



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

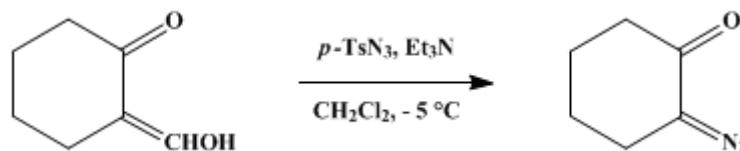
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.389 (1988); Vol. 51, p.86 (1971).

2-DIAZOCYCLOALKANONES: 2-DIAZOCYCLOHEXANONE

[Cyclohexanone, 2-diazo-]



Submitted by Manfred Regitz¹, Jörn Rüter, and Annemarie Liedhegener.
Checked by John D. Fenwick and Peter Yates.

1. Procedure

Caution! 2-Diazocyclohexanone may explode, especially on being heated. The workup and distillation should be carried out in a fume hood behind a safety shield.

A. 2-l., wide-necked Erlenmeyer flask is charged with 66.2 g. (0.525 mole) of 2-(hydroxymethylene)cyclohexanone (Note 1), 400 ml. of dichloromethane, and 106 g. (1.05 moles) of triethylamine (Note 2). The flask is cooled in an ice-salt bath at -12 to -15° , and 98.0 g. (0.500 mole) of *p*-toluenesulfonyl azide (Note 3) is added with vigorous mechanical stirring over a period of approximately 1 hour, at such a rate that the temperature of the reaction mixture does not rise above -5° . Stirring is continued for an additional 2 hours as the cooling bath melts. A solution of 30.8 g. (0.550 mole) of potassium hydroxide in 400 ml. of water is added, and the mixture is stirred for 15 minutes at room temperature. The resulting emulsion is placed in a 2-l. separatory funnel, the dichloromethane layer is separated after the emulsion has broken, and the aqueous, alcoholic layer is washed with two 100-ml. portions of dichloromethane. The combined dichloromethane solutions are washed with a solution of 2.8 g. of potassium hydroxide in 200 ml. of water, then with 200 ml. of water, and dried over anhydrous sodium sulfate (Note 4). The solvent is removed on a rotary evaporator at 35° (15 mm.) until the weight of the residue is constant, yielding 51.5–59.0 g. (83–95%) of yellow-orange 2-diazocyclohexanone (Note 5). Distillation with magnetic stirring (Note 6) of 20 g. of this crude product from a hot-water bath at 80° gave 17.0 g. of yellow-orange liquid, b.p. 46° (0.1 mm.) or 60° (0.4 mm.) (Note 7). The IR spectrum (liquid film) has a strong band at 2083 cm^{-1} attributable to the diazo function.

2. Notes

1. 2-(Hydroxymethylene)cyclohexanone was prepared from cyclohexanone [*Org. Synth.*, **Coll. Vol. 4**, 536 (1963)] and was freshly distilled before use.
2. Freshly distilled; b.p. 88.5 – 90.5° .
3. *p*-Toluenesulfonyl azide was prepared from *p*-toluenesulfonyl chloride and sodium azide [*Org. Synth.*, **Coll. Vol. 5**, 179 (1973)]. The submitters found that when somewhat less than the stoichiometric quantity of *p*-toluenesulfonyl azide is used, 2-diazocyclohexanone is obtained free of azide; the excess 2-(hydroxymethylene)cyclohexanone is readily removed in the alkaline workup. The crude product obtained by the checkers, however, contained *p*-toluenesulfonyl azide (Note 5).
4. The basic, aqueous solution on acidification with 6 *N* hydrochloric acid gives *N*-formyl-*p*-toluenesulfonamide in almost quantitative yield. Crystallization from benzene gave crystals, m.p. 101 – 102° (lit.² 102 – 103°).
5. The submitters found that this product gave a single spot by TLC (Note 8), and that it can be used for most preparative purposes without distillation. The checkers found by ¹H NMR spectroscopy that the product contained *p*-toluenesulfonyl azide (ca. 5%) and triethylamine.
6. If the distillation is carried out with a capillary leak, decomposition of the diazo compound occurs. The checkers found that distillation on a larger scale led to extensive decomposition.

7. The distillation is not carried to completion because of the danger of explosion. It is carried out with the usual safety precautions (safety shield), although no explosion has yet occurred.
8. TLC was carried out on DC-Fertigplatte Merck Kieselgel F₂₅₄ supplied by Firma Merck AG, 61 Darmstadt, Germany. For the solvent system [dichloromethane/methanol](#) (97/3) the product has an *R_f* value of 0.45.

3. Discussion

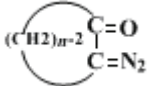
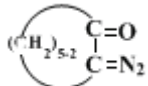
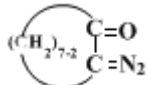
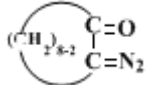
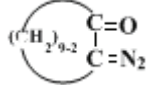
In addition to previously described syntheses^{2,3} by diazo group transfer with deformylation,⁴ 2-diazocyclohexanone has been prepared by two variants of this method. In one, the reaction of 2-(hydroxymethylene)cyclohexanone with *p*-toluenesulfonyl azide is carried out in ether/diethylamine, and an enamine is assumed to be formed as an intermediate;⁵ in the other, the sodium salt of the hydroxymethylene compound was treated with the lithium salt of *p*-carboxybenzenesulfonyl azide in ether/tetrahydrofuran.⁶ Its preparation from 1,2-cyclohexanedione mono-*p*-toluenesulfonylhydrazone was described earlier.⁷

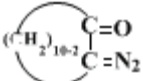
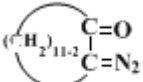
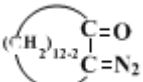
2-Diazocycloalkanones with five- to twelve-membered rings can be synthesized by the present procedure in good yields (Table I).² Diazo transfer with deformylation can also be used for the preparation of bicyclic α -diazo ketones.^{8,9} A related procedure involving reaction of the sodium salt of an α -(hydroxymethylene) ketone with *p*-toluenesulfonyl azide in ethanol has been applied to the synthesis of diazoalkyl ketones, α -diazo aldehydes, and α -diazo carboxylic esters.¹⁰

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 9, 197](#)
- [Org. Syn. Coll. Vol. 9, 400](#)

TABLE I
PREPARATION OF 2-DIAZOCYCLOALKANONES

	Boiling Point or [Melting Point], °C.	Yield, %
5		
	34–37 (0.8 mm.)	98
7		
	62 (0.4 mm.)	83
8		
	a	87
9		
	a	73

	[54–55]	81
11		
	b	79
12		
	[42–43]	57

^a Liquid, purified by crystallization from [ether](#) at -60° .

^b Liquid, purified by crystallization from [ethanol](#) at -20° .

References and Notes

1. Institut für Organische Chemie der Universität des Saarlandes, 66 Saarbrücken 11, Germany. [Present address: Fachbereich Chemie, Universität Kaiserslautern, 675 Kaiserslautern, Germany.]
 2. M. Regitz and J. Rüter, *Chem. Ber.*, **101**, 1263 (1968).
 3. M. Regitz, F. Menz, and J. Rüter, *Tetrahedron Lett.*, 739 (1967).
 4. M. Regitz, *Angew. Chem.*, **79**, 786 (1967); *Angew. Chem. Int. Ed. Engl.*, **6**, 733 (1967).
 5. M. Rosenberger, P. Yates, J. B. Hendrickson, and W. Wolf, *Tetrahedron Lett.*, 2285 (1964).
 6. J. B. Hendrickson and W. A. Wolf, *J. Org. Chem.*, **33**, 3610 (1968).
 7. H. Stetter and K. Kiehs, *Chem. Ber.*, **98**, 1181 (1965).
 8. T. Gibson and W. F. Erman, *J. Org. Chem.*, **31**, 3028 (1966).
 9. K. B. Wiberg and A. de Meijere, *Tetrahedron Lett.*, 519 (1969).
 10. M. Regitz and F. Menz, *Chem. Ber.*, **101**, 2622 (1968).
-

Appendix

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

sodium salt of the hydroxymethylene

2-Diazocycloalkanones

sodium salt of an α -(hydroxymethylene) ketone

[ethanol](#) (64-17-5)

[hydrochloric acid](#) (7647-01-0)

[Benzene](#) (71-43-2)

[methanol](#) (67-56-1)

[ether](#) (60-29-7)

Cyclohexanone (108-94-1)

sodium sulfate (7757-82-6)

potassium hydroxide (1310-58-3)

diethylamine (109-89-7)

sodium azide (26628-22-8)

dichloromethane (75-09-2)

Tetrahydrofuran (109-99-9)

triethylamine (121-44-8)

2-(hydroxymethylene)cyclohexanone (823-45-0)

p-Toluenesulfonyl chloride (98-59-9)

2-Diazocyclohexanone,
Cyclohexanone, 2-diazo- (3242-56-6)

p-toluenesulfonyl azide (941-55-9)

N-formyl-p-toluenesulfonamide

1,2-cyclohexanedione mono-p-toluenesulfonylhydrazone

lithium salt of p-carboxybenzenesulfonyl azide