[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Effect of Surfaces on the McFadyen–Stevens Aldehyde Synthesis; An Improved Procedure

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Heating of a homogeneous solution of the sodium salt of benzenesulfonylbenzhydrazide in ethylene glycol at 160–165° does not bring about reaction. However, the addition of powdered solids causes a rapid reaction which is complete in a few minutes. An improved McFadyen–Stevens aldehyde synthesis, developed from this fact, is described.

The McFadyen–Stevens reaction[2] provides one route for the reduction of a carboxylic acid to the corresponding aldehyde *via* the arylsulfonhydrazide

$$ArCONHNHSO_2Ar' \xrightarrow[Na_2CO_3]{\Delta} ArCHO + N_2 + Ar'SO_2Na$$

The original object of the research herein reported was to measure the kinetics of this decomposition in homogeneous solution and thereby to gain further insight as to the mechanism. A suggested mechanism[2] is shown in equation 1.

$$\begin{aligned} &C_6H_5CONHNHSO_2C_6H_5 + RO^- \longrightarrow \\ &\qquad C_6H_5CON{=}NH + C_6H_5SO_2^- + ROH \\ &\qquad \hookrightarrow C_6H_5CHO + N_2 \quad (1) \end{aligned}$$

We thought to test this proposal by studying the effect of varying the benzenesulfonyl group on the rate of decomposition. Preliminary studies were carried out on benzenesulfonylbenzhydrazide (I). Surprisingly, it was discovered that when *homogeneous* solutions of the sodium or potassium salt of I in ethylene glycol were heated to 160–165° *no appreciable evolution of nitrogen occurred.* In the conventional procedure for carrying out the McFadyen–Stevens reaction, *only a few minutes at 160–165° are required for complete reaction.* The only difference in these two procedures is that in the conventional procedure solid sodium carbonate is present whereas in our experiments the reaction mixture was homogeneous. Accordingly we studied the effect of adding solids to a hot solution (160–165°) of the sodium salt of I in ethylene glycol. Nitrogen evolution occurred rapidly when the following finely divided solids were added: charcoal, copper, zinc, diatomaceous earth (Super Cel), glass wool (Pyrex), powdered soft glass, sodium carbonate, barium carbonate and barium hydroxide. A blank experiment ruled out supersaturation of ethylene glycol with nitrogen as a possible reason for the surface effect. If thus appears that the conventional McFadyen–Stevens reaction[3] requires a surface for completion and almost any solid is effective. Since glass was convenient and the yield of benzaldehyde was somewhat better with this than with some of the other solids, glass was used in further studies.

Before describing the studies which led to an improved procedure for the McFadyen–Stevens reaction, it is well to describe the conventional procedure[4] which we and others have used for the preparation of benzaldehyde from I. About a five-fold excess of solid sodium carbonate is added to a solution of I in ethylene glycol held at 160°. A rapid evolution of nitrogen occurs and after a short time (1.25 minutes) the reaction mixture is rapidly cooled. The yield of benzaldehyde is stated to be 73% and to fall considerably if the heating time is prolonged even as little as a minute or two beyond the recommended period. We have confirmed the rapid drop in yield with longer heating periods.

In the improved procedure, a solution of the sodium salt of N′-benzenesulfonylbenzhydrazide is heated to 160–165° in ethylene glycol, an addition of powdered soft glass or of glass wool is made, and, after a few minutes, the reaction mixture is cooled. In Fig. 1 are plotted the results of several experiments in which the time of heating and temperature were varied. Even after a 35-minute heating period the yield of benzaldehyde is only a few per cent. less than the maximum.

A more convenient way to carry out the McFadyen–Stevens reaction for synthetic purposes involves the addition of 1.1 moles of solid sodium carbonate to a stirred suspension of powdered soft glass in a solution of I in ethylene glycol at 160–165°. After four minutes of heating the mixture is cooled and processed (see Experimental part) to yield 76–81% of benzaldehyde. In Table I are listed the yields of several aldehydes prepared by this procedure together with the yields reported when the conventional procedure was employed.

The improvement in the new procedure lies not so much in the slightly higher yield in the case of benzaldehyde as in the decrease in sensitivity of the yield to length of time of heating. In the case of pyridine-3-carboxaldehyde the yield was almost doubled and a small (15%) yield of *p*-nitrobenzaldehyde was obtained as compared to the complete failure reported for this aldehyde.[2] *p*-Aminobenzaldehyde, 2,4,6-trimethylbenzaldehyde and furane-2-carboxaldehyde were prepared for the first time by the McFadyen–Stevens reaction.

It seems of interest to call attention to the fact that the rapid evolution of nitrogen from a solution of the sodium salt of N′-benzenesulfonylbenzhydra-

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[1] Holder of the Union Carbide and Carbon predoctoral fellowship, 1952–1953. The material presented was taken from the Ph.D. thesis of E. G. C. which may be consulted for many details not covered herein.

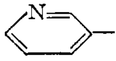
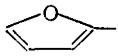
[2] J. S. McFadyen and T. S. Stevens, *J. Chem. Soc.*, 584 (1936).

[3] See, however, reference 7 in this paper.

[4] E. Mosettig, "Organic Reactions," Vol. VIII, edited by R. Adams, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 232. The following additional references to the McFadyen–Stevens reaction are appended: J. W. Baker, *et al.*, *J. Chem. Soc.*, 2831 (1952); S. Kushner, *et al.*, THIS JOURNAL, **74**, 3617 (1952); M. D. Libermann, *et al.*, *Bull. soc. chim. France*, 957 (1953); J. H. T. Ledrut, U. S. Patent 2,651,638, Sept. 8, 1953, and British Patent 694,204, July 15, 1953; R. Huisgen and H. Nakaten, *Ann.*, **586**, 84 (1954); W. H. Linnel, D. W. Mathieson and D. T. Modi, *J. Chem. Soc.*, 3257 (1953); T. P. C. Mulholland and G. Ward, *ibid.*, 4676 (1954); G. Cauquil and A. Casadevall, *Compt. rend.*, **238**, 908 (1954).

TABLE I

ALDEHYDES PREPARED BY IMPROVED PROCEDURE[a]

Aldehyde[b]	Hydrazide, mmoles	Na_2CO_3, equiv.	Heating, min.	Yield,[c] %
C_6H_5CHO (73)	1.82	0.99	4.0	77
	1.82	1.11	4.0	81
	1.82	1.51	4.0	76
	50	4.6	2.0	70[d,e]
2-HOC_6H_4CHO (55)	1.67	5.3	3.0	59[d]
	1.67	5.3	3.0	57[d,f]
	1.73	1.17	3.0	38[g]
3-$O_2NC_6H_4CHO$ (42)	1.29	1.10	3.0	52
4-$O_2NC_6H_4CHO$ (0)[i]	1.57	1.00	4.0	15[h]
4-$H_2NC_6H_4CHO$[i]	1.16	1.16	3.0	36
2,4,6-$(CH_3)_3C_6H_2CHO$[i]	0.33	1.17	3.0	38
 —CHO (36)	1.1	1.10	3.0	64
	1.1	1.10	2.0	61
 —CHO[i]	1.93	1.16	3.0	64
	1.88	1.16	15.0	62

[a] Unless otherwise noted sodium carbonate was added to a stirred solution of benzenesulfonylacylhydrazide containing powdered soft glass. About 17 ml. of ethylene glycol per millimole of hydrazide was used. The temperature was held at 160–165° unless otherwise noted. [b] The numbers in parentheses refer to the best yield reported by the conventional procedure. [c] Yields usually checked in duplicate (see Experimental). [d] No surface other than Na_2CO_3. [e] Isolated by distillation. [f] Temperature 155°. [g] This case was the only one in which glass was inferior. [h] Thiosemicarbazide hydrochloride added to prevent decomposition. [i] Aldehyde prepared for first time by McFadyen–Stevens reaction.

zide in ethylene glycol at 150–165° *does not occur unless a solid is present. It may be a general phenomenon that solid surfaces catalyze reactions in solution in which a gas is formed.*

One of the most notable examples of such catalysis is the decarbonylation of a glyoxalate ester by powdered soft glass in the first synthesis of equilenin.[5] This reaction failed or gave very poor yields in the absence of powdered glass. Other well known examples include the formation of aryl halides from aryl diazonium salts by the catalytic action of freshly prepared copper powder (Gattermann method) and the formation of diaryls from the coupling of aryl diazonium salts catalyzed by copper powder (Gattermann reaction). It should be of interest to see whether copper is necessary or other surfaces would be effective.

Various workers in our laboratories have found that, in the modification[6] of the Wolff rearrangement part of the Arndt–Eistert synthesis, when it becomes necessary to make additions of silver benzoate after the initial part of the reaction has occurred, it is more effective to add powdered silver benzoate than a solution of silver benzoate in triethylamine.

Experimental

Materials.—The benzenesulfonylhydrazides usually were prepared by the conventional procedure in which the corresponding methyl or ethyl esters reacted with hydrazine hydrate and then with benzenesulfonyl chloride. The yields for these two steps ranged from 50 to 93% and from 29 to 98% respectively. The N′ is used in this paper to designate the second nitrogen atom from the carbonyl group in hydrazides.

2,4,6-Trimethylbenzhydrazide.—To an ice-cold mixture 1.5 g. of anhydrous hydrazine and 3 ml. of pyridine was added dropwise with shaking 1.56 g. of 2,4,6-trimethylbenzoyl chloride. After 10 minutes the excess hydrazine and pyridine were removed by vacuum distillation. Recrystallization of the residue from mixtures of ethanol and water gave impure 2,4,6-trimethylbenzhydrazide (about 98% yield, m.p. about 153°) and N,N′-bis-(2,4,6-trimethylbenzoyl)-hydrazine in about 2% yield as a colorless solid, m.p. 251.0–252.8°.

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.0; H, 7.5; N, 8.6. Found: C, 73.8; H, 7.3; N, 8.7.

The crude 2,4,6-trimethylbenzhydrazide was converted directly to the benzenesulfonyl derivative.

N′-Benzenesulfonyl-2,4,6-trimethylbenzhydrazide.—Benzenesulfonyl chloride, 1.0 g., was added dropwise with shaking and ice cooling to 0.5 g. of the impure 2,4,6-trimethylbenzhydrazide in 2 ml. of pyridine. After one hour the mixture was poured over ice and hydrochloric acid and the resulting precipitate (56% yield) was collected, washed with water and recrystallized from 60% ethanol to yield a colorless solid, m.p. 205.0–206.0° dec. with little loss.

Anal. Calcd. for $C_{16}H_{18}N_2O_3S$: C, 60.3; H, 5.7; N, 8.8. Found: C, 60.4; H, 5.8; N, 8.9.

N′-Benzenesulfonyl-4-aminobenzhydrazide.—To a stirred and ice-cooled mixture of 16.6 g. of 4-aminobenzhydrazide,[7] m.p. 222–225°, and 80 ml. of pyridine was added dropwise 17.6 g. of benzenesulfonyl chloride. After standing for 2 hours at room temperature the mixture was poured over ice and hydrochloric acid. When the resulting oil solidified it was collected, washed with water and recrystallized from 95% ethanol. The desired product obtained in 29% yield as a colorless solid, m.p. 200.5–203.0°, was much less soluble in this solvent than the major product (unidentified).

Anal. Calcd. for $C_{13}H_{13}N_3O_3S$: C, 53.6; H, 4.5; S, 11.0. Found: C, 53.8; H, 4.5; S, 11.2.

N′-Benzenesulfonylfurane-2-carbohydrazide.—In a similar manner 19.3 g. of benzenesulfonyl chloride was allowed to react with 12.6 g. of furane-2-carbohydrazide in 80 ml. of pyridine. The orange precipitate (89% yield) was recrystallized from 95% ethanol to yield colorless crystals, m.p. 185.5–187.2° dec. with little loss.

Anal. Calcd. for $C_{11}H_{10}N_2O_4S$: C, 49.6; H, 3.8; N, 10.5; S, 12.0. Found: C, 49.9; H, 3.7; N, 10.6; S, 12.2.

Sodium Salt of N′-Benzenesulfonylbenzhydrazide.—To a hot solution of 28 g. of N′-benzenesulfonylbenzhydrazide in 800 ml. of absolute ethanol was added rapidly a solution of 50 ml. of absolute ethanol in which 2.4 g. of sodium had been dissolved under nitrogen. The mixture was allowed to cool slowly so the salt crystallized as large colorless needles (93% yield) which were collected and washed with a little ethanol.

Anal. Calcd. for $C_{13}H_{11}N_2NaO_3S$: C, 52.4; H, 3.7; N, 9.4; S, 10.8. Found: C, 51.0; H, 4.1; N, 9.2; S, 10.6; non-alkaline ash, 23.0 (calcd. for Na_2SO_4, 23.8).

Less than 0.1 g. of water-insoluble material was found when a 2.00-g. sample of the salt was placed in 10 ml. of water. Acidification of this aqueous solution with hydrochloric acid gave N′-benzenesulfonylbenzhydrazide in 96% recovery. The stability of this salt was demonstrated by duplicate results which were obtained on a sample of the salt kept for 17 months.

Surface Effect.—Very little nitrogen evolution resulted when solutions of sodium hydroxide (or ethoxide) in ethanol, potassium *t*-butylate in *t*-butyl alcohol or potassium *n*-butylate in butanol were added to refluxing solutions of N′-benzenesulfonylbenzhydrazide in the respective alcohols. In each case the precipitate which formed on cooling the solutions was shown to be the sodium or potassium salt of the hydrazide, for acidification of aqueous solutions of these precipitates with hydrochloric acid gave the hydrazide in good recovery.

When sodium N′-benzenesulfonylbenzhydrazide was placed in ethylene glycol and heated rapidly, nitrogen evolution started at about 70° but almost ceased when the last of the salt went into solution. Brisk nitrogen evolution occurred, however, when a finely-divided insoluble solid was added to this hot solution (about 160°). All solids tested, including activated carbon, copper dust, zinc dust, dia-

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(5) W. E. Bachmann, W. Cole and A. L. Wilds, THIS JOURNAL, **62**, 824 (1940).

(6) M. S. Newman and P. F. Beal, III, *ibid.*, **72**, 5163 (1950).

(7) T. Curtius, *J. prakt. Chem.*, [2] **95**, 336 (1917).

tomaceous earth (Super Cel), Pyrex glass wool, powdered soft glass, barium carbonate and barium hydroxide, catalyzed nitrogen evolution even if previously wetted with ethylene glycol. The surface of glass reaction vessels caused slow evolution of nitrogen from rough spots or scratches.

No difficulty was experienced in reproducing the conventional[2] procedure for conversion of N'-benzenesulfonylbenzhydrazide to benzaldehyde. However, if the sodium carbonate was added as a solution in ethylene glycol essentially no nitrogen was evolved even though the ratio of sodium carbonate to hydrazide was the same. Again the addition of solids initiated nitrogen evolution. Supersaturation by nitrogen was ruled out by the fact that no nitrogen was evolved when the solid was not added until after the solution had been cooled to room temperature and by the fact that the hydrazide could be recovered from heated solutions from which nitrogen had not been evolved.

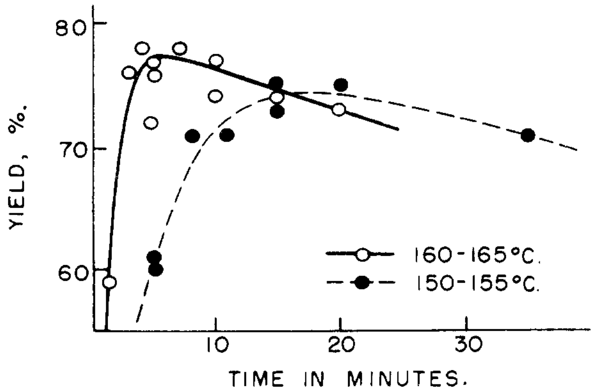

Fig. 1.

Surface-catalyzed Pyrolysis of Sodium N'-Benzenesulfonylbenzhydrazide.—A series of experiments were made to determine yields of benzaldehyde. One procedure was to add 0.6 g. (0.002 mole) of sodium N'-benzenesulfonylbenzhydrazide into 5 ml. of hot ethylene glycol in a test-tube and to stir with a wad of glass wool. At the end of the reaction period the test-tube was quickly transferred from the heating bath to an ice-bath. The reaction mixture was then washed through a sintered glass filter with methanol into a 0.05 *M* solution of 2,4-dinitrophenylhydrazine in 0.5 *M* methanolic hydrochloric acid. After several hours the precipitate was washed with 5–10 ml. of acidic methanol and dried to constant weight. An alternate procedure was to add water to the cooled reaction mixture, extract the benzaldehyde with ether, concentrate the extract and determine the yield by the Bryant-Smith titration.[8] Results are plotted in Fig. 1.

Improved Procedure for Benzaldehyde.—To a stirred hot mixture of 0.5 g. of N'-benzenesulfonylbenzhydrazide, 0.2 g. of powdered soft glass (finer than 30 mesh) and 5 ml. of ethylene glycol in a test-tube was added anhydrous sodium carbonate. The reaction mixture was then worked up as above with the 2,4-dinitrophenylhydrazine reagent and the results are shown in Table I.

2,4,6-Trimethylbenzaldehyde.—N'-Benzenesulfonyl-2,4,-6-trimethylbenzhydrazide was treated with sodium carbonate, 0.05 g. of powdered soft glass and 1.5 ml. of ethylene glycol in a manner similar to the above preparation of benzaldehyde. After recrystallization from alcohol, 2,4,6-trimethylbenzaldehyde 2',4'-dinitrophenylhydrazone was obtained as a red solid, m.p. 256–257°.

Anal. Calcd. for $C_{16}H_{16}N_4O_4$: N, 17.5. Found: N, 17.1.

Pyridine-3-carboxaldehyde.—N'-Benzenesulfonylpyridine-3-carbohydrazide, 0.27 g., was treated with sodium carbonate, 0.1 g. of powdered soft glass and 3 ml. of ethylene glycol as above. The pyridine-3-carboxaldehyde 2',4'-dinitrophenylhydrazone[9] was obtained as an orange solid, m.p. 258.5–259.5°, after recrystallization from alcohol.

Anal. Calcd. for $C_{12}H_9N_5O_4$: C, 50.2; H, 3.1; N, 24.4. Found: C, 50.2; H, 3.1; N, 23.8.

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[8] W. M. D. Bryant and D. M. Smith, THIS JOURNAL, **57**, 57 (1935).

[9] J. P. Wibaut and R. Huls, *Rec. trav. chim.*, **71**, 1021 (1952); S. J. Angyal, G. B. Barlin and P. C. Wailes, *J. Chem. Soc.*, 1740 (1953).

COLUMBUS 10, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

5-Phenyl-2-penten-4-yn-1-ol and Related Compounds[1]

BY THOMAS L. JACOBS, DAVID DANKNER AND ARLYN R. DANKNER

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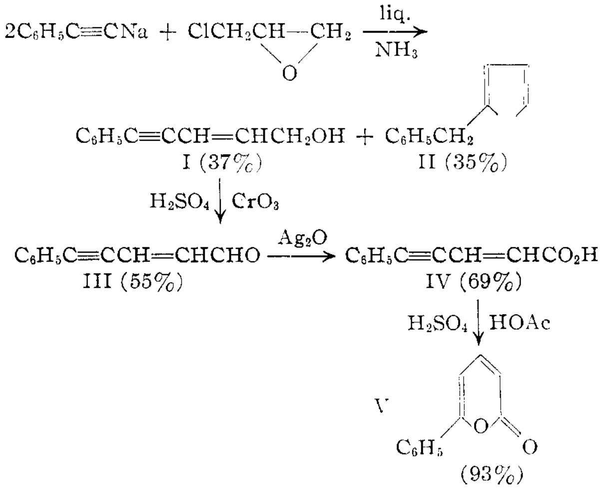
The synthesis of 5-phenyl-2-penten-4-yn-1-ol from sodium phenylacetylide and epichlorohydrin was repeated and the by-product shown to be α-benzylfuran. The alcohol was oxidized to the corresponding aldehyde and acid; the latter was cyclized to phenylcoumalin.

The physiological activity of highly unsaturated systems containing acetylenic and allenic bonds, such as Mycomycin,[2] $HC\equiv CC\equiv CCH=C=CH-CH=CHCH=CHCH_2CO_2H$, and Diatretyne 2,[3] $N\equiv CC\equiv CC\equiv CCH=CHCO_2H$, suggested an investigation of more stable and more readily available related compounds. As part of this general program 5-phenyl-2-penten-4-yn-1-ol and compounds easily derived from it were submitted[4] for screening and certain of them were found to possess interesting physiological properties.



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[1] This work was supported by a grant from the Los Angeles County Tuberculosis and Health Association.

[2] W. D. Celmer and I. A. Solomons, THIS JOURNAL, **74**, 1870, 2245, 3838 (1952); **75**, 1372 (1953).

[3] M. Anchel, *Science*, **121**, 607 (1955).

[4] The physiological testing of these compounds is being carried out by Dr. Charles M. Carpenter, Mr. A. W. C. Naylor-Foote and their colleagues in the Department of Infectious Diseases, University of California at Los Angeles Medical Center.