A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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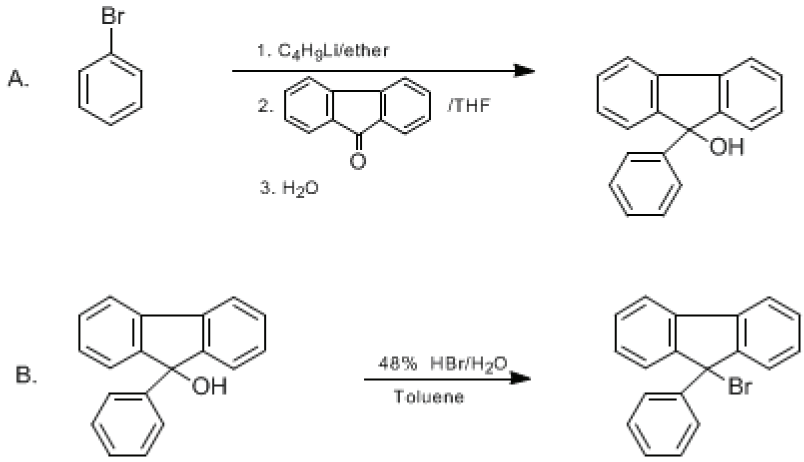
9-BROMO-9-PHENYLFLUORENE

[9H-Fluorene, 9-bromo-9-phenyl-]



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1. Procedure

CAUTION! Butyllithium is an air-sensitive, pyrophoric material and should be kept under an inert atmosphere at all times. Persons following this procedure should be thoroughly familiar with the handling of air-sensitive solutions(Note 1). Bromobenzene is an irritant and a potential carcinogen.

A. *9-Phenyl-9-fluorenol.* A flame-dried, 3-L, three-necked, round-bottomed flask equipped with an overhead stirrer, rubber septum, and glass stopper, under a nitrogen atmosphere, is charged with bromobenzene (158 mL, 1.5 mol, (Note 2)) and ethyl ether (800 mL, (Note 2)). The solution is cooled in an ice bath and stirred at 0°C. A flame-dried, 1-L, graduated cylinder fitted with a rubber septum is filled with 767 mL of a 1.5 M solution of butyllithium in hexane (1.15 mol, (Note 3)) under a nitrogen atmosphere. The butyllithium solution is then added to the 0°C ether solution over 30 min via a Teflon cannula with a positive nitrogen pressure. After the addition is complete, the solution is stirred for 20 min at 0°C and a solution of fluorenone (180 g, 1 mol, (Note 4)) in tetrahydrofuran (THF) (300 mL, (Note 5)) is added over 25 min via a Teflon cannula using positive nitrogen pressure. The ice bath is removed, the mixture is allowed to reach room temperature (24°C), and stirred for 2 hr. During this time, lithium bromide precipitates out of the reaction mixture. Water (250 mL) is added to dissolve the precipitate, the layers are separated, and the organic layer is washed with 800 mL of water and 800 mL of brine. The brine wash is discarded, and the other aqueous layers are combined and extracted with ethyl ether (2 × 200 mL). The combined organic layers are evaporated on a rotary evaporator at an initial bath temperature of 30–35°C and, when most of the volatile material has been removed, at a bath temperature of 70–75°C until a yellow solid is obtained (Note 6).

B. 9-Bromo-9-phenylfluorene. The yellow solid obtained in Step A is dissolved in toluene (800 mL, (Note 7)) and transferred to a three-necked, 2-L Morton flask (Note 8) equipped with an overhead stirrer, a nitrogen-filled balloon, and a glass stopper. Aqueous hydrobromic acid (HBr) (48%, 400 mL, (Note 9)) is added, and the heterogeneous mixture is vigorously stirred at room temperature (ca. 20–25° C) for 24 hr (Note 10). The layers are separated, the aqueous layer is extracted with toluene (400 mL), the combined organic layers are dried over sodium sulfate (Na_2SO_4) and filtered. The filter cake is washed with ethyl acetate (2 × 50 mL), and the combined organic filtrate and washings are evaporated to a yellow solid. Recrystallization from isooctane (1.25 L, (Note 7)) gives 270 g (84%) of 9-bromo-9-

phenylfluorene (Note 11),(Note 12),(Note 13),(Note 14).

2. Notes

1. A pamphlet describing techniques for the handling of air-sensitive solutions can be ordered from Aldrich Chemical Company, Inc.

2. Bromobenzene and ethyl ether were obtained from the Fisher Scientific Company. Bromobenzene was distilled from calcium hydride (CaH_2) under vacuum, and ethyl ether was distilled from sodium/benzophenone. Each liquid was transferred to the reaction vessel via glass syringe or Teflon cannula under a positive nitrogen pressure.

3. Butyllithium was obtained as a solution in hexane from Foote Mineral Ltd. and titrated with 0.5 M 2-propanol in tetrahydrofuran (THF) with 1,10-phenanthroline as the indicator. The butyllithium was transferred via Teflon cannula under positive nitrogen pressure. The checkers used a 1.6 M solution of butyllithium purchased from Aldrich Chemical Company, Inc.

4. Fluorenone was obtained from Chemical Dynamics Corporation or Fluka Chemical Corporation and recrystallized from absolute ethanol to remove fluorene.

5. Tetrahydrofuran was obtained from the Fisher Scientific Company and distilled from lithium aluminum hydride ($LiAlH_4$). (See warning: *Org. Synth., Coll. Vol. V* **1973**, 976).

6. The physical properties of 9-phenyl-9-fluorenol, which was recrystallized from isooctane to give pale yellow, translucent needles, are as follows: ^{13}C NMR (Nicolet, 200 MHz) δ: 83.5, 120.0, 124.7, 125.3, 127.1, 128.1, 128.4, 129.0, 139.5, 143.1, 150.3; mp 107–108°C (lit. mp 85°C,[2] 107°C[3]). The checkers observed mp 85–86°C. Anal. Calcd for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.39; H, 5.60.

7. Toluene and isooctane (2,2,4-trimethylpentane) were obtained from the Fisher Scientific Company and used without further purification.

8. Use of a Morton flask and an overhead stirrer allows for better mixing of the two-phase system and gives conversion to product faster than does use of a standard round-bottomed flask with an overhead stirrer.

9. Aqueous hydrobromic acid (HBr) (48%) was obtained from the J. T. Baker Chemical Company.

10. The relative amounts of 9-phenyl-9-fluorenol and 9-bromo-9-phenyl-fluorene were determined as follows: A ^{13}C NMR spectrum ($CDCl_3$ solution, Bruker 400 MHz) of an authentic sample of 9-bromo-9-phenylfluorene was recorded and then doped in 1% increments with authentic 9-phenyl-9-fluorenol. A ^{13}C NMR spectrum ($CDCl_3$ solution, Bruker 400 MHz) was recorded after each doping, and the heights of the peaks at 120.3 ppm (bromide) and 120.0 ppm (alcohol) were monitored. These spectra were compared with a ^{13}C NMR spectrum ($CDCl_3$ solution, Bruker 400 MHz) of the sample in question. Application of this technique to an evaporated aliquot of the reaction mixture in Step B, indicated >97% conversion of alcohol to bromide after 24 hr.

11. 9-Bromo-9-phenylfluorene is greater than 99% pure as shown by ^{13}C NMR, (determined by the procedure in (Note 10)); mp 99°C (lit.[4] mp 99°C).

12. The physical properties of 9-bromo-9-phenylfluorene, which was recrystallized from isooctane to give light-yellow, lustrous flakes, are as follows: ^{13}C NMR δ: 67.5, 120.3, 126.1, 127.4, 128.0, 128.3, 128.5, 129.0, 138.1, 141.1, 149.6; mp 99°C (lit.[4] mp 99°C); IR ($CHCl_3$) cm^{-1}: 3060 (m), 3000 (m), 1600 (w), 1485 (m), 1445 (s), 1150 (m), 830 (w), 690 (m), 620 (m); UV (EtOH) λ, nm, (ε): 310 (8,000), 276 (29,000), 238 (59,000), 230 (70,000), 213 (78,000). Anal. Calcd. for $C_{19}H_{13}Br$: C, 71.04; H, 4.08; Br, 24.88. Found: C, 71.11; H, 4.13; Br, 25.07.

13. The submitters report that 9-bromo-9-phenylfluorene of poorer quality can also be prepared on an identical scale in a lower yield using phenyllithium (obtained from Aldrich Chemical Company, Inc.) following the procedure given in Step A with minor modifications: A black solution of phenyllithium (632 mL, 1.14 mol, (Note 14)) was added to a 0°C solution of fluorenone (180.2 g, 1 mol, (Note 4)) in THF (1360 mL, (Note 5)) over 30 min, and the solution was stirred for 2 hr at room temperature (24°C). Isolation as described in Step A and conversion to the bromide as described in Step B, afforded 234 g (72.8%) of 9-bromo-9-phenylfluorene as an orange/yellow solid (mp 98°C, lit.[4] mp 99°C); >99% pure [^{13}C NMR (Note 10)] that was contaminated with approximately 20 g of a black solid; mp 91–94.5°C. This alternative procedure was not checked by the checkers.

14. Phenyllithium ("2.0 M" in cyclohexane/ether, 70/30, found to be 1.8 M by titration as described in (Note 3)) was obtained from the Aldrich Chemical Company, Inc., as a black solution and was added to the solution of fluorenone via Teflon cannula under positive nitrogen pressure.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Alkylation of α-amino esters with 9-bromo-9-phenylfluorene serves as the principal step in the preparation of N-(9-phenylfluoren-9-yl)-α-amino carbonyl compounds which are useful chiral educts for asymmetric synthesis. A discussion of the synthetic utility of N-9-phenylfluoren-9-yl derivatives of amino acids and amino acid esters appears on p. 348.

The preparation reported here is based on the method of Christie and Rapoport.[5] 9-Bromo-9-phenylfluorene has also been prepared by a light-initiated reaction of bromine and 9-phenylfluorene in carbon disulfide,[4] by addition of phenylmagnesium bromide to fluorene[3] followed by treatment with acetyl bromide,[6] and by treatment of 9-phenylfluorene with N-bromosuccinimide.[7]

References and Notes

1. Department of Chemistry, University of California, Berkeley, CA 94720.
2. Two distinct melting points (85°C and 107°C) are reported for 9-phenyl-9-fluorenol: (a) 85°C: Arcus, C. L.; Coombs, M. M. *J. Chem. Soc.* **1954**, 3977; Bolton, R.; Chapman, N. B.; Shorter, J. *J. Chem. Soc.* **1964**, 1895;
3. 107°C: Ullmann, F.; von Wurstemberger, R. *Chem. Ber.* **1904**, *37*, 73.
4. Kliegl, A. *Chem. Ber.* **1905**, *38*, 284.
5. Christie, B. D.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1239.
6. Bachmann, W. E. *J. Am. Chem. Soc.* **1930**, *52*, 3287.
7. Buu-Höi, Ng. Ph. *Justus Liebigs Ann. Chem.* **1944**, *556*, 1.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

brine

ethanol (64-17-5)

ethyl acetate (141-78-6)

ether,
ethyl ether (60-29-7)

HYDROBROMIC ACID (10035-10-6)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

cyclohexane (110-82-7)

toluene (108-88-3)

Benzophenone (119-61-9)

sodium (13966-32-0)

2-propanol (67-63-0)

bromobenzene (108-86-1)

carbon disulfide (75-15-0)

Phenylmagnesium bromide (100-58-3)

Phenyllithium (591-51-5)

butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

acetyl bromide (506-96-7)

lithium aluminum hydride (16853-85-3)

N-bromosuccinimide (128-08-5)

hexane (110-54-3)

fluorenone (486-25-9)

calcium hydride (7789-78-8)

isooctane (592-27-8)

1,10-phenanthroline (66-71-7)

lithium bromide (7550-35-8)

9-Bromo-9-phenylfluorene,
9-bromo-9-phenyl-fluorene,
9H-Fluorene, 9-bromo-9-phenyl- (55135-66-5)

9-Phenyl-9-fluorenol (25603-67-2)

2,2,4-trimethylpentane (540-84-1)

9-phenylfluorene (789-24-2)