevens and Bisacchi, we noticed a similar variability in the benzyne reaction. After some study, we were able to correlate the occurrence of the induction period with the purity of the $NaNH_2$. A freshly opened jar of commercially available $NaNH_2$ always reacted without an in-

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