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Studies of Hydrazine Derivatives. I. A Convenient Method of Preparing Chloroacetylhydrazones*1

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Although chloroacetylhydrazones are expected to be useful for synthetic purposes, only those of benzaldehyde[1,2] and of *m*-nitro- and *o*-hydroxy-benzaldehyde[1] have been reported in the literature.

Talik and Plazek[1] prepared benzaldehyde chloroacetylhydrazone by the chloroacetylation of benzaldehyde hydrazone with chloroacetyl chloride; it was also obtained by Buyle[2] from benzaldehyde and chloroacetohydrazide hydrochloride, which had been prepared from hydrazine and *p*-nitrophenyl

Table 1. Yields and melting points of chloroctylhydrazones

Original carbonyl compound	Yield (%)	Solvent for recrystallization	Melting point (°C)[a]	Crystal form
Benzaldehyde	84	Methanol	165.5—166.5 (dec.)[b]	colorless fine needles
Acetophenone	81	Methanol	137.5—138.5	colorless long needles
Benzophenone	83	Methanol	105.5—106.5	colorless prisms
Furfural	77	Methanol	151.0—152.0 (dec.)	almost colorless columns
d-Camphor	60	Methanol	189.0—190.0	colorless needles
Cyclohexanone	69	Methanol	114.0—115.0	cololress plates
Cyclopentanone	62	Methanol	123.5—124.5	colorless prisms
Pinacolone	67	Methanol	94.5— 95.5	colorless needles
Ethyl methyl ketone	72	*n*-Hexane	76.0— 77.0	colorless prisms
Acetone	53	Benzene	96.0— 97.0	colorless prisms
Acetaldehyde	73	Benzene	109.0—110.0	colorless fine plates

a) All melting points were determined in capillary, and are uncorrected.
b) Reported mp: 164°C,[1] 166°C.[2]

Table 2. Analytical data of chloroacetylhydrazones

Original carbonyl compound	Molecular weight[a,c]	Elemental analysis[b,c]		
		C%	H%	N%
Benzaldehyde	197 (197)	55.15 (54.97)	4.67 (4.61)	14.31 (14.25)
Acetophenone	218 (211)	57.07 (57.02)	5.32 (5.26)	13.39 (13.30)
Benzophenone	283 (273)	65.77 (66.06)	4.81 (4.80)	10.18 (10.27)
Furfural	174 (187)	44.99 (45.06)	3.76 (3.78)	14.88 (15.01)
d-Camphor	241 (243)	60.53 (59.38)	8.06 (7.89)	11.67 (11.54)
Cyclohexanone	224 (189)	50.84 (50.93)	7.01 (6.95)	14.78 (14.85)
Cyclopentanone	178 (175)	48.43 (48.15)	6.43 (6.35)	16.05 (16.04)
Pinacolone	203 (191)	50.70 (50.39)	8.06 (7.93)	15.09 (14.69)
Ethyl methyl ketone	157 (163)	43.94 (44.32)	6.92 (6.82)	17.03 (17.23)
Acetone	165 (149)	40.62 (40.42)	6.19 (6.11)	19.01 (18.55)
Acetaldehyde	151 (135)	35.59 (35.70)	5.22 (5.24)	20.64 (20.82)

a) A Takara Twin-type Ebulliometer Model L4 was used for the molecular weight measurement.
b) A Perkin-Elmer Elemental Analyzer Model 240 was employed for the micro-analysis.
c) Figures in parentheses are calcd values.

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1) Z. Talik and E. Płażek, *Roczniki Chem.*, **33**, 379 (1959); *Chem. Abstr.*, **53**, 21660e (1959).

2) R. Buyle, *Helv. Chim. Acta*, **47**, 2449 (1964).

chloroacetate. Kupcik and others[3] reported a method for the preparation of chloroacetohydrazide and its hydrochloride from hydrazine hydrate and methyl chloroacetate.

The method of Talik and Płażek[1] is not general, but is limited in its application to carbonyl compounds that can easily give hydrazones. Buyle's method,[2] though universally applicable, is complicated and expensive. The present authors attempted to prepare chloroacetohydrazide and its hydrochloride by the method of Kupcik and others,[3] but a considerable evolution of nitrogen was observed at the reported reaction temperature (25°C) and the expected hydrazide could not be obtained even at a low reaction temperature (−25°C).

An alternative method for the preparation of chloroacetylhydrazones was devised. It consists of the previous preparation of a chloroacetohydrazide solution by the reaction of ethyl or methyl chloroacetate with 80—90% hydrazine hydrate in methanol at −30——40°C and the addition of an equimolar amount of aldehyde or ketone to the solution, without any isolation of the chloroacetohydrazide. By this simple and convenient procedure, several chloroacetylhydrazones were obtained with a higher purity and in satisfactory yields (see Tables 1 and 2).

The IR spectra of these chloroacetylhydrazones show absorptions at 3260—3350 (γ_{NH}) and 1690—1700 cm^{-1} (γ_{CO}).

Each of the NMR spectra (1—2% in CCl_4 or $CDCl_3$) shows a singlet assigned to the methylene protons of the $ClCH_2CO$- group at about 5.5 ppm (τ value) and a proton signals of the –NH– group (broad singlet) at 0—1.5 ppm (τ value).

Chloroacetylhydrazones of acetophenone and benzophenone were also synthesized by Talik and Płażek's method[1] and confirmed to be identical with those prepared by the present method.

The study of the syn-anti isomerism and tautomerism of the chloroacetylhydrazones by means of NMR analysis is now in progress.

Experimental

General Procedure. Into a stirred solution of 0.5 mol of ethyl or methyl chloroacetate (61 or 54 g) in 75 ml[4] of methanol, was added 0.5 mol (30 g) of 85% hydrazine hydrate over a period of 20—30 min at −30——40°C. After the addition was completed, the temperature of the reaction mixture was allowed to rise slowly to 0—10°C while the mixture was being stirred for an additional hour.

To this solution, was then added 0.5 mol of a carbonyl compound[5] with external cooling at such a rate that the temperature of the reaction mixture did not rise over 10°C.[6] Crystalline precipitates appeared almost immediately or after a while, so it was necessary to continue the cooling. After the reaction was over, the precipitates were collected by filtration. Washing with methanol,[7] followed by drying under a vacuum, gave fairly-pure chloroacetylhydrazone.

Further purification of the product was achieved by recrystallization from an appropriate solvent.

3) F. Kupcik, M. Liska and M. Konupcik, *Czech.*, 101955 (1961); *Chem. Abstr.*, **60**, 1606a (1964).

4) As the chloroacetylhydrazones of aliphatic carbonyl compounds are fairly soluble in methanol, it was necessary to change the quantity of the solvent as follows:

Carbonyl compound	Quantity of methanol (m*l*)
Benzaldehyde, acetophenone, and furfural	125
Benzophenone and cyclohexanone	75
Cyclopentanone, *d*-camphor, and acetaldehyde	50
Pinacolone, ethyl methyl ketone, and acetone	35

5) When it was solid, it was dissolved in a small quantity of methanol.

6) In the reaction of benzaldehyde or furfural, it was necessary to cool the reaction mixture below −30°C.

7) For aliphatic carbonyl compounds, the procedure was modified as follows. After the addition of the carbonyl compound, the reaction mixture was kept at −20——30°C for 2—3 hr, and then filtered. The resulting solid were washed with a small amount of cold methanol diluted with water (−20——30°C, 50%).