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Photo-induced Transformation of Polyalkylbenzyl Thiocyanates into Polyalkylbenzyl Isothiocyanates. A Synthesis of Some Bis- and Tris(isothiocyanatomethyl)polymethylbenzenes by Multiple Thiocyanate Isomerization[1]

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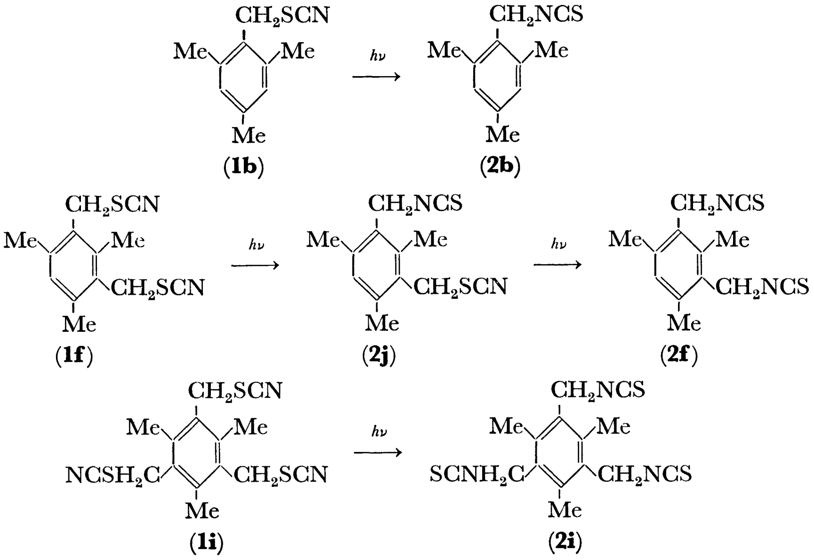
Polyalkylbenzyl thiocyanates, upon irradiation in acetic acid, readily undergo reversible photoisomerization, giving an equilibrium mixture composed mostly of the corresponding isothiocyanates. Several new bis- and tris(isothiocyanatomethyl)polymethylbenzenes have been prepared by utilizing the photoinduced multiple thiocyanate isomerization.

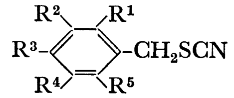
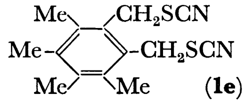
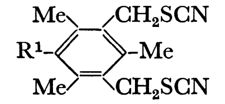
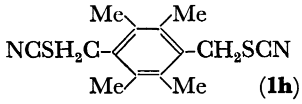
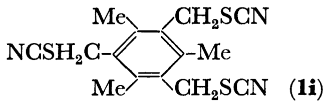
In connection with our studies on the *ipso*-thiocyanation of arenes, we needed several polyalkylbenzyl isothiocyanates as reference compounds for comparison. The classical synthesis of alkyl isothiocyanates[2] has been based on the reaction of alkyl halides with alkali thiocyanates,[3] thermal isomerization of thiocyanates,[4] and treatment of dithiocarbamate derivatives with heavy metal salts,[5] ethyl chloroformate,[6] aqueous potassium hydroxide,[7] sodium hypochlorite or chlorite,[8] and iodine.[9] Other methods of limited generality include the reaction of primary amines with thiophosgen,[10] action of sulfur and alkali cyanide upon alkyl halides,[11] addition of thiocyanic acid to olefins,[12] reaction of carbon disulfide and carbodiimide at high temperatures,[13] and treatment of isocyanates with phosphorus pentasulfide under pressure.[14] Recent proposals involve the reaction of primary amines with bis(trichloromethyl)pentathiodiperoxycarbonate,[15] treatment of dithiocarbamate derivatives with butyllithium,[16] phenylpropiolamidines,[17] phosphoryl chloride,[18] cyanuric chloride,[19] or dicyclohexylcarbodiimide,[20] pyrolysis of alkyldithiourethanes,[21] reaction of phosphoramidate anions with carbon disulfide,[22] and cleavage of secondary carboxamides by successive treatment with sodium hydride and carbon disulfide.[23] Many of these, however, suffer from either the lack of wide applicability, or the use of less common starting materials, and often require relatively tedious manipulative procedures.

Of the various methods previously reported, the isomerization of thiocyanates appeared attractive for our purpose, since the starting materials are easily accessible from aromatic hydrocarbons by chloromethylation and subsequent treatment with potassium thiocyanate. However, mild heating of polyalkylbenzyl thiocyanates in *N*,*N*-dimethylformamide (DMF) with or without potassium thiocyanate does not bring about isomerization; forced thermal isomerization under drastic conditions is accompanied by extensive decomposition. Conversions are generally slow and incomplete, rendering the reaction unfeasible for preparative purposes. Irradiation of benzyl thiocyanates in inert solvents in the absence of oxygen has been known to give a photo-stationary mixture of thiocyanate and isothiocyanate,[24] although the photoisomerization itself is not a general process for alkyl thiocyanates. In order to examine the synthetic potentials of obtaining polyalkylbenzyl isothiocyanates by a photochemical process, a series of polyalkylbenzyl thiocyanates were prepared from the corresponding chlorides and irradiated in dry acetic acid with a high-pressure mercury lamp. Solutions of 1.0—0.1 mM in compounds **1a**—**1d** afforded upon irradiation photo-equilibria which were composed mostly of the corresponding isothiocy-



Scheme 1.

Table 1. Physical properties of some polyalkylbenzyl thiocyanates and poly(thiocyanatomethyl)polyalkylbenzenes

Compound	Mp (°C)	Yield[a)] (%)	PMR spectra (δ, ppm)	IR spectra (cm^{-1})	Elemental analysis (%)	
					Found	Calcd
 (**1**)						
a: R^1, R^4=Me; R^2, R^3, R^5=H	49—50	74	2.37 (Me), 2.40 (Me), 4.22 (CH_2), 7.10 (3 aromatic H)	2150, 1500, 880, 805, 725	C: 67.6 H: 6.3 N: 7.8	67.7 6.3 7.9
b: R^1, R^3, R^5=Me; R^2, R^4=H	81—82	88	2.23 (Me), 2.36 (2Me), 4.23 (CH_2), 6.83 (2 aromatic H)	2140, 1605, 1225, 1195, 845	C: 69.0 H: 6.9 N: 7.2	69.1 6.9 7.3
c: R^1, R^2, R^3, R^4, R^5=Me	122—124	70	2.22 (3Me), 2.33 (2Me), 4.40 (CH_2)	2150, 1225, 1055, 1010, 795	C: 71.1 H: 7.8 N: 5.9	71.2 7.8 6.4
d: R^1, R^3, R^5=*i*-Pr R^2, R^4=H	113—114	68	1.24 (2Me, d; *J*=7 Hz), 1.29 (4Me, d; *J*=7 Hz), 2.7—3.6 (3CH, m), 4.48 (CH_2), 7.05 (2 aromatic H)	2140, 1605, 1225, 935, 870	C: 74.0 H: 9.2 N: 5.0	74.1 9.2 5.1
 (**1e**)	155—156	77	2.27 (2Me), 2.37 (2Me), 4.47 ($2CH_2$)	2150, 1285, 1220, 805, 710	C: 60.5 H: 5.8 N: 9.9	60.8 5.8 10.1
 (**1**)						
f: R^1=H	110—111	69	2.40 (2Me), 2.47 (Me), 4.37 ($2CH_2$), 6.97 (aromatic H)	2140, 1230, 1020, 875, 790	C: 59.4 H: 5.3 N: 10.6	59.5 5.4 10.7
g: R^1=Me	128—130	75	2.23 (Me), 2.37 (2Me), 2.48 (Me), 4.40 ($2CH_2$)	2155, 1230, 1000, 800, 760	C: 61.1 H: 5.9 N: 9.9	60.8 5.8 10.1
 (**1h**)	205—207 (lit,[27] 199—201)	84	2.35 (4Me), 4.42 ($2CH_2$)	2145, 1220, 1005, 800, 765	—	
 (**1i**)	143—145	76	2.52 (3Me), 4.40 ($3CH_2$)	2150, 2140, 1235, 1000, 785, 755	C: 54.2 H: 4.5 N: 12.3	54.0 4.5 12.6

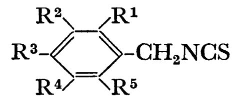
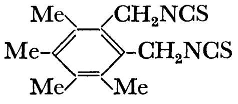
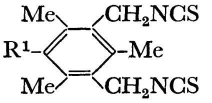
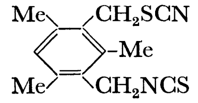
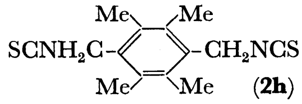
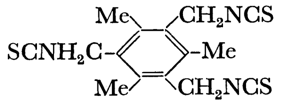
a) Based on the isolated pure product.

anates **2a**—**2d**. Photo-equilibrium was reached within 1 h when these dilute solutions were used. Longer irradiations were not advantageous, since the formation of tarry substances began to occur. Acetic acid was apparently a solvent of choice; in hexane an insoluble polymeric solid deposited, while in ethanol the formation of side products was prominent. Ordinary work-up of the reaction mixture gave a light brown solid or oily substance, which was chromatographed on a short silica gel column using hexane as eluant, giving the isothiocyanates as an early eluate. Unchanged material and small amounts of benzyl acetate were retained on the column or eluted quite slowly.

In order to ascertain the scope of photochemical isothiocyanate synthesis, we extended the present procedure to some poly(thiocyanatomethyl)benzenes. Upon irradiation in acetic acid, bis(thiocyanatomethyl)-polymethylbenzenes **1e**—**1h** likewise underwent isomerization, giving the corresponding bis(isothiocyanatomethyl)polymethylbenzenes **2e**—**2h** in fair to moderate yields (Table 2). The two vicinally disposed thiocyanatomethyl groups did not seem to interfere with each other during isomerization, since **1e** was smoothly transformed into **2e**. When the reaction was interrupted at early stages, (isothiocyanatomethyl)(thiocyanatomethyl)benzenes were obtained as intermediates along with the expected diisothiocyanates. Until now, no direct method was available for the preparation of such mixed benzylic thiocyanate–isothiocyanates.

Under similar irradiation, tris(thiocyanatomethyl)-benzene **1i** readily isomerized to tris(isothiocyanatomethyl)benzene **2i**. A patent description claims that

Table 2. Physical properties of some polyalkylbenzyl isothiocyanates and poly(isothiocyanatomethyl)polyalkylbenzenes

Compound	Mp (°C)	Yield[a)] (%)	PMR spectra (δ, ppm)	IR spectra (cm^{-1})	Elemental analysis (%)	
					Found	Calcd
 (**2**)						
a: R^1, R^4=Me; R^2, R^3, R^5=H	oil[b)]	51	2.30 (Me), 2.33 (Me), 4.60 (CH$_2$), 6.97 (3 aromatic H)	2160, 2100, 2050, 1505, 1335, 1155	C: 67.5 H: 6.3 N: 7.6	67.8 6.3 7.9
b: R^1, R^3, R^5=Me; R^2, R^4=H	33—34	54	2.27 (Me), 2.37 (2Me), 4.60 (CH$_2$), 6.87 (2 aromatic H)	2150, 2070, 2040, 1610, 1330, 845	C: 68.8 H: 6.9 N: 7.0	69.1 6.9 7.3
c: R^1, R^2, R^3, R^4, R^5=Me	116—117	45	2.23 (3Me), 2.30 (2Me), 4.67 (CH$_2$)	2180, 2090, 1380, 1055, 1025, 795	C: 71.1 H: 7.9 N: 6.2	71.2 7.8 6.4
d: R^1, R^3, R^5=*i*-Pr; R^2, R^4=H	oil[b)]	61	1.26 (2Me, d; *J*=7 Hz), 1.29 (4Me, d; *J*=7 Hz), 2.6—3.4 (3CH, m), 4.65 (CH$_2$), 6.90 (2 aromatic H)	2140, 2070, 2040, 1605, 1330, 870	C: 74.6 H: 9.3 N: 4.8	74.1 9.2 5.1
 (**2e**)	147—149	20	2.27 (2Me), 2.35 (2Me), 4.73 (2CH$_2$)	2160, 2100, 1335, 1235, 700	C: 61.1 H: 6.0 N: 9.6	60.9 5.8 10.1
 (**2**)						
f: R^1=H	99—100 (lit,[26)] 92—95)	27	2.35 (2Me), 2.42 (Me), 4.65 (2CH$_2$), 6.91 (aromatic H)	2130, 2050, 1320, 805	—	
g: R^1=Me	141—143	55	2.27 (Me), 2.37 (2Me), 2.43 (Me), 4.72 (2CH$_2$)	2155, 2070, 1325, 1010, 810	C: 61.0 H: 5.9 N: 9.8	60.8 5.8 10.1
 (**2j**)	80—82	27	2.38 (Me), 2.42 (Me), 2.46 (Me), 4.37 (CH$_2$), 4.67 (CH$_2$), 6.98 (aromatic H)	2150, 2070, 1330, 860, 805	C: 59.5 H: 5.4 N: 10.6	59.5 5.4 10.7
 (**2h**)	153—155	18	2.35 (4Me), 4.70 (2CH$_2$)	2170, 2075, 2045, 1335, 790	C: 61.0 H: 6.1 N: 9.2	60.8 5.8 10.1
 (**2i**)	137—139	24	2.48 (3Me), 4.73 (3CH$_2$)	2175, 2090, 1335, 790, 760	C: 54.2 H: 4.7 N: 12.3	54.0 4.5 12.6

a) Based on the isolated pure product. b) The PMR spectra were measured in carbon tetrachloride.

the reaction of poly(chloromethyl)benzenes with potassium thiocyanate in the presence of potassium iodide in *N*,*N*-dimethylformamide under reflux gives the corresponding poly(isothiocyanatomethyl)benzenes in high yields.[25)] This procedure was carefully repeated using several poly(chloromethyl)polymethylbenzenes as substrate, and the products obtained were shown by TLC and PMR analyses to be a mixture of various benzylic compounds. Although polyisothiocyanates could be isolated pure by preparative thick-layer chromatography, this method was unsuitable for laboratory purposes, especially when pure compounds were needed. The photochemical conversion of polythiocyanates into polyisothiocyanates represents, to our knowledge, the first example of a multiple thiocyanate isomerization and the results summarized in Table 2 indicate the general character of this reaction. All the polyisothiocyanates obtained are colorless fine needles, slightly soluble in hexane, benzene, and carbon tetrachloride, and soluble in dichloromethane and hot ethanol. They can be recrystallized without alteration from ethanol and stored indefinitely, without appreciable deterioration, when kept in a dessicator protected against the daylight.

Although yields were only fair to modest (no attempt was made to optimize the reaction conditions), the easy availability of the starting compounds, the ease of performance, and the mild reaction conditions render this procedure quite useful for the laboratory-scale preparation of various poly(isothiocyanatomethyl)-benzenes, which are otherwise only laboriously accessible.

Experimental

The melting points were taken on a hot-stage apparatus and are uncorrected. The IR spectra were determined in Nujol mulls on a Hitachi 215 spectrophotometer. The PMR spectra were obtained on a Varian T-60 spectrometer, using deuteriochloroform as solvent and TMS as internal standard, unless otherwise stated. The UV spectra were recorded on a Hitachi 124 spectrophotometer in 95% ethanol solutions. All photochemical reactions were conducted using a Halōs PlH 100 high-pressure mercury lamp in a water-cooled quartz immersion well. The solution was flushed with dry nitrogen prior to irradiation and was stirred during the reaction by a magnetic stirring bar.

The benzyl thiocyanates and poly(thiocyanatomethyl)-benzenes were prepared by the reaction of the corresponding chlorides with potassium thiocyanate and recrystallized from ethanol or hexane prior to use. All the new thiocyanates were characterized by elemental analyses as well as by the IR and PMR spectral data summarized in Table 1. The following is a typical experimental procedure.

*2,4,6-Tris(thiocyanatomethyl)-1,3,5-*trimethylbenzene *(**1i**).* A solution of 2,4,6-tris(chloromethyl)-1,3,5-trimethylbenzene (2.0 g (7.5 mM)) and potassium thiocyanate (15.0 g (156 mM)) in DMF (100 ml) was allowed to stand at room temperature for 4 h and then diluted with water (200 ml). The precipitated solid was filtered off and recrystallized from ethanol to give **1i** as white needles, mp 143—145 °C. Yield, 1.90 g (76%).

The general procedure of photo-induced transformation of thiocyanates into isothiocyanates is illustrated below with the representative preparation of two isothiocyanates. Other isothiocyanates obtained are shown in Table 2, along with the corresponding isolation yields as well as IR and PMR spectral data.

*2,4,6-Trimethylbenzyl Isothiocyanate (**2b**).* A solution of 2,4,6-trimethylbenzyl thiocyanate (**1b**; 100 mg (0.524 mM)) in acetic acid (40 ml) was irradiated with a high-pressure mercury lamp for 0.5 h in an atomosphere of nitrogen at room temperature. Thin-layer chromatography showed that the conversion to a single photo-product was nearly complete within this period of time, with only a little starting material recovered. A pale yellow photo-equilibrium mixture was diluted by the addition of water (200 ml) and the product was extracted with ether. The ethereal extract was washed successively with water, aqueous sodium hydrogencarbonate, and water again, dried over anhydrous magnesium sulfate, and evaporated to dryness on a rotary evaporator. The residue was placed on a top of a short silica gel column and eluted with hexane. Evaporation of early eluates followed by recrystallization of the residue from ethanol gave isothiocyanate **2b** as colorless needles, mp 33—34 °C. Yield, 54 mg (54%).

*4,6-Bis(isothiocyanatomethyl)-1,2,3,5-tetramethylbenzene (**2g**).* A solution of 4,6-bis(thiocyanatomethyl)-1,2,3,5,-tetramethylbenzene (**1g**; 100 mg (0.362 mM)) in dry acetic acid (100 ml) was irradiated under nitrogen for 0.5 h at room temperature and worked up in a manner similar to the above. The solid residue obtained after removal of the solvent was chromatographed on a short column of silica gel; evaporation of the early eluates gave bis(isothiocyanatomethyl) compound **2g** as fine needles, 55 mg (55%). Mp 110—111 °C (ethanol).

*2-(Isothiocyanatomethyl)-4-(thiocyanatomethyl)-1,3,5-trimethylbenzene (**2j**).* The photoisomerization was carried out essentially as described for **2b**, using 2,4-bis(thiocyanatomethyl)-1,3,5-trimethylbenzene (**1f**; 300 mg (1.1 mM)) and acetic acid (70 ml). After 15 min the reaction was stopped and the solution was diluted with water, extracted with ether, and the solvent removed *in vacuo*. The crude product mixture was separated by silica gel chromatography and further purified by preparative thin-layer chromatography to give **2j** (80 mg (27%)), mp 80—82 °C, and **2f** (57 mg (19%)), mp 99—100 °C.

References

1) The reaction of polysubstituted aromatics. Part LIII. Part LII: H. Suzuki, T. Mishina, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **52**, 191 (1979).

2) For a general survey of the chemistry of isothiocyanates, see M. Bögemann, S. Petersen, O. E. Schultz, and H. Söll, in "Houben-Weyl Methoden der Organischen Chemie," 4th ed, ed by E. Müller, Georg Thieme Verlag, Stuttgart (1955), Vol. IX, p. 867.

3) E. Schmidt, W. Striewsky, M. Seefelder, and F. Hitzler, *Justus Liebigs Ann. Chem.*, **568**, 192 (1950).

4) O. Mumm and H. Richter, *Chem. Ber.*, **73**, 843 (1940); P. A. S. Smith and D. W. Emerson, *J. Am. Chem. Soc.*, **82**, 3076 (1960); J. Kalamar, J. Hrivnak, A. Kovac, and J. Obertas, Czech. Patent, 131547 (1969); *Chem. Abstr.*, **72**, 100264u (1970).

5) M. Delépine, *Bull. Soc. Chim. Fr.*, **[4]**, **3**, 642 (1908).

6) M. L. Moore and F. S. Crossley, *Org. Synth.* Coll. Vol. III, 599 (1955).

7) J. E. Hodgkins and M. G. Ettlinger, *J. Org. Chem.*, **21**, 404 (1956).

8) E. Schmidt, F. Zaller, F. Moosmüller, and E. Kammerl, *Justus Liebigs Ann. Chem.*, **585**, 230 (1954); E. Schmidt, E. Kammerl, D. Ross, and F. Zaller, *ibid.*, **594**, 233 (1955).

9) J. von Braun and H. Deutsch, *Chem. Ber.*, **45**, 2188 (1912).

10) A. Rathke, *Justus Liebigs Ann. Chem.*, **167**, 218 (1873).

11) N. E. Searle, U. S. Patent, 2462433 (1946); *Chem. Abstr.*, **43**, 3843d (1949).

12) M. S. Kharasch, E. M. May, and F. R. Mayo, *J. Am. Chem. Soc.*, **59**, 1580 (1937).

13) W. Weith, *Chem. Ber.*, **7**, 1303 (1874).

14) A. Michael and G. M. Palmer, *Am. Chem. J.*, **6**, 258 (1884); W. V. Wirth, U. S. Patent, 2681358 (1954); *Chem. Abstr.*, **49**, 6303f (1955).

15) R. Gottfried, *Angew. Chem. Int. Ed. Engl.*, **5**, 963 (1966).

16) S. Sakai, T. Aizawa, and T. Fujinami, *J. Org. Chem.*, **39**, 1970 (1974).

17) H. Fujita, R. Endo, and K. Murayama, *Chem. Lett.*, **1973**, 883.

18) D. Martin, E. Beyer, and H. Gross, *Chem. Ber.*, **98**, 2425 (1965).

19) W. Schwarze and W. Weigert, Ger. Patent, 1935302, 2002903 (1971); *Chem. Abstr.*, **74**, 87457d (1971), **75**, 88101r

(1971).

20) J. C. Jochims and A. Seeliger, *Angew. Chem. Int. Ed. Engl.*, **6**, 174 (1967).

21) Y. E. Moharir, *J. Indian Chem. Soc.*, **58**, 148 (1975).

22) W. S. Wadsworth, Jr. and W. D. Emmons, *J. Org., Chem.*, **29**, 2816 (1964).

23) I. Shahak and Y. Sasson, *J. Am. Chem. Soc.*, **95**, 3440 (1973).

24) U. Mazzucato, G. Beggiato, and G. Favaro, *Tetrahedron Lett.*, **1966**, 5455; T. E. Parks and L. A. Spurlock, *J. Org. Chem.*, **38**, 3922 (1973).

25) E. J. Tarlton and A. F. McKay, Ger. Patent, 1148540 (1963); *Chem. Abstr.*, **60**, 2825 g (1964).

26) H. Teubner, W. Weuffen, and H. Höppe, *Arch. Exper. Vet. Med.*, **29**, 621 (1975).

27) I. Rosen, U. S. Patent, 3109015 (1963); *Chem. Abstr.*, **60**, 2827a (1964).