

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF DEPAUW UNIVERSITY]

1,4-Dimethyl-3-alkylcarbostyrils

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Recently the preparation of various 3-alkyl-4-methylcarbostyrils has been reported.² Since the preparation of several N-alkyl-4-methylcarbostyrils has been described,³ it was of interest to prepare a series of 1,4-dimethylcarbostyrils with alkyl substituents in the 3 position. As intermediate products the corresponding N-methyl- α -alkylacetoacetanilides have also been prepared. Ring closure of these compounds with concentrated sulfuric acid gave the corresponding 1,4-dimethyl-3-alkylcarbostyril. The properties of the substituted acetoacetanilides are given in Table I and the data for the 1,4-dimethyl-3-alkylcarbostyrils are recorded in Table II.

TABLE I
N-METHYL- α -ALKYLACETOACETANILIDES OF THE TYPE
 $\text{CH}_3\text{COCH(R)CON(CH}_3\text{)C}_6\text{H}_5$

R—	B. p., °C. at 1 mm.	Yield, %	Formula	N Analyses, %		2,4-Di- nitro- phenyl- hydra- zone, m. p., °C.
				Calcd.	Found	
Methyl	136–137	41	$\text{C}_{13}\text{H}_{15}\text{NO}_2$	6.83	7.14	134–135
Ethyl	144–145	42	$\text{C}_{14}\text{H}_{17}\text{NO}_2$	6.39	6.48	104–105
Propyl	160–163 ^a	40	$\text{C}_{14}\text{H}_{19}\text{NO}_2$	6.00	6.33	73–74
Butyl	152–154	37	$\text{C}_{15}\text{H}_{21}\text{NO}_2$	5.67	6.01	
Allyl	142–144	37	$\text{C}_{14}\text{H}_{17}\text{NO}_2$	6.03	6.38	
Benzyl	184–187	47	$\text{C}_{18}\text{H}_{19}\text{NO}_2$	4.98	5.18	165–167

^a Pressure was 3 mm.

TABLE II
1,4-DIMETHYL-3-ALKYLCARBOSTYRIL ($\text{C}_{11}\text{H}_{10}\text{NO}$)R

R—	M. p., °C.	Yield, %	Formula	N Analyses, %	
				Calcd.	Found
Methyl	106.5–107.5	96.5	$\text{C}_{12}\text{H}_{12}\text{NO}$	7.48	7.26
Ethyl	99	75	$\text{C}_{14}\text{H}_{14}\text{NO}$	6.96	6.63
Propyl	79	85.5	$\text{C}_{14}\text{H}_{17}\text{NO}$	6.51	6.29
Butyl	62.5–63	70.6	$\text{C}_{16}\text{H}_{16}\text{NO}$	6.11	5.81
Propanol-2	140	60.0	$\text{C}_{14}\text{H}_{17}\text{NO}_2$	6.06	6.01

In treating N-methyl- α -allylacetoacetanilide with concentrated sulfuric acid not only did the condensation take place to give the carbostyril, but also the sulfuric acid treatment hydrated the unsaturated bond in the allyl side chain to give the secondary alcohol 1,4-dimethyl-3-(propanol-2)-carbostyril.

This alcohol was characterized by the preparation of the phenylurethan.

It is to be noted that even though the N-methyl- α -benzylacetoacetanilide could be prepared, ring closure of this compound to the corresponding carbostyril could not be accomplished.

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(2) Searles and Lindwall, *THIS JOURNAL*, **68**, 988 (1946).

(3) Kaslow and Cook, *ibid.*, **67**, 1969 (1945).

Experimental^{4,5}

N-Methylacetoacetanilide.—This starting material was prepared as described by Kaslow and Cook.³

The preparations of N-methyl- α -methylacetoacetanilide and 1,3,4-trimethylcarbostyril can be used as general methods to describe the preparation of the series of N-methyl- α -alkylacetoacetanilides and 1,4-dimethyl-3-alkylcarbostyrils.

N-Methyl- α -methylacetoacetanilide.—To 300 ml. of absolute alcohol in a 3-necked, round-bottomed flask equipped with a reflux condenser, stirrer and dropping funnel was added slowly 4.6 g. (0.20 mole) of sodium metal. When the sodium had reacted completely, 38.2 g. (0.20 mole) of N-methylacetoacetanilide was added to the mixture and the solution then heated on the steam-bath with constant stirring. To the refluxing solution 28.4 g. (0.20 mole) of methyl iodide was added dropwise and the refluxing continued for twelve hours. The alcohol was then removed under vacuum and the residue extracted with 300–400 ml. of ethyl ether. The ether was removed and the product then recovered by distillation under vacuum. After a small forerun, the product distilled at 136–137° (1 mm.); yield 16.8 g. (41%).

The other N-methyl- α -alkylacetoacetanilides were prepared in an analogous manner using ethyl, *n*-propyl, *n*-butyl and allyl bromides and benzyl chloride.

N-Methyl- α -alkylacetoacetanilide 2,4-Dinitrophenylhydrazone.—The 2,4-dinitrophenylhydrazones of the N-methyl- α -alkylacetoacetanilides were prepared according to the directions given by Shriner and Fuson.⁶ These derivatives were purified by recrystallization from alcohol.

1,3,4-Trimethylcarbostyril.—To 50 ml. of concentrated sulfuric acid was added 12.8 g. (0.062 mole) of N-methyl- α -methylacetoacetanilide at such a rate as to maintain the temperature at 75°. During the addition the mixture was stirred continuously. After the addition was complete, the mixture was heated on a steam-bath for ten to fifteen minutes. The mixture was then cooled and poured with vigorous stirring into 500 ml. of a 50:50 mixture of ice and water. The solution was then neutralized with a solution of sodium hydroxide. After standing overnight, the white precipitate was recovered by filtration and dried at 70–75°. The crude product weighed 11.3 g. (96.5%) and melted at 100–101°. One gram of the product was recrystallized by dissolving it in 6–8 ml. of hot alcohol, filtering and adding water to faint turbidity. Upon cooling and scratching the inside of the flask, white needles formed, m. p. 106.5–107.5°.

The other 1,4-dimethyl-3-alkylcarbostyrils were prepared in an analogous manner by ring closure of the corresponding N-methyl- α -alkylacetoacetanilide.

1,4-Dimethyl-3-(propanol-2)-carbostyril.—This compound was prepared in a manner analogous to the preparation of 1,3,4-trimethylcarbostyril by treating 12.0 g. (0.052 mole) of N-methyl- α -allylacetoacetanilide with 50 ml. of concentrated sulfuric acid. White needles were obtained upon dilution with water and subsequent neutralization with sodium hydroxide. The yield was 6.7 g. (60%). The product when recrystallized from alcohol-water gave a m. p. of 140–140.5°. This compound did not change upon drying at 90° in a vacuum oven. It would not add bromine and gave no iodine number. The analysis as given in Table II corresponds to the alcohol and not the allyl substituted carbostyril. The prepara-

(4) All melting points were taken on a Fisher-Johns melting block.

(5) Microanalyses were carried out by Mr. Lorne MacBeth.

(6) Shriner and Fuson, "Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 143.

tion of the phenylurethan is proof of the secondary alcohol being the compound.

The Phenylurethan of 1,4-Dimethyl-3-(propanol-2)-carbostyryl.—This derivative was prepared as described by Shriner and Fuson.⁷ The compound was recrystallized from carbon tetrachloride. The m. p. was 178–179°.

Anal. Calcd. for $C_{21}H_{22}N_2O_5$: N, 8.00. Found: N, 8.28, 7.93.

Summary

1. Several N-methyl- α -alkylacetoacetanilides have been prepared by condensation of N-methyl-

(7) Ref. 6, p. 136.

acetoacetanilide with the corresponding alkyl halide.

2. Ring closure of the N-methyl- α -alkylacetoacetanilides with concentrated sulfuric acid resulted in the formation of the 1,4-dimethyl-3-alkylcarbostyryls.

3. N-Methyl- α -allylacetoacetanilide when subjected to the sulfuric acid treatment gave the hydrated product, 1,4-dimethyl-3-(propanol-2)-carbostyryl.

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[CONTRIBUTION FROM SOUTHERN REGIONAL RESEARCH LABORATORY¹]

Trimethylsilylcellulose

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Silicon tetrachloride and aryl- and alkylhalosilanes react easily and rapidly with organic hydroxyl groups,^{2,3,4} to yield hydrogen chloride and silicic esters. A number of patents have been issued dealing with the treatment of cellulose with organosilicon halides to impart water repellency.^{5,6,7} In one case⁵ a surface reaction either with adsorbed moisture or with hydroxyl groups of the cellulose was postulated. However, the amount of product formed was too small to be measured or analyzed. Jullander⁸ has studied the reaction of silicon tetrachloride with nitrocellulose and reports the formation of gels due to cross linkage. The present investigation concerns the reaction of some organo-silanes with cellulose, particularly to obtain trimethylsilylcellulose.

It was found that halosilanes will react with cellulose in the presence of pyridine to form rela-

tively stable compounds. The reaction will take place slowly at room temperature and rapidly at reflux temperatures. A group substitution as high as 2.75 trimethylsilyl groups per glucose unit was attained with cotton linters (Fig. 1). With partially substituted cellulose acetate, the total substitution approached 3.0 (Table I).

TABLE I
REACTIONS OF ALKYLCHLOROSILANES WITH CELLULOSE ACETATE

Reagent	Acetyl groups per glucose		Mole ratio Silane: Cell-OAc	Silyl groups per glucose by Weight	%Si	Total groups
	Before	After				
$(CH_3)_3SiCl$	2.30	2.24	2.79	0.69	0.65	2.89–2.93
$(C_2H_5)_3SiCl$	2.30	2.24 ^a	4.08	.66	.58	2.82–2.90
$(CH_3)_2SiCl$	2.90	2.87	4.86	.16	.14	3.01–3.03

^a Assumed.

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted. Presented at the Southwestern Regional Meeting, Houston, Texas, September, 1947.

(2) J. J. Ebelman, *Compt. rend.*, **18**, 1202; **19**, 398 (1844).

(3) M. N. Kalinin, *Compt. rend. acad. sci. URSS*, **26**, 365 (1940).

(4) G. Martin, *J. Chem. Soc.*, **105**, 2880 (1914).

(5) W. I. Patnode, U. S. Patent 2,306,222 (Dec. 22, 1942).

(6) British Thomson-Houston Co., British Patent 575,698 (Feb. 28, 1946).

(7) J. F. Hyde, U. S. Patent 2,413,050 (Dec. 24, 1946).

(8) I. Jullander, "Studies of Nitrocellulose," Almquist and Wiksells Boktryckeri-A.-B., Stockholm, 1945, or H. K. Lewis and Co., Ltd., London, pp. 109–117.

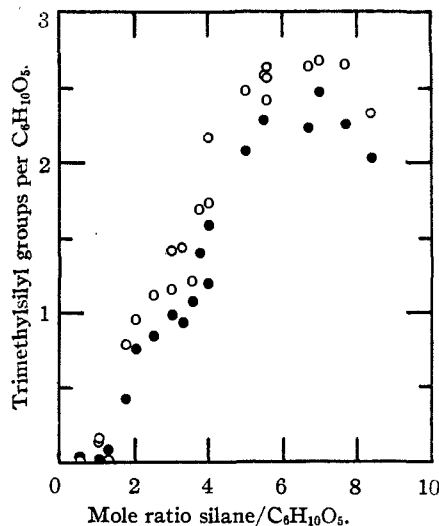


Fig. 1.—Change in trimethylsilyl substitution of cellulose with change in mole ratio of reactants: O, calculated from gain in weight; ●, calculated from silicon content.

Trimethylsilylcellulose is stable in dry air at room temperature but at elevated temperatures or in the presence of atmospheric moisture will decompose slowly. The compound is insoluble in the usual organic solvents and in mixtures of solvents such as are used in dissolving cellulose acetate and other cellulose derivatives.

Materials.—The trimethylchlorosilane used was commercial grade and the acetoxy silanes were prepared according to the method of