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Synthesis of *N*-Phenylalkanehydrazonoyl Chlorides

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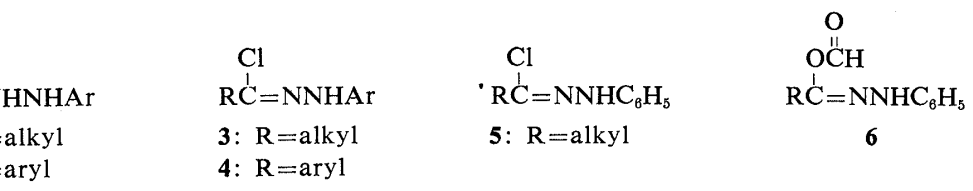
N-Phenylalkanehydrazonoyl chlorides (**5**), hitherto unknown, were synthesized from the corresponding arylhydrazides of aliphatic carboxylic acids (**1**) with triphenylphosphine–carbon tetrachloride in good yields.

Keywords——*N*-phenylalkanehydrazonoyl chloride; arylhydrazide; triphenylphosphine; carbon tetrachloride; chlorination

In the course of investigations on the chemistry of imidoyl chlorides, a simple and convenient method for the synthesis of *N*-phenylalkanehydrazonoyl chlorides (**5**) was required. *N*-Arylarenecarbohydrazonoyl chlorides (**4**) were prepared easily from arylhydrazides of aromatic carboxylic acid (**2**) by the usual methods; however, *N*-arylalkanehydrazonoyl chlorides (**3**) have been prepared only in the case of the arylhydrazides of aliphatic acids (**1**) containing electron-withdrawing substituents such as a nitro group in the arene ring.[1] As no report has appeared on the synthesis of **5** bearing no substituents on the phenyl ring, we searched for a facile synthetic method for **5**. Attempted synthesis of **5** by using usual chlorination reagents, such as phosphoryl chloride,[2] phosphoryl chloride–pyridine,[1] phosphorus pentachloride,[3] or thionyl chloride[2] was unsuccessful. In the case of phosphoryl chloride–pyridine employed at room temperature for 6.5 h, the desired chloro compound was obtained in low yield (about 20%) by the direct and rapid silica gel column chromatography of the reaction mixture, as the chloro compound was labile in the usual work-up. In other cases, the reaction did not proceed at low temperature, while at elevated temperature the starting material was decomposed to several compounds, none of which corresponded to the desired chloro compound. Finally we applied the triphenylphosphine–carbon tetrachloride system,[2b,4] which was used earlier for the synthesis of *N*-arylbenzenecarbohydrazonoyl



	R
a	C_2H_5
b	$C_6H_5CH_2CH_2$
c	$C_6H_5CH=CH$
d	$CH_3(CH_2)_6$

RCONHN(CHO)C_6H_5
7: R=alkyl

Chart 1

TABLE I. Preparation of Compounds **5**

Compd. No.	Ratio of PPh_3/**1** (mol)	Ratio of CCl_4/**1** (mol)	Reaction time (h)	Yield (%)	mp (°C)	IR ν_{max}^{neat} (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ (ppm)	Formula MS (*m/z*, M^+, $M^+ + 2$)
5a	1.25	1.25	12	86	Oil	3290, 1600, 1500	1.25 (t, 3H, $J=7$ Hz), 2.62 (q, 2H, $J=7$ Hz), 6.56—7.35 (m, 5H), 7.5 (br s, 1H)	$C_9H_{11}ClN_2$ (182, 184)
5b	1.25	1.25	12	92	Oil	3340, 1600, 1500	2.57—3.27 (m, 4H), 6.57—7.87 (m, 11H)	$C_{15}H_{15}ClN_2$ (258, 260)
5c	2	12	2	68	150—152	3320, 1600, 1500[a]	6.73—7.60 (m, 12H), 7.93 (br s, 1H)	$C_{15}H_{13}ClN_2$ (256, 258)
5d	1.5	5	2	84	Oil	3350, 1600, 1505	0.63—2.05 (m, 13H), 2.59 (t, 2H, $J=7$ Hz), 6.63—7.03 (m, 5H), 7.65 (br s, 1H)	$C_{14}H_{21}ClN_2$ (252, 254)

a) KBr.

TABLE II. Preparation of Compounds **7**

Compd. No.	Reaction time (h)	Yield (%)	mp (°C) Recrystn. solvent[a]	Formula	Analysis (%) Calcd (Found)		
					C	H	N
7a	0.25	84	66—67 A	$C_{10}H_{12}N_2O_2$	62.49 (62.57	6.29 6.41	14.75 14.67)
7b	1	98	128—129 A	$C_{16}H_{16}N_2O_2$	71.62 (71.42	6.01 5.98	10.44 10.17)
7c	12	69	145—146 A	$C_{16}H_{14}N_2O_2$	72.17 (72.07	5.30 5.10	10.52 10.49)
7d	2	84	56—57 B	$C_{15}H_{22}N_2O_2$	68.67 (68.58	8.45 8.74	10.68 10.54)

a) A, chloroform–hexane; B, ether–pet. ether.

chlorides,[5] to the synthesis of **5** in satisfactory yields. The products **5** could be purified by silica gel column chromatography and are stable for a few hours, as the neat liquid at room temperature. For the preparation of analytically pure samples, compounds **5** were converted to **7** with ammonium formate in methanol in good yields. The reaction is thought to take place through the intermediate **6** followed by O→N migration of the formyl group.[6] The products **7** were identified by microanalysis and by mixed melting point measurement with authentic samples prepared by the formylation of **1** ($Ar=C_6H_5$) with acetic formic anhydride.[7] Compounds **5** may be utilized for the synthesis of nitrogen-containing heterocyclic compounds by 1,3-dipolar cycloaddition with dipolarophiles,[8] and also after dechlorination for the synthesis of indole compounds by the Fischer indolization, because these compounds **5** are structurally related to aldehyde hydrazones.

Experimental

Melting points were determined on Yanaco micro melting point apparatus and are uncorrected. Mass spectra (MS) were measured with a JEOL DX-300 mass spectrometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured with a JEOL JNM-PMX60SI spectrometer using tetramethylsilane as an internal standard. In-

frared (IR) spectra were measured with a JASCO IR810 spectrometer.

Alkanehydrazonoyl Chlorides (5a—d); Typical Procedure——Freshly distilled carbon tetrachloride (0.3 ml, 3.05 mmol) was added to a suspension of *N*-phenyl-*N'*-propionoylhydrazine (**1a**) (400 mg, 2.44 mmol) and triphenylphosphine (800 mg, 3.05 mmol) in dry acetonitrile (3 ml) with stirring at room temperature. The reaction mixture was stirred overnight. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel using benzene–hexane (1 : 1) as an eluent to give *N*-phenylpropanehydrazonoyl chloride (**5a**) (303 mg, 68.0%).

Formylhydrazines (7a—d); Typical Procedure——Ammonium formate (523 mg, 8.30 mmol) was added to a solution of *N*-phenylpropanehydrazonoyl chloride (**5a**) (303 mg, 1.66 mmol) in absolute methanol (3 ml) at room temperature. The mixture was stirred for 30 min, then the solvent was evaporated off *in vacuo*. The residue was dissolved in ethyl acetate (25 ml), and the solution was washed with water (20 ml), dried with sodium sulfate and concentrated. The crude product was chromatographed on silica gel using benzene–ethyl acetate (2 : 1) as an eluent to give 1-formyl-1-phenyl-2-propionylhydrazine (**7a**) (268 mg, 84.0%).

References

1) B. I. Buzykin, L. P. Sysoeva, and Yu. P. Kitaev, *J. Org. Chem. USSR*, **12**, 1649 (1976) [*Chem. Abstr.*, **85**, 159354*v* (1976)].
2) *a*) B. C. Challis and J. A. Challis, "The Chemistry of Amides," ed. by J. Zabicky, Interscience Publishers, London, 1970, pp. 801—803; *b*) G. Tennant, "Comprehensive Organic Chemistry," Vol. 2, ed. by I. O. Sutherland, Pergamon Press, New York, 1979, pp. 469—487.
3) F. Pochat, *Synthesis*, **1984**, 146.
4) R. Appel and M. Halstenberg, "Organophosphorus Reagents in Organic Synthesis," ed. by J. I. G. Cadogan, Academic Press, London, 1979, pp. 387—432.
5) P. Wolkoff, *Can. J. Chem.*, **53**, 1333 (1975).
6) J. T. Edward and S. A. Samad, *Can. J. Chem.*, **41**, 1638 (1963).
7) J. C. Sheehan and D.-D. H. Yang, *J. Am. Chem. Soc.*, **80**, 1154 (1958).
8) A. S. Shawali and C. Párkányi, *J. Heterocycl. Chem.*, **17**, 833 (1980).