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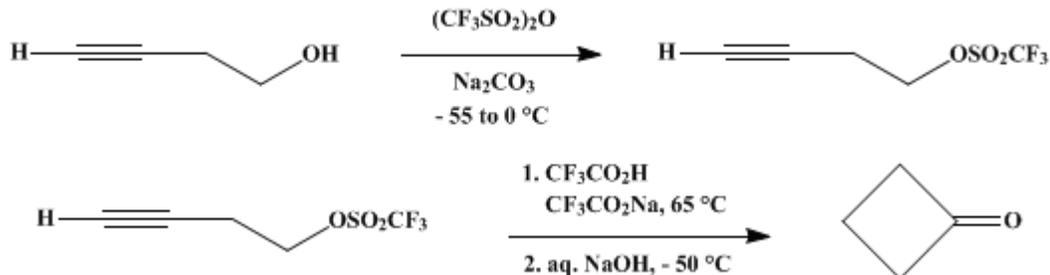
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.324 (1988); Vol. 54, p.84 (1974).

CYCLOBUTANONE *via* SOLVOLYTIC CYCLIZATION

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1. Procedure

A. *3-Butyn-1-yl trifluoromethanesulfonate*. A 500-ml., three-necked flask is fitted with a mechanical stirrer, a pressure-equalizing dropping funnel, and a stopper. The system is flushed with nitrogen through a gas-inlet tube attached to the top of the funnel. To 150 ml. of dry dichloromethane (Note 1) in the flask is added 75 g. (0.27 mole) of trifluoromethanesulfonic anhydride (Note 2), and the solution is cooled to −40°. After addition of 14.5 g. (0.175 mole) of finely powdered anhydrous sodium carbonate (Note 3), 15g. (0.21 mole) of 3-butyn-1-ol (Note 4) is added dropwise over a 20-minute period to the well-stirred reaction mixture maintained at −40° to −55°. Stirring is continued at −30° for 2 hours, at 0° for another hour, and finally the reaction is quenched by dropwise addition of 50 ml. of water. The organic layer is separated, dried over anhydrous sodium sulfate, filtered and concentrated with a rotary evaporator, the temperature of the water bath not exceeding 25° The resulting residue is placed in a flask directly connected with a liquid nitrogen trap and distilled at 1 mm. The fractions boiling in the range from 40° to 50° are sufficiently pure for use in the next step. The yield of the sulfonate is 38.94 g. (90%) (Note 5) and (Note 6).

B. *Cyclobutanone*. A 500-ml., thick-walled ampoule is charged with 210 g. (137 ml.) of trifluoroacetic acid, 11.5 g. (0.0846 mole) of sodium trifluoroacetate (Note 7), and 17 g. (0.084 mole) of 3-butyn-1-yl trifluoromethanesulfonate, in this order. A magnetic stirring bar is added, and the ampoule is sealed. The stirred reaction mixture is immersed in a constant temperature bath kept at 65° (±2°) for 1 week. The ampoule is cooled slowly to −50° with a methanol–dry-ice bath (Note 8) and opened. With the aid of 200 ml. of diethyl ether the reaction mixture is transferred to a 1-l. Erlenmeyer flask to which 74 g. (1.83 mole) of sodium hydroxide in 150 ml. of water is added carefully. During the addition the flask is immersed in the bath, maintained at approximately −50° (Note 8). After the ethereal layer is separated, the aqueous layer is saturated with sodium chloride and extracted twice with ether. The original organic layer and ethereal extracts are combined, dried over anhydrous sodium sulfate, and directly distilled into a liquid nitrogen trap. The total condensate in the trap is placed in a distillation flask attached to a 40-cm. Vigreux column and a condenser cooled to −40° with a circulating cold bath (Note 9). After the ether is distilled, all volatile materials are collected by raising the bath to 130°, yielding 1.84–2.05 g. (31–36%) of cyclobutanone. The purity of the product is greater than 95% by ¹H NMR, the only impurity being diethyl ether (Note 10), (Note 11).

2. Notes

1. The submitters treated dichloromethane first with sulfuric acid, then with sodium hydroxide, and distilled it before use. The checkers used reagent grade solvent, supplied by Fisher Scientific Company, stored overnight over 4A Molecular Sieves.
2. The submitters prepared the anhydride, following basically the procedure described by Burdon, Farazmand, Stacey, and Tatlow.[2] Trifluoromethanesulfonic acid (32.1 g., 0.214 mole) (supplied by Minnesota Mining and Manufacturing Company) maintained at 0°, is treated with 25 g. of phosphorus

pentoxide in three portions. The resulting anhydride is distilled by gradually heating the reaction mixture to a bath temperature of 110° over a 1-hour period. The fractions boiling at 80–100° (760 mm.) are collected and redistilled from approximately 8 g. of phosphorus pentoxide until the distillate no longer fumes on exposure to air. Normally three distillations are necessary. The presence of the trifluoromethanesulfonic acid can be detected by dipping a glass rod into the distillate and waving the wet rod in the air. The anhydride, in contrast, does not fume. The final yield of the product is 25 g. (83%), b.p. 84°. The checkers purchased the anhydride from Pierce Chemical Company and used it without further purification.

3. Anhydrous sodium carbonate was ground into fine powder and dried in vacuum at 200° for 4 hours.

4. In one experiment the checkers used 3-butyn-1-ol available from Aldrich Chemical Company, Inc., and found that its purity was satisfactory. In other experiments, both the submitters and the checkers prepared the hydroxy compound from sodium acetylide and ethylene oxide in liquid ammonia according to the procedure described by Schulte and Reiss[3] and further attempted to maximize the yield by varying the ratio of sodium: ethylene oxide: liquid ammonia used in the reaction. While the submitters obtained 3-butyn-1-ol in a yield of 60%, the checkers failed to obtain consistent results in repeated experiments and consequently could not define the optimum conditions for the reaction. Thus, the yield of 3-butyn-1-ol varied from 15 to 45% and 15 to 31% on the basis of sodium and ethylene oxide, respectively. Unknown and apparently subtle experimental factors affect the yield significantly.

5. When 3-butyn-1-ol was added to a solution of the anhydride, cooled to 0°, and the mixture was allowed to react at room temperature for 3 hours, the yield of the sulfonate dropped to 70–75%.

6. ^{1}H NMR of 3-butyn-1-ol trifluoromethanesulfonate (CCl_4) δ, (multiplicity, coupling constant J in Hz., number of protons): 2.05 (t, $J_{2,4} = 2.6$, 1H), 2.76 (d of t, $J_{1,2} = 6.7$, $J_{2,4} = 2.6$, 2H), 4.57 (t, $J_{1,2} = 6.7$, 2H).

7. The salt is available from Aldrich Chemical Company Inc. However, the checkers readily prepared it in the following way. To a stirred solution of 8.8 g. (0.22 mole) of sodium hydroxide in 400 ml. of 98% ethanol was added dropwise 25 g. (0.22 mole) of trifluoroacetic acid. After the addition was completed, the ethanol was removed under reduced pressure, and the residue was suspended in approximately 100 ml. of ether, filtered, and washed several times with ether. The yield was 25 g. (83.8%), and the salt was dried to a constant weight in a vacuum desiccator containing calcium sulfate (2 days).

8. Due to the high volatility of cyclobutanone, a substantial amount of the product is lost unless the mixture is sufficiently cooled during the process of neutralization.

9. The cooling to −40° was necessary to prevent the loss of highly volatile cyclobutanone.

10. The checkers redistilled this product through a 3-cm. column and determined its b.p. to be 96.5–97.5° (710 mm.); IR ($CHCl_3$), cm.$^{-1}$: 1780; ^{1}H NMR (CCl_4), δ (multiplicity, number of protons): 3.05 (m, 4H), 1.96 (m, 2H).

11. Subsequent to the publication of this procedure in the annual volume, the submitter has suggested the following changes, which have not been checked: After neutralization of the cyclobutanone with 1.83 moles of sodium hydroxide, the aqueous layer is made neutral or weakly alkaline with additional sodium hydroxide solution. Often the neutralization point can be observed as a weak color change (to a lighter color) of the dark brown reaction mixture. After separation of the ethereal layer and saturation of the aqueous layer with sodium chloride, the aqueous layer is extracted repeatedly (more than twice) with ether. The submitters obtained cyclobutanone in 66% yield.

3. Discussion

Cyclobutanone has been prepared by (1) reaction of diazomethane with ketene,[4] (2) treatment of methylenecyclobutane with performic acid, followed by cleavage of the resulting glycol with lead tetraacetate,[5] (3) ozonolysis of methylenecyclobutane,[6] (4) epoxidation of methylenecyclopropane followed by acid-catalyzed ring expansion,[7] (5) oxidative cleavage of cyclobutane trimethylene thioketal, which is prepared from 2-(ω-chloropropyl)-1,3-dithiane,[8] and (6) by hydrolytic conversion of 1-tosylcyclobutyl isocyanide, which is obtained by a one-step cyclodialkylation of tosylmethyl isocyanide with 1,3-dibromopropane.[9]

The present procedure[10] represents another synthesis of cyclobutanone through the unique acetylenic bond participation in solvolysis. Cyclobutane derivatives prepared in this way include 2-methyl-, 2-ethyl-, 2-isopropyl-, and 2-trifluoromethylcyclobutanone from the corresponding acetylenic compounds.[11] Condensed cyclobutanones are also easily accessible in good preparative yields by homopropargylic rearrangement: 7-methylbicyclo[3.2.0]heptan-6-one and 9-methylbicyclo[5.2.0]

nonan-8-one are prepared by solvolyzing the corresponding *trans*-2-(1-propynyl)cycloalkyl-4-dimethylaminobenzenesulfonates in 67% sulfuric acid.[12]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 320
- Org. Syn. Coll. Vol. 6, 737
- Org. Syn. Coll. Vol. 7, 114

References and Notes

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

performic acid

cyclobutane trimethylene thioketal

2-methyl-, 2-ethyl-, 2-isopropyl-, and 2-trifluoromethylcyclobutanone

ethanol (64-17-5)

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

ether,
diethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

1,3-dibromopropane (109-64-8)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

sodium (13966-32-0)

Ethylene oxide (75-21-8)

Ketene (463-51-4)

dichloromethane (75-09-2)

Diazomethane (334-88-3)

sodium acetylide

trifluoroacetic acid (76-05-1)

Cyclobutanone (1191-95-3)

3-butyn-1-ol (927-74-2)

trifluoromethanesulfonic acid (1493-13-6)

methylenecyclobutane (1120-56-5)

Methylenecyclopropane (6142-73-0)

3-Butyn-1-yl trifluoromethanesulfonate (32264-79-2)

tosylmethyl isocyanide (36635-61-7)

Trifluoromethanesulfonic anhydride (358-23-6)

sodium trifluoroacetate (2923-18-4)

2-(ω-chloropropyl)-1,3-dithiane

1-tosylcyclobutyl isocyanide

7-methylbicyclo[3.2.0]heptan-6-one

9-methylbicyclo[5.2.0]nonan-8-one

phosphorus pentoxide (1314-56-3)

lead tetraacetate (546-67-8)