Hydrazinolysis of Urazoles: A Convenient and Mild Method for the Preparation of Azoalkanes

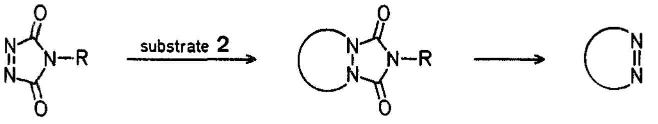
Waldemar ADAM[1], Luis A. ARIAS[2], Ottorino DE LUCCHI[2]

Institute of Organic Chemistry, University of Würzburg, Am Hubland, D-8700 Würzburg, Federal Republic of Germany

and Department of Chemistry, University of Puerto Rico, Rio Piedras, Puerto Rico 00931, U.S.A.

The importance of azoalkanes as mechanistic probes for diradical chemistry[3] and as synthons for the preparation of unusual molecules[4] has come clearly into focus during the last decade. One of the more important syntheses of the azoalkanes (**4**) involves cycloaddition of 1,2,4-triazolin-3,5-dione (**1**) to suitable diene substrates **2** to afford urazoles (**3**), followed by oxidative hydrolysis (Scheme **A**).

0039-7881/81/0732-0543 $ 03.00



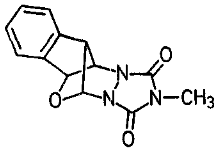
1 (TAD) **3** **4**

Scheme A

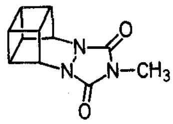
The latter step can be a handicap in this synthetic sequence, because the drastic conditions which are usually necessary in the hydrolysis step[5] lead frequently to low yields (< 30%) due-to destruction of the product. The best method to date, which is even effective for sterically hindered urazoles[6], requires such strongly basic conditions as potassium *t*-butoxide in wet dimethyl sulfoxide, but at room temperature. Some alternative attempts to solve this problem have been the use of more easily hydrolizable urazole analogs derived from cycloaddition of 4-thia-1,2-diazoline-3,5-dione[7]. Unfortunately, this dienophile is too labile thermally and survives cycloaddition only with the most reactive dienes.

Hydrazinolysis has been employed as an effective and convenient method to release primary amines from *N*-substituted phthalimides (the Gabriel synthesis)[8]. Consequently, we felt that this reagent should be useful in the conversion of urazoles **3** into azoalkanes **4**. Thus, a large variety of bicyclic urazoles, prepared via cycloaddition of **1** to the appropriate substrate **2**, were submitted to hydrazinolysis and subsequently oxidized with copper(II) chloride to the respective azoalkanes **4**. The results are summarized in the Table and compared with the usual oxidative hydrolysis methods.

Clearly, the present hydrazinolysis procedure has definite merits in view of its relatively mild and moderately basic conditions. In all cases studied here, the hydrazinolysis method is

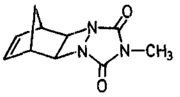
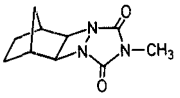
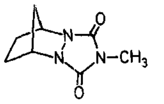
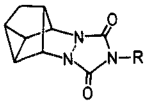
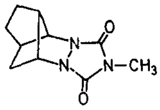
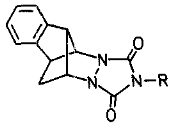
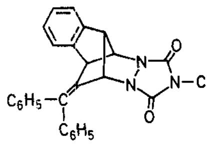
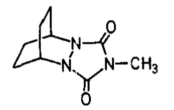
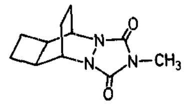


3m



3n

Table. Hydrazinolysis of Urazoles **3** to Azoalkanes **4**

Urazole 3		Hydrazinolysis conditions[a]	Yield [%] of 4	m.p. [°C][b] of 4	Lit. m.p. [°C] of 4
	**3a**	$N_2H_4/C_2H_5OH/\sim 22\,°C$	92	65-66°	65-66°[9]
	**3b**	$N_2H_4/C_2H_5OH/\sim 22\,°C$	70	129-130°	128-129°[9]
	**3c**	N_2H_4/C_2H_5/reflux	71	99-101°	99-100°[5a]
	**3d** R = CH_3	N_2H_4/C_2H_5OH/reflux	67	95-96°	95-97°[5b]
	3e R = C_6H_5	N_2H_4/C_2H_5OH/reflux	57		
	**3f**	N_2H_4/C_2H_5OH/reflux	72	145-146°	147-149°[10]
	**3g** R = CH_3	N_2H_4/C_2H_5OH/reflux	74	75-77°	74°[10]
	3h R = C_6H_5	N_2H_4/C_2H_5OH/reflux	66		
	3i R = $N{=}CH{-}C_6H_5$	N_2H_4/C_2H_5OH/reflux	56		
	**3j**	N_2H_4/C_2H_5OH/reflux	90	99-101°	99-100°[11]
	**3k**	$N_2H_4/\sim 130\,°C$	60	140-141°	139-140°[12]
	**3l**	$N_2H_4/\sim 130\,°C$	33	141-143°	142-144°[12]

---

[a] Usually a large excess of hydrazine was used except for **3a** for which stoichiometric quantities were used to avoid reduction of the double bond.

[b] Uncorrected.

at least as good or better than the previous methods[4]. Qualitative observations revealed that the more strained urazoles react faster, e.g. diazetidine **(3a)** > pyrazoline **(3c)** > pyridazine **(3h)**. When no double bonds are present, a large excess of hydrazine can be used to drive the reaction faster to completion; but in the case of the urazole **(3a)**, stoichiometric amounts of hydrazine must be used to avoid reduction of the double bond. Even under a nitrogen atmosphere, the double bond reduction could not be suppressed. Use of polar aprotic solvents such as dimethyl sulfoxide instead of ethanol did not increase the yields of azoalkane significantly. Furthermore, the use of hydroxylamine in place of hydrazine did not effect hydrolysis of the urazoles.

Unfortunately, the present hydrazinolysis method could not be used to prepare the azoalkanes derived from the urazoles **(3m)** and **(3n)**. In both cases only intractable tars were isolated; not even traces of the respective azoalkanes had formed.

Hydrazinolysis of Urazoles 3; General Procedure:

A 50-ml, one-necked, round-bottomed flask, provided with a magnetic spinbar and reflux condenser, is charged with urazole **3** (1-2 mmol) and hydrazine hydrate (100%; 1-6 mmol) in 95% ethanol (20 ml). The reaction mixture is stirred at room temperature (~20 °C) or refluxed, depending on the reactivity of the urazole, while monitoring the progress of reaction by T.L.C. (silica gel, ethyl acetate). After complete hydrazinolysis, the reaction mixture is roto-evaporated (~25-40 °C/10-20 torr), the residue is dissolved in 95% ethanol (~30 ml), and immediately treated with saturated aqueous copper(II) chloride solution until precipitation. The precipitated copper complex of the azoalkane is collected on a sintered glass funnel, the pH of the filtrate adjusted to ~6.0-6.5 with aqueous ammonium hydroxide and again saturated aqueous copper(II) chloride solution is added until precipitation. This process is repeated until no more copper complex precipitates (usually 2-3 cycles). The combined precipitates are dissolved in 25% ammonium hydroxide solution (20-25 ml), the solution is extracted with dichloromethane (3 × 30 ml), the extracts are washed with 20% aqueous sodium chloride solution (2 × 30 ml), and dried with anhydrous magnesium sulfate. After roto-evaporation of the solvent (~10-20 °C/15-20 torr) [care must be taken in the solvent removal because some of the azoalkanes are easily lost through volatilization] the crude azoalkane **4** is purified through sublimation and subsequent recrystallization. The results are given in the Table.

Acknowledgements are made to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the National Institutes of Health, the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society for financial support.

Received: March 2, 1981

---

[1] Correspondence should be addressed to this author at Würzburg.

[2] An Alexander-von-Humboldt Foundation travel grant is gratefully acknowledged.

[3] P. S. Engel, *Chem. Rev.* **80**, 99 (1980).

[4] W. Adam, O. De Lucchi, *Angew. Chem.* **92**, 813 (1980); *Angew. Chem. Int. Ed. Engl.* **19**, 762 (1980).

[5] (a) S. G. Cohen, R. Zand, *J. Am. Chem. Soc.* **84**, 586 (1962).
(b) R. C. Cookson, S. S. H. Gilani, I. D. R. Stevens, *J. Chem. Soc.* **1967**, 1905.
(c) H. Ulsen, J. P. Snyder, *J. Am. Chem. Soc.* **99**, 1524 (1977).

[6] L. A. Paquette, personal communication.

[7] (a) E. J. Corey, B. B. Snider, *J. Org. Chem.* **38**, 3632 (1973).
(b) S. W. Mojé, P. Beak, *J. Org. Chem.* **39**, 2951 (1974).

[8] M. S. Gibson, R. W. Bradshaw, *Angew. Chem.* **80**, 986 (1968); *Angew. Chem. Int. Ed. Engl.* **7**, 919 (1968).

[9] D. M. Lemal, *J. Am. Chem. Soc.* **91**, 5668 (1969).

[10] W. Adam, O. De Lucchi, I. Erden, *J. Am. Chem. Soc.* **102**, 4806 (1980).

[11] W. Adam, O. De Lucchi, unpublished results.

[12] M. Hexman, V. T. Bandurco, J. P. Snyder, *J. Chem. Soc. Chem. Commun.* **1971**, 297.

[13] (a) R. J. Boyd, J.-C. G. Bünzli, J. P. Snyder, *J. Am. Chem. Soc.* **98**, 2398 (1976).
(b) E. L. Allred, J. C. Hinshaw, *J. Chem. Soc. Chem. Commun.* **1969**, 1021.

0039-7881/81/0732-0545 $ 03.00