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SYNTHESES OF 1-ARYLOXYACETYL-4-(3-TOLYLOXYACETYL) THIOSEMICARBAZIDES VIA SOLID-LIQUID PHASE TRANSFER CATALYSIS

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ABSTRACT: A series of new 1-aryloxyacetyl-4-(3-tolyloxyacetyl) thiosemicarbazides is synthesized under the condition of soid-liquid phase transfer catalysis.

1,4-disubstituted thiosemicarbazides have been found to exhibit wide spectrum of biological activities. Some of them can be used as insecticides, herbicides and plant-growth regulators[1]. Meanwhile, aryloxyacetic acid derivatives have also been used as herbicides and plant-growth regulators[2-5]. These applications prompt us to synthesize a new series of compounds bearing both thiosemicarbazide and aryloxyacetyl moiety, with the objective of obtaining new biologically active compounds.

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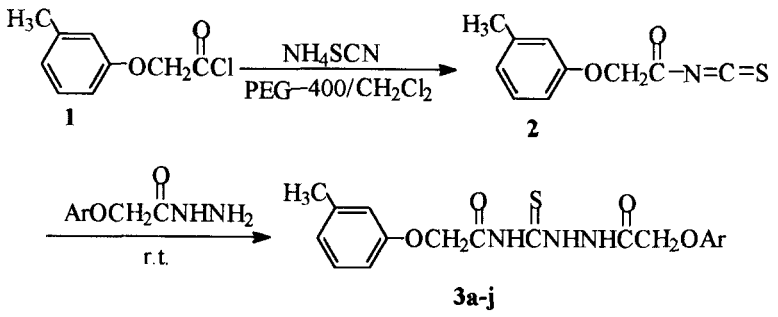
In this paper, we report a convenient and efficient method for the preparation of new 1,4-disubstituted thiosemicarbazide derivatives under the condition of solid-liquid phase transfer catalysis using polyethylene glycol 400 (PEG-400) as the catalyst.

3- tolyloxyacetyl isothiocyanate (**2**) has been synthesized by the reaction of 3-tolyloxyacetyl chloride (**1**) with ammonium thiocyanate catalyzed by PEG-400 at room temperature. Further, compound **2** on treatment with aryloxyacetic acid hydrazides at room temperature gives 1-aryloxyacetyl-4-(3-tolyloxyacetyl) thiosemicarbazides (**3a-j**) in excellent yields (Scheme).

Scheme



3	Ar	3	Ar
a	C_6H_5	**f**	1-Naphthyl
b	2-$CH_3C_6H_5$	**g**	2-Naphthyl
c	4-$CH_3C_6H_5$	**h**	2-$O_2NC_6H_5$
d	4-$CH_3OC_6H_5$	**i**	3-$O_2NC_6H_5$
e	4-ClC_6H_5	**j**	4-$O_2NC_6H_5$

Acyl isothiocyanates are usually prepared by refluxing acyl chloride with potassium thiocyanate in acetone, but the yields are always very low. Harrison[6] reported that polymer-supported thiocyanate on treatment with acyl chloride in benzene can afford acylisothiocyanate, but the preparation of the polymer-supported reagent required long reaction time and vacuum condition. Reeves and coworkers[7] carried out the same reactions under the liquid-liquid phase transfer catalysis using tetrabutyl ammonium bromide as phase transfer catalyst, however, hydrolysis reactions of the acyl chloride were taken place frequently because of the presence of water, and the yields of the acylisocyanate were not high yet. In addition, a great excess of ammonium thiocyanate had to be used.

However, acylisocyanate can be easily obtained under the solid-liquid phase transfer catalysis using PEG-400 as catalyst. It is found that acyl chlorides are quantitatively converted to corresponding acyl isothiocyanates, which on reaction with the acyloxyacetic acid hydrazides to afford compound **3a-j** in high yields. From these reactions, it is seen that solid-liquid phase transfer catalytic method as the condition of main step to prepare **3a-j** has great advantages of mild reaction condition, high yield, short reaction time and low cost of catalyst.

EXPERIMENTAL SECTION

IR spectra were recorded using KBr pellets on an Alpha Centauri FTIR spectrophotometer and ^{1}H NMR spectra on a FT-80A instrument using $(CD_3)_2SO$

Table 1 Physical data and elemental analyses of **3a-j**

Product	m.p. (℃)	Yield(%)	%C	%H	%N
			Found (Calculated)		
3a	118-119	94	57.93(57.89)	5.24(5.13)	11.05(11.25)
3b	162-163	87	59.17(58.90)	5.57(5.46)	10.73(10.85)
3c	167-168	95	58.73(58.90)	5.32(5.46)	10.94(10.85)
3d	117-118	89	56.40(56.56)	5.13(5.25)	10.57(10.41)
3e	137-138	90	52.81(53.00)	4.57(4.45)	10.49(10.30)
3f	208-209	91	62.63(62.40)	4.81(5.00)	10.14(9.92)
3g	182-183	87	62.56(62.40)	4.79(5.00)	10.20(9.92)
3h	180-181	92	51.79(51.67)	4.45(4.34)	13.51(13.39)
3i	197-198	89	51.40(51.67)	4.23(4.34)	13.54(13.39)
3j	201-202	93	51.57(51.67)	4.25(4.34)	13.20(13.39)

as solvent and Me_4Si as internal standard. Elemental analyses were performed on a Carlo-Erba 1106 Elemental Analysis instrument. Melting points were observed in an open capillary tube and uncorrected. 3-tolyloxyacetyl chloride[8] (**1**) and aryloxyacetic acid hydrazides[9] were prepared according to literature procedures.

Ammonium thiocyanate and PEG-400 were commercially available and used as received.

General procedure for preparation of 3a-j

A suspension of 3-tolyloxyacetyl chloride (1.5mmol), ammonium

Table 2 IR data of **3a-j**

Product	IR ν (cm^{-1})			
	N-H	C=O	C=S	ArO
3a	3390 3275 3164	1712	1184	1243
3b	3386 3290 3221	1707	1190	1247
3c	3382 3279 3172	1702	1192	1245
3d	3393 3271 3192	1713	1189	1250
3e	3371 3268 3180	1716	1186	1248
3f	3386 3272	1701	1191	1252
3g	3392 3280	1704	1195	1250
3h	3380 3287 3201	1708	1187	1247
3i	3384 3271 3185	1713	1189	1251
3j	3392 3278 3189	1705	1191	1244

Table 3 ^{1}H NMR data of **3a-j**

Product	N-H[a]	N-H[b]	N-H[c]	Ar-H	OCH_2	CH_3	OCH_3
3a	12.83 (1H,s)	10.06 (1H,s)	9.37 (1H,s)	6.76-7.50 (9H,m)	4.69 (4H,s)	2.33 (3H,s)	
3b	12.85 (1H,s)	10.11 (1H,s)	9.41 (1H,s)	6.80-7.52 (8H,m)	4.65 (4H,s)	2.29 (6H,s)	
3c	12.82 (1H,s)	10.08 (1H,s)	9.38 (1H,s)	6.75-7.54 (8H,m)	4.70 (4H,s)	2.27 (6H,s)	
3d	12.79 (1H,s)	10.03 (1H,s)	9.44 (1H,s)	6.70-7.33 (8H,m)	4.65 (4H,s)	2.31 (3H,s)	3.81 (3H,s)
3e	12.76 (1H,s)	10.10 (1H,s)	9.52 (1H,s)	6.79-7.54 (8H,m)	4.68 (4H,s)	2.33 (3H,s)	
3f	12.75 (1H,s)	10.59 (1H,s)	9.50 (1H,s)	6.75-7.52 (11H,m)	4.71 (4H,s)	2.38 (3H,s)	
3g	12.77 (1H,s)	10.61 (1H,s)	9.48 (1H,s)	6.78-7.53 (11H,m)	4.73 (4H,s)	2.35 (3H,s)	
3h	12.83 (1H,s)	10.09 (1H,s)	9.47 (1H,s)	6.80-7.47 (8H,m)	4.66 (4H,s)	2.20 (3H,s)	
3i	12.79 (1H,s)	10.12 (1H,s)	9.53 (1H,s)	6.85-7.46 (8H,m)	4.71 (4H,s)	2.31 (3H,s)	
3j	12.80 (1H,s)	10.19 (1H,s)	9.58 (1H,s)	6.91-7.58 (8H,m)	4.72 (4H,s)	2.33 (3H,s)	

thiocyanate (2.63mmol) and PEG-400 (3% based on ammonium thiocyanate) in methylene chloride was stirred for 1h at room temperature, then a kind of aryloxyacetic acide hydrazides (1.45mmol) was added. The mixture was stirred for another 0.5h, and a precipitate was observed immediately. The resulting mixture was filtered and washed with water to remove inorganic salts. The residue was recrystallized from DMF-EtOH-H_2O, and crystals of compound **3** were given. The physical and analytical data and spectral results were shown in Table 1-3.

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