From these results, the configuration of the first eluting and herbicidally active enantiomer can be assumed to be (–)-D-isomer. However, there is some confusion in the literature, as in the paper of *Chan et al.* [11] describing the synthesis of napropamide enantiomers, the herbicidally active D-stereoisomer was found levorotatory ($[\alpha]_{20}^{D} = -121.35$), whereas a patent to *Stauffer* mentions the dextrorotatory form as being the active one [12]. This situation clearly illustrates the necessity of using unambiguous designations for stereoisomers, as stated in a recent report of the WHO expert committee [10]. To our knowledge, the absolute configuration according to the rule of *Cahn, Ingold,* and *Prelog* [16] of the herbicidally active isomer has not yet been published.

In conclusion, the data presented in this paper indicate a considerable difference in the herbicidal activities of (*R*)- and (*S*)-napropamide with, at lower concentrations, virtually all herbicidal activity being present in one enantiomer. However, we are fully aware of the complexity of transferring laboratory data to field experiments, as other mechanisms such as racemization or stereochemical inversion in soil [17], in plants and animals [18] or different uptakes of enantiomers [19] may strongly influence the biological activity of optically active pesticides under field conditions. Therefore, these findings would require a verification under field conditions. Nevertheless, we are convinced that a careful evaluation of desired and undesired biological activities including the possibly different environmental fate of optical isomers is an important tool for a deeper understanding of environmental effects and fate of pesticides and is currently implemented in the pesticide registration procedure in Switzerland.

This work is part of a joint project of the *Federal Office for Environmental Protection* (*BUWAL*) and of the *Research Station* for evaluation of the potential for reducing pesticides application by omitting isomeric ballast where one of us (*R.W.*) is engaged. The support of *BUWAL* is kindly acknowledged. We wish to thank *E. Barben* for carrying out the bioassay of the napropamide samples.

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Chemo- and Regioselectivity in the Reaction of Tetrachloro- and Tetrabromophthalic Anhydrides and Imides with Thiolates

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Abstract. The reaction of tetrachloro- and tetrabromophthalic anhydrides and -imides with *in situ* generated aryl and alkyl thiolates gives mono- to tetrathio-substituted derivatives depending on reagent, stoichiometry, and reaction conditions. The halogens non-vicinal to the carbonyl groups react regio- and chemoselectively under appropriate conditions. By this reaction, novel types of photosensitizers useful to photocross-link polymers are prepared.

Introduction

Aryl and alkyl thiolates are highly reactive and versatile nucleophiles in aromatic nucleophilic substitution reactions [1][2]. This formation of aryl thioethers continues to be of interest from both a mechanistic and synthetic point of view [3] and has found a wide range of applications, *e.g.* in the fields of polymer synthesis [4], preparation of pigments [5], thioxanthone photosensitizers [1][6], and in the synthesis of natural products [7]. In polyhalogen compounds, some chemo- and regioselectivities were found, *e.g.* in tetrahalo cyanobenzoates [5], polychlorobenzenes [3], or halogenated pyridines [2a].

We recently found particularly high regioselectivities in the reaction of 3,5-dinitrophthalimides and -anhydrides with thiolates [6a], and we now report similar effects in the reaction with tetrachloro- and tetrabromo phthalimides and anhydrides.

Results and Discussion

In several cases, isolated alkali thiolates were used as nucleophiles [2][8]. We prefer to prepare the thiolate anions *in situ* by adding a base (mostly anhydrous K_2CO_3, in one case Et_3N) to the reaction mixture [1][6a]. When stirred with tetrachloro- or tetrabromophthalic anhydrides or imides **1** (*Scheme*) in THF, mono- and dithio-substituted derivatives **2** and **3** can be prepared regio- and chemoselectively depending on reagents, stochiometry, and reaction conditions (*Table 1*) [9][10].

If *ca.* 1 equiv. of a thiophenol bearing in 4-position a *+I-* or *+M*-substituent (such as Me or MeO) is used the monosubstitution products **2** can be isolated in fair yields.

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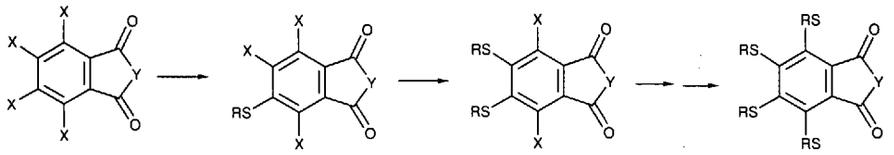

1 **2** **3** **4**

	X	Y	R	R	R
1a	Cl	O	**2a** Ph	**3a** Ph	**4a** Ph
1b	Br	O	**3b** Ph		
1c	Cl	NBu	**2c** Ph	**3c** Ph	**4c** Ph
1d	Cl	$N(CH_2)_2OH$	**2d** *p*-Tolyl	**3d** *p*-Tolyl	**4d** *p*-Tolyl
1d	Cl	$N(CH_2)_2OH$		**4e** Decyl	
1d	Cl	$N(CH_2)_2OH$		**4f** $(CH_2)_2OH$	
1g	Cl	NCH_3	**3g** Ethyl		
1g	Cl	NCH_3	**2h** *p*-$MeOC_6H_4$	**4h** *p*-$MeOC_6H_4$	
1i	Cl	NH		**4i** *p*-$O_2NC_6H_4$	

Here the phthalic-acid aromatic system is deactivated enough by the donor group in the thioether to be protected from further substitution. With thiophenol, the products **2a**, **2c** are formed in rather low yields, whereas 4-nitrothiophenol even with only 1 or 2 equiv. of nucleophile exclusively gives the tetrasubstituted product **4g** besides starting material **1g**.

With 2 (or slightly more) equiv. of thiol, the 4,5-disubstituted derivatives 3 are normally obtained in good yields (*Table 1*).

With 4 or more equiv. of thiol, the tetrasubstituted derivatives **4** are readily accessible (*Table 2*) (for a recent publication in the same field, see [8]).

When tested in a photoresist material containing pendent dimethylmaleinimide units as photosensitive functional groups [11], the imides **2** and **3** exhibit good properties as triplet photosensitizers for the cross-linking [2+2] cycloaddition [10] comparable to the normally used thioxanthones [1][6b]. Keeping in mind the short and efficient syntheses of **2** and **3** from inexpensive starting materials, a competitive performance/cost ratio of these new photosensitizers may be expected.

Table 1. *Chemo- and Regioselectivities in the Reaction of Tetrahalophthalic-Acid Derivatives with Thiolates* (K_2CO_3/THF) *to Give* **2** *and* **3**

Start. mat. [mmol][equiv.]	Thiol	K_2CO_3 [equiv.]	THF [ml]	Time [h]	Yield[a]) [%]	Product	M.p.[a]) [°]
1a (20)	PhSH (2.2)	3[b])	50[b])	18	13	**2a**[b])	162–4
				30	**3a**[b])	204–7	
1b (4.31)	PhSH (4.1)	4.05	20	2	75	**3b**	183–4
1c (5.86)	PhSH (1.05)	3	15	6	7	**2c**	159–63
1c (58.6)	PhSH (2.1)	4.14	150	18	83	**3c**	215–6
1d (6.08)	*p*-TolSH (1.05)	3	20	20	56	**2d**	205–9
1d (60.8)	*p*-TolSH (2.1)	4.05	200	60	86	**3d**	211–2
1g (138)	*p*-MeOPhSH (1)	3	410	24	64	**2h**	182–6
1g(10.04)	EtSH (2)	4	30[c])	4[c])	63	**3g**	154–5

[a]) Isolated products, recrystallized from toluene/cyclohexane [9].
[b]) Reaction in $Et_3N/CHCl_2$–$CHCl_2$ at 60°; the products were separated by fractional crystallization.
[c]) Reaction in DMF at 0°.

Table 2. *Tetrasubstitution of Tetrahalophthalic-Acid Derivatives with Thiolates at 25° to Give* **4**

Start. mat. [mmol]	Thiol [equiv.]	K_2CO_3 [equiv.]	Solvent [ml]	Time [h]	Yield[a]) [%]	Product	M.p.[a]) [°]
1a (108)	PhSH (4.1)	6	THF (300)	3	71	**4a**	141–2
1c (58.7)	PhSH (4.1)	6.05	EA[b]) (200)	18	97	**4c**	159–60
1d (6.08)	*p*-TolSH (4.1)	6.05	DMF (20)	1	78	**4d**	161–2
1g (6.7)	*p*-MeOPhSH(4.5)	6.75	THF (20)	4	98	**4h**	168–70
1i (7.02)	*p*-O_2NPhSH (4)	6	THF (30)	14	57[c])	**4i**	297–9
1d (6.08)	DecSH (5)	7.5	DMF (20)	7	70[d])	**4e**	57–8
1d (6.08)	$HOCH_2CH_2SH$(4.5)	6.5	DMF (20)	4	24	**4f**	152–7

[a]) Isolated products, recrystallized from toluene/cyclohexane [9].
[b]) EA = Ethyl acetate.
[c]) Recrystallized from dioxane/toluene.
[d]) Recrystallized from hexane.

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[9] All new compounds gave satisfactory elemental analyses [10] and ^{1}H-NMR spectra. Representative procedures are as follows:
4,5-Bis(phenylthio-)-3,6-dichlorophthalic anhydride (**3a**) and *4-(phenylthio)-3,5,6-trichlorophthalic anhydride* (**2a**): Tetrachlorophthalic anhydride (5.72 g, 20 mmol), thiophenol (4.84 g, 44 mmol), Et_3N (6.08 g, 60 mmol), and 1,1,2,2-tetrachloroethane (50 ml) were stirred at 60° for 18 h. The mixture was evaporated, and the residue was dissolved in 1N NaOH soln. The soln. was acidified with 2N HCl, and the products were extracted with CH_2Cl_2/acetone 1:1. The extracts were dried (Na_2SO_4) and evaporated. The residue was refluxed with toluene to form the anhydrides by azeotropic removal of H_2O. The soln. was filtered while hot, some cyclohexane added, until turbidity occurred, and the suspension cooled slowly to give in a first crop 2.41 g (30%) of **3a**. M.p. 204–207°. ^{13}C-NMR ($CDCl_3$): 158.3 (C=O); 151.4 (C(3)); 136.6 (C(2)); 134.2 (C(1')); 129.8 (C(2')); 129.6 (C(3')); 128.5 (C(1)); 127.9 (C(4')).
Addition of more cyclohexane to the filtrate gave 0.91 g (13%) of **2a**. M.p. 162–164°.
4-(p-Tolylthio-)-3,5,6-trichlorophthalic acid N-(2-hydroxyethyl)imide (**2d**): Tetrachlorophthalic acid *N*-(2-hydroxyethyl)imide (2 g, 6.08 mmol), *p*-thiocresol (0.79 g, 6.38 mmol), powdered anh. K_2CO_3 (2.52 g, 18.24 mmol), and THF (20 ml) were stirred at 25° for 20 h. The mixture was acidified with 2N HCl, extracted with CH_2Cl_2, and the extracts dried (Na_2SO_4), and evaporated. Recrystallization from toluene/cyclohexane gave 1.41 g (56%) of **2d**. M.p. 205–209°.
4,5-Bis(p-tolylthio-)-3,6-dichlorophthalic acid N-(2-hydroxyethyl)imide (**3d**): Tetrachlorophthalic acid *N*-(2-hydroxyethyl)imide (20 g, 60.8 mmol), *p*-thiocresol (15.86 g, 127.67 mmol), K_2CO_3 (34.03 g, 246.22 mmol), and THF (200 ml) were stirred at 25° for 60 h. Workup as above gave 26.42 g (86%) of **3d**. M.p. 211–212°.

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