Stereochemistry and Regiochemistry of the Addition of Iodonium Nitrate to Alkenes

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Iodonium nitrate in the presence of pyridine adds *trans*-stereospecifically and regiospecifically to a series of *Z*–*E* pairs of alkenes to give iodoalkyl nitrate esters and iodoalkyl pyridinium nitrates. The stereochemistry of the products was confirmed by relating them chemically with known compounds. Addition to the less hindered (*Z*)-[β-^{2}H]styrene is also stereospecific, eliminating the possibility of restricted rotation during addition. Ring closure by neighbouring sulphur in the addition of iodonium nitrate to 1-allyl-3,3-diethylthiourea affords a thiazole. The failure to obtain addition and phenyl migration in 3,3,3-triphenylpropene may be due to steric hindrance of the approach of the $[IPy_2]^+$ complex. The latter was isolated as its nitrate salt and was shown to undergo a stoicheiometric and stereospecific addition to (*E*)-4,4-dimethylpent-2-ene to give *erythro*-2-iodo-1,3,3-trimethylbutyl nitrate (IIIa).

THE addition of pseudo-halogens to unsaturated substrates provides stereospecific routes to, *e.g.*, β-iodoazides,[1] vinyl azides,[2] azirines,[3] aziridines,[4] (*E*)-*N*-(2-iodoalkyl)-carbamates,[4e] (*Z*)- and (*E*)-2-amino-alcohols,[4e] oxazolidones,[4a] 1,2-diamines,[5] aminosugars,[6] and azepines.[7]

Significant differences in reactivity and in the types of reaction undergone have been observed for different pseudohalogens. Thus iodine isocyanate is unreactive towards unsaturated substrates possessing electron-withdrawing groups,[4a-e] αβ-unsaturated esters and ketones, and some trisubstituted olefins and stilbenes.[4a,e] Iodine azide, in contrast, is much more reactive and versatile.[1,4a] Nitrosyl chloride, being less reactive, requires a tetra-alkyl substituted olefin if an aziridine is desired.[8]

Differences in the mechanism of addition are also apparent; thus whereas the pseudo-halogens mentioned above appear to react exclusively by an ionic pathway involving a bridged halogenonium ion,[9] in contrast, the non-stereospecific additions of *NN*-dichlorourethan proceed by a free radical pathway and are often accompanied by allylic chlorinations.[10] The additions of bromonium azide have a substantial free radical component and selection of an ionic or free radical pathway is contingent upon the nature of the solvent and the presence of oxygen.[11] Assignment of the mechanistic pathway is complicated by the sensitivity of the regiochemistry of ionic additions of pseudo-halogens to both electronic and steric factors.[1,2a]

Recently we have shown that iodonium nitrate (generated by the reaction of iodine chloride with silver nitrate in chloroform–pyridine) readily undergoes addition to alkenes to form (i) iodoalkyl nitrates, (ii) iodoalkylpyridinium nitrates, or (iii) alkenylpyridinium iodides depending on the substrate.[12] With certain olefinic alcohols iodonium nitrate affords (iv) hydroxyiodoalkyl nitrates and (v) hydroxyiodoalkylpyridinium nitrates.[13] Parallel reactions in *sym*-collidine–chloroform gave three, four, and five-membered cyclic ethers as well as products of the type (iv) signifying neighbouring hydroxy-participation in contrast to the known chemistry of iodine isocyanate [9b] and iodine azide,[14] and differing in scope from the additions of iodine to unsaturated alcohols.[15] Iodonium nitrate in pyridine–chloroform adds to cyclohex-2-enol in a stereospecific *trans*-fashion in which the iodonium ion is formed *cis* to the hydroxy-group.[13] The additions of pseudo-halogens in general are quite sensitive to steric hindrance so this result signified some compensating interaction between iodine and hydroxy which was controlling the stereochemistry. This is potentially useful for the stereospecific control of the introduction of the aziridine portion in Mitomycin analogues.[16]

The differences in the reactions and reactivity of iodonium nitrate compared with other pseudo-halogens warranted further study, and we examined the mechanism of iodonium nitrate additions in greater detail.

Pure (*E*)-4,4-dimethylpent-2-ene (Ia) was treated with

[1] F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, 1967, **89**, 2077.

[2] (*a*) A. Hassner and F. W. Fowler, *J. Org. Chem.*, 1968 **33**, 2686; (*b*) A. Hassner, G. L'Abbe, and M. J. Miller, *J. Amer. Chem. Soc.*, 1971, **93**, 981; (*c*) G. L'Abbe and A. Hassner, *J. Org. Chem.*, 1971, **36**, 258; (*d*) G. L'Abbe, M. J. Miller, and A. Hassner, *Chem. and Ind.*, 1970, 1321.

[3] (*a*) A. Hassner and F. W. Fowler, *J. Amer. Chem. Soc.*, 1968, **90**, 2869; (*b*) A. Hassner and F. W. Fowler, *Tetrahedron Letters*, 1967, 1545.

[4] (*a*) A. Hassner, G. J. Matthews, and F. W. Fowler, *J. Amer. Chem. Soc.*, 1969, **91**, 5046; (*b*) A. Hassner and C. Heathcock, *J. Org. Chem.*, 1965, **30**, 1748; (*c*) C. G. Gebelein, G. Swift, and D. Swern, *ibid.*, 1967, **32**, 3314; (*d*) T. A. Foglia and D. Swern, *ibid.*, p. 75; (*e*) A. Hassner, M. E. Lorber, and C. Heathcock, *ibid.*, p. 540.

[5] (*a*) G. Swift and D. Swern, *J. Org. Chem.*, 1967, **32**, 511; (*b*) 1966, **31**, 4226.

[6] (*a*) R. U. Lemieux, T. L. Nagabhushan, and I. K. O'Neill, *Tetrahedron Letters*, 1964, 1909; (*b*) R. U. Lemieux, and T. L. Nagabhushan, *ibid.*, 1965, 2143.

[7] L. A. Paquette and D. E. Khula, *Tetrahedron Letters*, 1967, 4517.

[8] G. L. Closs and S. J. Brois, *J. Amer. Chem. Soc.*, 1960, **82**, 6068.

[9] (*a*) A. Hassner, F. P. Boerwinkle, and A. B. Levy, *J. Amer. Chem. Soc.*, 1970, **92**, 4879; (*b*) A. Hassner, R. P. Hoblitt, C. Heathcock, J. E. Kropp, and M. Lorber, *ibid.*, p. 1326; (*c*) C. G. Gebelein, S. Rosen, and D. Swern, *J. Org. Chem.*, 1969, **34**, 1677.

[10] (*a*) T. A. Foglia and D. Swern, *J. Org. Chem.*, 1966, **31**, 3625; (*b*) 1968, **33**, 766.

[11] A. Hassner and F. Boerwinkle, *J. Amer. Chem. Soc.*, 1968, **90**, 216.

[12] (*a*) U. E. Diner and J. W. Lown, *Canad. J. Chem.*, 1971, **49**, 403; (*b*) *Chem. Comm.*, 1970, 333.

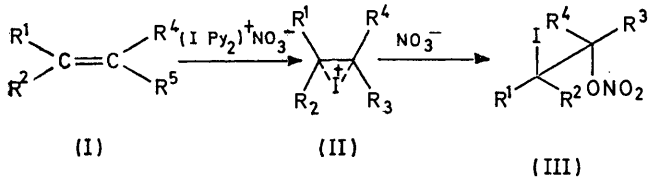
[13] U. E. Diner, M. Worsley, and J. W. Lown, *J. Chem. Soc.* (*C*), 1971, 3131.

[14] A. Hassner, R. J. Isbister, and A. Friederang, *Tetrahedron Letters*, 1969, 2939.

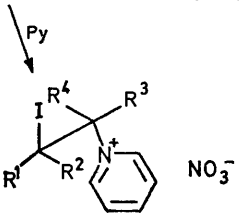
[15] D. L. H. Williams, *Tetrahedron Letters*, 1967, 2001.

[16] J. W. Lown, T. Itoh, and N. Ono, *Canad. J. Chem.*, 1973, **51**, 856.

1 equiv. of iodonium nitrate in pyridine–chloroform to afford a single stereoisomer of the iodonitrate ester (IIIa) (76% yield) in a regiospecific anti-Markovnikov addition together with the pyridinium salt (IVa) (5% yield), which also subsequently proved to be regiospecific and stereospecific in its formation.



(I) (II) (III)

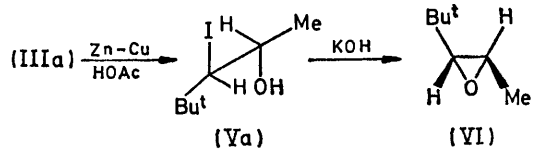


(IV)

	R^1	R^2	R^3	R^4
a;	Bu^t	H	Me	H
b;	Me	H	Me	H
c;	Et	H	Me	H
d;	Me	H	Et	H
e;	Pr^i	H	Me	H
f;	Me	H	Pr^i	H
g;	Et	Me	Me	H
h;	H	Me	Me	Et
i;	H	^{2}H	Ph	H
j;	Bu^t	H	Et	H
k;	Ph	H	Ph	H

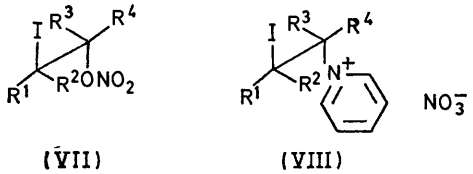
No conformational preference is implied by the saw-horse projection formulae.

The regiochemistry of the additions was assigned from the n.m.r. spectra as described previously.[12,13] The stereochemistry of (IIIa) (*erythro*) was proven by relating it to that of the independently prepared (*E*)-epoxide (VI)[17] derived from (I) by the transformations shown below.



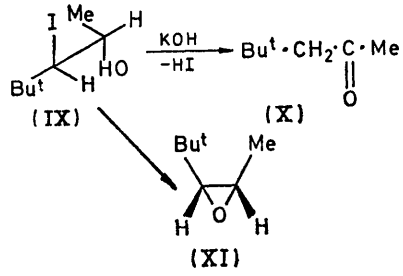
(IIIa) (Va) (VI)

Similarly, treatment of pure (*Z*)-4,4-dimethylpent-2-ene with iodonium nitrate afforded only one stereoisomerically pure *threo*-iodonitrate ester (VIIa) together with pyridinium salt (VIIIa) in regiospecific reactions.



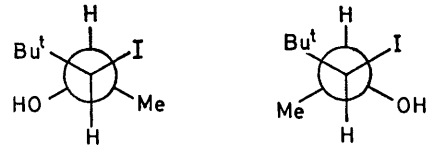
(VII) (VIII)

The configuration of (VIIa) was proven by relating it to that of the (*Z*)-epoxide (XI) except that in this case considerable base catalysed elimination of the intermediate iodohydrin to give 4,4-dimethylpentan-2-one



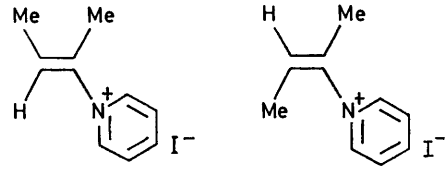
(IX) (X) (XI)

(X) accompanied ring closure to the epoxide. The relative ease of *trans*-displacement of iodide from the *erythro*-iodohydrin (Va) to form epoxide (VI) compared with the slow formation of the (*Z*)-epoxide (XI) from (IX) indicates preferred conformations (VA) for the former and (IXA) for the latter. Whereas no trace of ketone is formed from (VA), (IXA) may rotate with equal facility to two conformers comparable in energy giving rise to (X) and (XI) in equal proportion. Thus the addition



(VA) (IXA)

of iodonium nitrate to the 4,4-dimethylpent-2-enes is stereospecific and regiospecific at least with regard to the iodonitrate esters. The iodopyridinium nitrate salts (IVa) and (VIIa), although clearly epimers, were produced in such low yields that it was inconvenient to ascertain the stereochemistry in this particular example. When the but-2-enes were used the relative yields of the pyridinium salts were much higher, reflecting the reduced steric hindrance during the addition, and permitting an examination of their stereochemistry. From (*E*)-but-2-ene were produced (IIIb) and (IVb) in 32 and 55% yields respectively, both stereoisomerically pure. Treatment of (IVb) with sodium methoxide in methanol at

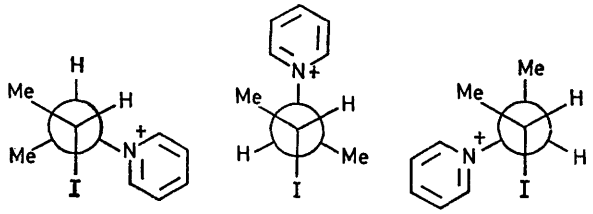


(XII) (XIII)

room temperature or at 50° afforded the single diastereoisomeric elimination product (XII). Similar treatment of (*Z*)-but-2-ene produced stereospecifically compounds (VIIb) and (VIIIb). Treatment of (VIIIb) with sodium

[17] (*a*) P. D. Bartlett, *Rec. Chem. Progr.*, 1950, **11**, 51; (*b*) B. M. Lynch and K. H. Dausaker, *J. Chem. Soc.*, 1955, 1525; (*c*) A. C. Cope, S. W. Fenton, and C. F. Spencer, *J. Amer. Chem. Soc.*, 1952, **74**, 5884; (*d*) A. C. Cope, A. Fournier, and H. E. Simmons, *ibid.*, 1957, **79**, 3905.

methoxide in methanol at 65° for 48 h gave (XIII). The configurational assignments of (XII) and (XIII) were made by n.m.r., compound (XIII) showing the larger homoallylic coupling.[18] The marked difference in the relative ease of elimination of hydrogen iodide from (IVb) and (VIIb) can be accounted for by conformational analysis. Of the three staggered conformations for the

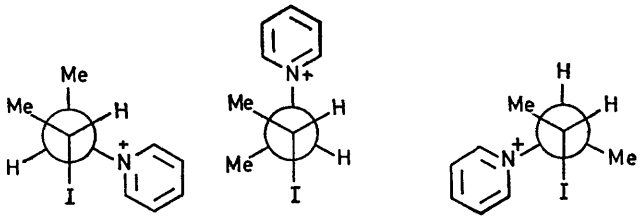


(IVb)

erythro-epimer (IVb) conformer B might be predicted to be the preferred conformation. However, the rapid *trans*-elimination of hydrogen iodide at room temperature suggests a significant contribution from conformation A, implying a compensating attractive force between *gauche* iodo and pyridinium groups. As reported earlier, the *X*-ray crystallographic study of 1-(2-methyl-3-iodobutyl)pyridinium nitrate shows that the largest groups, iodo and pyridinium, are similarly oriented *gauche* to one another.[12]

Hassner has reported that London attractive forces between vicinal iodo and azide groups in IN_3 adducts similarly favour an adoption of gauche relative positions for these groups.[4,19]

In the case of the *threo*-epimer the three conformers to be considered are D—F. For this isomer the most stable



(VIIIb)

conformer should be D in accord with the observation that base catalysed *trans*-elimination of hydrogen iodide requires much more vigorous conditions than for (IVb) (*i.e.* sodium methoxide in refluxing methanol for 48 h) and is still incomplete. The attractive *gauche* iodo–pyridinium interaction in D may reinforce the conformational preference.

Addition of iodonium nitrate to (Z)-pent-2-ene was regioselective in the formation of the *threo*-iodonitrates (VIIc) and (VIId) in a ratio of 70 : 30 (by n.m.r.) (67% yield), and regiospecific in the formation of the *threo*-iodopyridinium nitrate (VIIIc) (*ca.* 5% yield).

[18] (*a*) J. H. Richards and W. F. Beach, *J. Org. Chem.*, 1961, **26**, 623; (*b*) p. 3011; (*c*) R. R. Fraser, *Canad. J. Chem.*, 1960, **38**, 549.

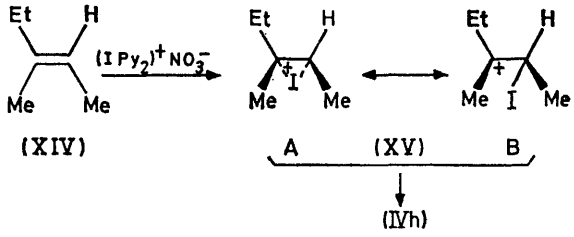
The corresponding reaction with (*E*)-pent-2-ene similarly afforded a mixture of the regioisomeric *erythro*-iodonitrate esters (IIIc) and (IIId) (combined yield 53%) together with the *erythro*-iodopyridinium salt (IVc) (12% yield).

Electrophilic addition of INO_3 to 4-methylpent-2-ene represents a border-line case in that the addition to the (*E*)-isomer is 80% regioselective while addition to the (*Z*)-isomer is regiospecific in formation of the iodonitrate esters. The nucleophilic attack of the larger pyridine is regiospecific with both isomers.

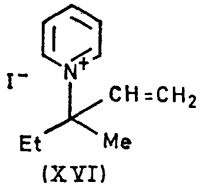
Compounds (IIIe) and (IIIf) were formed in a combined yield of 70% and (IVe) in a yield of 15%. The corresponding yields of regiospecific iodonitrate ester (VIIe) and iodopyridinium salt (VIIIe) obtained from the (*Z*)-isomer were 63 and 14% respectively.

The greater steric bulk offered by the t-butyl group in 2,2-dimethylhex-3-ene ensures regiospecific anti-Markovnikov addition [1,20] producing the *threo*-isomer in 80% yield from the (*Z*)-isomer and the *erythro*-isomer in 55% yield from the (*E*)-alkene. Only traces of the corresponding pyridinium salts were formed.

Addition of INO_3 to (*Z*)- and to (*E*)-3-methylpent-2-enes (XIV), although they do not contain especially bulky groups, afford exclusively the diastereoisomeric iodopyridinium salts (IVh) and (VIIIh) in stereospecific



and regiospecific additions. The regiochemistry of the addition is proved by the sodium methoxide catalysed elimination of hydrogen iodide from (IVh) to form (XVI), the n.m.r. spectrum of which showed a clear ABC pattern for the vinyl protons. Addition of iodonium nitrate to (*Z*)- and (*E*)-stilbenes to form the pyridinium nitrates is also stereospecific (see Tables 1—4) and



(XVI)

base catalysed *trans*-elimination of hydrogen iodide proceeded normally.

To eliminate the possibility that the stereospecificity observed in the addition to (*Z*)- and (*E*)-(XIV) and to stilbene is due to restricted rotation in the intermediate

[19] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Interscience Publishers, New York, 1965, chapter 1.

[20] W. H. Puterbaugh and M. S. Newman, *J. Amer. Chem. Soc.*, 1957, **79**, 3469.

TABLE 1

Iodo-nitrate esters

Alkene	Iodo-nitrate ester	B.p. (°C/mmHg)	Yield (%)	Molecular formula	Required (%) C	H	N	Found (%) C	H	N
(*E*)-But-2-ene	(IIIb)	40/0·05	32	$C_4H_8INO_3$	19·5	3·25	5·7	19·55	3·3	5·75
(*Z*)-But-2-ene	(VIIb)	44·0·03	32	$C_4H_8INO_3$	19·5	3·25	5·7	19·85	3·25	5·75
(*E*)-4-Methylpent-2-ene	(IIIe) (IIIf)	44—45·5/0·04	70	$C_6H_{12}INO_3$	26·35	4·4	5·15	25·95	4·45	5·15
(*Z*)-4-Methylpent-2-ene	(VIIe)	58—58·5/0·02	62	$C_6H_{12}INO_3$	26·35	4·4	5·15	25·85	4·55	5·25
(*E*)-Pent-2-ene	(IIIc) (IIId)	43—44/0·05	53	$C_5H_{10}INO_3$	23·2	3·9	5·40	22·7	3·9	5·5
(*Z*)-Pent-2-ene	(VIIc) (VIId)	43—44/0·05	67	$C_5H_{10}INO_3$	23·2	3·9	5·4	23·2	4·0	5·71
(*E*)-2,2-Dimethylhex-3-ene	(IIIj)	58—60/0·02	51	$C_8H_{16}INO_3$	[*M* Required 301·0175			*M* Found 301·0179]*		
(*Z*)-2,2-Dimethylhex-3-ene	(VIIj)	63—64/0·04	77	$C_8H_{16}INO_3$	31·9	5·3		31·8	5·3	
					[*M* Required 301·0175			*M* Found 301·0179]*		

* Determined by mass spectrometry.

TABLE 2

Iodo-pyridinium salts

Starting alkene	Iodo-pyridinium salt	M.p. (°C)	Yield (%)	Molecular formula	Required (%) C	H	N	Found (%) C	H	N
(*E*)-But-2-ene	(IVb)		55*	$C_9H_{13}IN_2O_3$						
(*Z*)-But-2-ene	(VIIIb)	108—112	54	$C_9H_{13}IN_2O_3$	33·35	4·0	8·65	33·15	4·15	8·75
(*E*)-4-Methylpent-2-ene	(IVe)	125—128	15	$C_{11}H_{17}IN_2O_3$	37·5	4·85	7·95	37·6	5·05	7·2
(*Z*)-4-Methylpent-2-ene	(VIIIe)	84—87	14	$C_{11}H_{17}IN_2O_3$	37·5	4·85	7·95	37·5	4·8	8·5
(*Z*)-3-Methylpent-2-ene	(IVh)		43†	$C_{11}H_{17}IN_2O_3$						
(*E*)-3-Methylpent-2-ene	(VIIIh)	126—129	39	$C_{11}H_{17}IN_2O_3$	37·5	4·85		37·05	4·85	
(*E*)-Pent-2-ene	(IVc)	96—99	12	$C_{10}H_{15}IN_2O_3$	35·5	4·45	8·3	35·9	4·65	8·6
(*Z*)-Pent-2-ene	(VIIIc)	94—97	6	$C_{10}H_{15}IN_2O_3$	35·5	4·45		36·8	4·55	
(*E*)-Stilbene	(IVk)	144—145	62	$C_{19}H_{17}IN_2O_3$	50·9	3·8	6·25	50·85	3·8	6·35
(*E*)-Stilbene	(E)-1-(α-*Phenylstyryl*)-*pyridinium iodide*	242—245	86	$C_{19}H_{16}IN$	59·2	4·15	3·65	59·45	4·3	3·8
(*Z*)-Stilbene	(Z)-1-(α-*Phenylstyryl*)-*pyridinium iodide*	264—266	83	$C_{19}H_{16}IN$	59·2	4·15	3·65	59·3	4·25	3·75

* Viscous liquid, not obtained analytically pure. Characterized by its elimination product. † Viscous liquid, not obtained analytically pure.

TABLE 3

N.m.r. data for iodo-nitrate esters (δ/p.p.m. in $CDCl_3$; *J* in Hz)

Iodo-nitrate ester*	>CH-I	>CHONO$_2$	$J_{CH,CH}$	Additional signals
(IIIb)	4·23 (octet)	4·69 (octet)	5·1	1·39 (3H, d, *J* 6·2, *Me*CHONO$_2$)
				1·83 (3H, d, *J* 7·1, *Me*CHI
(VIIb)	4·29 (octet)	5·07 (octet)	4·0	1·47 (3H, d, *J* 6·2, *Me*CHONO$_2$)
				1·88 (3H, d, *J* 7·1, *Me*CHI)
(IIIe)	4·20 (q)	5·08 (sextet)		1·0 (3H, d, *J* 6, *Me*$_2$CH–)
(IIIf)	4·25 (quint)	(Overlapping above sextet)	7·0	1·03 (3H, d, *J* 6, *Me*$_2$CH–)
				1·59 (3H, d, *J* 6, *Me*CHONO$_2$)
[Regioisomer ratio (IIIe) : (IIIf) = 80 : 20]				1·95 (3H, d, *J* 7, *Me*CHI)
				1·24 (1H, m, C*H*Me$_2$)
(VIIe)	4·04 (q)	5·1 (quint)	6·3	1·03 (3H, d, *J* 6·2, *Me*$_2$CH–)
				1·05 (3H, d, *J* 6·2, *Me*$_2$CH–)
				1·40 (1H, m, *J* 4·5, C*H*Me$_2$)
				1·49 (3H, d, *J* 6·3, *Me*CHONO$_2$)
(VIIc)	4·1 (sextet)	5·15(octet)	4·0	1·06 (3H, t, *J* 7, *Me*CH$_2$)
				1·51 (3H, d, *J* 6·5, *Me*CHONO$_2$)
				1·82 (2H, m, J_{CH,CH_3} 7, *CH*$_2$Me)
(VIId)	4·33 (octet)	4·81 (quint)	4·0	1·0 (3H, t, *J* 7, *Me*CH$_2$)
[Regioisomer ratio (VIIc) : (VIId) = 70 : 30]				1·89 (3H, d, *J* 7, *Me*CHI)
(IIIc)	4·09—4·45 (m)	4·68—4·92 (m)		1·07 (3H, t, *J* 7·1, *Me*CH$_2$)
				1·48 (3H, d, *J* 6·2, *Me*CHONO$_2$)
(IIId)				1·77 (2H, q, *J* 7·1, CH$_2$)
[Regioisomer ratio (IIIc) : (IIId) = 55 : 45]				1·03 (3H, t, *J* 7·1, *Me*CH$_2$)
				1·81 (3H, d, *J* 6·1, *Me*CHONO$_2$)
(IIIj)	4·32 (d)	4·6 (octet)	2·75	1·06 (3H, t, *J* 7·7, *Me*CH$_2$)
				1·18 (9H, s, C*Me*$_3$)
				1·70—1·93 (2H, m, C*H*$_2$)
(VIIj)	4·05 (d)	4·71 (sextet)	1·5	0·98 (3H, t, *J* 8, *Me*CH$_2$)
				1·35 (9H, s, C*Me*$_3$)
				1·89—2·21 (2H, m, $J_{CH_2,CHONO_2}$ 6·5, CH$_2$)

* All these compounds exhibited ONO_2 i.r. absorption between 1620 and 1640 cm^{-1}.

(XV), an addition to (*Z*)-[β-^{2}H]styrene[9a] (XVII) (>95% deuterium) was performed. The sole product isolated was the unsaturated pyridinium nitrate (XVIII)

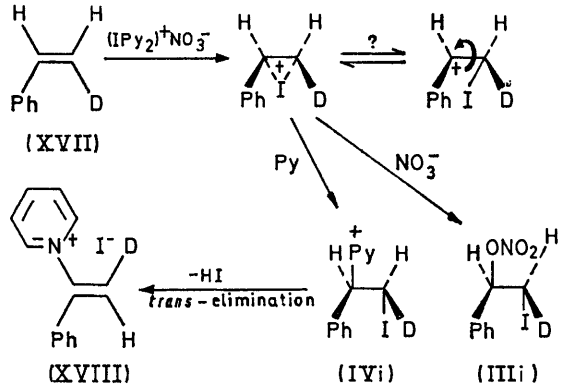
TABLE 4

N.m.r. data for iodoalkyl-pyridinium nitrates (δ/p.p.m. in $CDCl_3$; *J* in Hz)

Pyridinium salt *	Methine absorptions	Additional signals †
(IVb)	4·6—5·35 (2H, m)	1·83 (6H, 2 overlapping d, 2Me)
(VIIIb)	4·5—5·4	1·7 (3H, d, *J* 6·5, *Me*CHI)
	(2H, m)	1·92 (3H, d, *J* 6·5 *Me*CHN⁺≤)
(IVe)	4·7—5·4	0·9 (7H, septet, –C*H*Me$_2$)
	(2H, m)	1·9 (3H, d, *J* 6·2, *Me*CHN⁺≤)
(VIIIe)	4·7—5·65 (2H, m)	0·73 (6H, 2 overlapping d, *Me*$_2$CH–) 1·17 (1H, m, C*H*Me$_2$) 1·8 (3H, d, *J* 6·5, *Me*CHN⁺≤)
(IVh)	5·02 (1H, q, *J* 7)	0·72 (3H, t, *J* 7 *Me*CH$_2$) 1·7 (3H, d, *J* 7, *Me*CHI) 1·98 (3H, s, Me–C(I)–N⁺≤) 2·33 (2H, m, C*H*$_2$Me)
(VIIIh)	5·18 (1H, q, *J* 6·8)	0·65 (3H, t, *J* 7 *Me*CH$_2$ 1·93 (3H, s, MeC–N) 2·05 (3H, d, *J* 6·8, *Me*CHI) 2·3 (2H, m, –CH$_2$–)
(IVc)	4·4—5·5	1·02 (3H, t, *J* 6·5, *Me*CH$_2$)
	(2H, m)	1·76 (3H, d, *J* 6·5, *Me*CHN⁺≤) 1·8 (2H, m, overlapped by d, CH$_2$Me)
(VIIIc)	4·4—5·4 (2H, m)	1·01 (3H, t, *J* 6·5, *Me*CH$_2$) 1·75 (3H, d, *J* 6·5, *Me*CHN⁺≤) 1·9 (2H, m, overlapped by d, C*H*$_2$–Me)

* All these compounds had ONO_2^- i.r. absorption between 1620 and 1640 cm^{-1}. † All these compounds had absorption due to Py^+ between δ 8 and 9·5.

produced from spontaneous *trans*-elimination of hydrogen iodide from intermediate (IVi). The structure of

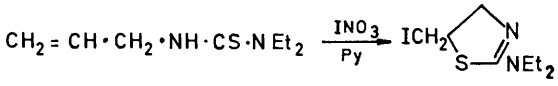


(XVIII) follows from comparison of the n.m.r. spectrum (vinyl singlet at δ 6·43) with that of the protium analogue (vinyl ABq at δ 6·43, 6·10, *J* 2·5 Hz). In such compounds the proton *cis* to phenyl absorbs at lower field than the *trans*-proton.[9a]

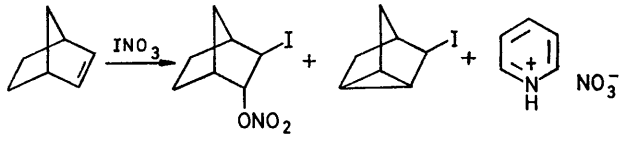
The observation has been made previously, as in this case, that when a tertiary cationic centre is generated during the addition of iodonium nitrate, exclusive attack at the more stable centre results, despite the increased steric hindrance offered.[12,13]

Evidently the iodonium ion implicated in iodonium nitrate addition, unlike that formed in other pseudohalogen additions,[1,9a,b] has sufficient free cation character [*e.g.* (XVB)], to permit nucleophilic attack despite increased steric hindrance and to permit neighbouring hydroxy-group attack to form three, four, and five-membered cyclic ethers,[13] but sufficient stability through the bridged form (XVA) to ensure that its stereochemical integrity is maintained, leading to the observed stereospecificity of formation of *e.g.* (IVh) and its diastereoisomer, and of (IVi). It appears therefore that the intermediate iodonium ion should be represented by the unsymmetrically bridged species (XVA) with a contribution from the free cationic form (XVB).

Participation by sulphur occurred in the addition of iodonium nitrate to the allylthiourea (XIX) which gives a cyclised product tentatively assigned as the thiazoline (XX) together with some pyridinium nitrate. These

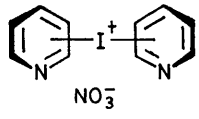


results suggested the possibility of rearrangements of suitable substrate olefins. Norbornene with iodonium nitrate gives the 'normal' iodonitrate ester (XXI) (60% yield) and the rearranged tricycloheptanyl iodide



(XXII) (40% yield) together with the corresponding amount of pyridinium nitrate.[12a] Hassner and Teeter reported phenyl migration during the addition of iodine azide and iodine isocyanate to 3,3,3-triphenylpropene. A comparable experiment with iodonium nitrate produced no addition in contrast to the easy addition to (*Z*)- and (*E*)-4,4-dimethylpent-2-ene. This unexpected result may indicate steric hindrance of approach of the bulky complex (XXIII) to the 3,3,3-triphenylpropene.

Although the intermediate in the additions has been represented as an unsymmetrically bridged iodonium ion for the purposes of discussion, the iodine is complexed to two pyridine molecules in this solvent. The complex (XXIII) may be isolated as a very unstable crystalline solid which is soluble in polar solvents.



(*E*)-4,4-Dimethylpent-2-ene with 1 equiv. of the complex (XXIII) in rigorously dried dimethyl sulphoxide gave compound (IIIa) stereospecifically. Rate data for

the addition of iodonium nitrate to unsaturated substrates and kinetic evidence for neighbouring group participation controlling the stereochemistry of addition will be discussed in a subsequent publication.

EXPERIMENTAL

M.p.s. were determined on a Fisher–Johns apparatus. I.r. spectra were recorded on a Perkin-Elmer model 421 spectrophotometer. N.m.r. spectra were recorded on Varian A-60 and A-100 analytical spectrometers. The spectra were measured on *ca.* 10—15% (w/v) solutions usually in $CDCl_3$, with tetramethylsilane as a standard. Mass spectra were determined on an A.E.I. MS9 double focusing high resolution mass spectrometer. The ionisation energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15,000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for thin layer chromatography. Microanalyses were carried out by Mrs. D. Mahlow of this department.

General Procedure for the Reaction of Iodonium Nitrate with Stereoisomeric Alkenes.—Representative examples of additions to (*E*)–(*Z*) pairs of alkenes leading predominantly to iodoalkyl nitrate esters and iodopyridinium nitrate salts, respectively are given. Thereafter the results are summarised in Tables 1—4.

Addition of iodonium nitrate to (E)-4,4-*dimethylpent*-2-*ene in the presence of pyridine.* Using a modification of the reported procedure, silver nitrate (6·8 g, 0·04 mol) was dissolved in a mixture of anhydrous chloroform (50 ml) and anhydrous pyridine (15 ml). Iodine monochloride (Alfa Inorganics) (6·5 g, 0·04 mol) in dry chloroform (20 ml) was added dropwise to the stirred solution. The silver chloride produced was collected and washed with a mixture of chloroform (10 ml) and pyridine (10 ml). (*E*)-4,4-Dimethylpent-2-ene (3·925 g, 0·04 mol) was added all at once to the filtrate. The mixture was stirred at room temperature for 3 h, then poured into an excess of ether and chilled. The resulting precipitate was collected and the filtrate concentrated *in vacuo*. The oil obtained was washed with water (4 × 50 ml) to remove pyridine and any remaining pyridinium salt, then taken up in ether and dried ($MgSO_4$). Evaporation *in vacuo* gave erythro-2-*iodo*-1,3,3-*trimethylbutyl nitrate* (IIIa) (8·7 g, 76%), b.p. 48·5—50° at 3·4 mmHg (Found: C, 28·9; H, 4·9; N, 5·0%, M^+, 287. $C_7H_{14}INO_3$ requires C, 29·25; H, 4·9; N, 4·88%, *M*, 287), $\nu_{max.}$ (neat) 1625 cm^{-1} (ONO_2), δ ($CDCl_3$) 1·22 [9H, s, $C(CH_3)_3$], 1·52 (3H, d, $J_{CH_3-CHONO_2}$ 6·2 Hz, CH_3), 4·42 (1H, d, $J_{CHI-CHONO_2}$ 2·75Hz, CHI), and 4·8 (1H, octet, $J_{CH_3-CHONO_2}$ 6·2, $J_{CHI-CHONO_2}$ 2·75 Hz, $CHONO_2$).

The ether-insoluble residue after washing several times with ether was extracted with ethanol–propan-2-ol (1 : 1), then filtered. Ether was added to the filtrate dropwise until the solution turned cloudy, and it was left in the refrigerator overnight. The resulting precipitate was collected and washed with ether containing a little ethanol to afford erythro-1-(2-*iodo*-1,3,3-*trimethylbutyl*)*pyridinium nitrate* (IVa) (0·7 g, 4·8%), m.p. 89—92° (Found: C, 39·35; H, 5·0. $C_{12}H_{19}IN_2O_3$ requires C, 39·35; H, 5·2), $\nu_{max.}$ (KBr) 1620 cm^{-1} (ONO_2), δ [$(CD_3)_2SO$] 1·2 [9H, s, $C(CH_3)_3$], 1·74 (3H, d, $J_{CH_3-\overset{+}{C}H-\overset{+}{N}\lesssim}$ 7 Hz, CH_3), and 4·6—5·15 (2H, m, CHI, $CH-\overset{+}{N}\lesssim$).

Addition of iodonium nitrate to (Z)-4,5-*dimethylpent*-2-*ene in the presence of pyridine.* A solution of iodonium nitrate was prepared from iodine monochloride (6·5 g, 0·04 mol) and silver nitrate (6·8 g, 0·04 mol) in chloroform–pyridine as described above. (*Z*)-4,4-Dimethylpent-2-ene (3·925 g, 0·04 mol) was added all at once to the filtrate, the mixture stirred at room temperature for 3 h then worked up according to the procedure described above affording threo-2-*iodo*-1,3,3-*trimethylbutyl nitrate* (VIIa) (10·59 g, 91·5%) which was purified by distillation under reduced pressure, b.p. 52—53° at 3 mmHg (Found: C, 29·6; H, 4·9; N, 4·9%, M^+ 287. $C_7H_{14}INO_3$ requires C, 29·25; H, 4·9; N, 4·9%, *M*, 287), $\nu_{max.}$ (film) 1625 cm^{-1} (ONO_2), δ ($CDCl_3$) 1·19 [9H, s, $C(CH_3)_3$], 1·53 (3H, d, $J_{CH_3-CHONO_2}$ 6·15 Hz, CH_3), 3·99 (1H, d, J_{CH-CH} 1·5 Hz, CHI), and 4·93 (1H, octet, J_{CH-CH} 1·5, J_{CH-CH_3} 6·15 Hz, $CHONO_2$).

From the ether-insoluble residue and according to the crystallisation procedure discussed above was isolated threo-1-(2-*iodo*-1,3,3-*trimethylbutyl*)*pyridinium nitrate* (VIIIa) (0·8 g, 5·46%), m.p. 82—85° (Found: C, 40·1; H, 5·25. $C_{12}H_{19}IN_2O$ requires C, 39·35; H, 5·2), $\nu_{max.}$ (KBr) 1620 cm^{-1} (NO_3^-), δ ($CDCl_3$) 1·17, [9H, s, $(CH_3)_3C$], 1·87 (3H, d, J_{CH_3-CH} 6·5 Hz, CH_3), and 4·9—5·4 (2H, m, CHI, $CH-\overset{+}{N}\lesssim$).

Reduction of erythro-2-*Iodo*-1,3,3-*trimethylbutyl Nitrate* (IIIa).—The *erythro*-nitrate (IIIa) (16·5 g, 0·0575 mol) was added dropwise to a stirred mixture of glacial acetic acid (230 ml) and zinc–copper couple (14·3 g). The mixture was stirred at room temperature for 24 h, filtered into water–ether and the residue was washed with a small amount of ether. The filtrate was neutralised with sodium hydrogen carbonate, the ether layer removed, and the aqueous layer extracted with ether (2 × 50 ml). The combined ether extracts were dried ($MgSO_4$) and the solvent removed *in vacuo* to give erythro-3-*iodo*-4,4-*dimethylpentan*-2-*ol* (Va) (4 g, 29%). Purification was effected by chromatography on neutral alumina (120 g) and elution with pentane–methanol (96 : 4), m.p. 59—60°, $\nu_{max.}$ ($CHCl_3$) 3450 cm^{-1} (OH), δ ($CDCl_3$), 1·15 [9H, s, $C(CH_3)_3$], 1·28 (3H, d, J_{CH_3-CHOH} 6 Hz, CH_3), 1·9 (1H, s, OH), 3·11 (1H, octet, J_{CH_3-CHOH} 6, J_{CH-CH} 2·9 Hz, *CH*OH), and 4·58 (1H, d, $J_{CHI-CHOH}$ 2·9 Hz, CHI).

(*E*)-2,3-*Epoxy*-4,4-*dimethylpentane* (VI).—The iodohydrin (Va) (2·4 g, 0·01 mol) was dissolved in ether (80 ml). Powdered potassium hydroxide (0·85 g, 0·015 mol) was added in small portions to the stirred solution and stirred at room temperature for 1·5 h, filtered, and the residue washed with a small amount of ether. The combined extracts were washed with water (50 ml), dried ($MgSO_4$), and evaporated *in vacuo* at room temperature to afford the *epoxide* (VI) (0·8 g, 70%), identical with the authentic epoxide prepared below.

Epoxidation of (E)-4,4-*Dimethylpent*-2-*ene.*—A mixture of *m*-chloroperbenzoic acid (80% pure; 6·6 g, 0·03 mol), anhydrous sodium hydrogen carbonate (5 g), and methylene chloride (80 ml) was cooled in ice–water. (*E*)-4,4-Dimethylpent-2-ene (2 g, 0·02 mol) was added all at once and the mixture stirred at 0° for 3 h. The mixture was kept in the refrigerator overnight, filtered, and the residue was washed with a small amount of methylene chloride. The methylene chloride solution was washed with aqueous potassium carbonate solution (10%; 2 × 40 ml) and then with water (40 ml), dried ($MgSO_4$), and evaporated *in vacuo* at room temperature to afford (E)-2,3-*epoxy*-4,4-*dimethylpentane* (VI) (2 g) (1·5 g, 68% after distillation), b.p. 102—103° at 700 mmHg [Found: *m/e*, 99·0811. $C_6H_{11}O$ ($M - CH_3$) requires 99·0810], δ ($CDCl_3$) 0·90 [9H, s, $(CH_3)_3C$], 1·25

(3H, d, J_{CH_3-CH} 5·1 Hz, CH_3), 2·35 [1H, d, J_{CH-CH} 2·2 Hz, OC*H*·$C(CH_3)_3$], and 2·79 (1H, octet, J_{CH-CH_3} 5·1, J_{CH-CH} 2·1 Hz, OC*H*CH_3); $\nu_{max.}$ (neat) 1250, 907, 760 (oxiran), and 3010 cm^{-1} (CH).

Reduction of 2-*Iodo*-1,3,3-*trimethylbutylnitrate* (VIIa).—The *threo*-nitrate (VIIa) was subjected to zinc–copper couple reduction according to the conditions described above for (IIIa) to give 3-*iodo*-4,4-*dimethylpentan*-2-*ol* (IX) (41% yield), δ ($CDCl_3$) 1·15 [9H, s, $C(CH_3)_3$], 1·2 (3H, d, overlapped by Bu^t, CH_3), 1·66 (1H, s, OH), 3·11 (1H, m, CH_3CHOH), and 4·13 (1H, d, *J* 1·5 Hz, Bu^tCHI), $\nu_{max.}$ (film) 3430 cm^{-1} (OH).

(Z)-2,3-*Epoxy*-4,4-*dimethylpentane* (IX).—Treatment of 3-iodo-4,4-dimethylpentan-2-ol (IX) with potassium hydroxide according to the conditions described for (Va) above gave a mixture of (Z)-2,3-*epoxy*-4,4-*dimethylpentane* (XI) and a ketonic fraction (0·5 g, 44%). The epoxide was identical with an authentic sample (see below). The ketone was shown to be 4,4-dimethylpentan-2-one by comparison of its g.l.c. retention time with that of an authentic sample.

Epoxidation of (Z)-4,4-*Dimethylpent*-2-*ene*.—An authentic sample of (*Z*)-2,3-epoxy-4,4-dimethylpentane (XI) was prepared from (*Z*)-4,4-dimethylpent-2-ene by treatment with *m*-chloroperbenzoic acid. Distillation gave the pure *epoxide* (68% yield), b.p. 110—111·5 at 700 mmHg [Found: *m/e*. 99·0811. $C_6H_{11}O$ ($M - CH_3$) requires 99·0810], δ ($CDCl_3$) 1·04 [9H, s, $C(CH_3)_3$], 1·43 (3H, d, J_{CH-CH_3} 5·7 Hz, CH_3), 2·6 [1H, d, J_{CH-CH} 4·5 Hz, OC*H*$C(CH_3)_3$], and 2·97 (1H, octet, J_{CH-CH_3} 5·7, J_{CH-CH} 4·5 Hz, CH_3CHO), $\nu_{max.}$ (neat) 1260, 900, (oxiran), 3010 cm^{-1} (CH–O).

Base Catalysed Elimination of Hydrogen Iodide from erythro-1-(2-*Iodo*-1-*methylpropyl*)*pyridinium Nitrate*.—The *erythro*-nitrate (IVb) (14 g, 0·0432 mol) was dissolved in methanol (70 ml), sodium methoxide (3 g, 0·0555 mol), was added, and the mixture stirred at 50° for 20 h, cooled, and the precipitated salts were collected. The filtrate was poured into excess of ether, chilled and the resulting precipitate collected. Recrystallisation from ethanol–propan-2-ol–ether gave (E)-1-(1-*methylprop*-1-*enyl*)*pyridinium iodide* (XII) (9·5 g, 84%), m.p. 138—139° (Found: C, 40·8; H, 4·7; N, 5·35. $C_9H_{12}IN$ requires C, 41·4; H, 4·6; N, 5·35), δ [$(CD_3)_2SO$] 1·9 (3H, 2 q, J_{CH_3-CH} 7·3, $J_{CH_3C=CCH_3}$ 1·3 Hz, CH_3CH=), 2·36 (3H, quintet, $J_{CH_3C=CCH_3} = J_{CH=CCH_3}$ 1·3 Hz, $CH_3-\overset{\|}{C}-\overset{+}{N}<$), 6·16 (1H, octet, J_{CH_3CH} 7·3, $J_{CH=CCH_3}$ 1·3 Hz, $-CH$=), and 8·20—9·33 (5H, m, Py).

Base Catalysed Elimination of Hydrogen Iodide from threo-1-(2-*Iodo*-1-*methylpropyl*)*pyridinium Nitate* (VIIIb).—Similar sodium methoxide catalysed elimination of hydrogen iodide from compound (VIIIb) afforded (Z)-1-(1-*methylprop*-1-*enyl*)*pyridinium iodide* (XIII) (2·8 g, 87%), m.p. 182—184° (Found: C, 39·2; H, 4·6; N, 5·15. $C_9H_{12}IN$ requires C, 41·4; H, 4·6; N, 5·35), δ[$(CD_3)_2SO$] 1·47 (3H, 2 q, $J_{CH_3C=CCH_3}$ 1·7, J_{CH_3CH} 7 Hz, CH_3CH=), 2·38 (3H, quintet. $J_{CH_3=CH} \simeq J_{CH_3C=CCH_3}$ 1·7 Hz, $CH_3\overset{\|}{C}-\overset{+}{N}<$), 6·14 (1H, m, J_{CH_3CH} 7, $J_{CH_3C=CH}$ 1·5 Hz, CH=), and 8·2—9·15 (5H, m, Py).

Proof of Regiochemistry of Addition of Iodonium Nitrate to (E)-3-*Methylpent*-2-*ene by Base Catalysed Elimination of Hydrogen Iodide from* threo-1-(1-*Ethyl*-2-*iodo*-1-*methylpropyl*)*pyridinium Nitrate* (IVh).—A mixture of the *threo*-pyridinium nitrate (IVh) (1·6 g, 4·5 mmol), sodium methoxide (1 g, 19 mmol), and methanol (40 ml) was stirred under reflux for 48 h, cooled, poured into ether, and then chilled. The resulting precipitate was collected and recrystallisation from ethanol–ether gave 1-(1-*ethyl*-1-*methylprop*-2-*enyl*)*pyridinium iodide* (XVI) (0·5 g, 38%), m.p. 72—75°, δ [$(CD_3)_2SO$] 0·75 (3H, t, *J* 7·5 Hz, CH_3CH_2), 1·87 (3H, s, $CH_3\overset{|}{C}-\overset{+}{N}<$), 2·27 (3H, q, *J* 7·5 Hz, CH_2CH_3), 5·37—5·70 (2H, q, $=CH_2$), 6·1—6·57 (1H, q, =CH–), and 8·1—9·31 (5H, m, Py).

Addition of Iodonium Nitrate to (Z)-[β-^{2}H]*Styrene in the Presence of Pyridine*.—Iodonium nitrate (0·02 mol) was prepared in chloroform (30 ml) and pyridine (12·5 ml). (*Z*)-[β-^{2}H]Styrene (2·1 g, 0·02 mol; >97% D) [9a] was added all at once to the solution. The mixture was stirred at room temperature for 3·5 h and then poured into water–ether. The ethereal layer was washed successively with water (50 ml), sodium thiosulphate (10%; 50 ml), water (2 × 50 ml), hydrochloric acid (5%; 70 ml), and then with water (2 × 50 ml). Evaporation *in vacuo* after drying ($MgSO_4$) gave a trace of *threo*-α-(iodo[^{2}H]methyl)benzyl nitrate (IIIi). The aqueous layer was washed with ether (50 ml) and the ether discarded. A control experiment with unlabelled styrene showed that the water-soluble material was a mixture of uneliminated pyridinium salt, eliminated pyridinium salt, and pyridinium nitrate, which were not separable by usual procedures. Therefore the aqueous solution was treated with solid potassium carbonate (4 g) and extracted several times with ether, and the ether discarded. The solution was adjusted to pH 7 with dilute nitric acid, and evaporated to dryness *in vacuo*. Ether was added to an ethanolic solution of the residue until the solution turned cloudy. Crystallisation by the method described before gave (Z)-1-(α-[^{2}H]methylenebenzyl)pyridinium iodide (XVIII) (2·0 g, 32%),[12a] δ [$(CD_3)_2SO$] 6·43 (1H, s, =CHD), 7·45 (5H, m, Ph), and 8·17—9·27 (5H, m, Py).

Iodonium Nitrate–Pyridine Complex.—Iodonium nitrate (0·04 mol) was prepared in chloroform (50 ml) and pyridine (25 ml). Excess of ether was added and the mixture chilled. The resulting precipitate was collected and washed several times with ether. Recrystallisation from propan-2-ol–pyridine–ether gave *iodonium nitrate–pyridine complex* (XXIII) (8·6 g), m.p. 72°, as a crystalline solid which was very unstable out of solution (Found: C, 36·25; H, 3·65; N, 13·5. $C_{10}H_{10}IN_3O_3$ requires C, 34·6; H, 2·9; N, 12·1%).

Addition of Iodonium Nitrate–Pyridine Complex to (E)-4,4-*Dimethylpent*-2-*ene in Dimethyl Sulphoxide*.—A mixture of iodonium nitrate–pyridine complex (3·47 g, 0·01 mol), (*E*)-4,4-dimethylpent-2-ene (0·98 g, 0·01 mol), and dimethyl sulphoxide (20 ml) was stirred at room temperature for 5 h, and then poured into water–ether. The ether layer was removed and the aqueous layer extracted with a small amount of ether. The combined ether extracts were washed successively with water (50 ml), sodium thiosulphate (10%; 40 ml), water (2 × 50 ml), hydrochloric acid (5%; 40 ml), and water (2 × 50 ml). Drying ($MgSO_4$), and evaporation *in vacuo* gave the *erythro*-nitrate (IIIa) (60% yield), b.p. 48·5—50 at 3·4 mmHg.

Addition of Iodonium Nitrate to 1-*Allyl*-3,3-*diethylthiourea in the Presence of Pyridine*.—Iodonium nitrate (0·02 mol) was prepared in chloroform (4 ml) and pyridine (15 ml). 1-Allyl-3,3-diethylthiourea (3·49 g, 0·02 mol) was added all at once to the stirred solution. An exothermic reaction took place and the colour changed to dark brown. The mixture was stirred at room temperature for 3 h, then poured into excess of ether and chilled. The resulting residue was collected, washed several times with ether, and

extracted with cold methanol, filtered, and reprecipitated with ether. The residue was chromatographed on silica gel (100 g) and eluted with benzene–methanol (85 : 15). Evaporation of the first fraction gave an oily residue (3·3 g) which solidified slowly on standing to give 2-*diethylamino*-4,5-*dihydro*-5-*iodomethyl*-1,3-*thiazole* (XX), δ [$(CD_3)_2SO$] 1·03 (6H, t, J 6·5 Hz, CH_3CH_2); $\nu_{max.}$ ($CHCl_3$) 1597—1625 cm^{-1} (C=N) [Found: M^+, 298·0003. $C_8H_{15}IN_2S$ requires 298·0001].

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