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of Organic Compounds

Working with Hazardous Chemicals

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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.

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TRIFLOROACETYL TRIFLATE

[Acetic acid, trifluoro-, anhydride with trifluoromethanesulfonic acid]

$$CF_3CO_2H + CF_3SO_3H \xrightarrow{P_2O_5} CF_3CO_2SO_2CF_3$$

Submitted by Stephen L. Taylor, T. R. Forbus, Jr., and J. C. Martin[1].
Checked by Thomas W. Panunto and Edwin Vedejs.

1. Procedure

Caution! The volatile product reacts rapidly with water to give corrosive strong acids. It also reacts rapidly with other nucleophiles. Care should therefore be exercised to avoid inhalation of its vapors. It should be handled in a well-vented fume hood.

To a 1-L flask containing 160 g (1.13 mol) of powdered phosphorus oxide (P_2O_5), thoroughly mixed with an equal volume of dried fine sand (Note 1), is added a mixture of 85.5 g (0.75 mol) of trifluoroacetic acid (TFA) (Note 2) and 56.5 g (0.376 mol) of triflic acid (TfOH) at −20°C (Note 3). The stoppered flask (Note 4) is vigorously shaken for 5 min and then fitted for simple distillation, with the receiving flask cooled to −78°C, and allowed to stand at room temperature under a dry nitrogen atmosphere for 2.5 hr. The liquid is removed from the solid mixture by simple distillation at a bath temperature of 240°C (Note 5) for 3.5 hr (Note 6). The distillate is then carefully fractionally distilled (Note 7) from 5 g of powdered P_2O_5 (Note 8) with the receiving flasks cooled at −78°C. The colorless liquid collected at 62.5–63°C (760 mm) (Note 9), 69 g (75%) of trifluoroacetyl triflate (TFAT), is of 99% purity (Note 10), as determined by fluorine magnetic resonance (Note 11).

2. Notes

1. In recent synthetic applications of this method the powdered phosphorus oxide was mixed with *twice* as much volume of dried fine sand. The increased volume of sand makes it easier to remove the TFAT by distillation and reduces the probability that the flask will be broken after the distillation.
2. The 99% TFA obtained from Aldrich Chemical Company, Inc. was used without further purification.
3. Triflic acid (TfOH), obtained from Minnesota Mining & Manufacturing Company, (3M), in kilogram quantities was used without further purification.
4. Ground-glass joints were connected using Teflon sleeves or a chlorofluorocarbon stopcock grease.
5. High temperatures are needed to distill the products from P_2O_5. The use of temperatures higher than 250°C, however, causes the round-bottomed flask to break when the temperature is lowered to near room temperature. On completion of the reaction, the P_2O_5 sand mixture can be removed from the flask by careful, slow addition of water. The checkers used an equilibrated bath of sand in a large heating mantle; the flask always broke after distillation (see (Note 1)).
6. The nitrogen outlet from the distillation apparatus should be well vented.
7. An 8-mm × 1-m jacketed column packed with a coiled tantalum wire was used by the submitters. The checkers used a Vigreux column of similar size.
8. Since the distillate contains 1–3% of the starting acids, P_2O_5 is added to prevent the reaction of TFA and TFAT, which gives trifluoroacetic anhydride (TFAA) and TfOH.
9. The first fraction is TFAA, bp 38.5–41°C (760 mm).
10. The impurity is TFAA.
11. The reactants and products show only singlets in their fluorine magnetic resonance spectra with the following chemical shifts (downfield from fluorotrichloromethane internal standard) δ: TFA, −76.3; TfOH, −77.3; TFAT, −73.3 and −74.8; TFAA, −75.9; triflic anhydride, −72.6 ppm.

3. Discussion

Trifluoroacetyl triflate is probably the most powerful trifluoroacetylating agent known, as evidenced by its reactivity toward several types of nucleophiles under mild conditions. A sterically hindered base, 2,6-di-*tert*-butyl-4-methylpyridine,[2] may be used to scavenge the triflic acid produced in the reactions, since it does not react with TFAT under these conditions.

Trifluoroacetylation occurs at carbon in activated arenes such as anthracene[3] under milder conditions using TFAT than when using T FAA. Trifluoroacetate esters are formed from alcohols and phenols,[4] while ketones are acylated at oxygen to yield enol trifluoroacetates.[3] Amines[4] give the corresponding amides on reaction with 1 equiv of TFAT or imides on reaction with 2 equiv. Some covalent halides (fluorides[5] and chlorides[3]) are acylated at halogen by TFAT to yield the very volatile trifluoroacetyl halides and ionic triflates. It was recently reported that TFAT reacts with a thioketone to give a stable cation.[6] Reaction of TFAT with the methyl ester of glutaconic acid gives 2,6-dimethoxypyrylium triflate, the first member of a new class of pyrylium salts[4] with alkoxy groups at positions-2 and -6.

The high reactivity of TFAT limits the number of solvents that can be used for its reactions. We have found that TFAT is unreactive towards saturated hydocarbons, benzene, and common halogenated solvents. It reacts only very slowly with nitromethane, but reacts relatively rapidly with ether, tetrahydrofuran, ethyl acetate, and acetonitrile.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 7, 144

References and Notes

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

TRIFLOROACETYL TRIFLATE

Triflic acid (TfOH)

trifluoroacetic anhydride (TFAA)

Benzene (71-43-2)

ethyl acetate (141-78-6)

ether (60-29-7)

acetonitrile (75-05-8)

oxygen (7782-44-7)

carbon (7782-42-5)

anthracene (120-12-7)

Nitromethane (75-52-5)

Tetrahydrofuran (109-99-9)

fluorotrichloromethane (75-69-4)

trifluoroacetic acid (76-05-1)

Acetic acid, trifluoro-, anhydride (407-25-0)

trifluoromethanesulfonic acid,
triflic acid (1493-13-6)

triflic anhydride (358-23-6)

Trifluoroacetyl triflate (68602-57-3)

2,6-dimethoxypyrylium triflate

TFA

phosphorus oxide (1314-56-3)

2,6-Di-tert-butyl-4-methylpyridine (38222-83-2)

methyl ester of glutaconic acid