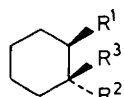


## Reactions of Thallium(I) Azide and Iodine with Alkenes

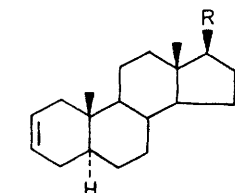
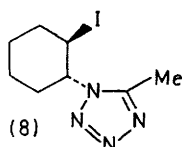
By Richard C. Cambie,\* Rodney C. Hayward, Peter S. Rutledge, Truis Smith-Palmer, and Paul D. Woodgate, Department of Chemistry, University of Auckland, New Zealand

The action of thallium(I) azide and iodine on some alkenes has been examined. This reagent gives different product ratios from those given by sodium azide and iodine chloride, and it differs from the latter reagent in that iodine azide cannot be preformed. Solvent incorporation occurs when thallium(I) azide-iodine is added to cyclohexene in acetonitrile. In addition to products arising from diaxial opening of  $\alpha$ - and  $\beta$ -iodonium ions, products of *cis*-addition have been obtained from the reactions of both thallium(I) azide-iodine and sodium azide-iodine chloride on  $\Delta^2$ -steroids. The mode of formation of these products is discussed.

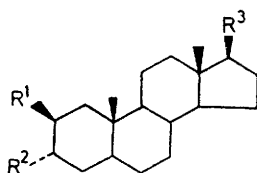
TREATMENT of an alkene with iodine(I) azide has been reported to result in regio- and stereo-selective formation of vicinal iodo-azides which can serve as starting



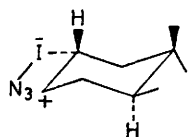
- (1)  $R^1 = I, R^2 = N_3, R^3 = H$   
 (2)  $R^1 = I, R^2 = N: CMe, R^3 = H$   
 (3)  $R^1 = OAc, R^2 = N_3, R^3 = H$   
 (4)  $R^1 = OH, R^2 = N_3, R^3 = H$   
 (5)  $R^1 = I, R^2 = N_3, R^3 = Me$   
 (6)  $R^1 = OAc, R^2 = N_3, R^3 = Me$   
 (7)  $R^1 = OH, R^2 = N_3, R^3 = Me$



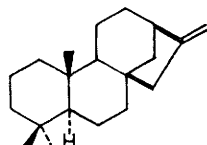
- (9)  $R = H$   
 (10)  $R = C_8H_{17}$



- (11)  $R^1 = N_3, R^2 = I, R^3 = H$  (15)  $R^1 = I, R^2 = N_3, R^3 = H$   
 (12)  $R^1 = I, R^2 = N_3, R^3 = H$  (16)  $R^1 = N_3, R^2 = I, R^3 = H$   
 (13)  $R^1 = N_3, R^2 = I, R^3 = C_8H_{17}$  (17)  $R^1 = I, R^2 = N_3, R^3 = C_8H_{17}$   
 (14)  $R^1 = I, R^2 = N_3, R^3 = C_8H_{17}$



(18)



(19)

materials for the preparation of vinyl azides, amines, amino-ketones, azirines, aziridines, and other *N*-hetero-

cycles.<sup>1</sup> In a continuation of our study of the utilization of thallium(I) salts in organic synthesis,<sup>2,3</sup> we have examined the reaction of thallium(I) azide<sup>4</sup> with alkenes in the presence of iodine or iodine chloride.

The reaction of cyclohexene with thallium(I) azide and iodine in dichloromethane gave the same *trans*-iodo-azide (1) as obtained from the reaction with sodium azide and iodine chloride in acetonitrile.<sup>5</sup> However, in acetonitrile the major product was the result of solvent incorporation, the *trans*-iodo-tetrazole (8).<sup>6</sup> The tetrazole presumably arises from a Ritter type intermediate (2) by reaction with azide ion and subsequent cyclization,<sup>7</sup> since no reaction occurred when the iodo-azide (1) was treated with thallium(I) azide and acetonitrile. Similar solvent incorporation has been reported for the analogous addition of bromine(I) azide<sup>8</sup> but in the case of iodine(I) azide only with  $\alpha$ - and  $\beta$ -pinenes<sup>9</sup> or  $C_9$  and  $C_{10}$  medium-ring dienes<sup>10</sup> where the cationic or incipient cationic centre is generated at a site remote from the double bond attacked initially. When cyclohexene was treated with sodium azide and iodine in dichloromethane, no iodo-azide was formed, but with acetonitrile as the solvent the iodo-azide was again obtained. The reaction of cyclohexene with thallium(I) azide and iodine chloride in dichloromethane gave the iodo-azide (1), whereas in acetonitrile a mixture of the iodo-azide (1), the tetrazole (8), and a minor unidentified product was formed.

In contrast to the case of sodium azide and iodine chloride in acetonitrile, where Hassner was able to form iodo-azides from a preformed filtered mixture of the reagents, no iodo-azide was formed if cyclohexene was added to the filtrate from a mixture of thallium(I) azide and iodine or of thallium(I) azide and iodine chloride in dichloromethane. Thallium(I) azide thus appeared to react in a different way to sodium azide and it was found that the presence of all three components [cyclohexene, thallium(I) azide, and iodine] was necessary to

<sup>1</sup> F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, 1967, **89**, 2077.

<sup>2</sup> A. Hassner, L. A. Levy, and R. Gault, *Tetrahedron Letters*, 1966, 3119.

<sup>3</sup> J. H. Boyer and E. J. Miller, *J. Amer. Chem. Soc.*, 1959, **81**, 4671.

<sup>4</sup> F. Boerwinkle and A. Hassner, *Tetrahedron Letters*, 1968, 3921.

<sup>5</sup> S. Ranganathan, D. Ranganathan, and A. K. Mehrotra, *Tetrahedron Letters*, 1973, 2265; *Synthesis*, 1973, 356; B. Bochwic and B. Olejniczak, *Roczniki Chem.*, 1973, **47**, 315.

<sup>10</sup> S. N. Moorthy, D. Devaprabhakara, and K. G. Das, *Tetrahedron Letters*, 1975, 257.

<sup>1</sup> A. Hassner, *Accounts Chem. Res.*, 1971, **4**, 9.

<sup>2</sup> R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J.C.S. Perkin I*, 1974, 1858.

<sup>3</sup> R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J.C.S. Perkin I*, 1974, 1864.

<sup>4</sup> W. S. McEwan and M. M. Williams, *J. Amer. Chem. Soc.*, 1954, **76**, 2182.

obtain iodo-azide adducts. A similar situation exists when thallium(I) carboxylates are used in place of silver(I) carboxylates in the Prévost reaction.<sup>2</sup>

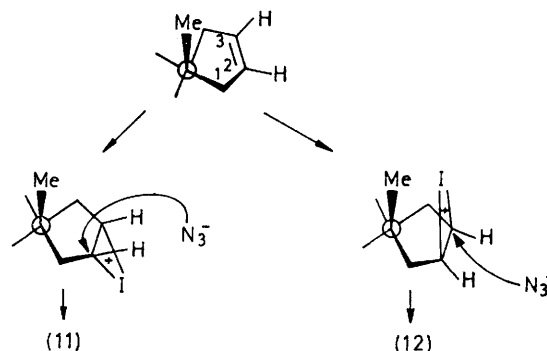
Solvolysis of the *trans*-iodo-azide (1) with silver(I) acetate in acetic acid gave a near quantitative yield of *trans*-2-azidocyclohexyl acetate (3).<sup>\*</sup> The splitting patterns for its C-1 and C-2 proton signals at  $\delta$  3.35 and 4.67 were consistent with a conformation in which the iodo- and acetate groups are *trans*-diequatorial. Hydrolysis of the acetate (3) with ethanolic potassium hydroxide gave the azido-alcohol (4). Solvolysis of the iodo-azide (5)<sup>5</sup> formed by addition of sodium azide and iodine chloride in acetonitrile, or of thallium(I) azide and iodine in dichloromethane, to 1-methylcyclohexene, gave a product which was tentatively identified as the azido-acetate (6) since its n.m.r. spectrum showed a C-2 proton signal at higher field ( $\delta$  3.85) than expected. Hydrolysis gave the azido-alcohol (7).

In order to examine any regio- and stereo-selectivity which might result from using thallium(I) azide and iodine rather than sodium azide and iodine chloride, the reaction with  $\Delta^2$ -steroids was investigated. Reaction with 5 $\alpha$ -androst-2-ene<sup>11</sup> (9) gave three isomeric iodo-azides in the ratio 3:2:1, which were separated by preparative t.l.c. Two of the products had very similar  $R_F$  values and were identified as 2 $\beta$ -azido-3 $\alpha$ -iodo-5 $\alpha$ -androstane (11) and 3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -androstane (12) on the basis of their n.m.r. spectra. The spectrum of the major component (11), m.p. 96–98°, showed signals at  $\delta$  4.17 and 4.60 assigned to the C-2 and C-3 protons, which from their  $W_{1/2}$  values (8 and 7 Hz, respectively) are equatorial.<sup>12a</sup> The iodine atom is therefore axial and must be at either C-2 $\beta$  or C-3 $\alpha$ . It is assigned to the latter position since the signal of the C-19 protons ( $\delta$  0.98) showed a downfield shift of ca. 0.2 p.p.m. from that of 5 $\alpha$ -androstane.<sup>12b</sup> If we assume that ring A is in a chair form, a 2 $\beta$ -iodo-substituent would be expected to cause a shift of the 19- $H_3$  signal of ca. 0.4 p.p.m.<sup>13</sup> The spectrum of the minor component (12), m.p. 108–110.5°, possessed two downfield equatorial proton signals ( $\delta$  4.27 and 4.60) but in this case the 19- $H_3$  signal ( $\delta$  1.17) was shifted ca. 0.4 p.p.m. downfield from that of 5 $\alpha$ -androstane, indicating a 2 $\beta$ -iodo-substituent.

The spectrum of the third isomer, m.p. 175–181°, showed signals at  $\delta$  4.50 and 4.56 with  $W_{1/2}$  values (6 and 22 Hz) indicating an equatorial and an axial proton, respectively. Since the 19- $H_3$  signal ( $\delta$  0.83) shows only a slight downfield shift (0.02 p.p.m.) from that of 5 $\alpha$ -androstane, no substituent is present in the 2 $\beta$ -

position. Of the two possible structures (15) and (16) the former, viz. 3 $\alpha$ -azido-2 $\alpha$ -iodo-5 $\alpha$ -androstane, is favoured since Hassner has reported that a proton adjacent to a secondary iodide resonates further downfield than a proton adjacent to a secondary azide.<sup>5</sup> All three of the above products were obtained, albeit in a different ratio (7:2:1), when 5 $\alpha$ -androst-2-ene was treated with sodium azide and iodine chloride in ether-acetonitrile.

Formation of the compounds (11) and (12) can be rationalized in terms of initial formation of both  $\alpha$ - and  $\beta$ -iodonium ion intermediates (cf. refs. 2 and 14) which are opened in a diaxial manner.<sup>15</sup> Formation of an iodonium ring  $\alpha$  to the steroid face is more favoured for



steric reasons, thereby leading to (11) as the major product. Attack at C-3 of the  $\alpha$ -iodonium ion and at C-2 of the  $\beta$ -iodonium ion is not favoured since, although each would ultimately lead to a more stable configuration with diequatorial substituents, the reaction must pass through a boat transition state.<sup>16</sup> Formation of the product (15) requires *cis*-addition of the elements of iodine(I) azide to the alkene (9), which could be explained by radical addition or by formation of a carbocation. Radical addition would be unexpected since, although Hassner has obtained *cis*-adducts from the radical addition of bromine(I) azide to cyclohexene and 5 $\alpha$ -cholest-2-ene (10),<sup>17</sup> radical addition of iodine(I) azide has hitherto been obtained only when styrene was the alkene and pentane was used as the solvent under a nitrogen atmosphere.<sup>18</sup> *cis*-Addition has also been observed recently for addition of iodine(I) azide to a strained and hindered cyclobutene.<sup>19</sup> In the present work addition of thallium(I) azide and iodine to 5 $\alpha$ -androst-2-ene in pentane under nitrogen gave a low yield of product in which the ratio of *cis*- to *trans*-adducts had decreased, suggesting that radical addition was not operating. On the other hand radical addition cannot be entirely discounted since under the same

<sup>15</sup> D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, p. 114.

<sup>16</sup> A. Hassner and C. Heathcock, *J. Org. Chem.*, 1965, **30**, 1748.

<sup>17</sup> A. Hassner and F. Boerwinkle, *J. Amer. Chem. Soc.*, 1968, **90**, 216.

<sup>18</sup> A. Hassner and F. Boerwinkle, *Tetrahedron Letters*, 1969, 3309.

<sup>19</sup> G. Mehta, P. K. Dutta, and P. N. Pandey, *Tetrahedron Letters*, 1975, 445.

\* The complete retention of the *trans*-configuration implies that the azide has acted as a neighbouring group.

<sup>11</sup> J. M. Evans, G. D. Meakins, Y. Morisawa, and P. D. Woodgate, *J. Chem. Soc. (C)*, 1968, 2841.

<sup>12</sup> N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, (a) p. 79; (b) p. 17.

<sup>13</sup> A. Hassner, J. E. Kropp, and G. J. Kent, *J. Org. Chem.*, 1969, **34**, 2628.

<sup>14</sup> A. Bowers, E. Denot, and R. Becerra, *J. Amer. Chem. Soc.*, 1960, **82**, 4007.

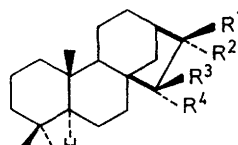
conditions a mixture of sodium azide and iodine chloride gave a low yield of product in which the ratio of *cis*- to *trans*-adduct was greater.

One possibility for *cis*-addition is that molecular iodine(I) azide reacts from the  $\alpha$ -face to give a zwitterion (18) in which the azide group is positioned for intramolecular attack at C-3. However, the absence of the alternative *cis*-adduct (16) among the products is difficult to explain. Depending on the solvent, the azide anion may be more intimately involved in the formation of some iodine(I) azide adducts than hitherto supposed. Insufficient evidence exists to warrant a full discussion of the mechanism but it appears likely that the addition of iodine(I) azide may involve different pathways and multiple intermediates of similar energy, in a manner similar to that proposed by de la Mare and his co-workers for additions of molecular chlorine.<sup>20</sup>

The above results prompted a reinvestigation of the action of iodine(I) azide on 5 $\alpha$ -cholest-2-ene (10).<sup>5,21</sup> Addition of sodium azide and iodine chloride in acetonitrile under Hassner's conditions was very slow, giving only a low yield of product after the reported time of 24 h. However, the reaction was faster in a mixture of dry ether and acetonitrile as solvent, giving a moderate yield of product after 24 h. Although Hassner reported that the *trans*-diaxial adduct (13) was the sole product, two products were consistently obtained in a 3 : 1 ratio during the present work. Neither possessed a melting point similar to that of Hassner's product (102–103°) but the n.m.r. data of the major product, m.p. 71–74°, were identical with those recorded for Hassner's adduct (13). By analogy with the 5 $\alpha$ -androst-2-ene case it is assumed that the material of m.p. 71–74° contains two inseparable components. Unlike the 5 $\alpha$ -androst-2-ene case where there is a simplified methyl signal region, the complexity of the methyl region in the n.m.r. spectrum of 5 $\alpha$ -cholest-2-ene adducts does not permit a clear distinction between two closely related isomers. However, the material showed only diequatorial downfield protons in its n.m.r. spectrum indicating that, if present, both components were *trans*-diaxial adducts. One is assumed to correspond with Hassner's product (13) and, by analogy with the work on 5 $\alpha$ -androst-2-ene, the second is assigned the structure (14). The n.m.r. spectrum of the other product, m.p. 136–139°, showed low-field signals at  $\delta$  4.10 and 4.57 with  $W_{\frac{1}{2}}$  (8 and 21 Hz) which indicated an equatorial and axial proton, respectively. By analogy with the products from 5 $\alpha$ -androst-2-ene this compound is identified as 3 $\alpha$ -azido-2 $\alpha$ -iodo-5 $\alpha$ -cholestane (17). Treatment of 5 $\alpha$ -cholest-2-ene with thallium(I) azide and iodine also gave the products [(13) and (14)] and (17) in the ratio 2 : 1.

The action of sodium azide and iodine chloride on some diterpenoid alkenes was also investigated. Reaction with phyllocladene (19) gave the expected regioisomer (20) as the sole product. Reaction with

isophyllocladene (24) gave two major but unstable products which, assuming *trans*-addition, were identified as 15 $\beta$ -azido-16 $\alpha$ -iodo-13 $\beta$ -kaurane (21) and 16 $\beta$ -azido-15 $\alpha$ -iodo-13 $\beta$ -kaurane (22), respectively. In addition to starting material, minor products were the allylic azide (25) and the diazido-iodo-adduct (23). Although a pure sample of the allylic azide was not isolated, support for its structure was obtained when an enriched sample afforded further quantities of the diazido-iodo-compound after further treatment with sodium azide and iodine chloride.

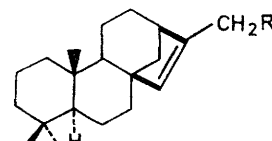


(20)  $R^1 = \text{CH}_2\text{I}$ ,  $R^2 = \text{N}_3$ ,  $R^3 = R^4 = \text{H}$

(21)  $R^1 = \text{Me}$ ,  $R^2 = \text{I}$ ,  $R^3 = \text{N}_3$ ,  $R^4 = \text{H}$

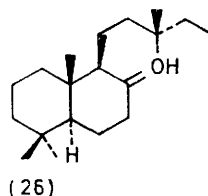
(22)  $R^1 = \text{N}_3$ ,  $R^2 = \text{Me}$ ,  $R^3 = \text{H}$ ,  $R^4 = \text{I}$

(23)  $R^1 = \text{CH}_2\text{N}_3$ ,  $R^2 = \text{I}$ ,  $R^3 = \text{N}_3$ ,  $R^4 = \text{H}$

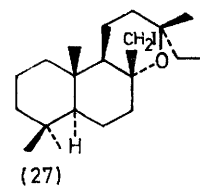


(24)  $R = \text{H}$

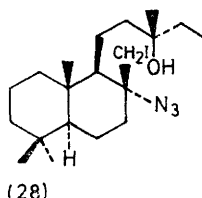
(25)  $R = \text{N}_3$



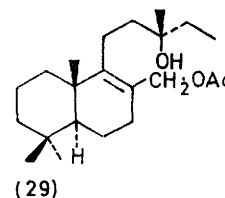
(26)



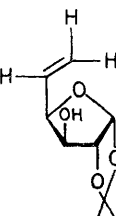
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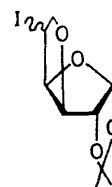
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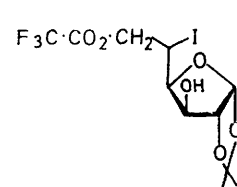
(29)



(30)



(31)



(32)

Reaction of labd-8(17)-en-13-ol (26) with sodium azide and iodine chloride gave a mixture of two products identified as 8,13-epoxy-17-iodolabdane (27) and 8-azido-17-iodolabdane-13-ol (28). The epoxy-iodide (27) has been obtained previously along with 17-acetoxylabd-8-

<sup>20</sup> P. B. D. de la Mare, M. A. Wilson, and M. J. Rosser, *J.C.S. Perkin II*, 1973, 1480.

<sup>21</sup> A. Hassner and L. A. Levy, *J. Amer. Chem. Soc.*, 1965, **87**, 4203.

en-13-ol (29) by the action of silver(I) acetate and iodine in benzene on labd-8(17)-en-13-ol.<sup>22</sup> In the present work a mixture of intramolecularly and intermolecularly derived products, (27) and (29), was again obtained by using thallium(I) acetate and iodine in dichloromethane.<sup>2</sup> The formation of the product (27) from the reaction of sodium azide and iodine chloride is of interest in view of the reported lack of neighbouring group participation of these reagents with the alkene (30), but the formation of compound (31) and the iodo-trifluoroacetate (32) with silver trifluoroacetate and iodine.<sup>23</sup> The i.r. spectrum of the adduct (28) showed a strong azide peak at 2 100 cm<sup>-1</sup> and the n.m.r. spectrum exhibited an AB quartet centred at  $\delta$  3.68 due to the C-17 protons. Assignment of the structure (28) is in agreement with Hassner's observations that most terminal alkenes yield adducts with the iodine atom at the primary position.<sup>5</sup>

#### EXPERIMENTAL

Unless otherwise indicated i.r. spectra were recorded for solutions in CHCl<sub>3</sub> with a Perkin-Elmer 237 or 337 spectrophotometer. N.m.r. spectra were measured for solutions in CDCl<sub>3</sub> with a Varian T60 spectrometer (tetramethylsilane as internal reference). Alumina for chromatography was Spence type H deactivated with 5% (v/v) of aqueous 10% acetic acid. T.l.c. was carried out on plates of kieselgel DG (Riedel de Haen) and preparative t.l.c. (p.l.c.) was carried out on 1 mm thick plates of kieselgel PF<sub>254</sub>+336 (Merck). Dichloromethane was purified before use by passage through a short column of alumina.

**Reaction of Cyclohexene with Thallium(I) Azide and Iodine.**—(i) *In dichloromethane.* A solution of iodine (0.32 g, 1.25 mmol) in dichloromethane (20 ml) was added dropwise over 2 days to a stirred slurry of thallium(I) azide<sup>4</sup> (0.62 g, 2.5 mmol) in dichloromethane (10 ml) and cyclohexene (82 mg, 1.0 mmol). The mixture was stirred at 20 °C for 18 h and the precipitate was removed by filtration. The dichloromethane was removed and ether was added. Work-up as previously described<sup>5</sup> gave *trans*-1-azido-2-iodocyclohexane (1) (0.17 g, 68%) as an oil (i.r. and n.m.r. spectra as reported<sup>5</sup>). If a mixture of thallium(I) azide and iodine in dichloromethane was filtered before addition of cyclohexene, no iodo-azide adduct was obtained.

(ii) *In acetonitrile.* A solution of iodine (0.32 g) in acetonitrile (5 ml) was added dropwise to a stirred suspension of thallium(I) azide (0.62 g) in acetonitrile (2 ml) and cyclohexene (82 mg). The mixture was stirred at 20 °C for 18 h, filtered, poured into water, and extracted with ether. Work up and p.l.c. (benzene-acetone, 9:1) gave the *trans*-iodo-tetrazole (8) (0.17 g, 58%) as needles (from pentane-ether), m.p. 144–146° (lit.,<sup>6</sup> 143°),  $\nu_{\max}$  1 440 cm<sup>-1</sup> (tetrazole),  $\delta$  2.60 (s, Me), and 3.81 and 4.32 (2 overlapping m, CHI and CHN).

**Reaction of Cyclohexene with Sodium Azide and Iodine.**—Iodine (0.32 g, 1.25 mmol), sodium azide (0.165 g, 2.5 mmol), and cyclohexene (82 mg, 1.0 mmol) were treated as described above. In dichloromethane (30 ml) as solvent no iodo-azide adducts were obtained, but from a reaction in acetonitrile (30 ml) a yellow oil (0.14 g) containing two products was isolated. P.l.c. (hexane-ether, 9:1) gave *trans*-1-

azido-2-iodocyclohexane (70 mg, 28%) and an unidentified azide (20 mg),  $\nu_{\max}$  2 100 cm<sup>-1</sup> (N<sub>3</sub>), which was not the iodo-tetrazole (8).

**Reaction of Cyclohexene with Thallium(I) Azide and Iodine Chloride.**—(i) *In acetonitrile.* Iodine chloride (0.18 g, 1.1 mmol) in acetonitrile (3.5 ml) was added dropwise to a stirred slurry of thallium(I) azide (0.62 g, 2.5 mmol) in acetonitrile (2 ml). After 10 min cyclohexene (82 mg, 1.0 mmol) was added and the mixture was stirred at 20 °C for 18 h. Work-up gave a yellow oil (0.20 g) which was separated by p.l.c. (benzene-acetone, 9:1) into *trans*-1-azido-2-iodocyclohexane (40 mg, 16%), the *trans*-iodo-tetrazole (8) (0.10 g, 34%), and unidentified material (trace).

(ii) *In dichloromethane.* The previous experiment was repeated with dichloromethane as solvent. Work-up gave a pale yellow oil (0.18 g) which was separated by p.l.c. (hexane-ether, 9:1) into *trans*-1-azido-2-iodocyclohexane (60%) and *trans*-1-chloro-2-iodocyclohexane (30%). If a mixture of thallium(I) azide and iodine chloride in dichloromethane was filtered before addition of cyclohexene, no iodo-azide adduct was obtained.

**Solvolysis of *trans*-1-Azido-2-iodocyclohexane.**—A solution of the iodo-azide (1) (0.50 g, 2.0 mmol) in dry acetic acid (10 ml) was stirred with silver(I) acetate (0.36 g, 2.2 mmol) at 60 °C for 1 h. Silver iodide was removed and the mixture was worked up to give *trans*-2-azidocyclohexyl acetate (3) (0.36 g, 95%) as an oil,  $\nu_{\max}$  2 100 (N<sub>3</sub>) and 1 720 cm<sup>-1</sup> (OAc),  $\delta$  2.10 (s, OAc), 3.35 (6 lines,  $J_{\text{obs.1,2}} = J_{\text{obs.1,6ax}} 10$ ,  $J_{\text{obs.1,6eq}} 5$  Hz, CHN<sub>3</sub>), and 4.67 ( $J_{\text{obs.1,2}} = J_{\text{obs.2,3ax}} 10$ ,  $J_{\text{obs.2,3eq}} 5$  Hz, CH·OAc).

**Hydrolysis of *trans*-2-Azidocyclohexyl Acetate.**—The acetate (3) was hydrolysed with 0.6% potassium hydroxide in 95% ethanol. Work-up gave *trans*-2-azidocyclohexanol (4) (95%) as an oil (Found: C, 51.3; H, 7.9; N, 29.5. C<sub>6</sub>H<sub>11</sub>N<sub>3</sub>O requires C, 51.0; H, 7.85; N, 29.8%),  $\nu_{\max}$  3 380 (OH) and 2 100 cm<sup>-1</sup> (N<sub>3</sub>),  $\delta$  2.65 (s, OH, exchanged with D<sub>2</sub>O) and 3.27 (m, CH·OH and CHN<sub>3</sub>).

***trans*-1-Azido-2-iodo-1-methylcyclohexane** (5).—*trans*-1-Azido-2-iodo-1-methylcyclohexane was prepared in 93% yield by using sodium azide and iodine chloride<sup>5</sup> or in 90% yield by using thallium(I) azide and iodine;  $\nu_{\max}$  2 100 cm<sup>-1</sup> (N<sub>3</sub>),  $\delta$  1.46 (Me) and 4.20 (q,  $J_{2,3ax} 8$ ,  $J_{2,3eq} 5$  Hz, CHI).

**Solvolysis of *trans*-1-Azido-2-iodo-1-methylcyclohexane.**—A solution of the iodo-azide (5) (0.60 g, 2.3 mmol) in glacial acetic acid (10 ml) was stirred with silver(I) acetate (0.42 g, 2.5 mmol) at 20 °C for 1 h and then at 50 °C for 30 min. Work-up and chromatography on alumina gave *trans*-2-azido-2-methylcyclohexyl acetate (6) as an oil (0.40 g, 90%),  $\nu_{\max}$  2 100 (N<sub>3</sub>) and 1 720 cm<sup>-1</sup> (OAc),  $\delta$  1.50 (s, Me), 2.00 (s, OAc), and 3.85 (q,  $J_{2,3ax} 7$ ,  $J_{2,3eq} 5$  Hz, CHOAc).

Hydrolysis of the acetate (6) as above gave *trans*-2-azido-2-methylcyclohexanol (7) as an oil (96%),  $\nu_{\max}$  3 350 (OH) and 2 100 cm<sup>-1</sup> (N<sub>3</sub>),  $\delta$  1.28 (s, Me), 1.96 (s, OH, exchanged with D<sub>2</sub>O), and 3.43 (q,  $J_{2,3ax} 10$ ,  $J_{2,3eq} 5$  Hz, CHOAc).

**Reaction of 5 $\alpha$ -Androst-2-ene with Thallium(I) Azide and Iodine.**—A solution of iodine (98 mg, 0.39 mmol) in dichloromethane (20 ml) was added dropwise over 48 h to a stirred suspension of thallium(I) azide (0.19 g, 0.76 mmol) in a solution of 5 $\alpha$ -androst-2-ene<sup>11</sup> (9) (0.10 g, 0.39 mmol) in dichloromethane (10 ml). The mixture was stirred for

<sup>22</sup> P. K. Grant, R. T. Weavers, and C. Huntrakul, *Tetrahedron*, 1973, 29, 245.

<sup>23</sup> J. S. Brimacombe, J. G. H. Bryan, and T. A. Hamor, *J. Chem. Soc. (B)*, 1970, 514; R. G. S. Ritchie and W. A. Szarek, *Canad. J. Chem.*, 1972, 50, 507.

18 h and worked up to give an oil (0.15 g), which was separated by p.l.c. (n-hexane) into (decreasing  $R_F$  values) (i) **3 $\alpha$ -azido-2 $\alpha$ -iodo-5 $\alpha$ -androstane** (15) (15%), which crystallized from methanol-ether as needles, m.p. 175–181° (Found: C, 53.4; H, 7.1; I, 29.6; N, 9.6.  $C_{19}H_{30}IN_3$  requires C, 53.4; H, 7.1; I, 29.7; N, 9.8%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.68 (s, 18- $H_3$ ), 0.83 (s, 19- $H_3$ ), 4.50 (m,  $W_{\frac{1}{2}}$  6 Hz, CHN), and 4.56 (m,  $W_{\frac{1}{2}}$  22 Hz, CHI); (ii) **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -androstane** (12) (30%), which crystallized from methanol-ether as needles, m.p. 108–110.5° (Found: C, 53.7; H, 7.0; N, 9.8.  $C_{19}H_{30}IN_3$  requires C, 53.4; H, 7.1; N, 9.8%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.69 (s, 18- $H_3$ ), 1.17 (s, 19- $H_3$ ), 4.27 (m,  $W_{\frac{1}{2}}$  9 Hz, CHN), and 4.60 (m,  $W_{\frac{1}{2}}$  9 Hz, CHI); (iii) **2 $\beta$ -azido-3 $\alpha$ -iodo-5 $\alpha$ -androstane** (11) (45%), which crystallized from methanol-ether as plates, m.p. 96–98° (Found: C, 53.1; H, 7.3; I, 29.6; N, 9.7.  $C_{19}H_{30}IN_3$  requires C, 53.4; H, 7.1; I, 29.7; N, 9.8%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.70 (s, 18- $H_3$ ), 0.98 (s, 19- $H_3$ ), 4.17 (m,  $W_{\frac{1}{2}}$  8 Hz, CHN), and 4.60 (m,  $W_{\frac{1}{2}}$  7 Hz, CHI).

Repetition of the experiment in pentane under nitrogen gave a 20% yield of compounds (15), (12), and (11) in the ratio 1 : 2 : 12.

**Reaction of 5 $\alpha$ -Androst-2-ene with Sodium Azide and Iodine Chloride.**—A mixture of sodium azide (74 mg, 1.14 mmol), and iodine chloride (76 mg, 0.42 mmol) in acetonitrile-ether (1 : 1; 5.5 ml) was treated with a solution of 5 $\alpha$ -androst-2-ene (0.10 g, 0.39 mmol) in the same solvent (5 ml). The mixture was stirred at 20 °C for 17 h and worked up to give a pale yellow oil (0.13 g), which was shown (n.m.r. analysis) to contain **3 $\alpha$ -azido-2 $\alpha$ -iodo-5 $\alpha$ -androstane** (7%), **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -androstane** (14%), **2 $\beta$ -azido-3 $\alpha$ -iodo-5 $\alpha$ -androstane** (50%), and starting material (29%).

Repetition of the experiment in pentane under nitrogen gave a 30% yield of compounds (15), (12), and (11) in the ratio 2 : 1 : 4. In dichloromethane the yield was 95% and the ratio 2 : 1 : 25.

**Reaction of 5 $\alpha$ -Cholest-2-ene with Sodium Azide and Iodine Chloride.**—5 $\alpha$ -Cholest-2-ene (10) (0.18 g, 0.49 mmol) was treated with sodium azide and iodine chloride as previously described<sup>5</sup> for 48 h with acetonitrile-dry ether (1 : 1) as solvent. T.l.c. (hexane) showed that addition of iodine azide was still taking place slowly after 24 h. Work-up gave a pale yellow solid (0.23 g) which was shown (n.m.r. analysis) to contain iodo-azide adducts (33%) and starting material (66%). P.l.c. gave (decreasing  $R_F$  values) (i) a mixture (25%) of **2 $\beta$ -azido-3 $\alpha$ -iodo-5 $\alpha$ -cholestane** (13) and **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -cholestane** (14), which crystallized from methanol-ether as plates, m.p. 71–74° [lit.,<sup>5</sup> 102–103° for (13)] (Found: C, 60.1; H, 8.5; N, 8.2. Calc. for  $C_{27}H_{46}IN_3$ : C, 60.1; H, 8.6; N, 7.8%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.66 (s, 18- $H_3$ ), 0.93 (s, 19- $H_3$ ), 0.90, 0.93, and 0.99 (3  $\times$  Me), 4.13 (m,  $W_{\frac{1}{2}}$  9 Hz), and 4.54 (m,  $W_{\frac{1}{2}}$  7 Hz); and (ii) **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -cholestane** (17) (8%), which crystallized from methanol as needles, m.p. 136.5–139° (Found: C, 60.0; H, 8.6; N, 7.9.  $C_{27}H_{46}IN_3$  requires C, 60.1; H, 8.6; N, 7.8%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.83, 0.93, and 0.93 (3  $\times$  Me), 4.10 (m,  $W_{\frac{1}{2}}$  8 Hz, CHN), and 4.57 (m,  $W_{\frac{1}{2}}$  21 Hz, CHI).

**Reaction of 5 $\alpha$ -Cholest-2-ene with Thallium(I) Azide and Iodine.**—A solution of iodine (0.25 g, 1.0 mmol) in dichloromethane (10 ml) was added dropwise over 48 h to a stirred suspension of thallium(I) azide (0.49 g, 2.0 mmol) in a solution of 5 $\alpha$ -cholest-2-ene (0.37 g, 1.0 mmol) in dichloromethane (20 ml). The mixture was stirred for 18 h and worked up to give a product which was chromatographed

on neutral alumina. Elution with hexane gave starting material (60 mg) and a 2 : 1 mixture of iodo-azide adducts (0.36 g, 82%), which were separated by p.l.c. (hexane) into (i) a mixture of **2 $\beta$ -azido-3 $\alpha$ -iodo-5 $\alpha$ -cholestane** (13) and **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -cholestane** (14); and (ii) **3 $\alpha$ -azido-2 $\beta$ -iodo-5 $\alpha$ -cholestane** (17).

Repetition of the experiment in acetonitrile-ether (1 : 1) gave identical products.

**Reaction of Phyllocladene with Sodium Azide and Iodine Chloride.**—Phyllocladene (19) (0.54 g, 2.0 mmol) was added to a stirred mixture of sodium azide (0.32 g, 5.0 mmol) and iodine chloride (0.26 g, 2.2 mmol) in acetonitrile-ether (1 : 1; 20 ml) at 0 °C. The mixture was warmed slowly to 20 °C and stirred for 24 h. Work-up and chromatography gave **16 $\alpha$ -azido-17-iodo-13 $\beta$ -kaurane** (20) (0.87 g, 98%), which crystallized from chloroform-pentane as needles, m.p. 170–172° (decomp.) (Found: C, 54.6; H, 7.4; I, 28.2; N, 9.3.  $C_{20}H_{32}IN_3$  requires C, 54.4; H, 7.3; I, 28.8; N, 9.5%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.80 (s, 10-Me), 0.86 and 0.90 (2s, *gem*-Me<sub>2</sub>), and 3.40 and 3.48 (2d, *J*<sub>gem</sub> 11 Hz, 17- $H_2$ ).

**Reaction of Isophyllocladene with Sodium Azide and Iodine Chloride.**—Isophyllocladene (24) (0.82 g, 3.0 mmol), sodium azide (0.32 g, 5.0 mmol), and iodine chloride (0.26 g, 2.2 mmol) were treated as above in acetonitrile-ether (1 : 1; 50 ml) for 24 h. Work-up gave an oil (0.69 g) containing two major components, and starting material, in the ratio 6 : 6 : 1. Two other compounds were present in trace amounts. P.l.c. (hexane) gave (decreasing  $R_F$  values) (i) **15 $\beta$ -azido-16 $\alpha$ -iodo-13 $\beta$ -kaurane** (21), which crystallized from methanol-ether as needles, m.p. 130–133° (decomp.) (Found: C, 54.9; H, 7.4; N, 9.4.  $C_{20}H_{32}IN_3$  requires C, 54.4; H, 7.3; N, 9.5%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.80 and 0.82 (2s, *gem*-Me<sub>2</sub>), 0.93 (s, 10-Me), 2.21 (s, 16-Me), and 3.09 (s, 15 $\alpha$ -H); (ii) a trace of **17-azido-13 $\beta$ -kaur-15-ene** (25) as an oil from the mother liquors of (21),  $\delta$  0.80 and 0.84 (2s, 10-Me and *gem*-Me<sub>2</sub>), 3.71 (d, *J* 0.5 Hz, 17- $H_2$ ), and 5.61 (s, 15-H); (iii) **16 $\beta$ -azido-15 $\alpha$ -iodo-13 $\beta$ -kaurane** (22), which crystallized from chloroform-pentane as needles, m.p. 165–168° (Found: C, 55.0; H, 7.3; N, 9.4.  $C_{20}H_{32}IN_3$  requires C, 54.4; H, 7.3; N, 9.5%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.85 (s, 10-Me and *gem*-Me<sub>2</sub>), 1.38 (s, 16-Me), and 3.46 (s, 15 $\beta$ -H); and (iv) a trace of **15 $\beta$ ,17-diazido-16 $\alpha$ -iodo-13 $\beta$ -kaurane**, which crystallized from methanol-ether as needles, m.p. 125° (decomp.; gas evolution) (Found: C, 50.3; H, 6.6; N, 16.8.  $C_{20}H_{31}IN_6$  requires C, 49.8; H, 6.3; N, 17.4%),  $\nu_{\max}$  2 100  $cm^{-1}$  ( $N_3$ ),  $\delta$  0.81 and 0.84 (2s, *gem*-Me<sub>2</sub>), 0.93 (s, 10-Me), 3.20 (s, 15 $\alpha$ -H), and 3.86 (s, 17- $H_2$ ), *m/e* 482 ( $M^+$ ) (<0.5%), 327 ( $M^+ - IN_2$ ) (84%), 313 ( $M^+ - IN_3$ ) (11%), 299 ( $M^+ - IN_4$ ) (30%), and 69 (100%).

**Reaction of Labd-8(17)-en-13-ol with Thallium(I) Acetate and Iodine.**—A solution of iodine (0.48 g, 1.87 mmol) in dichloromethane (10 ml) was added to a stirred suspension of thallium(I) acetate (0.74 g, 2.80 mmol) in a solution of labd-8(17)-en-13-ol<sup>22</sup> (26) (0.55 g, 1.90 mmol) in dichloromethane (15 ml). The mixture was stirred at 20 °C for 24 h, thallium(I) iodide was removed, and the mixture was worked up in the usual manner.<sup>2</sup> P.l.c. (chloroform) gave **8,13-epoxy-17-iodolabdan** (27) (0.19 g) and **17-acetoxy-labd-8-en-13-ol** (29) (0.17 g), each identified by comparison with an authentic sample.<sup>22</sup>

**Reaction of Labd-8(17)-en-13-ol with Sodium Azide and Iodine Chloride.**—Labd-8(17)-en-13-ol (0.29 g, 1.0 mmol) was treated with sodium azide and iodine chloride as

described above. Three major products were isolated by p.l.c. (chloroform) and identified by n.m.r. and i.r. spectra as (i) 8-azido-17-iodolabdan-13-ol (28), obtained as an oil,  $\nu_{\text{max.}}$  2 100  $\text{cm}^{-1}$  ( $\text{N}_3$ ),  $\delta$  0.69—1.17 ( $5 \times \text{Me}$ ), and 3.68 (q,

$J$  6 Hz, long-range coupling  $J$  2 Hz, 17- $\text{H}_2$ ); (ii) starting material; and (iii) 8,13-epoxy-17-iodolabdane (27).

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