NEW COMPOUNDS

Halogenation of Substituted Hydrazones. A Facile Route for the Synthesis of Some New Hydrazidoyl Halides

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A wide variety of new alkyl, aryl, acyl, and ethoxycarbonyl derivatives of hydrazidoyl halides have been synthesized by the electrophilic attack of the halogen atom on the corresponding hydrazone chain. The structural assignments of the products are based on spectral and analytical studies.

Taking advantage of the marked superiority (*1–4*) and applicability of hydrazidoyl halides in the syntheses of heterocyclic (*5–7*) and acyclic systems (*9–10*), we thought it to be of interest to synthesize a wide variety of substituted hydrazones and study their reactivity toward chlorine and bromine, with a view to synthesize a wide range of hydrazidoyl halides.

Results and Discussion

Syntheses of hydrazones **5a–t** (Scheme I) (*11–16*, *18*), which are the precursors of hydrazidoyl halides, have been accomplished by employing two distinct approaches, one of which comprises the condensation of aliphatic or aromatic aldehydes with 2,4-dinitrophenylhydrazine in alcohol at room temperature (*15*) while the other involves the coupling reaction of aryldiazonium salts with ethylacetoacetate or acetylacetone (*12*, *16*).

Treatment of these hydrazones (**5a–t**) with chlorine or bromine (*17*) under different conditions afforded only α-halo derivatives (**6a–t**) in appreciable yields (Scheme I). Various hydrazidoyl halides (**6a–t**) synthesized during this study are listed in Table I. Their structures are supported by microanalyses, which are in good accord with calculated values (Table I) and also with spectral evidence (Table II).

Experimental Section

All of the reagents were obtained from commercial sources (BDH, E. Merek and S. Merek). Hydrazones were prepared according to the references cited in the literature (*12*, *14*, *15*, *18*). Chlorine gas was prepared by the method described by Vogel (*18*). All melting points were determined on a Gallenkamp apparatus and are uncorrected. A Perkin-Elmer Infracord spectrophotometer was used to determine the IR spectra (KBr). NMR spectra ($CDCl_3$ or CCl_4) were run on a Varian A-60 or A-100 spectrophotometer with Me_4Si as an internal standard. UV spectra were recorded on a Beckman Du spectrophotometer. Column chromatography was done to purify the products, and purity was checked by TLC.

Methods of Preparation

***Hydrazidoyl Chlorides* 6a–e,g,h.** A stream of dry chlorine gas was cautiously passed into a well-cooled solution of thrice-crystallized hydrazones (**5a–e,g,h**) (2.0 g) in 30 mL of chloroform until the hydrazones turned into a clear red solution. The solution finally lightened in color, and hydrazidoyl chlorides (**6a–e,g,h**) were separated out as a bright yellow crystalline mass. The solid was filtered out of the mother liquor after slight concentration, and further treatment with methanol afforded

Scheme I

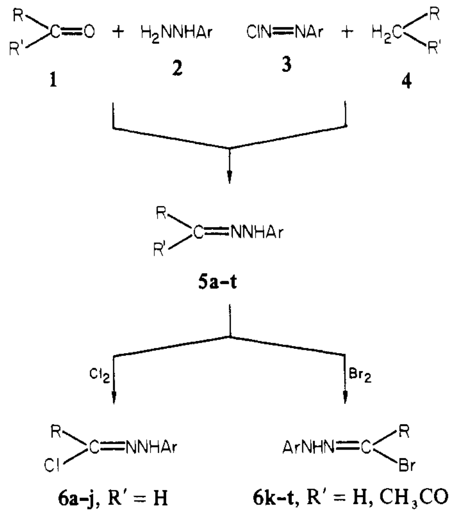
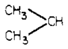
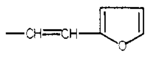
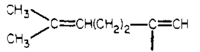


Table I. Physical Characteristics of Hydrazidoyl Halides (6a–t)

compd no.[a]	R[b]	crystallizing solvent	mp, °C	yield, %
6a	CH_3	$CHCl_3$-MeOH	149–150	92
6b	CH_3CH_2	$CHCl_3$-MeOH	142–144	86
6c	$CH_3CH_2CH_2$	$CHCl_3$-MeOH	90–91	87
6d	 $(CH_3)_2CH$	$CHCl_3$-MeOH	105–107	80
6e	$CH_3CH{=}CH$	$CHCl_3$-MeOH	96–97	81
6f	CCl_3	AcOH	130–131	82
6g	$C_6H_5CH{=}CH$	$CHCl_3$-MeOH	233–234	80
6h		$CHCl_3$-MeOH	155–156	79
6i	C_6H_5	AcOH	190–192	62
6j	4-$(OCH_3)C_6H_4$	AcOH	205–208	64
6k	$CH_3(CH_2)_7$	$CHCl_3$-MeOH	128–129	70
6l	 $(CH_3)_2C{=}CH(CH_2)_2{-}C(CH_3){=}CH$	C_6H_6-PE	141	75
6m	$CH_2{=}CH$	AcOH	130	70
6n	C_6H_5	AcOH	216–218	40
6o	4-$(OCH_3)C_6H_4$	AcOH	241–242	32
6p	3-$(OH)C_6H_4$	AcOH	160–161	40
6q	CH_3CO	EtOH	132–133	82
6r	CH_3CO	EtOH or MeOH	230–232	74
6s	$C_2H_5CO_2$	MeOH	90–91	66
6t	$C_2H_5CO_2$	EtOH	201–203	69

[a] Compounds **5a–p**, R' = H; compounds **5q–t**, R' = CH_3CO.
[b] **6a–p**, Ar = 2,4-$(NO_2)_2C_6H_3$; **6q,s**, Ar = 4-$(CH_3)C_6H_4$; **6r,6t**, Ar = 4-$(NO_2)C_6H_4$.

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Table II. Spectral Studies of the Hydrazidoyl Halides

	¹H NMR		IR (KBr)^b		
compd	δ^a	assignment (no. of protons)	ν, cm^{-1}	assignment	UV λ_{max}, nm
6a	2.57, s	methyl (3)	1430, 1130	C–N	364
	7.95, 8.07, s; 8.40, 8.57, 9.07, d; J = 3.0 Hz	aromatic (3)	640	C–Cl	
	11.50, s	imino (1)			
6b			1435, 1140	C–N	
			645	C–Cl	
6c			1420, 1225	C–N	370
			730	C–Cl	
6d	1.23, s	methyl (3)	2990, 2940	C–H aliphatic	
	1.34, s	methyl (3)	1620, 1490	C=C aromatic	
	2.70–3.15, m	methine (1)	1420, 1140	C–N	
	7.16, 7.60, 7.77, s; 8.10, 8.29, 8.92, d; J = 3.0 Hz	aromatic (3)	645	C–Cl	
	11.15, s	imino (1)			
6e	1.71, d, J = 6.0 Hz	methyl (3)			280, 390
	4.18–4.50, m	olefinic (1)			
	4.63–4.86, m	olefinic (1)			
	7.23–9.06, m	aromatic (3)			
	11.13, s	imino (1)			
6f			1590, 1510, 1450	C–C aromatic	
			1428, 1150	C–N	
			735	C–Cl	
			3110, 830, 860	C–H aromatic	
6h			2960	C–H olefinic	
			1610	C=C olefinic	
			1580, 1510, 1450	C=C aromatic	
			1430, 1130	C–N	
			740	C–Cl	
6k			2985, 2930	C–H aliphatic	
			1610, 1485	C=C aromatic	
			1410, 1160	C–N	
			670	C–Cl	
6l	0.65–2.99, m	methyl (9), methylene (4)			260, 850
	4.06–4.40, m	methine (1)			
	5.00–5.21, m	methine (1)			
	7.36–8.25, m	aromatic (3)			
	11.37, s	imino (1)			
6n	7.41–9.38, m	aromatic (8)			370
	11.94, s	imino (1)			
6o			1620, 1560, 1490	C=C aromatic	
			1428, 1160	C–N	
			2940	C–H methoxy	
6p			3430	O–H	
			1580, 1510, 1480	C=C aromatic	
			1430, 1130	C–N	
6q			1670	C=O	
			1610, 1590, 1510	C=C aromatic	
			1410, 1315	C–H deformation	
			1450, 1165	C–N	
6r	2.52, s	acetyl (3)			
	7.51–8.40, m	aromatic (4)			
	11.40, s	imino (1)			
6s			2910	C–H aliphatic	
			1700	C=O	
			1600, 1565, 1500	C=C aromatic	
6t	1.42, t, J = 7.2 Hz	methyl (3)	1710	C=O	
	4.41, q, J = 7.2 Hz	methylene (2)	1610, 1540, 1490	C=C aromatic	
	7.27–8.64, m	aromatic (4)	3000, 2980, 2900	C–H aliphatic	
	11.36, s	imino (1)	600	C–Br	

[a] s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. [b] In general, IR spectra show N–H bonds at 3290–3260 cm^{-1} and C=N bonds at 1610–1590 cm^{-1}, and NO_2 bonds show absorptions at 1530–1520 and 1345–1340 cm^{-1}.

another crop of hydrazidoyl chloride. Products were obtained in ~70–90% yields.

***Hydrazidoyl Chlorides* 6f,i,j.** A mixture of hydrazone (1.0 g) in glacial acetic acid (20.0 mL) was saturated with dry chlorine gas. In the case of hydrazone **5f**, the solid went into solution and an orange solution was obtained which upon cooling gradually at room temperature afforded pale yellow crystals of compound **6f**, which was then filtered and recrystallized from acetic acid as bright shining crystals.

The solution of hydrazones **5i,j** was warmed on a water bath with continuous passage of chlorine gas through the hot solution. After 0.5 h a clear solution was obtained, which upon cooling started to deposit crystals of hydrazidoyl chloride. The products were recrystallized from acetic acid (Table I).

***Hydrazidoyl Bromides* 6k–p.** The dinitrophenylhydrazones (DNPs) **5k–p** (0.01 mol) were suspended in glacial acetic acid (10 mL) containing 4% acetic anhydride and vigorously stirred, while bromine (0.03 mol) in 2 mL of the same solvent was added dropwise with constant stirring. The hydrazones immediately dissolved, and the bromides precipitated out in 80–85% yields after 10–30 min, the time depending mainly on the reactivity of the DNPs. In the case of hydrazidoyl bromides **6n–p**, usually a 4-fold excess of bromine was used, and, after 4 h of stirring, the solution was warmed on a sand bath. The hydrazidoyl bromides thus obtained were separated from the solution, washed with a little acetic acid and then with petroleum ether, and recrystallized from appropriate solvents (Table I).

***Hydrazidoyl Bromides* 6q–t.** Hydrazones **5q–t** (0.04 mol) were added to a mixture of 200 mL of glacial acetic acid and 120 mL of acetic anhydride containing sodium acetate (27 g), and the temperature was lowered to 0–5 °C by means of an ice-salt bath. To this was added over a 1-h period bromine (0.04 mL) dissolved in 5 mL of acetic acid. After additional stirring for 3 h, the solution was poured into 2 L of water. A yellow product so obtained was stirred for some time and then left overnight at room temperature. The product was filtered, washed with water, and dried under vacuum. The products so obtained were generally crystallized from alcohol or aqueous alcohol.

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Synthesis of 2,2-Disubstituted 5-Cyanocyclopentanones and Comparison of Their Enol Contents with the Corresponding Cyclohexanones

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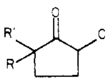
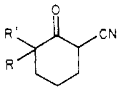
The enol contents of 14 2,2-disubstituted 5-cyanocyclopentanones and the analogous 2,2-disubstituted 6-cyanocyclohexanones are reported. The Brown–Brewster–Schechter prediction of less enolization for the five-membered alicyclics vs. the six-membered analogues is valid for all but three cases (Ph, *i*-C_3H_7; Ph, CH_2Ph; Ph, *n*-C_4H_9).

We previously reported (*2*) the development of a procedure for determining the percent enol for 2-cyanocyclohexanones by an infrared technique. Using this method for 14 compounds in the cyclohexanone series and 7 analogous compounds, which were available to us, in the cyclopentanone series (*3*, *4*) gave data which led to a correlation attempt via the Brown–Brewster–Schechter proposal (*5*) to exo/endo bonds in five- or six-membered rings. The rule predicts less enolization in the five-membered compounds.

We now report the synthesis of the remaining seven 2,2-disubstituted 5-cyanocyclopentanones and their enol contents as well as the necessary 1-cyano-2-methoxy-3,3-disubstituted cyclopentenes (H, H; Me, Me; Ph, *n*-C_5H_{11}; Ph, Ph) employed as conjugated nitrile standards.

Table I. Percent Enol of 2-Cyanocyclohexanones and 2-Cyanocyclopentanones in Dioxane

substituents		mol % enol	
R	R′		
H	H	1	37
Et	Et	2	18
Me	Me	4	20
C_6H_5	*i*-butyl	6	6
C_6H_5	*i*-propyl	6	5
C_6H_5	Et	6	10
C_6H_5	cyclohexyl	6	6
C_6H_5	*n*-amyl	7	10
C_6H_5	$CH_2C_6H_5$	8	4
C_6H_5	*n*-propyl	8	10
C_6H_5	*n*-butyl	8	5
C_6H_5	C_6H_5	9	24
C_6H_5	$(CH_2)_2C_6H_5$	13	13
C_6H_5	Me	13	19

Absorption of the keto nitriles in dioxane at 2210 cm^{-1} (conjugated CN) gave the concentration of the enol form by reference to a calibration plot for a related 1-cyano-2-meth-

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