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THE McFADYEN-STEVENS SYNTHESIS OF ALIPHATIC ALDEHYDES CONTAINING α-HYDROGENS

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The alkaline decomposition of 1-acyl-2-arylsulfonylhydrazines to yield aldehydes was first described by McFadyen and Stevens (1) and a comprehensive review of the reaction has since been published (2).

$$R-\overset{O}{\overset{\|}{C}}-NHNH-SO_2Ar + OH^- \longrightarrow RCHO + ArSO_2^- + N_2 + H_2O$$

The work of McFadyen and Stevens (1,2) established that the method was applicable, in varying yields, only to the preparation of aromatic and heterocyclic aldehydes. Recently Sprecher (3) extended this reaction to the aliphatic series for compounds having no hydrogen atoms on the carbon atom alpha to the carbonyl group, the yields being highly dependent on the reaction time. The reduction of N'-p-toluenesulfonylpivalhydrazide (I) resulted in a 40% yield of pivalaldehyde when the reaction time was limited to 30 seconds, but only a 12% yield when the contact time was extended to 120 seconds, under the usual McFadyen-Stevens conditions (2,3). Aldehydes having a "neopentyl-type" structure should be less susceptible to destruction by secondary processes, than compounds having alpha hydrogens. This suspicion was confirmed when a survey of the literature showed that in all the aliphatic cases cited, the expected aldehydes contained an α-hydrogen and would therefore be subject to self-condensation reactions in the hot alkaline medium. In addition, the factor that seems critical in the application of the McFadyen-Stevens reaction to the aliphatic series is the reaction time.

In recent work on the decomposition of simple carbonyl derivatives of p-toluenesulfonylhydrazide (PTSH) with base (4), we have demonstrated that the reaction time as well as the nature of the solvent is critical in determining the nature and numbers of the products (5). We have applied the flash pyrolytic technique* developed in this study to the McFadyen-Stevens reaction for a number of simple aliphatic aldehydes.

The direct reaction of the aliphatic acid chloride with PTSH in ether solution containing an excess of pyridine or triethylamine was found to be superior (yields increased by 20-40%) to the usual route through the acylhydrazide, although both gave identical products. N'-p-toluenesulfonylpivalhydrazide (I) (m.p. 158-160°), N'-p-toluenesulfonyl-i-butyrylhydrazide (II) (m.p. 130-132°), and N'-p-toluenesulfonyl-n-butyrylhydrazide (III) (m.p. 125-127°) were prepared in 75-85% yields from the appropriate acyl halide, and then were decomposed under flash pyrolytic conditions as described in Table I.

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* The PTSH derivative is added slowly to a refluxing suspension or solution of base and the products are distilled from the reaction mixture as rapidly as formed. See reference 4.

TABLE I

Decomposition of PTSH[a] Derivatives of Aliphatic Acid Chlorides

Compound[b] (RCOTsH)	Mole Ratio RCOTsH:Base[c]	Solvent[d]	Total Yield	Yield of A	Product Distribution[e]		
					A	B	C
I	1:1	E.G.	82%	49%	60	22	18
I	1:2	E.G.	77%	47%	61	21	18
I	1:2	E.G.(aq.)	81%	50%	62	21	17
II	1:1	E.G.	48%	34%	71	17	12
II	1:2	E.G.	69%	33%	48	30	22
II	1:2	E.G.(aq.)	73%	13%	18	47	35
III	1:1	E.G.	31%	19%	62	22	16
III	1:1	E.G.(aq.)	38%	22%	57	25	18
III	1:2	E.G.	48%	12%	25	44	31
III	1:2	E.G.(aq.)	75%	10%	14	50	36

(a) *p*-Toluenesulfonylhydrazide. (b) Compounds (RCOTsH):I - *p*-toluenesulfonylpivalhydrazide, II - *p*-toluenesulfonyl-*i*-butyrylhydrazide, and III - *p*-toluenesulfonyl-*n*-butyrylhydrazide. (c) The mono sodium salt of ethylene glycol (prepared *in situ*). (d) Solvent: E.G. is ethylene glycol(anhydrous), and E.G.(aq.) ethylene glycol containing an equivalent of water for each equivalent of RCOTsH. (e) The distribution of products was obtained on an SE-30 preparative column at 150° by v.p.c. by consecutive analysis. The reaction products were found to be identical to authentic samples by I.R., N.M.R. and chemical analysis. A is the aldehyde, B is the alcohol and C is the acid, all materials having the same carbon skeleton. C was recovered from the alkaline residues by acidification and extraction.

It is evident from the results in Table I that aliphatic aldehydes, regardless of the structure at the α-carbon atom, are formed from 1-acyl-2-arylsulfonylhydrazines under flash pyrolytic conditions in ethylene glycol with sodium ethyleneglycolate as base. The reaction also results in a mixture of the aliphatic alcohol and aliphatic acid having the same carbon skeleton as the aldehyde**. In addition to the results listed in Table I, we have demonstrated that in aqueous ethylene glycol, under the normal reaction conditions, n-butyraldehyde is converted to a 1:1 mixture (after correction for extraction losses) of n-butanol and n-butyric acid. The extraction procedure used to recover the aliphatic acid was tested with samples of n-butyric acid and pivalic acid in a reaction blank, and only 75-85% of the acid was recovered from the alkaline reaction medium. The conversion of I, II, and III to a mixture of aldehyde and Cannizzaro products (6) further demonstrates the effect of reaction time on the pyrolysis of PTSH derivatives and the general utility of the flash technique in the preparation of sensitive compounds.

$$2\ R\text{-}CHO + OH^- \longrightarrow R\text{-}CH_2OH + R\text{-}CO_2^-$$

It is to be noted that the sensitivity of the aldehyde toward reaction by secondary processes increases with the number of alpha hydrogens present in the molecule. As the protonicity of the solvent is increased (added water) the yield of aldehyde falls off even though the overall yield of products increases. In the presence of excess alkali the yield of aldehyde also decreases. Extrapolation of our experimental results suggests that the optimum conditions for the formation of aldehydes from 1-acyl-2-arylsulfonylhydrazines consist of the use of one equivalent of base and a relatively aprotic solvent. Friedman (7) has reported verbally that good yields (70-

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** The Cannizzaro reaction is usually limited to aldehydes having no alpha hydrogens. Reference 6.

85%) of aliphatic aldehydes can be obtained by treatment of 1-acyl-2-arylsulfonylhydrazines with one equivalent of base in diglyme at 140°. We have been unable to duplicate these results, under a variety of reaction conditions.

When the decomposition of II and III was attempted in diglyme under aprotic conditions using either sodium methoxide or anhydrous sodium carbonate as base, the evolution of nitrogen was extremely slow and no detectable volatile products were formed. When a mixture of III and one equivalent of sodium carbonate were refluxed for 8 hours, and the solvents and products were analyzed by v.p.c., a 6% yield of n-butyraldehyde was obtained and there was less than 1% n-butanol in the reaction mixture. We are currently investigating these anamolous results further, and also probing more deeply into the scope of the unusual Cannizzaro reaction reported here.

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