ORGANIC SYNTHESES

VOLUME 65
1987

ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

VOLUME 65
1987

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NOTICE

With Volume 62, the Editors of *Organic Syntheses* began a new presentation and distribution policy to shorten the time between submission and appearance of an accepted procedure. The soft cover edition of this volume is produced by a rapid and inexpensive process, and is sent at no charge to members of the Organic Division of the American Chemical Society. The soft cover edition is intended as the personal copy of the owner and is not for library use. A hard cover edition is published by John Wiley and Sons, Inc. in the traditional format, and differs in content primarily in the inclusion of an index. The hard cover edition is intended primarily for library collections and is available for purchase through the publisher. Annual Volumes 60–64 will be included in a new five-year version of the collective volumes of *Organic Syntheses* which will appear as *Collective Volume Seven* in the traditional hard cover format, after the appearance of annual volume 64. It will be available for purchase from the publishers. The Editors hope that the new *Collective Volume* series, appearing twice as frequently as the previous decennial volumes, will provide a permanent and timely edition of the procedures for personal and institutional libraries. The Editors welcome comments and suggestions from users concerning the new editions.

NOMENCLATURE

Both common and systematic names of compounds are used throughout this volume, depending on which the Editor-in-Chief felt was more appropriate. The *Chemical Abstracts* indexing name for each title compound, if it differs from the title name, is given as a subtitle. Systematic *Chemical Abstracts* nomenclature, used in both the 9th and 10th Collective Indexes for the title compound and a selection of other compounds mentioned in the procedure, is provided in an appendix at the end of each preparation. Registry numbers, which are useful in computer searching and identification, are also provided in these appendixes. Whenever two names are concurrently in use and one name is the correct *Chemical Abstracts* name, that name is adopted. For example, both diethyl ether and ethyl ether are normally used. Since ethyl ether is the established *Chemical Abstracts* name for the 8th Collective Index, it has been used in this volume. The 9th Collective Index name is 1,1′-oxybisethane, which the Editors consider too cumbersome.

SUBMISSION OF PREPARATIONS

Organic Syntheses welcomes and encourages submission of experimental procedures which lead to compounds of wide interest or which illustrate important new developments in methodology. The Editorial Board will consider proposals in outline format as shown below, and will request full experimental details for those proposals which are of sufficient interest. Submissions which are longer than three steps from commercial sources or from existing *Organic Syntheses* procedures will be accepted only in unusual circumstances.

Organic Syntheses Proposal Format

1. Authors
2. Literature reference or enclose preprint if available.
3. Proposed sequence
4. Best current alternative(s)

5. a. Proposed scale, final product:
   b. Overall yield:
   c. Method of isolation and purification:
   d. Purity of product (%):
   e. How determined?
6. Any unusual apparatus or experimental technique:
7. Any hazards?
8. Source of starting material?
9. Utility of method or usefulness of product.

Submit to: Dr. Jeremiah P. Freeman, Secretary
Department of Chemistry
University of Notre Dame
Notre Dame, IN 46556

Proposals will be evaluated in outline form, again after submission of full experimental details and discussion, and finally, by checking experimental procedures. A form that details the preparation of a complete procedure (Notice to Submitters) may be obtained from the Secretary.

Additions, corrections, and improvements to the preparations previously published are welcomed; these should be directed to the Secretary. However, checking of such improvements will only be undertaken when new methodology is involved. Substantially improved procedures have been included in the Collective Volumes in place of a previously published procedure.

PREFACE

This volume reflects intensive activity in several areas of synthetic organic chemistry. The volume begins with enol/carbonyl condensations and several variants for synthesis of 5-membered carbocycles. Next comes a series of examples illustrating the synthesis of alkynes, alkenes, and aromatic carbocycles. Heteroelement chemistry is featured in the extensive use of organosilicon reagents, in several applications of transition element chemistry, in reactive nitrogen intermediates, and in the preparation of β-lactams, indoles, and other heterocycles. The last and largest section of the volume deals with a variety of chiral auxiliaries which are important in asymmetric synthesis. This field is in the midst of explosive growth and will undoubtedly see major changes and improvements in techniques and results over the next decade.

I would like to thank Carole Klingbeil, Joyce Bohling, and Professor Jeremiah P. Freeman and his office staff for their extensive help and patience in the preparation of text for this volume. Mr. P. Kierkus deserves credit for the structures, drawn with the ChemDraw™ program and for transforming a great deal of rough copy into final diagrams. Lastly, my thanks to those of my students over the past several years who have spent their time and energy checking procedures and contributing in other ways which left me time for this volume.

E. VEDEJS

Madison, Wisconsin
January 1987

A. HAROLD BLATT

January 9, 1903–March 19, 1986

A. Harold Blatt, second Secretary to the Board of Editors of *Organic Syntheses, Inc.*, 1938-1943, and co-editor with Henry Gilman of the revised edition of Collective Volume 1 of *Organic Syntheses,* passed away on March 19, 1986 in Melbourne, Florida at the age of 83.

Dr. Blatt was born in Cincinnati, Ohio and received B.S., M.A., and Ph.D. degrees from Harvard University in 1923-1926. He held postdoctoral positions at the College de France in Paris, Harvard University, and the University of Buffalo before he joined the faculty at Howard University as an associate professor in 1932. He became a member of the newly-formed Queens College in 1939, where he was a professor, and stayed for 32 years. His academic pursuits were interrupted during World War II when he was a Science Liaison Officer, the London Mission, in the Office of Scientific Research and Development (1944-1945), and a Technical Aide to Division 8 during the latter year.

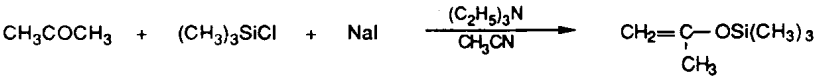
Dr. Blatt also edited Collective Volume 2 of *Organic Syntheses* (1943), and served for many years on the Board of Directors, where his expertise and knowledge of finance were of inestimable value. At corporation meetings, his versatility was shown by the skill he demonstrated in the selection of the dinner wines. His editorial expertise was used also by Organic Reactions, Inc. where he was a member of the Editorial Board (1948-1954), and then served on the Advisory Board until 1986.

Dr. Blatt's teaching and research activities covered the period from his Harvard days into the 1980's. He was a co-editor with James B. Conant of the well-known text, *The Chemistry of Organic Compounds,* 3rd edition, which was published in 1947, and used widely during the 1950's. The text offered a new approach for organic chemistry students to the subjects of reaction rates and equilibria. It also presented new physiochemical concepts and data, as well as an effort to cover some of the major topics of biochemistry and pharmacology, and relate their chemistry to the principles expounded in the book.

CONTENTS

ACETONE TRIMETHYLSILYL ENOL ETHER

(Silane, trimethyl[(1-methylethenyl)oxy]-)



Submitted by Nigel D. A. Walshe, Graham B. T. Goodwin, Graham C. Smith, and Frank E. Woodward.[1]

Checked by V. A. Palaniswamy and James D. White.

1. Procedure

To a 5-L, four-necked flask, equipped with a mechanical stirrer, reflux condenser with nitrogen inlet, thermometer and pressure-equalizing dropping funnel, are added 150 g (2.6 mol) of acetone (Note 1) and 192 g (1.9 mol) of triethylamine (Note 2) under a nitrogen atmosphere. To this mixture, stirred at room temperature under nitrogen, is added via the dropping funnel 200 g (1.84 mol) of chlorotrimethylsilane over 10 min (Note 3). The flask is then immersed in a waterbath and the contents are warmed to 35°C. The waterbath is removed and the dropping funnel is charged with a solution of 285 g (1.9 mol) of sodium iodide (Note 4) in 2.14 L of acetonitrile (Note 5). This solution is added to the stirred mixture in the flask at such a rate that the temperature of the reaction is maintained at 35-40°C without external heating or cooling (Note 6). The addition requires approximately 1 hr. When addition is complete, the reaction mixture is stirred for a further 2 hr at room temperature. The contents of the flask are then poured into 5 L of ice-cold water, and the aqueous mixture is extracted with two 1-L portions of pentane,

and once with 500 mL of pentane. The combined pentane extracts are dried over anhydrous potassium carbonate, and filtered into a 3-L, round-bottomed flask. This is arranged for distillation at atmospheric pressure, incorporating a 30-cm Vigreux fractionating column. The pentane is distilled off at atmospheric pressure, until a head temperature of 88°C is attained. The crude material is transferred to a 500-mL flask, and the product is then distilled at atmospheric pressure through a 20-cm Vigreux column. A forerun of 20 g is collected between room temperature and 94°C. The product is the fraction boiling at 94-96°C, the yield of which is 116-130 g (48-54%) (Note 7).

2. Notes

1. "AnalaR" grade acetone, as supplied by BDH, was used.

2. Triethylamine was dried over potassium hydroxide pellets for at least 24 hr.

3. Commercial chlorotrimethylsilane was used without purification. When it was added to the acetone/triethylamine mixture, only a very mild exothermic reaction occurred (ca. 2°C). Dense white fumes formed, and a turbid solution was obtained.

4. Sodium iodide was reagent grade. It is essential to dry this material thoroughly. Heating at 140°C for 8 hr under reduced pressure (ca. 20 mm) is satisfactory. The loss of weight on drying is roughly 5%. If this is not done, hexamethyldisiloxane is the principal product.

5. Acetonitrile was reagent grade, dried by passage through 1 kg of neutral alumina (grade 1), and then stored over 3 Å molecular sieves.

6. A copious white precipitate forms at this stage. If the reaction is not mildly exothermic, then very poor yields of product are obtained.

7. The yield is based on chlorotrimethylsilane. Two small-scale runs - 0.124 mol and 0.37 mol, also based on chlorotrimethylsilane - gave yields of 60% and 61%, respectively, which the submitters also reported on the larger scale. The material from the large-scale run was 92% pure by gas-chromatographic analysis. The impurities, identified by NMR, are triethylamine (0.5%) and hexamethyldisiloxane (7.5%). The product has the following spectral characteristics; IR (film) cm^{-1}: 1650, 1280, 1260, 1050; ^1H NMR ($CDCl_3$) δ: 0.13 (s, 9 H, $SiCH_3$), 1.69 (br s, 3 H, $=CCH_3$), 3.92 (m, 2 H, $=CH_2$).

3. Discussion

Trimethylsilyl enolates of aldehydes and ketones are now established as highly useful synthetic intermediates.[2] In particular, their Lewis acid-catalyzed reactions - e.g., alkylation[3] and mild, regiospecific aldol condensations[4] - provide useful alternatives to classical, base-generated metal enolate chemistry. This new methodology would be ideal for the introduction of the commonly-encountered acetonyl residue. However the required silyl enol ether of acetone is not commercially available, nor is a simple, reliable and economical synthesis adequately described in the literature. The above procedure is an adaptation of a literature method,[5] and relies on the generation of iodotrimethylsilane in situ. We have found that the precautions described in Notes 4 and 6 are crucial to the success of the preparation. This procedure makes available a useful reagent by a cheap, reliable route, starting from readily available materials, and in large or

small quantity. The trimethylsilyl enol ether of acetone has been prepared previously in good yield by reaction of acetone with trimethylsilyl triflate and triethylamine.[6] However, the silyl triflate reagent is expensive for large-scale work. Another route[7] involves the mercuric iodide-catalyzed rearrangement of α-trimethylsilylacetone (obtained from trimethylsilylmethylmagnesium chloride and acetic anhydride). This is a laborious, low-yield process. Other methods include a synthesis from acetone, chlorotrimethylsilane, and triethylamine[8] (yields and exact procedure unspecified); or reaction of acetone with hexamethyldisilazane,[9] or bis(trimethylsilyl)acetamide,[10] and a catalytic amount of sodium in the presence of hexamethylphosphoric triamide. Two authors[11] who used the method of House[12] (no experimental details supplied) note that their product always contained about 30% of hexamethyldisiloxane, which could not be separated by fractional distillation.

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Appendix

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

Acetone trimethylsilyl enol ether: Silane, (isopropenyloxy)trimethyl- (8); Silane, trimethyl[(1-methylethenyl)oxy]- (9); (1833-53-0)

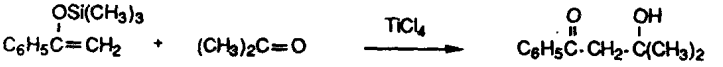
Acetone (8); 2-Propanone (9); (67-64-1)

Triethylamine (8); Ethanamine, N,N-diethyl- (9); (121-44-8)

Chlorotrimethylsilane: Silane, chlorotrimethyl- (8,9); (75-77-4)

3-HYDROXY-3-METHYL-1-PHENYL-1-BUTANONE BY CROSSED ALDOL REACTION

(1-Butanone, 3-hydroxy-3-methyl-1-phenyl-)



Submitted by Teruaki Mukaiyama and Koichi Narasaka.[1]

Checked by Kathleen Hug and Clayton H. Heathcock.

1. Procedure

A 500-mL, three-necked flask is fitted with a stirring bar, rubber stopper, 100-mL pressure-equalizing dropping funnel and a three-way stop-cock which is equipped with a balloon of argon gas (Note 1). The flask is charged with 140 mL of dry methylene chloride (Note 2) and cooled in an ice bath. Titanium tetrachloride (11.0 mL) (Note 3) is added by a syringe with stirring by a magnetic stirrer, and a solution of 6.5 g of acetone in 30 mL of methylene chloride is added dropwise over a 5-min period. On completion of this addition a solution of 19.2 g of 1-phenyl-1-trimethylsiloxyethylene (Note 4) in 15 mL of methylene chloride (Note 5) is added dropwise over a 10-min period, and the mixture is stirred for 15 min.

The reaction mixture is poured into 200 mL of ice water with vigorous stirring and the organic layer is separated. The aqueous layer is extracted with two 30-mL portions of methylene chloride. The combined methylene chloride extracts are washed with two 60-mL portions of a 1:1 mixture of saturated aqueous sodium bicarbonate and water, and then with brine. The methylene chloride solution is dried over sodium sulfate and the methylene chloride is removed using a rotary evaporator.