

Heterocycles in Organic Synthesis. Part 16.¹ The Conversion of Aliphatic, Aromatic, and Heteroaromatic Primary Amines into Iodides²

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22 Aliphatic primary and secondary carbylamines, aliphatic unsaturated-, hydroxy- and di-amines, benzylamines, anilines, 2-pyridylamines, and thiazolylamines have been converted in 62–96% (average 84%) yield into 1-substituted-2,4,6-triphenylpyridinium iodides by 2,4,6-triphenylpyrylium iodide. Pyrolysis of these at 135–300 °C gave the iodides corresponding to the starting amines in 52–86% (average 76%) yield.

NUMEROUS routes are available for the conversion of alcohols into iodides³ and new methods continue to appear.⁴ By contrast, useful preparative techniques for the conversion of non-diazotizable primary amines into iodides are rare: although *n*-hexylamine was converted (in two steps) into the *NN*-bis-*p*-nitrophenyl-

amines and yields are generally in the range 50–80%.⁸

The pyrolysis of tetra-alkylammonium iodides is a developed method for the preparation of methyl, allyl, and benzyl iodides,⁹ but the conversion of primary amines into tetra-alkylammonium salts is time-con-

TABLE 1
Preparation of pyridinium iodides

No.	Starting amine	Solvent	Procedure			M.p. (°C)	Crystalline form	Molecular formula	Required (%)			Found (%)		
			Temp. (°C)	Time (h)	Yield (%)				C	H	N	C	H	N
(1)	Ethyl	Et ₂ O	20	12	96	165	Yellow needles	C ₂₅ H ₂₂ IN			3.0			3.1
(2)	<i>n</i> -Butyl	Et ₂ O	20	12	87	185–187	Yellow needles	C ₂₇ H ₂₆ IN	66.0	5.3		66.0	5.4	
(3)	Tetramethylene *	Et ₂ O	20	12	90	243–247	Yellow prisms	C ₅₀ H ₄₂ I ₂ N ₂ , H ₂ O	63.7	4.7	3.0	63.6	4.7	2.7
(4)	Pentamethylene *	EtOH	20	24	96	147	Yellow prisms	C ₅₁ H ₄₄ I ₂ N ₂	65.3	4.7	3.0	64.7	4.8	2.9
(5)	Isopropyl	Et ₂ O	20	30	91	154 (decomp.)	Yellow prisms	C ₂₆ H ₂₄ IN	65.4	5.1	2.9	65.3	4.6	2.7
(6)	<i>s</i> -Butyl	Et ₂ O	20	12	73	158	Yellow prisms	C ₂₇ H ₂₆ IN			2.9			2.8
(7)	Cyclohexyl	Et ₂ O	20	30	84	162 (decomp.)	Yellow prisms	C ₂₉ H ₂₈ IN	67.3	5.5	2.7	67.1	5.6	2.8
(8)	Allyl	Et ₂ O	20	12	90	149	Yellow prisms	C ₂₆ H ₂₂ IN	65.7	4.7	3.0	65.3	4.7	2.6
(9)	3-Hydroxypropyl	Et ₂ O	20	12	90	177	Lemon yellow prisms	C ₂₆ H ₂₄ INO	63.3	4.9	2.8	62.9	4.8	2.9
(10)	Benzyl	EtOH	100	3	62	126–127	Yellow prisms	C ₃₀ H ₂₄ IN			2.7			3.0
(11)	<i>p</i> -Methylbenzyl	EtOH	20	2	68	115–116	Yellow prisms	C ₃₁ H ₂₆ IN			2.6			2.7
(12)	<i>p</i> -Chlorobenzyl	EtOH	100	3	73	112	Yellow prisms	C ₃₀ H ₂₃ ClIN			2.6			2.7
(13)	Phenyl	EtOH	100	3	81	281	Orange needles	C ₂₉ H ₂₂ IN	68.1	4.4	2.7	68.2	4.5	2.9
(14)	<i>p</i> -Tolyl	EtOH	100	3	83	288	Yellow needles	C ₃₀ H ₂₄ IN	68.6	4.6	2.7	68.0	4.6	2.9
(15)	<i>p</i> -Chlorophenyl	EtOH	100	3	84	180	Golden yellow prisms	C ₂₉ H ₂₁ ClIN			2.6			2.5
(16)	<i>m</i> -Phenylene *	EtOH	100	48	87	247–248	Yellow needles	C ₅₂ H ₄₂ I ₂ N ₂ O ₂ ^a	62.7	4.3	2.8	62.3	4.1	2.6
(17)	2-Pyridyl	Et ₂ O	20	12	85	>280	Yellow prisms	C ₂₈ H ₂₁ IN ₂			5.5			5.6
(18)	3-Methyl-2-pyridyl	Et ₂ O	20	12	80	>290	Yellow prisms	C ₂₉ H ₂₃ IN ₂	66.2	4.4	5.3	66.0	4.6	5.0
(19)	4-Methyl-2-pyridyl	Et ₂ O	20	12	78	>290	Yellow prisms	C ₂₉ H ₂₃ IN ₂	66.2	4.4	5.3	66.2	4.7	5.1
(20)	2-Thiazolyl	EtOH	100	3	92	254–255	Mustard prisms	C ₂₈ H ₁₉ IN ₂ S	60.2	3.7	5.4	59.8	4.1	5.0
(21)	4-Phenylthiazol-2-yl	EtOH	100	3	87	173–174	Red lustrous prisms	C ₃₂ H ₂₃ IN ₂ S ^b			4.7			4.3
(22)	Benzothiazol-2-yl	EtOH	100	3	91	256–257	Bright red prisms	C ₃₀ H ₂₁ IN ₂ S	63.4	3.7	4.9	62.9	3.8	4.7

* Di-NH₂.

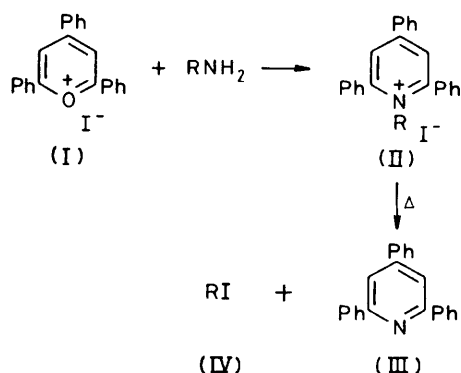
^a Compound crystallises with 2 H₂O of crystallisation: $\nu(\text{OH})$ at 3400 cm⁻¹ and the n.m.r. peak in CDCl₃ at δ 1.65 correctly integrates for 2H₂O and is shifted far down field in CF₃CO₂H. ^b S: Found 5.2, required 5.4%.

sulphonyl derivative which gave *n*-hexyl iodide (79%) by nucleophilic displacement with KI in dimethylformamide,⁵ this reaction has not been generalised, and *N*-benzylbenzene-1,2-disulphonamide was unreactive in a similar reaction.⁶ Talik and his co-workers⁷ have recently developed a useful method for the conversion of pyridylamines to the corresponding pyridyl iodides by heating intermediate nitramides with PI₃ (overall yields 40–60%), although both steps of this sequence utilise rather vigorous conditions. The chemical conversion of aniline *via* benzenediazonium salts into iodo-benzene is generally applicable to diazotizable aromatic

suming and the orientation of the pyrolysis is not always favourable. Conversion¹⁰ by Susan and Balaban of methylamine into 1-methyl-2,4,6-triphenylpyridinium iodide (81%) and its pyrolysis to give methyl iodide at 180 °C was, therefore, of considerable potential interest, but it has remained the sole example of its type. We now report the generalisation of this reaction into a widely applicable synthetic method.

Preparation of the Pyridinium Iodides.—2,4,6-Triphenylpyrylium iodide (I) (readily available in high yield from the corresponding perchlorate¹¹) reacts with aliphatic, aromatic, and heterocyclic amines to give the

pyridinium salts (II) in high yield (Table 1). For the more nucleophilic (generally aliphatic) amines ether was



used as a solvent because in ethanol spontaneous decomposition of the pyridinium iodide occurred; for the less nucleophilic amines reaction in ethanol is utilised often at reflux.

could usually be removed by careful drying. I.r. and ^1H n.m.r. spectra were obtained for all the pyridinium salts and were in agreement with the structures assigned.

Pyrolysis of the Pyridinium Iodides.—On heating at temperatures from 135–300 °C *in vacuo*, the pyridinium iodides (II) decomposed smoothly into 2,4,6-triphenylpyridine (III) and the iodides (IV) corresponding to the original amines which were isolated in yields of 52–86% (Table 2). For the iodopyridines, iodothiazoles, and 1,4-di-iodobutane, of which the corresponding pyridinium salts had m.p. >240 °C, it was found advantageous to mix the salt with 2,4,6-triphenylpyridine as a flux. The temperature used (Table 2) was that at which evolution of the iodide occurred rapidly.*

Pyrolysis of the 2-thiazolyl derivative (20) for 2 h gave a poor result: the distillate turned from a yellow oil into a brown pitch. However pyrolysis for 0.5 h gave a good result: 2-iodothiazole is reported to be thermally unstable.¹³

Pyrolysis of the *p*-tolyl derivative (14) without flux

TABLE 2
Pyrolysis of pyridinium iodides

No.	Procedure	Pyrolysis conditions			Product	Yield (%)	Characterisation ^a		Ref.
		Temp. (°C)	Pressure (mmHg)	Time (h)			M.p. (°C) or n_D^{20}	Found	
(1)	A	130	0.4	3	Ethyl iodide	83	1.5128	1.5133	<i>e</i> (i)
(2)	B	220	0.5	1	<i>n</i> -Butyl iodide	78	1.5006	1.5001	<i>f</i>
(3)	B	220	0.5	1	1,4-Di-iodobutane	85	1.6200	1.6200	<i>g</i>
(4)	A	190	0.1	3	1,5-Di-iodopentane	81	1.6021	1.6046	<i>h</i>
(5)	A	135	0.2	3	Isopropyl iodide	79	1.5026	1.5026	<i>e</i> (ii)
(6)	A	140	0.3	1	2-Iodobutane	83	1.4989	1.4991	<i>e</i> (iii)
(7)	A	140	0.4	3	Cyclohexene ^b	66	1.4464	1.4465	<i>e</i> (iv)
(8)	A	145	0.2	4	Allyl iodide	85	1.5528	1.5530	<i>e</i> (v)
(9)	A	140	0.2	3	3-Iodopropanol	78	1.5592	1.5586	<i>i</i>
(10)	A	270	0.5	2	Benzyl iodide	58	24–25	24.5	<i>e</i> (vi)
(11)	A	270	0.01	1	<i>p</i> -Methylbenzyl iodide	65	46–47	46.5–47.5	<i>j</i>
(12)	A	300	0.03	1	<i>p</i> -Chlorobenzyl iodide	52	60–61	62–63	<i>j</i>
(13)	A	240	0.05	4	Iodobenzene	75	1.6194	1.6200	<i>e</i> (vii)
(14)	B	220	0.1	2	<i>p</i> -Tolyl iodide	78	34–36	36–37	<i>e</i> (vi)
(15)	A	220	0.2	1	<i>p</i> -Chloroiodobenzene	77	54–56	57	<i>e</i> (viii)
(16)	B	220	0.1	2	<i>m</i> -Di-iodobenzene	70	38–40	40.4	<i>k</i>
(17)	B	220	0.5	3	2-Iodopyridine	75	118–120 ^c	119–120	<i>l</i>
(18)	B	220	0.5	3	3-Methyl-2-iodopyridine	71	163–164 ^d	164	<i>m</i>
(19)	B	220	0.5	3	4-Methyl-2-iodopyridine	62	162–164 ^d	164	<i>m</i>
(20)	B	220	0.1	0.5	2-Iodothiazole	72	1.6662	1.6670	<i>n</i>
(22)	B	260	0.2	2	2-Iodobenzothiazole	85	75–78	79	<i>n</i>

* I.r. and ^1H n.m.r. spectra were obtained for all iodides and were in agreement with the structures assigned. ^b Cyclohexene contained also iodocyclohexane (20% yield) as indicated by integration of n.m.r. spectrum of distillate. ^c Picrate. ^d HgCl_2 complex. ^e 'Handbook of Chemistry and Physics,' 53rd edn., ed. R. C. Weast, Chemical Rubber Company, Cleveland, Ohio, 1972–1973, (i) p. C-287; (ii) p. C-442; (iii) p. C-213; (iv) p. C-259; (v) p. C-458; (vi) p. C-520; (vii) p. C-161; (viii) p. C-148. ^f Beilstein's *Handbuch der Organischen Chemie*, eds. B. Prager, P. Jacobson, P. Schmidt, and D. Stern, Verlag von Julius Springer, Berlin, 1918, Vol. I, p. 123. ^g C. J. Pouchert, 'The Aldrich Library of Infrared Spectra,' Aldrich Chemical Co. Inc., U.S.A., 1970, p. 44. ^h Beilstein's *Handbuch der Organischen Chemie*, ed. F. Richter, Verlag von Julius Springer, Berlin, 1928, Suppl. I, vol. I, p. 44 (measured at 15 °C). ⁱ Ref. *h*, p. 182. ^j G. H. Daub and R. N. Castle, *J. Org. Chem.*, 1954, **19**, 1571. ^k Beilstein's *Handbuch der Organischen Chemie*, eds. B. Prager and P. Jacobson, Verlag von Julius Springer, Berlin, 1922, vol. V, p. 225. ^l Beilstein's *Handbuch der Organischen Chemie*, ed. F. Richter, Verlag von Julius Springer, Berlin, 1935, Suppl. I, vol. XX, p. 81. ^m Ref. *7a*. ⁿ P. E. Iversen, *Acta Chem. Scand.*, 1968, **22**, 1690.

The aliphatic bis-amines reacted readily under the normal conditions to give the expected products (3) and (4), but for *m*-phenylenediamine refluxing for 48 h was required: previous reactions¹² of this amine with pyrylium salts have given reactions at one amino-group. Aliphatic secondary carbylamines reacted smoothly at 20 °C.

Many of the pyridinium salts are hygroscopic and crystallise with water or ethanol of crystallisation: this

gave a mixture of *p*-tolyl iodide and toluene as shown by the n.m.r. spectrum. However, addition of 2,4,6-triphenylpyridine (3 parts by weight) gave a good result (Table 2).

Limits to the Applicability of the Synthetic Process.—

* We have found recently that the pyrolysis temperatures can be considerably reduced. The yields reported were for samples dried *in vacuo* at 60–70 °C: it is probable that significant decomposition occurred during the drying process particularly for the benzyl compounds.

Attempted reactions of *t*-butylamine, α -phenylethylamine, and of pyrimidin-2-ylamine with 2,4,6-triphenylpyrylium iodide failed to yield any pyridinium iodide: in the first two cases, ring opening occurred but reclosure was prevented by steric hindrance, whilst in the last, the nucleophilicity of the amino-group is probably too low (cf. ref. 14). These examples probably illustrate two general boundaries of applicability.*

Pyrolysis of the cyclohexylpyridinium iodide (7) gave 20% cyclohexyl iodide mixed with 66% cyclohexene. Pyrolysis of the *s*-butyl salt (6) at 160 °C for 3 h gave a significant amount of olefin, but at 140 °C a good yield of pure *s*-butyl iodide was obtained (Table 2). Olefin formation probably occurs largely for steric reasons and, although we have not tried β -phenylethylamine in the present sequence, it readily forms the analogous bromide.¹⁵

Mechanistic Considerations.—We believe that the mechanism of this displacement reaction is essentially S_N2 in character for the aliphatic and benzylic cases (as earlier suggested by Balaban¹⁰). The S_N2 mechanism is much less likely for the *N*-aryl displacements, and examination of models indicates the steric difficulty of iodide anion approach to the sp^2 -hybridised carbon. The known¹⁶ ability of pyridinium iodides to form charge-transfer complexes, where the iodide ion is located above the pyridinium ring plane near the centre of this ring,¹⁷ may promote an $S_{RN}1$ mechanism.¹⁸ The mechanism of the heteroaryl displacements is also uncertain and awaits further investigation.

EXPERIMENTAL

2,4,6-Triphenylpyrylium Iodide, m.p. 222 °C (lit.,¹¹ m.p. 224 °C) was prepared as in ref. 11 in 99% yield.

Preparation of Pyridinium Iodides: Typical Procedure (cf. Table 1).—2,4,6-Triphenylpyrylium iodide (0.01 mol) and the amine (0.012 mol) were allowed to react in the solvent, for the time, and at the temperature shown in Table 1. The precipitated product was filtered off, washed with Et₂O (15 ml), and recrystallised from EtOH.

Procedures for Pyrolysis of Pyridinium Iodides (cf. Table 2).—*Procedure A.* The pyridinium iodide (0.004 mol) was heated *in vacuo*; the distillate was collected and identified. *Procedure B.* The pyridinium iodide (0.005

* Recent work with other pyrylium salts shows promise to overcome both these limitations.

mol) and 2,4,6-triphenylpyridine (2 g) were heated *in vacuo*; the distillate was collected and identified.

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