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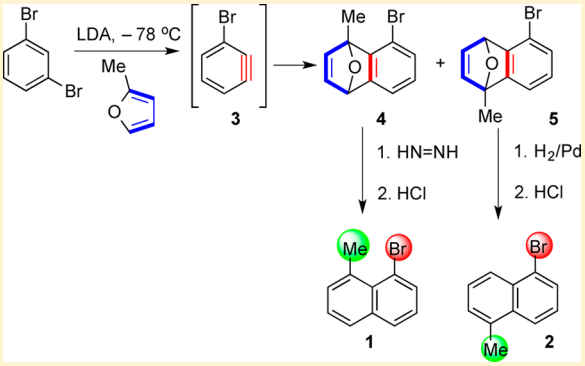
Syntheses of 1-Bromo-8-methylnaphthalene and 1-Bromo-5-methylnaphthalene

Evans O. Onyango, Anne R. Kelley, David C. Qian, and Gordon W. Gribble*

Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755-3564, United States

Supporting Information

ABSTRACT: The Diels–Alder reaction between 2-methylfuran and 3-bromobenzyne (**3**), which was generated under mild conditions from 1,3-dibromobenzene and lithium diisopropylamide (LDA), gives a mixture of regioisomeric 1,4-dihydro-1,4-epoxynaphthalenes **4** and **5**. A subsequent two-step deoxygenation affords the corresponding 1-bromo-8-methylnaphthalene (**1**) and 1-bromo-5-methylnaphthalene (**2**) in high yields.



In connection with a synthesis project, we needed sufficient quantities of pure 1-bromo-8-methylnaphthalene (**1**) and 1-bromo-5-methylnaphthalene (**2**) (Figure 1). Because the literature procedures[1−6] are either cumbersome or have low yields, and direct bromination of 1-methylnaphthalene leads mainly to 1-bromo-4-methylnaphthalene or 1-(bromomethyl)-naphthalene depending on the reaction conditions,[7,8] we employed the method described herein to achieve a practical synthesis of **1** and **2**. Thus, on the basis of our earlier studies of the Diels–Alder cycloaddition of 3-fluorobenzyne with 2-alkylfurans,[9] we anticipated that 3-bromobenzyne (**3**) would behave similarly in an approach to obtain desired isomeric naphthalenes **1** and **2**.

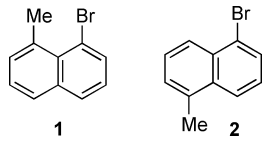
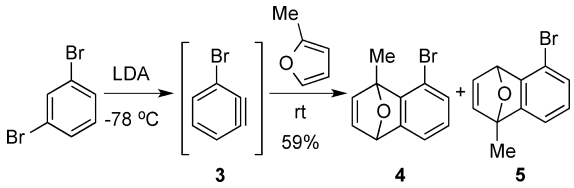


Figure 1.

As shown in Scheme 1, treatment of commercially available 1,3-dibromobenzene with lithium diisopropylamide (LDA) at −78 °C generated the transient 3-bromobenzyne (**3**), which upon warming to ambient temperature in the presence of excess 2-methylfuran was trapped to give 59% yield of a 3:2 (^{1}H NMR) mixture of separable 1,4-dihydro-1,4-epoxynaphthalenes **4** and **5**. Flash column chromatography followed by recrystallization from hexanes afforded **4** as white crystals and **5** as a yellow oil. The structures of these regioisomers were distinguished by NMR spectroscopy and by subsequent conversion to the respective naphthalenes (vide infra). The observed regioselectivity slightly favoring *syn*-cycloadduct **4** was consistent with our earlier studies.[9] This method is reproducible and was utilized to prepare multigram quantities of **4** and **5**.

Scheme 1



Hydrogenation of *syn*-cycloadduct **4** with hydrogen over Pd/C was not without incident (Scheme 2). Somewhat surprisingly, our initial attempts achieved direct deoxygenation of **4** to the desired 1-bromo-8-methylnaphthalene (**1**) instead of the expected epoxy naphthalene **6**. However, we also observed reductive debromination to give 1-methylnaphthalene (**7**). Analysis of a reaction aliquot by TLC and ^{1}H NMR showed that hydrogenation of the double bond occurs very rapidly to furnish **6**, which slowly dehydrates to **1** and is then further reductively debrominated to **7** upon prolonged hydrogenation. By monitoring the reaction by TLC, we could stop it after complete hydrogenation of the double bond in **4** to obtain a mixture consisting mainly of **6**, a small amount of **1**, and a trace of **7**. Acid-catalyzed dehydration of this mixture followed by recrystallization from hexanes gave **1** (65% yield for two steps) as colorless crystals, consistent with the known 1-bromo-8-methylnaphthalene.[1] Similarly, catalytic hydrogena-

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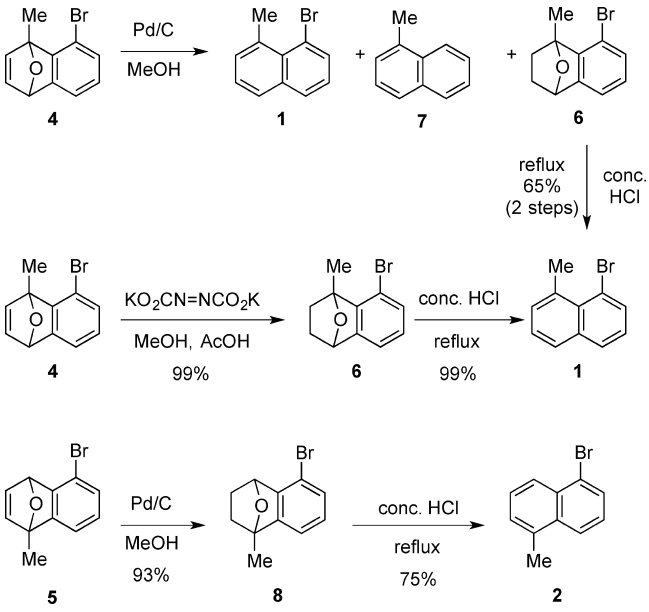
Scheme 2



tion of **5** to **8** and subsequent acid-catalyzed dehydration gave the known 1-bromo-5-methylnaphthalene (**2**),[10] a sequence that proceeded excellently without reductive debromination. Because the reductive debromination involving **4** lowered the overall yield of **1**, we chose a different reduction protocol. Thus, treatment of a methanol solution of **4** with dipotassium azodicarboxylate (PADA)[11] and glacial acetic acid at room temperature, which generates diimide, afforded **6** in 99% yield in less than 10 min. Dehydration in refluxing concentrated HCl gave 1-bromo-8-methylnaphthalene (**1**) in 99% yield.

The simplicity and scalability of these twin reaction sequences provide a useful alternative to the existing methods for the preparation of these two naphthalenes. Our results also showcase the generality and utility of our earlier studies on the regioselective Diels–Alder reaction between 3-halobenzynes with 2-alkylfurans to afford substituted naphthalenes.

EXPERIMENTAL SECTION

The general supplemental methods are provided in the Supporting Information.

8-Bromo-1-methyl-1,4-dihydro-1,4-epoxynaphthalene (4) and 5-Bromo-1-methyl-1,4-dihydro-1,4-epoxynaphthalene (5). To a solution of 1,3-dibromobenzene (22 g, 0.093 mol) in Et_2O (120 mL) at −78 °C was added LDA (2 M in THF; 49 mL, 0.098 mol) dropwise. The mixture was stirred for 1 h at −78 °C, treated dropwise with 2-methylfuran (17.2 g, 0.209 mol), and allowed to warm to room temperature overnight. The cooled reaction mixture was quenched with ice water and extracted twice with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to yield an orange oil. The crude mixture was purified via silica gel chromatography (60:1 hexanes/ethyl acetate) to afford **4** and **5** (13 g, 59%) as yellow-orange oils. The isomers were further separated by crystallization from hexanes.

8-Bromo-1-methyl-1,4-dihydro-1,4-epoxynaphthalene (4). Colorless crystalline solid; mp 41–42 °C; R_f = 0.28 (15:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, J = 6.95 Hz, 1H), 7.07 (dd, J = 8.2, 0.55 Hz, 1H), 7.02 (dd, J = 5.4, 1.7 Hz, 1H), 6.84–6.79 (m, 2H), 5.60 (d, J = 1.85 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.7, 149.5, 145.5, 144.7, 130.1, 127.1, 118.8, 114.6, 91.8, 81.7, 17.5; IR (NaCl) ν 1577, 1448, 1125, 1076, 892, 841, 771, 741, 713 cm^{-1}; HRMS (EI) calcd for $C_{11}H_9BrO$ $[M]^+$ 235.9837, found 235.9831.

5-Bromo-1-methyl-1,4-dihydro-1,4-epoxynaphthalene (5). Yellow oil; R_f = 0.33 (15:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09–7.08 (m, 2H), 7.06 (dd, J = 8.05, 0.6 Hz, 1H), 6.87 (dd, J = 8.2, 6.95 Hz, 1H), 6.81 (d, J = 5.45 Hz, 1H), 5.74 (d, J = 1.85 Hz, 1H), 1.92 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.0, 151.1, 145.9, 143.7, 128.1, 127.0, 117.5, 114.2, 90.4, 82.1, 15.3; IR (NaCl) ν 1585, 1449, 1382, 1302, 1069, 972, 857, 766, 714, 646 cm^{-1}; HRMS (EI) calcd for $C_{11}H_9BrO$ $[M]^+$ 235.9837, found 235.9836.

1-Bromo-8-methylnaphthalene (1). To a solution of **4** (150 mg, 0.633 mmol) in CH_2Cl_2/MeOH (1:1; 6 mL) was added 10% Pd–C (66.2 mg, 0.0633 mmol). The mixture was stirred vigorously at room temperature under H_2 until TLC showed the absence of starting material. The mixture was filtered through Celite and concentrated *in vacuo* to yield an orange oil. Proton NMR revealed the crude product to be a mixture of **1**, **6**, and **7**. This crude material was refluxed with concentrated hydrochloric acid (3 mL) overnight. The cooled reaction mixture was quenched with ice water and extracted twice with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give crude material. Recrystallization from hexanes gave **1** as a colorless crystalline solid (91 mg, 65%); mp 77–78 °C [lit.[2] mp 77–78 °C]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, J = 7.4, 1.1 Hz, 1H), 7.77 (dd, J = 8.1, 0.78 Hz, 1H), 7.71 (dd, J = 7.0, 2.3 Hz, 1H), 7.37–7.33 (m, 2H), 7.22–7.20 (m, 1H), 3.13 (s, 3H), which is in agreement with that reported.[1]

8-Bromo-1-methyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (6). To a solution of **4** (100 mg, 0.422 mmol) in MeOH (5 mL) was added potassium azodicarboxylate (248 mg, 1.28 mmol). The mixture was stirred while a solution of glacial acetic acid (0.2 mL) in MeOH (3 mL) was added dropwise. The crude mixture was treated with water and extracted twice with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to afford 8-Bromo-1-methyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (**6**) as a pale yellow solid in quantitative yield, which was used in the next step without further purification; mp 68–70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (dd, J = 8.05, 0.7 Hz, 1H), 7.14 (d, J = 7.15 Hz, 1H), 7.00 (dd, J = 8.0, 7.2 Hz, 1H), 5.29 (d, J = 5.1 Hz, 1H), 2.24–2.18 (m, 1H), 2.00 (s, 3H), 1.79–1.74 (m, 1H), 1.58–1.53 (m, 1H), 1.43–1.38 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.3, 145.3, 131.2, 128.5, 117.7, 113.9, 87.8, 78.1, 32.3, 29.4, 19.6; IR (NaCl) ν 1569, 1450, 1384, 1344, 1171, 1136, 1008, 912, 881, 834, 799, 754, 620 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}BrO$ $[M]^+$ 237.9993, found 237.9999. Crude **6** was refluxed with concentrated hydrochloric acid (5 mL) overnight. The cooled reaction mixture was quenched with ice water and extracted twice with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to afford **1** as a pale brown solid in quantitative yield. The NMR data agrees with that listed above.

5-Bromo-1-methyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (8). To a solution of **5** (150 mg, 0.633 mmol) in CH_2Cl_2/MeOH (1:1, 6 mL) was added 10% Pd–C (66.2 mg, 0.0633 mmol). The mixture was stirred vigorously at room temperature under H_2 until TLC showed the absence of starting material. The mixture was filtered through Celite and concentrated *in vacuo* to yield brown oil (141 mg, 93%), which was used in the next step without further purification; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 1.75 Hz, 1H), 7.25 (d, J = 1.75 Hz, 1H), 7.08–7.03 (m, 1H), 5.40 (d, J = 5.1 Hz, 1H), 2.25–2.19 (m, 2H), 1.83 (s, 3H), 1.56–1.42 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.0, 146.6, 129.6, 128.6, 116.5, 113.8, 86.8, 78.9, 32.6, 28.3, 17.8; IR (NaCl) ν 1576, 1455, 1382, 1343, 863, 759, 620 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}BrO$ $[M]^+$ 237.9993, found 238.0000.

1-Bromo-5-methylnaphthalene (2). Crude **8** was refluxed with concentrated hydrochloric acid (3 mL) overnight. The cooled reaction mixture was quenched with ice water and extracted twice with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to yield a mixture of brown and white solids. Recrystallization from hexanes gave **2** as a colorless crystalline solid (98 mg, 75%); mp 58–59 °C [lit.[4] mp 59–60 °C]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.6, 1H), 7.99 (d, J = 8.5, 1H), 7.79 (dd, J = 7.4, 1.0 Hz, 1H), 7.48 (dd, J = 8.5, 7.0 Hz, 1H), 7.38–7.34 (m, 2H), 2.71 (s, 3H), which is in agreement with that reported.[10]

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■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra for new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00730.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: gordon.w.gribble@dartmouth.edu.

Notes

The authors declare no competing financial interest.

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