Synthesis of Azoalkanes

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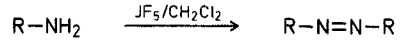
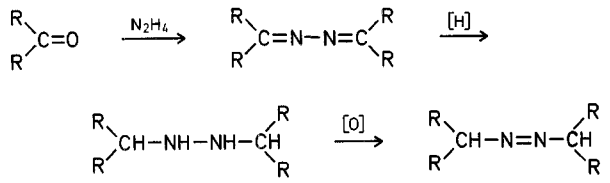
There are several widely used procedures for the synthesis of azoalkanes. Oxidative coupling of amines with iodine pentafluoride (Scheme **A**)[1,2,3] is a method which is difficult to work up, sometimes gives low yields[4], and is limited to preparation of symmetrical azoalkanes with tertiary alkyl groups.



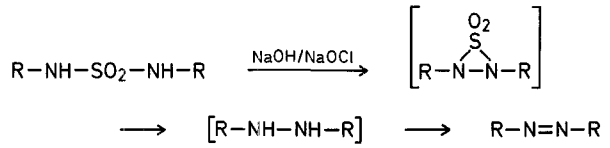
Scheme **A**

Oxidation of N,N′-dialkylhydrazines, prepared by condensation of hydrazine with an aldehyde or ketone followed by reduction of the carbon nitrogen double bond (Scheme **B**)[5], is a method which is applicable only to azo compounds with primary or secondary alkyl groups.



Scheme **B**

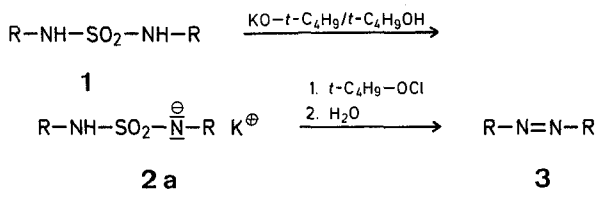
N,N′-Dialkylsulfamides can be cyclized, hydrolyzed, and oxidized to give azoalkanes by treatment with base and sodium hypochlorite (Scheme **C**)[6,7].



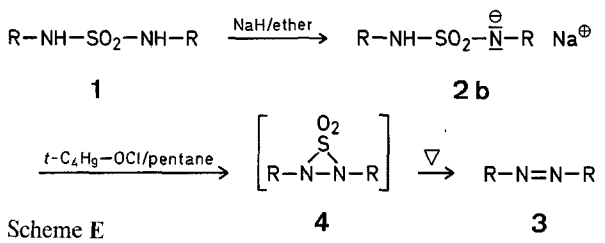
Scheme **C**

Although other approaches have been employed[8-14] Scheme **C** illustrates the method which seemed most likely to be generally adaptable to the widest variety of substrates. However, the present conditions are apparently too rigorous for isolating unstable azo compounds[15] and solubility problems in several cases led to quantitative return of starting sulfamides. Treatment of either N,N′-bis-[2,4,4-trimethyl-2-pentyl]-sulfamide or N,N′-bis-[2,3,3-trimethyl-2-butyl]-sulfamide under the conditions specified in Ref.[6] and Ref.[7] gave no azo compound.

We have investigated the conversion of N,N'-dialkylsulfamides (**1**) into azoalkanes (**3**) using a completely homogeneous mixture with potassium *t*-butoxide as the base, *t*-butyl hypochlorite as the chlorinating agent, and *t*-butanol as the solvent (Scheme **D**) and, alternatively, using a heterogeneous mixture with sodium hydride as the base and *t*-butyl hypochlorite as the chlorinating agent in an ether/pentane solvent (Scheme **E**).



Scheme **D**



Scheme **E**

The results are tabulated in Table 1. The reaction conditions are mild and should be amenable to preparation of relatively unstable azoalkanes.

It is noteworthy that we have been able to isolate the intermediate thiadiaziridine-1,1-dioxide (**4**) in one case and are presently investigating its chemistry.

Melting points are corrected. The N. M. R. spectra were recorded at 60 MHz using tetramethylsilane as an internal standard. The U. V. spectra were obtained with a Cary recording spectrophotometer model 15. Satisfactory analyses were obtained for all new compounds.

Commercial grades of *n*-butylamine (b. p. 77–78°), *sec*-butylamine (b. p. 67–68°), *t*-butylamine (b. p. 45–46°), and *t*-octylamine (b. p. 138–139°) were dried with potassium hydroxide and distilled immediately before use.

2-Amino-2,3,3-trimethylbutane (*t*-Heptylamine):
The amine was prepared by the procedure of Ritter and Kalish[16] with the indicated modifications. To a solution of conc. sulfuric acid (100 g, 1 mol) in glacial acetic acid (500 ml), acetonitrile (45 g, 1.1 mol) was added portionwise at 20°. 2,3,3-Trimethylbutan-2-ol (116 g, 1.0 mol) was added and the mixture stirred for 24 hr at room temperature. The mixture was then diluted with 5 volumes of ice water to give the crystalline N-acetyl derivative; yield: 113 g (72%); m. p. 115.5°–116°, after recrystallization from hexane. Hydrolysis of the acetamide was effected by refluxing with potassium hydroxide in ethylene glycol with removal of the amine by distillation. Fractionation of the distillate gave the amine as a colorless liquid; yield: 52 g (61%); b.p. 120–121° (Ref.[17], b.p. 121–122°).

N,N'-Dialkylsulfamides (1):
N,N'-Di-t-butylsulfamide was prepared according to the procedure of Stowell[18] and was recrystallized from benzene; yield: 66%; m. p. 141–142° (Ref.[18], m. p. 140–142°).

^{1}H-N. M. R. ($CDCl_3$): $\delta = 1.40$ (s, 18 H), 4.25 (s, 2 H) ppm.

N,N'-Dibutylsulfamide was prepared according to the procedure of Stowell[18] and was recrystallized from ethanol/water; yield: 71%; m. p. 126–127° (Ref.[7], m. p. 126°).

^{1}H-N. M. R. ($CDCl_3$): $\delta = 0.98$ (t, 6 H), 1.50 (m, 8 H), 3.08 (t, 4 H), 4.40 (t, 2 H) ppm.

N,N'-Bis-[2,4,4-trimethyl-2-pentyl]-sulfamide was prepared according to the procedure of Stowell[18] and was recrystallized from hexane; yield: 77%; m. p. 81–82°.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.04$ (s, 18 H), 1.42 (s, 12 H), 1.62 (s, 4 H), 4.41 (s, 2 H) ppm.

N,N'-Bis-[2,3,3-trimethyl-2-butyl]-sulfamide was prepared according to the procedure of Ohme and Preuschhof[7]; yield: 30%; m. p. 81–82°.

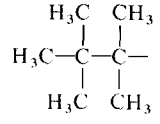
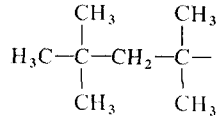
^{1}H-N.M.R. ($CDCl_3$): $\delta = 0.9$ (s, 18 H), 1.38 (s, 12 H), 4.0 (s, 2 H) ppm.

N,N'-Di-2-butylsulfamide was prepared according to the procedure of Sowada[19]; yield: 42%; m.p. 106–106.5° (Ref.[19], m.p. 104.5°).

^{1}H-N. M. R. ($CDCl_3$): $\delta = 0.97$ (d, 12 H, $J = 7.0$ Hz), 1.78 (m, 2 H), 2.87 (t, 4 H, $J = 6.5$ Hz), 4.50 (t, 2 H) ppm.

Preparation of Azoalkanes; General Procedure:
The dialkylsulfamide (**1**) is added in several portions to freshly washed sodium hydride (2 mol per 1 mol of **1**) suspended in

Table 1. Preparation of Azoalkanes (**3**) from N,N'-Dialkylsulfamides (**1**)

R	Yield %	b. p./mm	U.V. λ_{max} (ε) nm	N. M. R. (CCl_4) δ (ppm)
n-C_4H_9	37	60–62°/20	354 (19)	0.92 (m, 6 H), 1.40 (m, 6 H), 2.64 (t, 4 H)
sec-C_4H_9	64	41–43°/21	366 (18)	0.99 (d, 12 H, $J = 6.5$), 2.20 (m, 2 H), 3.53 (d, 4 H, $J = 7.0$)
t-C_4H_9	85	108–110°/760	368 (14)	1.17 (s)
	36	53–54°/1.5	376 (18)	1.00 (s), [($CCl_4 + CF_3COOH$): 1.00 (s, 18 H), 1.08 (s, 12 H)]
	78	70–71°/0.4	372 (23)	0.96 (s, 18 H), 1.12 (s, 12 H), 1.78 (s, 4 H)

purified pentane. (For sulfamides that are highly insoluble in pentane, ether can be substituted. However, the ether must be removed or the reaction mixture should be cooled to −20° before the next step, as *t*-butyl hypochlorite reacts with ether at room temperature.) The reaction mixture is stirred for a minimum of 2 hr at room temperature and then cooled to 0°. A 2 mol ratio of *t*-butyl hypochlorite in pentane (3 volumes) is added dropwise. After stirring overnight at room temperature, the excess sodium hydride is destroyed by the careful addition of water. The pentane extracts are dried with magnesium sulfate, concentrated, and passed through a neutral alumina column using pentane as an eluent. The pentane is removed and the azo compound distilled.

We appreciate helpful suggestions by Dr. J. C. Stowell and thank Dr. E. Elder for valuable library assistance. The Research Corporation is gratefully acknowledged for supporting this research.

Received: June 30, 1972

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