Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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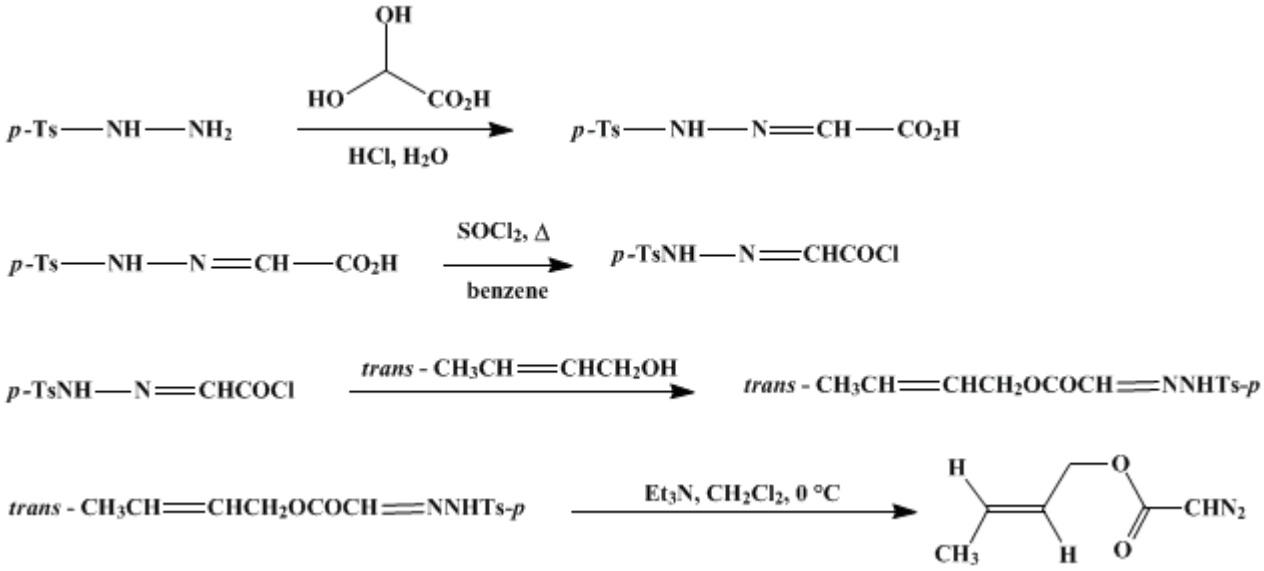
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.049.0022

Organic Syntheses, Coll. Vol. 5, p.258 (1973); Vol. 49, p.22 (1969).

CROTYL DIAZOACETATE

[Acetic acid, diazo-, *trans*-2-butenyl ester]



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Checked by J. H. Ham and R. E. Ireland.

1. Procedure

A. *Glyoxylic acid p-toluenesulfonylhydrazone*. A solution of 46.3 g. (0.50 mole) of 80% glyoxylic acid (Note 1) in 500 ml. of water is placed in a 1-l. Erlenmeyer flask and warmed on a steam bath to approximately 60°. This solution is then treated with a warm (approximately 60°) solution of 93.1 g. (0.50 mole) of *p*-toluenesulfonylhydrazide (Note 2) in 250 ml. (0.63 mole) of aqueous 2.5*M* hydrochloric acid. The resulting mixture is heated on a steam bath with continuous stirring until all the hydrazone, which initially separates as an oil, has solidified (about 5 minutes is required). After the reaction mixture has been allowed cool to room temperature and then allowed to stand in a refrigerator overnight, the crude *p*-toluenesulfonylhydrazone is collected on a filter, washed with cold water, and allowed to dry for 2 days (Note 3). The crude product (110–116 g., m.p. 145–149° dec.) is dissolved in 400 ml. of boiling ethyl acetate, filtered to remove any insoluble material, and then diluted with 800 ml. of carbon tetrachloride and allowed to cool. After the mixture has been allowed to stand overnight in a refrigerator, the *p*-toluenesulfonylhydrazone is collected and washed with cold mixture of ethyl acetate and carbon tetrachloride (1:2 by volume). The yield is 92.4–98.5 g. (76–81%) of the hydrazone as white crystals, m.p. 148–154° dec. (Note 4).

B. *The p-toluenesulfonylhydrazone of glyoxylic acid chloride*. *Caution! Since hydrogen chloride and sulfur dioxide are liberated during this reaction, it should be conducted in a hood.* To a suspension of 50.2 g. (0.21 mole) of glyoxylic acid *p*-toluenesulfonylhydrazone in 250 ml. of benzene is added 30 ml. (49 g. or 0.42 mole) of thionyl chloride (Note 5). The reaction mixture is heated under reflux with stirring until vigorous gas evolution has ceased and most of the suspended solid has dissolved (about 1.5–2.5 hours is required (Note 6)). The reaction mixture is then cooled immediately (Note 6) and filtered through a Celite mat on a sintered-glass funnel. After the filtrate has been concentrated to dryness under reduced pressure, the residual solid is mixed with 40–50 ml. of anhydrous benzene, warmed, and the solid mass is broken up to give a fine suspension. This suspension is cooled and filtered with suction. The crystalline product is washed quickly with two portions of cold benzene to remove most of the residual colored impurities, and then the remaining crude acid chloride is transferred to a flask for recrystallization.

The combined benzene filtrates from this initial washing procedure are concentrated under reduced pressure, and the washing procedure with benzene is repeated to give a second crop of the crude acid chloride which is transferred to a flask for recrystallization.

For recrystallization each crop of the crude acid chloride is dissolved in a minimum volume of boiling anhydrous benzene (about 100 ml. is required for the first crop) and petroleum ether (b.p. 30–60°; about 50 ml. is required for the first crop) is added to the hot solution. Crystallization begins on cooling. After the mixture has cooled to room temperature, it is allowed to stand overnight at room temperature and the acid chloride is collected on a filter and washed with a small portion of cold benzene. The yield of recrystallized acid chloride from the first crop of crude acid chloride is 27.6–33.4 g. (50–61%) of pale yellow prisms, m.p. 101–112° (Note 4). The product obtained from crystallization of the second crop of acid chloride amounts to 3.3–3.6 g. (6–7%), m.p. 104–108°.

C. *Crotyl diazoacetate*. A solution of 10.0 g. (0.038 mole) of the *p*-toluenesulfonylhydrazone of glyoxylic acid chloride in 100 ml. of methylene chloride is cooled in an ice bath. Crotyl alcohol (2.80 g. or 0.038 mole) (Note 7) is added to this cold solution, and then a solution of 7.80 g. (0.077 mole) of redistilled triethylamine (b.p. 88.5–90.5°) in 25 ml. of methylene chloride is added to the cold reaction mixture dropwise and with stirring over a 20-minute period. During the addition a yellow color develops in the reaction mixture and some solid separates near the end of the addition period. The resulting mixture is stirred at 0° for 1 hour and then the solvent is removed at 25° under reduced pressure with a rotary evaporator. A solution of the residual dark orange liquid in approximately 200 ml. of benzene is thoroughly mixed with 100 g. of Florisil (Note 8) and then filtered. The residual Florisil, which has adsorbed the bulk of the dark colored by-products, is washed with two or three additional portions of benzene of such size that the total volume of the combined benzene filtrates is 400–500 ml. This yellow benzene solution of the diazoester is concentrated under reduced pressure at 25° with a rotary evaporator, and the residual yellow liquid is distilled under reduced pressure. *(Caution! This distillation should be conducted in a hood behind a safety shield)* (Note 9). The diazo ester is collected as 2.20–2.94 g. (42–55%) of yellow liquid, b.p. 30–33° (0.15 mm)., n^{24}D 1.4853 — 1.4856 (Note 10).

2. Notes

1. The submitters used a practical grade of material containing 80% glyoxylic acid purchased from Eastman Organic Chemicals.
2. The submitters used *p*-toluenesulfonylhydrazide prepared as described in *Organic Syntheses*.[2] This material may be purchased from Eastman Organic Chemicals.
3. Difficulty was encountered in the subsequently described recrystallization if the crude product was not dry.
4. The broad melting range is presumably due to the presence of a mixture of stereoisomers.
5. If the thionyl chloride is not taken from a freshly opened bottle, it should be redistilled before use.
6. The heating period is critical to the success of this reaction. After a heating period of 45–90 minutes the initially white suspension begins to turn yellow and the color gradually deepens as heating is continued. The correct heating period is normally reached about 10 minutes after vigorous gas evolution ceases; at this time the color of the reaction mixture is yellow-orange to orange. At this point the mixture is not clear, but relatively little suspended material separates when the stirrer is stopped for a short period. If heating is stopped too soon, a large amount of acid is lost during the filtration and the product is difficult to crystallize. If heating is continued too long, the product is contaminated with a brown-colored impurity and is difficult to crystallize.
7. The submitters used material purchased from the Aldrich Chemical Company.
8. This material was purchased from Fisher Scientific Company.
9. Although this distillation has been performed repeatedly without incident, the product is potentially explosive and the operator should take suitable precautions including surrounding the distillation apparatus with a hood and a safety shield and wearing an effective face shield.
10. A pot residue amounting to 2–3 g. of orange liquid remains at the end of this distillation.

3. Discussion

Crotyl diazoacetate has been prepared by the procedure described here[3] and by the reaction of

diazomethane with crotyl chloroformate.[3] The lower homolog, allyl diazoacetate, has been prepared by the reaction of allyl glycinate with nitrous acid[4] and by the successive conversion of allyl chloroacetate to the corresponding azide, iminophosphorane, and, finally, the diazo ester.[5]

Other methods for the preparation of diazoacetic acid esters include the diazotization of glycine esters,[6] the thermal or base-catalyzed decomposition of N-acyl-N-nitrosoglycine esters,[7] the base-catalyzed cleavage of α-diazo-β-keto acetates,[8] the reaction of carboalkoxymethylenephosphoranes with arylsulfonyl azides,[9] the acid-catalyzed decomposition of acetic esters with α-aryl-triazene substituents,[10] and the reaction of chloroformate esters with diazomethane.[3,11] The present procedure is unique in that a diazoacetic ester may be prepared in one step by reaction of the desired alcohol with a relatively stable, solid acylating agent which may be prepared in quantity and stored (in a desiccator). Consequently, the method is of particular value for alcohols which are not readily available or for alcohols containing other functional groups which would be incompatible with the reaction conditions required in other diazoacetate syntheses.

Although the present procedure illustrates the formation of the diazoacetic ester without isolation of the intermediate ester of glyoxylic acid *p*-toluenesulfonylhydrazone, the two geometric isomers of this hydrazone can be isolated if only one molar equivalent of triethylamine is used in the reaction of the acid chloride with the alcohol.[3] The extremely mild conditions required for the further conversion of these hydrazones to the diazo esters should be noted. Other methods for decomposing arylsulfonyl-hydrazones to form diazocarbonyl compounds have included aqueous sodium hydroxide,[12] sodium hydride in dimethoxyethane at 60°,[13] and aluminum oxide in methylene chloride or ethyl acetate.[14] Although the latter method competes in mildness and convenience with the procedure described here, it was found not to be applicable to the preparation of aliphatic diazoesters such as ethyl 2-diazopropionate. Hence the conditions used in the present procedure may offer a useful complement to the last-mentioned method when the appropriate arylsulfonylhydrazone is available.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 7, 438

References and Notes

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

petroleum ether

p-toluenesulfonylhydrazone

p-toluenesulfonylhydrazone of glyoxylic acid chloride

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ethyl acetate (141-78-6)

sodium hydroxide (1310-73-2)

thionyl chloride (7719-09-7)

sulfur dioxide (7446-09-5)

carbon tetrachloride (56-23-5)

nitrous acid (7782-77-6)

methylene chloride (75-09-2)

glyoxylic acid (298-12-4)

Diazomethane (334-88-3)

aluminum oxide (1344-28-1)

sodium hydride (7646-69-7)

triethylamine (121-44-8)

dimethoxyethane (534-15-6)

Crotyl diazoacetate,
Acetic acid, diazo-, trans-2-butenyl ester (14746-03-3)

Crotyl alcohol

crotyl chloroformate

allyl diazoacetate

allyl glycinate

allyl chloroacetate (2916-14-5)

ethyl 2-diazopropionate

p-Toluenesulfonylhydrazide (1576-35-8)

Glyoxylic acid p-toluenesulfonylhydrazone (14661-68-8)