

THE USE OF *S*-ALKYL-*N*-PHENYLTHIURONIUM PICRATES, STYPHNATES AND PICROLONATES FOR THE CHARACTERISATION OF ALKYL HALIDES

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A series of *S*-alkyl-*N*-phenylthiuronium picrates, styphnates and picrolonates has been prepared and the melting points determined. By use of these derivatives it is possible to identify any of the lower primary and secondary alkyl halides examined. This has not previously been possible with *S*-alkylthiuronium salts. The reaction between tertiary alkyl halides and thiourea has been re-examined.

Primary and Secondary Alkyl Halides

S-Alkylthiuronium picrates are well known as derivatives for characterising primary and secondary alkyl halides^{1,2}. However, it was pointed out by Schotte³ that the usefulness of these derivatives is limited by the fact that derivatives of different homologues have the same or similar melting points. In an attempt to improve the analytical usefulness of the reaction, Schotte³ prepared the *S*-alkylthiuronium styphnates of many of the lower primary and secondary alkyl halides. While the combination of melting points of the picrate and the styphnate increased the usefulness of the method, it did not permit unambiguous identification of alkyl halides (Table I). Schotte³ also examined 2,4-dinitrophenol and 2,4-dinitroresorcinol, but reported that they did not form crystalline salts with *S*-alkylthiuronium halides. Other acidic precipitating reagents which have been examined⁴ are picrolonic acid, 3,5-dinitrobenzoic acid, *p*-toluenesulphonic acid, perchloric acid, oxalic acid and nitric acid. Jurecek⁶ selected 3,5-dinitrobenzoic acid as the most satisfactory and he reported the melting points of a series of *S*-alkylthiuronium 3,5-dinitrobenzoates. But the situation is not completely satisfactory (Table I).

We have now examined 3-nitrobenzoic acid, hexanitrodiphenylamine, flavionic acid, two sulphonic acids of fairly high molecular weight, R acid and H acid, and ammonium reineckate, as well as the acids listed above. From this work picric acid, styphnic acid and picrolonic acid were selected as the best precipitating agents. (For a detailed discussion of each precipitating agent see Baker⁵). A series of *S*-alkylthiuronium picrolonates was prepared and the melting points determined (Table I), in the vain hope that a combination of the melting points of *S*-alkylthiuronium picrate, styphnate and picrolonate would allow unambiguous identification.

A second method by which the general reaction may be modified is to replace the thiourea by a thiourea substituted on the nitrogen and determine the melting points of their picrates, styphnates and picrolonates. *N*-Phenylthiourea, *N*-ethylthiourea, 1,3-diphenylthiourea and 1,3-di-*n*-butylthiourea have been examined for their suitability for characterising alkyl halides. Both the disubstituted thioureas and *N*-ethylthiourea yielded thiuronium derivatives which had low melting points; several of

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the picrates and styphnates were oils which could not be induced to crystallise. *N*-Phenylthiourea condensed smoothly with alkyl halides and produced *S*-alkyl-*N*-phenylthiuronium salts whose picrates, styphnates and picrolonates were readily crystallisable and had sharp melting points. The melting points were scattered over a wide range of temperature (Table II) and in every example derivatives were obtained by which it is possible to identify an alkyl halide without ambiguity. It has been reported² that *N*-phenylthiourea does not react with branched chain alkyl halides; this has now been shown to be incorrect.

TABLE I

MELTING POINTS OF *S*-ALKYLTHIURONIUM PICRATES, STYPHNATES, PICROLONATES AND 3,5-DINITROBENZOATES. THE *S*-ALKYLTHIURONIUM PICROLONATES WERE PREPARED BY THE AUTHORS

Radical	Melting point °C			
	Picrate	Styphnate	Picrolonate	3,5-Dinitrobenzoate
Methyl	224 ³	226 ³ (decomp.)	243	205-206 ⁶
Ethyl	188	179	224	118
<i>n</i> -Propyl	177	161	221	176
Isopropyl	196	187	212	184
<i>n</i> -Butyl	177	164	197 (decomp.)	169
Isobutyl	167	150	127	158
<i>s</i> -Butyl	166	163	184	176
<i>n</i> -Pentyl	155	147	200	156
Isopentyl	173	159	225	—
2-Pentyl	155	112	174	—
3-Pentyl	159	114	177	—
<i>n</i> -Hexyl	157	153	190	—
Isohexyl	147	144	—	—
Heptyl	143	144	191	157-158
Octyl	134	122	191-195	—
Allyl	155	154	209	163
Benzyl	187	190	217	174-175
<i>p</i> -Nitrobenzyl	205	166	218-219 (decomp.)	—
Cetyl	137 ¹	—	—	—
Ethylene	260	—	—	—
	(267 ¹⁴ decomp.)	—	—	—
Trimethylene	229	—	—	—
1-Phenylethyl	167	—	—	—
Phenylethyl	139	—	—	—
<i>o</i> -Bromobenzyl	222	—	—	—
<i>m</i> -Bromobenzyl	205	—	—	—
<i>p</i> -Bromobenzyl	219	—	—	—
<i>o</i> -Chlorobenzyl	213	—	—	—
<i>m</i> -Chlorobenzyl	200	—	—	—
<i>p</i> -Chlorobenzyl	194	—	—	—
2-Octyl	131 ¹⁴	—	—	—
Nonyl	131	—	—	144
Decyl	137	—	188	145-146
Dodecyl	139	—	—	143
2-Hydroxyethyl	155-156	—	—	—
Pentamethylene	247	—	—	—
Hexamethylene	208	—	—	—
Octamethylene	214	—	—	—
Nonamethylene	193	—	—	—

Both the nature of the halide and of the alkyl radical influence the time required for any particular alkyl halide to react with thiourea and different times of reaction have been recommended for chlorides, bromides and iodides^{1,3}. To rationalise the method, a number of solvents and conditions have been investigated. Ethanol (absolute, 95 and 50 per cent) and acetone (80 and 50 per cent) were used for refluxing times varying from 5 minutes to 3 hours. Thiourea and *N*-phenylthiourea were found to react with all primary and secondary alkyl bromides and iodides examined when they were refluxed with any alkyl bromide or iodide in

ethanol (50 per cent) for 1 hour. The reaction with alkyl chlorides is slower, but may be accelerated by adding sodium iodide to the solution.

Tertiary Alkyl Halides

Levy and Campbell¹ reported that the *S*-ethylthiuronium salt was obtained when *t*-butyl iodide was refluxed with thiourea in ethanol as solvent. It was suggested that the *t*-butyl iodide reacted with ethanol to form ethyl iodide which then condensed with thiourea. This anomalous reaction of tertiary alkyl halides has since been quoted in books on organic analysis^{8,9}, even though the evidence is based on only two observations. It has been generally regarded that thiourea will not react with

TABLE II
MELTING POINTS OF *S*-ALKYL-*N*-PHENYLTHIURONIUM PICRATES, STYPHNATES AND PICROLONATES PREPARED AS DESCRIBED

Radical	Melting point °C		
	Picrate	Styphnate	Picrolonate
Methyl	179	205 (decomp.)	212 (decomp.)
Ethyl	198	176	206
<i>n</i> -Propyl	169	144	159
<i>n</i> -Butyl	144	125	154
<i>n</i> -Pentyl	142	131	173
<i>n</i> -Hexyl	128	112	143
<i>n</i> -Heptyl	127	112	163
<i>n</i> -Octyl	130	100	153
<i>n</i> -Nonyl	165	153	150
<i>n</i> -Decyl	128	97	94
<i>s</i> -Propyl	181	155	196-197
Isobutyl	134	105	160
<i>s</i> -Butyl	149	131	178
Isopentyl	153	149	165
2-Pentyl	130	86-87	151
3-Pentyl	137	84-86	145
Isohexyl	126	113	130-131 (decomp.)
Cetyl	113	101	102
Allyl	157	146	183
1-But-3-enyl	134	129	170
1-Pent-4-enyl	138	124	154
Benzyl	147	143	194 (decomp.)
<i>p</i> -Nitrobenzyl	195	162	192 (decomp.)

t-alkyl halides. However, Schotte³ was able to prepare *S*-*t*-alkylthiuronium salts by condensing a *t*-alkyl halide with thiourea using the corresponding tertiary alcohol as solvent. Later Schotte and Veibel¹⁰ obtained *S*-*t*-alkylthiuronium salts using aqueous ethanol (35 per cent) as solvent. The reactions between *t*-alkyl halides and thiourea and *N*-phenylthiourea have now been examined. *T*-alkyl halides will react with thiourea to produce the *t*-alkylthiuronium salts in aqueous ethanol, dioxan or acetone. The latter two solvents are better because there is no possibility of an abnormal product being formed and no solubility problems. Schotte and Veibel¹⁰ found that higher molecular weight *t*-alkyl halides were only slightly soluble in aqueous ethanol (35 per cent) with the consequence that the reaction was slow. No product was obtained when *t*-alkyl halides were refluxed with *N*-phenylthiourea in a number of solvents for 12 hours.

With the failure of *N*-phenylthiourea to react with *t*-alkyl halides, the possibility was considered of preparing *S*-alkyl-*N*-phenylthiuronium salts

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directly from alcohols by refluxing together an alcohol, a t-alkyl halide and *N*-phenylthiourea with either dioxan or acetone as solvent if required. With methanol, ethanol and propanol *S*-methyl-, *S*-ethyl- and *S*-propyl-*N*-phenylthiuronium picrates, respectively, have been prepared by this method.

Other applications of thiuronium and N-phenylthiuronium salts. Alkoxy groups have been identified by conversion with hydrogen iodide to the alkyl iodides which were then characterised as the thiuronium picrates^{6,12}.

Analysis of S-alkyl-N-phenylthiuronium picrates, styphnates and picrolonates. A spectrophotometric method has been developed for the determination of the picrate, styphnate and picrolonate ions present in the respective *S*-alkyl-*N*-phenylthiuronium salts¹³.

EXPERIMENTAL

Melting points. All melting points are corrected and were taken on a Kofler block.

Materials

All alkyl halides, except pent-3-yl bromide and isohexyl bromide, were obtained commercially and redistilled before use.

TABLE III
ANALYSIS OF *S*-ALKYL-*N*-PHENYLTHIURONIUM PICRATES, STYPHNATES AND PICROLONATES

	Picrate				Styphnate				Picrolonate			
	Found		Required		Found		Required		Found		Required	
	C	H	C	H	C	H	C	H	C	H	C	H
Methyl	42.6	3.41	42.5	3.29	40.6	3.25	40.9	3.16	50.2	4.52	50.0	4.63
Ethyl	44.2	3.8	44.0	3.67	42.2	3.38	42.3	3.53	51.1	4.9	51.1	4.93
n-Propyl	45.3	3.91	45.4	4.02	43.6	3.95	43.7	3.87	52.1	5.1	52.1	5.21
n-Butyl	46.5	4.36	46.7	4.35	45.2	4.0	45.0	4.19	53.0	5.4	53.1	5.49
n-Pentyl	48.2	4.63	47.9	4.66	46.4	4.6	46.3	4.5	54.1	5.69	54.1	5.74
n-Hexyl	49.0	4.8	49.0	4.95	47.2	4.66	47.4	4.78	55.0	5.82	55.0	5.98
n-Heptyl	50.1	5.4	50.1	5.22	48.7	5.01	48.5	5.05	55.8	6.0	55.8	6.2
n-Octyl	51.3	5.4	51.1	5.48	49.5	5.2	49.5	5.3	56.7	6.3	56.6	6.41
n-Nonyl	51.9	5.8	52.0	5.71	50.5	5.4	50.5	5.54	57.3	6.54	57.4	6.62
n-Decyl	53.1	5.82	53.0	5.95	51.6	5.76	51.4	5.77	58.3	6.64	58.1	6.81
s-Propyl	45.6	3.98	45.4	4.02	43.8	5.8	43.7	5.87	51.9	4.97	52.1	5.21
Isobutyl	46.5	4.26	46.7	4.35	45.1	4.38	45.0	4.19	52.9	5.4	53.1	5.49
s-Butyl	46.7	4.49	46.7	4.35	45.0	4.21	45.0	4.19	53.3	5.35	53.1	4.49
Isopentyl	48.0	4.46	47.9	4.66	46.1	4.54	46.3	4.5	54.4	5.61	54.1	5.74
2-Pentyl	47.7	4.84	47.9	4.66	46.5	4.32	46.3	4.5	54.2	5.63	54.1	5.74
3-Pentyl	47.6	4.71	47.9	4.66	46.4	4.5	46.3	4.5	54.1	5.65	54.1	5.74
Isohexyl	48.9	4.87	49.0	4.95	47.6	4.6	47.4	4.78	55.0	5.91	55.0	5.98
Cetyl	57.5	7.23	57.5	7.11	56.3	6.93	56.0	6.93	61.8	7.76	61.7	7.79
Allyl	45.5	3.58	45.6	3.56	44.0	3.46	43.9	3.44	52.5	4.61	52.4	4.8
1-But-3-enyl	47.0	4.1	46.9	3.91	45.0	3.68	45.2	3.77	53.7	4.99	53.4	5.09
1-Pent-4-enyl	47.9	4.13	48.1	4.23	46.3	3.97	46.4	4.09	54.4	5.15	54.3	5.35
Benzyl	50.9	3.5	51.0	3.61	49.1	3.7	49.3	3.49	56.8	4.66	56.7	4.72
p-Nitrobenzyl	46.7	3.2	46.5	3.1	45.1	2.87	45.1	3.01	52.2	3.9	52.1	4.16

Pent-3-yl bromide. Diethyl ketone was reduced by the Meerwein-Ponndorf-Verly reduction to give pentan-3-ol b.p. 114–117°. Pentan-3-ol was treated with hydrobromic acid and sulphuric acid. Pent-3-yl bromide b.p. 116–119° was collected.

Isohexyl bromide. Isohexanol was treated with potassium bromide and sulphuric acid. Isohexyl bromide b.p. 138–141° was collected.

Thiourea and all *N*-substituted thioureas were obtained commercially. Thiourea was recrystallised from aqueous ethanol m.p. 176°. *N*-Phenylthiourea was recrystallised from aqueous ethanol m.p. 153°. All the precipitating reagents except styphnic acid were obtained commercially. Picric acid m.p. 122° and picrolonic acid m.p. 118° (decomp.) were recrystallised from ethanol before use. A few samples of picrolonic acid were found to contain a dark yellow crystalline impurity which decomposed between 220–250°. This can be removed by crystallisation. Styphnic acid was prepared by the method of Merz and Zetter¹¹ by nitration of resorcinol. Recrystallisation from ethanol gave yellow crystals m.p. 175° (Lit.¹¹ 175°).

Standard procedure for preparing S-alkyl-N-phenylthiuronium picrates, styphnates and picrolonates. *N*-Phenylthiourea (1 g.) and the alkyl halide

TABLE IV
ANALYSIS OF *S*-ALKYLTHIURONIUM PICROLONATES

Radicals	Found		Required	
	C	H	C	H
Methyl	40.3	4.6	40.4	4.5
Ethyl	42.1	4.81	42.15	4.86
<i>n</i> -Propyl	43.9	5.27	43.8	5.21
<i>n</i> -Butyl	45.2	5.6	45.2	5.53
<i>n</i> -Pentyl	46.6	5.8	46.6	5.82
<i>n</i> -Hexyl	47.7	6.07	47.9	6.1
<i>n</i> -Heptyl	49.2	6.32	49.1	6.36
<i>n</i> -Octyl	50.0	6.7	50.2	6.6
<i>n</i> -Decyl	52.2	7.12	52.3	7.06
<i>s</i> -Propyl	43.6	5.2	43.8	5.21
Isobutyl	45.3	5.51	45.2	5.53
<i>s</i> -Butyl	45.3	5.46	45.2	5.53
Isopentyl	46.6	5.8	46.6	5.82
2-Pentyl	46.4	5.71	46.6	5.82
3-Pentyl	46.5	5.78	46.6	5.82
Allyl	43.7	4.75	44.0	4.71
Benzyl	50.1	4.58	50.0	4.63
<i>p</i> -Nitrobenzyl	45.4	4.01	45.3	3.99

(1 g.) were dissolved in turn in ethanol (10 ml. 50 per cent). The solution was refluxed for 1 hour and then divided into three aliquots.

Picrate. One aliquot was poured into a saturated aqueous solution of picric acid (25 ml.). The picrate was allowed to crystallise for half an hour then collected, washed and recrystallised from aqueous ethanol (50 per cent).

Styphnate. Styphnic acid (0.3 g.) was added to a second aliquot and the solution brought to the boil. Sufficient ethanol (50 per cent) was added dropwise to bring the styphnic acid into solution. The solution was allowed to cool when the *S*-alkyl-*N*-phenylthiuronium styphnate crystallised out. It was collected, washed and recrystallised from ethanol (50 per cent).

Picrolonate. The third aliquot was treated with picrolonic acid (0.3 g.) as described for styphnate.

Thiuronium picrates, styphnates and picrolonates were prepared by a similar procedure substituting thiourea for *N*-phenylthiourea.

S-T-butylthiuronium picrate, styphnate and picrolonate. *T*-butyl chloride (1.5 ml.) and thiourea (1 g.) were dissolved in dioxan (15 ml.) and water

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(1 ml.) and refluxed for 2 hours. The picrate, styphnate and picrolonate were prepared as described above. *S*-*T*-butylthiuronium picrate m.p. 150·5° (Lit.¹⁰ 151°). Found: C, 37·0; H, 4·3; N, 19·35. Calc. for $C_{11}H_{15}O_7N_5S$; C, 36·56; H, 4·15; N, 19·4.

S-*T*-butylthiuronium styphnate m.p. 149°—150°. $C_{11}H_{15}O_8N_5S$ requires N, 18·56. Found: N, 18·3.

S-*T*-butylthiuronium picrolonate m.p. 178°—179° (decomp.). $C_{15}H_{20}O_5N_6S$ requires N, 21·2. Found: N, 21·0.

Identical products were obtained when the reaction was repeated using (a) ethanol (95 per cent), (b) ethanol (50 per cent) and (c) acetone (very low yield).

Attempted preparation of S-t-butyl-N-phenylthiuronium picrate, styphnate and picrolonate. *N*-Phenylthiourea (1 g.) and *t*-butyl bromide (1 ml.) were dissolved in ethanol (10 ml.) (95 per cent) and the solution refluxed for 2 hours. The three salts were prepared as described above.

Picrate m.p. 198°, styphnate m.p. 176°, picrolonate m.p. 205—206°. These all correspond to the *S*-ethyl-*N*-phenylthiuronium salts (see Table II). *S*-Ethyl-*N*-phenylthiuronium picrate $C_{15}H_{15}O_7N_5S$ requires N, 17·11. Found N, 16·95.

The above experiment was repeated using (a) dioxan, (b) acetone, (c) formamide, (d) dimethylformamide as solvent and reaction times of up to 12 hours, but in no case was any product obtained. *S*-Methyl-*N*-phenylthiuronium picrate m.p. 179° and *S*-*n*-propyl-*N*-phenylthiuronium picrate m.p. 169° were obtained when the ethanol was replaced by methanol and *n*-propanol respectively in the above reaction. No product was obtained with butanol or isopropanol.

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