A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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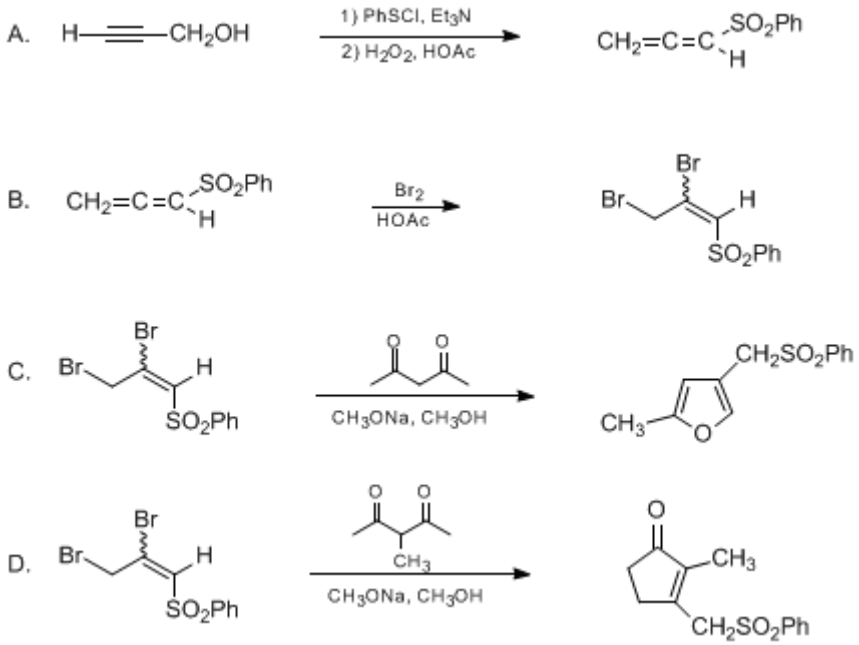
2,3-DIBROMO-1-(PHENYLSULFONYL)-1-PROPENE AS A VERSATILE REAGENT FOR THE SYNTHESIS OF FURANS AND CYCLOPENTENONES: 2-METHYL-4-[(PHENYL-SULFONYL) METHYL]FURAN AND 2-METHYL-3-[(PHENYLSULFONYL) METHYL]-2-CYCLOPENTEN-1-ONE

[Benzene, [(2,3-dibromo-1-propenyl)sulfonyl]-, Furan, 2-methyl-4-[(phenylsulfonyl)methyl]-, and 2-Cyclopenten-1-one, 2-methyl-3-[(phenylsulfonyl) methyl]-]



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Checked by Huguette Vanlierde, Amy Dekoker, and Leon Ghosez.

1. Procedure

A. *1-(Phenylsulfonyl)-1,2-propadiene*. In a 1-L, three-necked, round-bottomed flask equipped with a magnetic stirring bar, 100-mL addition funnel, and a septum fitted with a nitrogen inlet, are placed 10.5 mL (0.18 mol) of propargyl alcohol (Note 1), 30.1 mL (0.22 mol) of triethylamine, and 700 mL of dichloromethane. The flask is cooled with an ice-water bath and 26.0 g (0.18 mol) of phenylsulfenyl chloride (Note 2) in 50 mL of dichloromethane is added under a nitrogen atmosphere from the addition funnel. After the solution is warmed to room temperature and stirred for 3 hr, the mixture is washed with water (2 × 200-mL) and then concentrated under reduced pressure. The resulting residue (ca. 37 g) is dissolved in 100 mL of acetic acid in a 500-mL, round-bottomed flask fitted with a magnetic stirring bar, an addition funnel, and a thermometer. The solution is heated to 95°C and then 40 mL of hydrogen peroxide (30–35%) (Note 3) is slowly added over a 20-min period maintaining the internal temperature in the flask below 95°C. The mixture is heated for an additional 10 hr, maintaining the external temperature at 95°C (Note 4). After being cooled to 25°C, the mixture is poured into 200 mL of water, and extracted with dichloromethane (3 × 100 mL). The organic layer is washed with water (2 × 100 mL) followed by saturated sodium bicarbonate solution (100 mL), dried over magnesium sulfate, and filtered. The filtrate is concentrated to give 28.1 g (68%) of 1-(phenylsulfonyl)-1,2-propadiene as an oil, which is used in the next step (Note 5), (Note 6).

B. *2,3-Dibromo-1-(phenylsulfonyl)-1-propene*. To a solution containing 25.4 g (0.14 mol) of 1-(phenylsulfonyl)-1,2-propadiene in 100 mL of acetic acid in a 250-mL, round-bottomed flask fitted with a dropping funnel is added 8.0 mL (0.14 mol) of bromine over a period of 30 min. The solution is stirred at room temperature for 8 hr, poured into 200 mL of water, and extracted with dichloromethane (3 × 100 mL). The dichloromethane layer is washed with 50 mL of a 1.0 M aqueous sodium thiosulfate solution, water (2 × 100 mL) and saturated sodium bicarbonate solution (100 mL). The organic phase is dried over anhydrous magnesium sulfate, filtered under reduced pressure through a 60-mL fritted funnel containing 4.0 g of Celite topped with 6.0 g of silica gel. The mixture is concentrated under reduced pressure to give 41.5 g (87%) of 2,3-dibromo-1-(phenylsulfonyl)-1-propene (Note 7), which is used in the next step without further purification.

C. *2-Methyl-4-[(phenylsulfonyl)methyl]furan*. Into a flame-dried, 1-L, round-bottomed flask equipped with an addition funnel fitted with a nitrogen inlet are placed 20.0 g (58.8 mmol) of 2,3-dibromo-1-(phenylsulfonyl)-1-propene and 6.1 mL (59.4 mmol) of 2,4-pentanedione in 300 mL of methanol (Note 8). The flask is blanketed with nitrogen and cooled using an ice-water bath. To this mixture is added 140 mL (70.0 mmol) of a 0.5 N methanolic solution of sodium methoxide (Note 9) dropwise over 30 min. The solution is stirred at 25°C for 12 hr and cooled to 0°C. Another 140 mL (70.0 mmol) of the 0.5 N methanolic solution of sodium methoxide is added over 20 min. After being stirred at 25°C for 10 hr, the reaction is quenched by the addition of 50 mL of saturated ammonium chloride solution. The solvent is removed with a rotary evaporator at aspirator vacuum and the resulting residue is taken up in 100 mL of water and 200 mL of dichloromethane. The aqueous layer is extracted with dichloromethane (2 × 200 mL). The organic layer is washed with water (100 mL) and brine (100 mL) and then dried over anhydrous magnesium sulfate. After filtration and concentration, the residue is recrystallized from ethyl acetate to give 5.6 g (59%) of 2-methyl-4-[(phenylsulfonyl)methyl]furan (Note 6), (Note 10).

D. *2-Methyl-3-[(phenylsulfonyl)methyl]-2-cyclopenten-1-one*. In a flame-dried, 1-L, round-bottomed flask equipped with an addition funnel under a nitrogen atmosphere are placed 20.0 g (58.8 mmol) of 2,3-dibromo-1-(phenylsulfonyl)-1-propene and 7.0 mL (60.0 mmol) of 3-methyl-2,4-pentanedione in 300 mL of methanol (Note 8). The flask is cooled using an ice-water bath. To this mixture is added 140 mL (70.0 mmol) of a 0.5 N methanolic solution of sodium methoxide (Note 9) dropwise over 30 min. The solution is stirred at 25°C for 5 hr and cooled to 0°C. Another 140-mL (70.0 mmol) portion of the 0.5 N methanolic solution of sodium methoxide is added over 20 min. After being stirred at 25°C for 10 hr, the reaction is quenched by the addition of 50 mL of saturated ammonium chloride solution. The solvent is removed with a rotary evaporator at aspirator vacuum and the resulting residue is taken up in 100 mL of water and 200 mL of dichloromethane. The aqueous layer is extracted with dichloromethane (2 × 200 mL). The organic layer is washed with water (100 mL) and brine (100 mL) and then dried over anhydrous magnesium sulfate. After filtration and concentration, the residue is recrystallized from ethyl acetate to give 6.5 g (44%) of 2-methyl-3-[(phenylsulfonyl)methyl]-2-cyclopenten-1-one (Note 6), (Note 11).

2. Notes

1. Propargyl alcohol, 2,4-pentanedione and 3-methyl-2,4-pentanedione were purchased from Aldrich Chemical Company, Inc., and were used without further purification. Dichloromethane and triethylamine were distilled from calcium hydride prior to use. Methanol was dried and distilled from magnesium-iodine.
2. Phenylsulfenyl chloride was prepared according to the procedure of Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Org. Synth., Coll. Vol. VIII* **1993**, 550.
3. Hydrogen peroxide (30–35%), glacial acetic acid, and bromine were purchased from Fisher Scientific Company and were used without further purification.
4. For the next 30–60 min the internal temperature should not be allowed to exceed 95°C.
5. The submitters were able to obtain most of this product as a crystalline solid that could be recrystallized from ether at −20°C, mp 44–45°C [lit.[2] mp 44–45°C]. It has the following spectral properties: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.40 (d, 2 H, J = 6.3), 6.21 (t, 1 H, J = 6.3), 7.47–7.87 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 84.0, 100.7, 127.3, 129.0, 133.4, 140.9, 209.2.
6. The checkers were not able to purify the crude oil. As a result their overall yield of final product was

40%. The submitters obtained a 71% overall yield using the crystalline material.
7. This product contains a mixture of E- and Z-isomers in a 7:3 ratio, which could be separated by flash chromatography on silica gel eluting with hexane:ethyl acetate (4:1). The spectral properties of both isomers are as follows: E-isomer: mp 62–63°C (recrystallized from ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.96 (s, 2 H), 6.78 (s, 1 H), 7.50–8.15 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.8, 127.8, 129.6, 133.7, 134.4, 137.6, 139.6; Anal. Calcd for $C_9H_8Br_2O_2S$: C, 31.79; H, 2.37. Found: C, 31.86; H, 2.36. Z-Isomer (oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.20 (s, 2 H), 7.31 (s, 1 H), 7.50–7.95 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 35.7, 127.9, 128.5, 129.1, 133.8, 134.0, 139.4.
8. Both isomers gave similar yields. If the crystalline E-isomer was used, it took about 30 min for the solid to dissolve.
9. This solution was prepared from sodium and methanol and could be stored in a plastic bottle over a period up to several months without any effect on the reaction.
10. The product has the following spectral properties; mp 91–92°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.22 (s, 3 H), 4.10 (s, 2 H), 5.91 (s, 1 H), 7.01 (s, 1 H), 7.50–7.95 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.9, 53.0, 106.9, 112.5, 127.9, 128.3, 133.1, 137.3, 140.3, 152.6. Anal. Calcd for $C_{12}H_{12}O_3S$: C, 61.00; H, 5.12. Found: C, 60.91; H, 5.12.
11. The product has the following spectral properties; mp 166–167°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 (s, 3 H), 2.45 (m, 2 H), 2.73 (m, 2 H), 4.15 (s, 2 H), 7.40–7.95 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 7.2, 29.4, 33.7, 57.9, 127.5, 128.9, 133.7, 137.7, 142.4, 155.8, 207.8. Anal. Calcd. for $C_{13}H_{14}O_3S$: C, 62.38, H, 5.64. Found: C, 62.14, H, 5.47.

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

Many methods have been devised for the formation of multicyclic furans[3] and cyclopentenones[4] because of their importance in organic synthesis. The procedure described here provides a simple and general approach for the construction of 2-methyl-4-[(phenylsulfonyl)methyl]furan and 2-methyl-3-[(phenylsulfonyl)methyl]-2-cyclopenten-1-one using 2,3-dibromo-1-(phenylsulfonyl)-1,2-propene (DBP) as the key reagent.[5] Addition of bromine to 1-(phenylsulfonyl)-1,2-propadiene proceeds smoothly at 25°C and can be controlled so that the reaction may be terminated after 1 equiv of bromine is consumed. The resulting dibromide is a stable, crystalline solid, requiring no special precautions to prevent decomposition.[6] This dibromosulfone can be viewed as a multielectrophilic reagent with great potential as a nucleophilic acceptor for sequential addition. Functionalized allylic reagents that contain both a leaving group and a π-activating substituent have been used extensively in organic synthesis.[7,8,9,10] These substituted 1-propenes have been referred to as multicoupling reagents.[8] Because of the molecular weight and stability of the phenylsulfonyl group, the carbon backbone of DBP is very small, without the drawback of volatility or thermal lability seen in other synthetic intermediates with the same carbon skeleton. The synthetic potential of DBP is demonstrated here by taking advantage of two properties of the molecule: 1) the ability of the phenylsulfonyl group to activate the double bond toward Michael addition with soft dicarbonyl anions and 2) the facility with which both bromides can be displaced.

Treatment of 1,3-dicarbonyl compounds with DBP in a methoxide/methanol system affords 2-alkyl-4-[(phenylsulfonyl)methyl]furans, where reaction proceeds by initial addition-elimination on the vinyl sulfone moiety. In contrast, silyl enol ethers in the presence of silver tetrafluoroborate resulted in products derived from S_N2 displacement at the allylic site.[11] Anions derived from 1,3-dicarbonyls substituted at the C-2 position are found to induce a complete reversal in the mode of ring closure.[12] The major products obtained are 3-[(phenylsulfonyl)methyl]-substituted cyclopentenones. The internal displacement reaction leading to the furan ring apparently encounters an unfavorable $A_{1,3}$-interaction in the transition state when a substituent group is present at the 2-position of the dicarbonyl compound. This steric interaction is not present in the transition state leading to the cyclopentenone ring.

Since DBP can react with a variety of β-dicarbonyl anions, a wide assortment of furans and cyclopentenones is available. In addition to its ease of removal,[13] the pendant sulfone also offers a

convenient and versatile site for further elaboration (via alkylation[14] or Julia coupling[15]). This strategy toward furans and cyclopentenones can clearly be applied to more complex targets.

References and Notes

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

brine

Benzene, [(2,3-dibromo-1-propenyl)sulfonyl]-, Furan, 2-methyl-4-[(phenylsulfonyl)methyl]-, and 2-Cyclopenten-1-one, 2-methyl-3-[(phenylsulfonyl)methyl]-

2,3-dibromo-1-(phenylsulfonyl)-1,2-propene (DBP)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

methanol (67-56-1)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium bicarbonate (144-55-8)

bromine (7726-95-6)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

sodium methoxide (124-41-4)

carbon (7782-42-5)

sodium (13966-32-0)

hydrogen peroxide (7722-84-1)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

2,4-pentanedione (123-54-6)

hexane (110-54-3)

triethylamine (121-44-8)

silver tetrafluoroborate (14104-20-2)

calcium hydride (7789-78-8)

propargyl alcohol (107-19-7)

Phenylsulfenyl chloride (931-59-9)

3-methyl-2,4-pentanedione (815-57-6)

2,3-Dibromo-1-(phenylsulfonyl)-1-propene (132604-65-0)

2-METHYL-4-[(PHENYL-SULFONYL)METHYL]FURAN,
2-Methyl-4-[(phenylsulfonyl)methyl]furan (128496-98-0)

2-METHYL-3-[(PHENYLSULFONYL)METHYL]-2-CYCLOPENTEN-1-ONE

1-(Phenylsulfonyl)-1,2-propadiene (2525-42-0)

magnesium-iodine