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Assessment of Double-Barrelled Heck Cyclizations as a Means for Construction of the 14-Phenyl-8,9-dihydro-6H-[1]benzopyrano[4',3':4,5]pyrrolo[2,1-a]isoquinolin-6-one Core Associated with Certain Members of the Lamellarin Class of Marine Natural Product<sup>†</sup>

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The 1,2,4-trisubstituted pyrrole (4), which is readily prepared from pyrrole itself, undergoes doublebarrelled Heck cyclizations to give, *inter alia*, compounds (3) and (17) for which crystal structures have been determined. Product (3) constitutes the core associated with several key members, e.g. (1) and (2), of the lamellarin class of marine alkaloid.

#### Introduction

Lamellarins K  $(1)^1$  and N  $(2)^1$  are representative members of a small group of alkaloids that possess the hexacyclic framework (3)‡ (Scheme 1).§ A number of these natural products, which have been isolated from a diverse range of marine organisms, show some rather interesting biological activities. For example, lamellarin N (2) has been identified<sup>4</sup> as a type IV spindle toxin while the tri-*O*-acetyl derivative of congener (1) shows remarkable selectivity against the A549 human lung cancer cell line (IC<sub>50</sub> 0.005 mg/ml).<sup>5</sup> Furthermore, like a number of other lamellarins, compound (1) reverses multidrug resistance in certain cell lines by inhibiting P-glycoprotein mediated drug efflux and does so at non-cytotoxic concentrations.<sup>5</sup> In this regard, lamellarin K is even more effective than verapamil and, thus, has considerable potential for resensitizing cancer cells to various chemotherapeutic agents.<sup>5</sup>

Comprehensive investigations of the therapeutic potential of compounds such as (1) and (2) require access to gram quantities of material and the natural sources are unlikely to be useful in this regard. Consequently, several groups<sup>6–8</sup> have focused on developing total syntheses of various of the lamellarins as well as certain related compounds. We have recently disclosed<sup>9</sup> the first total synthesis of lamellarin K which involved, as the pivotal step, addition of an azomethine ylide to



† The work described herein is the subject of a patent application (AIPO Patent Office Provisional Application No. PP 4333/98, lodged 24 November 1998).

 $\ddagger 14-Phenyl-8,9-dihydro-6H-[1] benzopyrano [4',3':4,5] pyrrolo [2,1-a] isoquinolin-6-one.$ 

§ For other members of the lamellarin class which possess this or the corresponding fully unsaturated framework, see refs 1,2. A number of lamellarins possessing simpler frameworks have been isolated (Urban *et al.*<sup>3</sup>), and some of these have been synthesized (Banwell *et al.*<sup>3</sup>).

a tolan triple bond that are tethered to one another via an ester linkage. This reaction resulted in construction of the pyrrole core at a very late stage in the overall synthesis. Herein, we report on the almost exact opposite of this approach wherein the pyrrole core is in place at the start of the synthesis and the remainder of the lamellarin framework, as embodied in compound (3), is built around this core by using Negishi and double-barrelled Heck-type reactions to establish key carbon–carbon bonds.

#### **Results and Discussion**

#### (a) Retrosynthetic Analysis

The intramolecular Heck-type reactions of aryl bromides tethered to other aromatic nuclei have provided a useful means for the construction of various biaryl linkages including those observed in a number of natural products.<sup>10</sup> The seminal contributions of Bringmann and coworkers in this area<sup>11</sup> serve to highlight the utility of this strategy and prompted us to consider such an approach for construction of the title framework. In particular, we envisaged (Scheme 1) that the C13a/C13b and C14a/C14b bonds within compound (3) could be installed concurrently via double-barrelled intramolecular Heck reactions involving a substrate such as (4). During the course of the present study Steglich and coworkers reported<sup>6</sup> a novel variant on the intramolecular Heck reaction which they used to establish the C13a/C13b bond of lamellarin G trimethyl ether. However, to the best of our knowledge the double-barrelled Heck reaction sequence outlined above has not been employed for the construction of the title framework.

#### (b) Construction of Cyclization Substrate (4)

The synthetic sequence leading to the cyclization substrate (4) is shown in Scheme 2 and its implementation proved to be a relatively straightforward matter. Thus, following the procedure defined by Bailey et al.<sup>12</sup> pyrrole (5) was reacted with trichloroacetyl chloride. The resulting 2-substituted pyrrole (6) (80%)was treated with molecular iodine in the presence of silver trifluoroacetate and the 4-iodinated product  $(7)^{13}$  (82%) thereby obtained was hydrolysed with potassium carbonate in aqueous dimethyl sulfoxide to give the previously unreported acid (8) (92%). The corresponding acid chloride (9) was readily prepared by standard methods and reacted with o-bromophenol (10) to give the expected ester (11) in 92% yield [from (8)]. Treatment of this last compound with tosylate (13), derived by standard methods from the commercially available alcohol (12), resulted in alkylation at nitrogen and formation of the trisubstituted pyrrole (14) (89%) which contains the two tethered aryl bromide units required for the projected double-barrelled Heck cyclization studies. However, prior to conducting such studies compound (14) was subjected to a Negishi cross-coupling reaction<sup>14</sup> with phenylzinc chloride (15) at 18°C and in this manner the desired substrate (4) was obtained in 95% yield. There were no complications associated with coupling between organometallic (15) and the brominated carbon centres within compound (14), and this result is testimony to the impressive chemoselectivity usually encountered with the Negishi cross-coupling reaction. The proposed structures of compound (4) and all of its precursors were supported by the acquisition of the usual range of spectral data and substantiated through the X-ray crystallographic studies (see below) of the products derived from the foreshadowed Heck cyclization reactions.



#### (c) Cyclization Studies

Heck cyclization reactions of the type being contemplated here (Scheme 1) are usually carried out at elevated temperatures, often with dimethylformamide as solvent and with sodium acetate as the base.<sup>10,11</sup> The active Pd<sup>0</sup> species is generated *in situ* from palladium(II) acetate and triphenylphosphine. When such conditions were applied to substrate (4) and reaction temperatures of 135°C were employed (Scheme 3) then, after 6 h, the only isolable species was the desired double-barrelled cyclization product (3) although this was obtained in rather low (16%) yield. In the 70 eV electron impact mass spectrum of compound (3) the expected molecular ion was observed at m/z 363 but convincing spectroscopic characterization of this material could not be obtained because the <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra were rather non-descript. Consequently, a single-crystal X-ray analysis of compound (3) was undertaken (Fig. 1 and Tables 1–3) in order to provide rigorous proof of structure. The poor yields obtained when the conversion  $(4) \rightarrow (3)$  was run under the conditions defined above prompted an examination of the effects of lower reaction temperatures. However, when substrate (4) was reacted at  $110^{\circ}$ C for 19 h the target compound was not observed, rather the monocyclized materials (16) and (17) were obtained in yields of 17% and 8.5%, respectively. The structure of product (17) follows from an X-ray crystallographic study (Fig. 2 and Tables 4–6) while the structure of compound (16) derives from <sup>1</sup>H n.m.r. spectroscopic analysis. In particular, the upfield shift of the resonances due to the methylene protons at C9<sup> $\dagger$ </sup> ( $\delta$  3.05) relative to those of their counterparts in precursor (4)  $(\delta \ 3.32)$  is taken as a reflection of the loss of the bromine substituent in an ortho-relationship to the carbon bearing these protons. This, in turn, implies that the Heck reaction leading to compound (16) has involved formation of the  $C_{13a}/13b$  rather than the C14a/14b bond. Confirmation of these arguments follows from analysis of electron impact mass spectrum of compound (16) which reveals the presence of a fragment ion (base peak at m/z 272) corresponding to loss of an o-bromophenoxy radical from the molecular ion. This type of fragmentation process, which also features significantly in the mass spectra of the precursors to this compound, can be accommodated by structure (16) but not the alternate mono-Heck-type product derived from Pd<sup>0</sup>-mediated C14a/C14b bond closure within substrate (4). These results clearly suggest that Heck-type cyclization to form the C13a/C13bbond is more facile than the analogous process in which the C14a/C14b bond is produced. The rate of formation of the latter bond may be slowed by unfavourable rotamer populations about the 'doubly vinylogous' carbamate-type linkage within compounds such as (17) and/or poor orbital overlap associated with the 6-endo-trig-type ring closure that could be involved in converting this material into target (3)<sup>‡</sup>.

In an effort to improve the yield of compound (3) derived from precursor (4) several modifications to the standard conditions employed in Heck reactions were explored. For example, since various workers have shown<sup>15</sup> that the Heck reaction is promoted by the application of high pressures, a solution of



substrate (4) in 4:1 diethyl ether/tetrahydrofuran containing the much touted and readily prepared Herrmann–Beller catalyst<sup>16</sup> {trans-di( $\mu$ -acetato)bis[o-(di-o-tolylphosphino)benzyl]dipalladium(II)} was maintained at 15 kbar (1 bar =  $10^5$  Pa) and  $25^{\circ}$ C for Disappointingly, no reaction was observed 20 h. under these conditions. A related experiment using 1:3 tetrahydrofuran/acetonitrile as solvent and 10 kbar pressure was similarly unsuccessful. Use of the same catalyst under more conventional conditions (namely, dimethylformamide, sodium acetate, 130°C, 16 h) also failed to give any reaction. Similarly, the palladium carbene complexes Pd(dmiy)<sub>2</sub>MeCl and  $Pd(tmiy)_2(NC)_2C=C(CN)_2$ , which have recently been shown<sup>17</sup> to be especially effective catalysts for intermolecular Heck reactions, did not provide any useful conversion of compound (4) into (3) when used at elevated temperatures (110°C, N,N-dimethylacetamide, sodium acetate, 16 h) or pressures (15 kbar, 1:3 tetrahydrofuran/acetonitrile, triethylamine, 16 h). The Jeffrey<sup>18</sup> phase-transfer conditions for effecting Heck-type reactions were also investigated but no consumption of the substrate (4) was observed under these types of conditions. It has been reported<sup>19</sup> that when triphenylarsine, rather than triphenyphosphine, is used as a ligand for palladium in various coupling processes, including the Heck reaction,<sup>20</sup> then large rate accelerations can be observed. However, various efforts to apply such observations to the present case failed to provide a useful outcome. In fact the only other interesting reaction of compound (4) was observed when this material was

 $\dagger$  In order to facilitate structural comparisons, throughout the Results and Discussion section of this paper the lamellarin numbering scheme [see structure (3)] is used for compounds (1), (3), (4) and (16)–(19).



treated, in the presence of sodium acetate, with the Herrmann–Beller catalyst in N,N-dimethylacetamide at 115–140°C. Under these conditions (Scheme 3) a 1:3 mixture of compounds (18) and (19) (52% combined yield) was observed. In the 300 MHz <sup>1</sup>H n.m.r. spectrum of this mixture the resonances due to the three pyrrolic protons associated with compound (19) were readily discerned as were those due the vicinally related and mutually coupled protons attached to the five-membered ring within compound (18). The magnitude (J 2.7 Hz) of the spin–spin coupling

Table 1. Final fractional atomic coordinates and equivalent isotropic displacement factors (Å<sup>2</sup>) for (3),  $C_{25}H_{17}NO_2$ 

In Tables 1–6, estimated standard deviations are given in parentheses

$B_{eq} =$	$\frac{8}{3}\pi^2 [U_{11}(aa^*)^2 + U_{22}(bb^*)^2 +$
	$U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos\gamma +$
	$2U_{13}(aa^*cc^*)\cos\beta + 2U_{23}(bb^*cc^*)\cos\alpha]$

Atom	x	y	z	$B_{eq}$
O(5A)	-0.0947(2)	0.0979(3)	0.0482(1)	$3 \cdot 21(7)$
O(6A)	-0.0266(3)	0.0388(3)	0.1218(1)	3.67(8)
N(7A)	0.2294(3)	0.0860(3)	0.1065(1)	$2 \cdot 60(8)$
C(1A)	0.0432(4)	0.2297(4)	-0.0469(2)	$\frac{1}{3} \cdot 4(1)$
C(1'A)	0.3437(4)	0.2081(4)	0.0041(1)	2.8(1)
$C(2\Lambda)$	-0.0640(5)	0.2531(5)	-0.0790(2)	$\frac{2}{4.3(1)}$
$C(2'\Lambda)$	0.3411(4)	0.1512(4)	-0.0380(1)	3.2(1)
C(2A)	-0.1754(4)	0.1012(4) 0.2227(5)	-0.0689(2)	$\frac{3\cdot 2(1)}{4\cdot 3(1)}$
C(3'A)	0.4109(4)	0.1908(4)	-0.0710(1)	3.4(1)
C(4nA)	-0.0767(4)	0.1487(4)	0.0056(1)	3.1(1)
C(4aA)	-0.1830(4)	0.1705(4)	-0.0267(2)	3.0(1)
C(4II)	0.4862(4)	0.2884(4)	-0.0600(2)	3.3(1)
$C(5'\Lambda)$	0.4002(4)	0.3458(4)	-0.0175(2)	3.3(1)
$C(6 \times A)$	0.4903(4) 0.1902(4)	0.3408(4) 0.1005(4)	-0.0756(1)	2.6(1)
C(6A)	0.1202(4) 0.0017(4)	0.1003(4) 0.0758(4)	0.0850(1)	2.0(1)
C(6'A)	0.0017(4) 0.4101(4)	0.0738(4) 0.2070(4)	0.0639(2) 0.0142(1)	3.0(1) 2.1(1)
C(0 A)	0.4191(4) 0.2501(4)	0.3070(4)	0.0143(1) 0.1527(1)	$3 \cdot 1(1)$ $2 \cdot 2(1)$
C(0A)	0.2501(4) 0.2580(4)	0.0304(4)	0.1337(1) 0.1841(1)	$\frac{3 \cdot 2(1)}{2 \cdot 2(1)}$
C(9A)	0.3369(4) 0.4687(4)	0.0899(4)	0.1641(1) 0.1605(1)	$3 \cdot 2(1)$
C(9aA)	0.4007(4)	0.0892(4) 0.0715(4)	0.1000(1)	$\frac{2.8(1)}{2.9(1)}$
C(10A)	0.3837(4)	0.0713(4) 0.0750(4)	0.1640(2)	$3 \cdot 2(1)$
C(11A)	0.0800(4)	0.0759(4)	0.1042(2) 0.1158(2)	$3 \cdot 3(1)$
C(12A)	0.0702(4)	0.0955(4)	0.1138(2)	3.4(1)
C(13A)	0.3530(4)	0.1099(4)	0.0894(2)	$3 \cdot 2(1)$
C(13aA)	0.4500(4)	0.1082(4)	$0 \cdot 1111(1)$	$2 \cdot i(1)$
C(13DA)	0.3240(4)	0.1213(4)	0.0848(1)	$2 \cdot 6(1)$
C(14A)	$0 \cdot 2734(4)$	0.1604(4)	0.0390(1)	$2 \cdot 6(1)$
C(14aA)	0.1444(4)	0.1465(4) 0.1751(4)	0.0337(1)	$2 \cdot 5(1)$
C(14bA)	0.0394(4)	0.1751(4)	-0.0035(1)	$2 \cdot 9(1)$
C(1B)	-0.2769(4)	0.2287(4)	0.2894(1)	$3 \cdot 0(1)$
C(TB)	-0.0265(3)	0.2851(4)	0.2448(1)	$2 \cdot 7(1)$
C(2B)	-0.3541(4)	0.1860(4)	0.3180(1)	$3 \cdot 5(1)$
C(2 B)	0.0114(4)	0.3434(4)	0.2879(1)	$3 \cdot 1(1)$
C(3B)	-0.4769(4)	0.2180(4)	0.3102(2)	$3 \cdot 7(1)$
C(3 B)	0.1102(4)	0.3023(4)	0.3206(1)	$3 \cdot 3(1)$
C(4aB)	-0.4484(4)	0.3252(4)	0.2419(1)	$2 \cdot 8(1)$
C(4B)	-0.5260(4)	0.2881(4)	0.2717(2)	$3 \cdot 3(1)$
C(4 B)	0.1731(4)	0.2041(4)	0.3110(2)	$3 \cdot 3(1)$
O(5B)	-0.5076(2)	0.3874(3)	0.2017(1)	$3 \cdot 29(8)$
C(5 B)	0.1360(4)	0.1441(4)	0.2682(2) 0.1725(1)	$3 \cdot 5(1)$
C(6aB)	-0.3216(4)	0.3895(4)	0.1735(1)	$2 \cdot 5(1)$
O(6B)	-0.5129(3)	0.4589(3)	0.1295(1)	3.67(8)
C(6B)	-0.4491(4)	0.4142(4)	0.1643(1)	$2 \cdot 8(1)$
C(6, B)	0.0359(4)	0.1844(4)	0.2354(1)	$3 \cdot 0(1)$
N(7B)	-0.2422(3)	0.4087(3)	0.1427(1)	$2 \cdot 63(8)$
C(8B)	-0.2696(4)	0.4604(4)	0.0948(1)	$3 \cdot 1(1)$
C(9B)	-0.1885(4)	0.4010(4)	0.0655(2)	$3 \cdot 7(1)$
C(9aB)	-0.0557(4)	0.4037(4)	0.0894(2)	$3 \cdot 2(1)$
C(10B)	0.0384(5)	0.4189(4)	0.0640(2)	$4 \cdot 0(1)$
C(11B)	0.1890(4)	0.4209(4)	0.0867(2)	$4 \cdot 4(1)$
C(12B)	0.1889(4)	0.4094(4)	0.1355(2)	$4 \cdot 3(1)$
O(13B)	0.0972(4)	0.3960(4)	0.1613(2)	$3 \cdot 6(1)$
O(13aB)	-0.0252(4)	0.3910(4)	0.1389(2)	$2 \cdot 9(1)$
O(13DB)	-0.1265(4)	0.3739(4)	0.1642(1)	$2 \cdot 6(1)$
O(14B)	-0.1314(4)	0.3306(4)	0.2094(1)	$2 \cdot 7(1)$
O(14aB)	-0.2553(3)	0.3398(4)	0.2145(1)	$2 \cdot 46(9)$
C(14bB)	-0.3239(4)	0.3001(4)	0.2501(1)	$2 \cdot 6(1)$

between the latter protons supports the illustrated structure for compound (18) but not the isomeric one in which the phenyl substituent is attached at C 14a. Further confirmation of the gross structures assigned to compounds (18) and (19) followed from g.l.c./m.s. studies which revealed that the chromatographically more mobile compound [(18)] has a molecular ion at m/z 245 while the other [(19)] has a pair of equal intensity molecular ions at m/z 327 and 325. However, additional characterization of these compounds was not undertaken because of their instabilities and our inability to readily separate them on a preparative scale.



Fig. 1. ORTEP derived from X-ray crystallographic structure analysis of compound (3).

Table 2. Bond lengths (Å) for (3), C<sub>25</sub>H<sub>17</sub>NO<sub>2</sub>

Atoms	Distance	Atoms	Distance
O(5A)-C(4aA)	1.398(5)	O(5A)-C(6A)	$1 \cdot 390(5)$
O(6A) - C(6A)	$1 \cdot 208(5)$	N(7A) - C(6aA)	$1 \cdot 366(5)$
N(7A) - C(8A)	$1 \cdot 472(5)$	N(7A) - C(13bA)	$1 \cdot 375(5)$
C(1A)-C(2A)	$1 \cdot 382(6)$	C(1A)-C(14bA)	$1 \cdot 398(6)$
C(1'A) - C(2'A)	1.388(5)	$\hat{C(1'A)} - \hat{C(6'A)}$	$1 \cdot 393(6)$
C(1'A) - C(14A)	$1 \cdot 480(5)$	C(2A) - C(3A)	$1 \cdot 364(7)$
C(2'A) - C(3'A)	1.383(6)	C(3A)-C(4A)	$1 \cdot 367(6)$
C(3'A)-C(4'A)	1.384(6)	C(4aA)-C(4A)	$1 \cdot 382(6)$
C(4aA)-C(14bA)	1.390(5)	C(4'A)-C(5'A)	$1 \cdot 376(6)$
C(5'A)-C(6'A)	$1 \cdot 384(6)$	C(6aA)-C(6A)	$1 \cdot 424(5)$
C(6aA)-C(14aA)	1.381(5)	C(8A)-C(9A)	$1 \cdot 504(6)$
C(9A)-C(9aA)	$1 \cdot 497(6)$	C(9aA)-C(10A)	$1 \cdot 376(5)$
C(9aA)-C(13aA)	$1 \cdot 410(5)$	C(10A)-C(11A)	$1 \cdot 381(6)$
C(11A)-C(12A)	$1 \cdot 384(6)$	C(12A)-C(13A)	$1 \cdot 381(6)$
C(13A)-C(13aA)	$1 \cdot 398(5)$	C(13aA)-C(13bA)	$1 \cdot 463(5)$
C(13bA)-C(14A)	$1 \cdot 398(5)$	C(14A)-C(14aA)	$1 \cdot 416(5)$
C(14aA)-C(14bA)	$1 \cdot 459(5)$	C(1B)-C(2B)	$1 \cdot 379(6)$
C(1B)-C(14bB)	$1 \cdot 403(6)$	C(1'B)-C(2'B)	$1 \cdot 395(5)$
C(1'B)-C(6'B)	$1 \cdot 385(5)$	C(1'B)-C(14B)	$1 \cdot 482(5)$
C(2B)-C(3B)	$1 \cdot 383(6)$	C(2'B)-C(3'B)	$1 \cdot 379(6)$
C(3B)-C(4B)	$1 \cdot 384(6)$	C(3'B)-C(4'B)	$1 \cdot 366(6)$
C(4aB)-C(4B)	1.386(5)	C(4aB)-O(5B)	$1 \cdot 402(5)$
C(4aB)-C(14bB)	$1 \cdot 383(5)$	C(4'B)-C(5'B)	$1 \cdot 395(6)$
O(5B)-C(6B)	1.388(5)	C(5'B)-C(6'B)	$1 \cdot 388(6)$
C(6aB)-C(6B)	$1 \cdot 413(5)$	C(6aB)-N(7B)	$1 \cdot 376(5)$
C(6aB)-C(14aB)	$1 \cdot 383(5)$	${ m O(6B)-C(6B)}$	$1 \cdot 218(5)$
N(7B)-C(8B)	$1 \cdot 471(5)$	N(7B)-C(13bB)	$1 \cdot 370(5)$
C(8B)-C(9B)	$1 \cdot 499(6)$	C(9B)-C(9aB)	$1 \cdot 499(6)$
C(9aB)-C(10B)	$1 \cdot 390(6)$	C(9aB)-C(13aB)	$1 \cdot 405(6)$
C(10B)-C(11B)	$1 \cdot 374(6)$	C(11B)-C(12B)	$1 \cdot 383(6)$
C(12B)-C(13B)	$1 \cdot 373(6)$	C(13B)-C(13aB)	$1 \cdot 386(6)$
C(13aB)-C(13bB)	$1 \cdot 457(5)$	C(13bB)-C(14B)	$1 \cdot 398(5)$
C(14B)-C(14aB)	$1 \cdot 409(5)$	C(14aB)-C(14bB)	$1 \cdot 455(5)$

The formation of compound (18) can be rationalized by invoking initial conversion of precursor (4) into compound (17) which experiences extrusion of benzyne and concomitant migration of palladium from carbon to oxygen with the resulting formation of a palladium(II) carboxylate. Like other metal salts of pyrrole-2-carboxylic acids,<sup>21</sup> this latter species might be expected to undergo thermally promoted decarboxylation so as to give, after protonation, product (18). It is also conceivable that the above-mentioned palladium(II) carboxylate could be generated by simple hydrolysis of the ester linkage within a compound such as (16). Clearly, the production of compound (19) would likely involve the same sorts of reactions (except for the initial Heck process) as suggested above to account for the formation of co-product (18).

#### Conclusion

The work described herein suggests that the title reactions could provide a useful and rapid means for assembling the hexacyclic framework associated with certain members of the lamellarin class of marine natural product. Indeed, the synthetic sequence leading to the cyclization precursor (4) is an especially efficient one and should be capable of ready adaptation to the construction of highly oxygenated analogues as would be required for synthesis of the lamellarins themselves. However, the modest yields associated with the pivotal

Table 3. Bond angles (degrees) for (3), C<sub>25</sub>H<sub>17</sub>NO<sub>2</sub>

Atoms	Angle	Atoms	Angle
C(4aA)-O(5A)-C(6A)	$122 \cdot 6(3)$	C(6aA)-N(7A)-C(8A)	$127 \cdot 9(3)$
C(6aA)-N(7A)-C(13bA)	$109 \cdot 0(3)$	C(8A)-N(7A)-C(13bA)	$122 \cdot 8(3)$
C(2A)-C(1A)-C(14bA)	$120 \cdot 8(4)$	$\dot{C}(2'A) - \dot{C}(1'A) - \dot{C}(6'A)$	$118 \cdot 0(4)$
$\dot{C}(2'A) - \dot{C}(1'A) - \dot{C}(14A)$	120.5(4)	C(6'A) - C(1'A) - C(14A)	$121 \cdot 5(4)$
C(1A) - C(2A) - C(3A)	$120 \cdot 4(5)$	C(1'A) - C(2'A) - C(3'A)	$121 \cdot 4(4)$
C(2A) - C(3A) - C(4A)	$121 \cdot 0(4)$	C(2'A) - C(3'A) - C(4'A)	119.7(4)
O(5A) - C(4aA) - C(4A)	$114 \cdot 4(4)$	O(5A) - C(4aA) - C(14bA)	$122 \cdot 8(4)$
C(4A)-C(4aA)-C(14bA)	$122 \cdot 8(4)$	C(3A)-C(4A)-C(4aA)	$118 \cdot 5(4)$
C(3'A) - C(4'A) - C(5'A)	119.7(4)	$\dot{C}(4'A) - \dot{C}(5'A) - \dot{C}(6'A)$	$120 \cdot 4(4)$
N(7A) - C(6aA) - C(6A)	$125 \cdot 2(4)$	N(7A) - C(6aA) - C(14aA)	$108 \cdot 5(4)$
C(6A)-C(6aA)-C(14aA)	$126 \cdot 3(4)$	O(5A) - C(6A) - O(6A)	$116 \cdot 2(4)$
O(5A)-C(6A)-C(6aA)	$113 \cdot 8(4)$	O(6A) - C(6A) - C(6aA)	$129 \cdot 9(4)$
C(1'A) - C(6'A) - C(5'A)	120.7(4)	N(7A) - C(8A) - C(9A)	$108 \cdot 0(3)$
C(8A)-C(9A)-C(9aA)	$111 \cdot 4(4)$	C(9A) - C(9aA) - C(10A)	$121 \cdot 6(4)$
C(9A)-C(9aA)-C(13aA)	$118 \cdot 4(4)$	$\dot{C(10A)}$ - $\dot{C}(9aA)$ - $\dot{C}(13aA)$	$120 \cdot 1(4)$
$\dot{C}(9aA) - \dot{C}(10A) - \dot{C}(11A)$	$120 \cdot 9(4)$	C(10A)-C(11A)-C(12A)	$119 \cdot 8(4)$
$\dot{C(11A)} - \dot{C(12A)} - \dot{C(13A)}$	$120 \cdot 0(4)$	$\dot{C(12A)}$ - $\dot{C(13A)}$ - $\dot{C(13aA)}$	$120 \cdot 9(4)$
C(9aA) - C(13aA) - C(13A)	$118 \cdot 2(4)$	C(9aA) - C(13aA) - C(13bA)	$118 \cdot 6(4)$
C(13A)-C(13aA)-C(13bA)	$123 \cdot 1(4)$	$\dot{N(7A)}$ – $\dot{C(13bA)}$ – $\dot{C(13aA)}$	$118 \cdot 0(4)$
N(7A) - C(13bA) - C(14A)	$108 \cdot 3(3)$	C(13aA) - C(13bA) - C(14A)	$133 \cdot 7(4)$
C(1'A)-C(14A)-C(13bA)	$125 \cdot 6(4)$	C(1'A) - C(14A) - C(14aA)	$128 \cdot 1(4)$
C(13bA)-C(14A)-C(14aA)	$106 \cdot 3(3)$	C(6aA) - C(14aA) - C(14A)	$107 \cdot 9(3)$
C(6aA)-C(14aA)-C(14bA)	117.5(4)	C(14A)-C(14aA)-C(14bA)	$134 \cdot 5(4)$
C(1A)-C(14bA)-C(4aA)	$116 \cdot 6(4)$	C(1A)-C(14bA)-C(14aA)	$126 \cdot 6(4)$
$\dot{C}(4aA) - \dot{C}(14bA) - \dot{C}(14aA)$	$116 \cdot 8(4)$	C(2B) - C(1B) - C(14bB)	$120 \cdot 2(4)$
C(2'B) - C(1'B) - C(6'B)	118.9(4)	$\dot{C}(2'\dot{B}) - \dot{C}(1'\dot{B}) - \dot{C}(14\dot{B})$	$120 \cdot 6(4)$
C(6'B) - C(1'B) - C(14B)	120.5(4)	C(1B)-C(2B)-C(3B)	$120 \cdot 8(4)$
C(1'B) - C(2'B) - C(3'B)	120.7(4)	C(2B) - C(3B) - C(4B)	$120 \cdot 3(4)$
C(2'B) - C(3'B) - C(4'B)	$120 \cdot 4(4)$	$\dot{C}(4B) - \dot{C}(4aB) - \dot{O}(5B)$	$114 \cdot 3(4)$
C(4B)-C(4aB)-C(14bB)	$123 \cdot 1(4)$	O(5B)-C(4aB)-C(14bB)	$122 \cdot 6(4)$
C(3B)-C(4B)-C(4aB)	118.0(4)	C(3'B) - C(4'B) - C(5'B)	$119 \cdot 8(4)$
$\dot{C}(4aB) - \dot{O}(5B) - \dot{C}(6B)$	$122 \cdot 2(3)$	C(4'B) - C(5'B) - C(6'B)	$120 \cdot 0(4)$
C(6B)-C(6aB)-N(7B)	$125 \cdot 7(4)$	C(6B)-C(6aB)-C(14aB)	$126 \cdot 2(4)$
N(7B)-C(6aB)-C(14aB)	$108 \cdot 1(3)$	O(5B)-C(6B)-C(6aB)	$114 \cdot 0(4)$
O(5B) - C(6B) - O(6B)	$116 \cdot 3(4)$	C(6aB) - C(6B) - O(6B)	$129 \cdot 7(4)$
$\dot{C(1'B)} - \dot{C(6'B)} - \dot{C(5'B)}$	$120 \cdot 2(4)$	C(6aB) - N(7B) - C(8B)	$128 \cdot 3(3)$
C(6aB)-N(7B)-C(13bB)	$108 \cdot 7(3)$	C(8B) - N(7B) - C(13bB)	$123 \cdot 0(3)$
N(7B) - C(8B) - C(9B)	$107 \cdot 8(4)$	C(8B) - C(9B) - C(9aB)	$111 \cdot 9(4)$
C(9B) - C(9aB) - C(10B)	$122 \cdot 0(4)$	C(9B)-C(9aB)-C(13aB)	$119 \cdot 2(4)$
C(10B)-C(9aB)-C(13aB)	$118 \cdot 9(4)$	C(9aB) - C(10B) - C(11B)	$121 \cdot 0(5)$
C(10B) - C(11B) - C(12B)	$119 \cdot 9(4)$	C(11B) - C(12B) - C(13B)	$120 \cdot 1(4)$
C(12B) - C(13B) - C(13aB)	120.7(5)	C(9aB) - C(13aB) - C(13B)	$119 \cdot 4(4)$
$\dot{C(9aB)} - \dot{C(13aB)} - \dot{C(13bB)}$	$117 \cdot 2(4)$	$\dot{C(13B)} - \dot{C(13aB)} - \dot{C(13bB)}$	$123 \cdot 4(4)$
N(7B)-C(13bB)-C(13aB)	$118 \cdot 6(4)$	N(7B) - C(13bB) - C(14B)	$108 \cdot 7(3)$
C(13aB) - C(13bB) - C(14B)	$132 \cdot 6(4)$	$\dot{C(1'B)} - \dot{C(14B)} - \dot{C(13bB)}$	$126 \cdot 5(4)$
C(1'B) - C(14B) - C(14aB)	$127 \cdot 2(4)$	$\dot{C(13bB)}$ - $\dot{C}(14B)$ - $\dot{C}(14aB)$	$106 \cdot 3(3)$
$\dot{C(6aB)} - \dot{C(14aB)} - \dot{C(14B)}$	$108 \cdot 1(4)$	C(6aB) - C(14aB) - C(14bB)	$117 \cdot 4(4)$
$\dot{C(14B)} - \dot{C(14aB)} - \dot{C(14bB)}$	$134 \cdot 2(4)$	$\dot{C(1B)-C(14bB)-C(4aB)}$	117.5(4)
C(1B)-C(14bB)-C(14aB)	$125 \cdot 4(4)$	$\dot{C(4aB)}$ - $\dot{C}(14bB)$ - $\dot{C}(14aB)$	$116 \cdot 9(4)$

				U <sub>61</sub> Π <sub>48</sub> DrN	$0_2 P_2 P_4 . 0_4 \pi_{10}$	0			
Atom	x	y	z	$U_{\rm iso}$	Atom	x	y	z	$U_{\rm iso}$
Pd(1A)	0.7099(1)	$0 \cdot 2256(2)$	$0 \cdot 2219(1)$	0.035(0)	C(6B)	$0 \cdot 2609(10)$	-0.1096(18)	0.5656(3)	$0 \cdot 044(4)$
Br(1A)	0.7760(2)	0.2648(3)	$0 \cdot 1796(1)$	0.080(1)	O(6B)	$0 \cdot 2364(6)$	-0.1920(12)	0.5573(3)	0.048(4)
C1(4bA)	0.6579(9)	0.1970(6)	0.2556(6)	0.030(6)	C(6aB)	0.3171(9)	-0.1009(16)	0.5774(3)	0.046(4)
C(1A)	0.5655(9)	0.1907(11) 0.1701(14)	0.2419(6) 0.2661(7)	0.039(6) 0.046(7)	$\Gamma(B)$	0.3327(7)	-0.3037(14)	0.5810(3) 0.5736(4)	0.050(4)
C(2A) C(3A)	0.5851(10)	0.1761(14) 0.1560(11)	0.2001(7) 0.3048(7)	0.040(7) 0.042(6)	C(BB)	0.3399(7) 0.3899(7)	-0.3614(9)	0.5730(4) 0.5647(5)	0.000(4) 0.071(5)
C(4A)	0.6399(10)	0.1621(11)	0.3190(6)	0.040(6)	C(9aB)	0.4387(8)	-0.3398(7)	0.5877(5)	0.068(5)
C(4aA)	0.6747(10)	0.1822(9)	0.2945(6)	0.035(6)	C(10B)	0.4779(10)	-0.4169(16)	0.5963(6)	0.078(6)
O(5A)	0.7288(6)	0.1892(11)	0.3061(4)	0.038(4)	C(11B)	0.5255(9)	-0.3904(20)	0.6194(6)	0.074(7)
C(6A)	0.7512(10) 0.7241(6)	0.2533(13)	0.3345(5)	0.040(3)	C(12B) C(12P)	0.5343(8) 0.4056(7)	-0.2865(21)	0.6339(6)	0.064(6)
C(6aA)	0.7241(0) 0.8078(9)	0.3034(10) 0.2458(12)	0.3421(4)	0.042(3) 0.041(3)	C(13B) C(13aB)	0.4350(7) 0.4475(8)	-0.2351(15)	0.0230(3) 0.6024(3)	0.057(3) 0.057(4)
N(7A)	0.8410(7)	0.3025(11)	0.3697(4)	0.044(3)	C(13bB)	0.4045(8)	-0.1494(15)	0.5931(3)	0.052(4)
C(8A)	0.8243(9)	0.3816(15)	0.3967(6)	0.050(3)	C(14B)	0.4037(9)	-0.0352(16)	0.5976(3)	0.051(4)
C(9A)	0.8656(9)	0.3640(18)	0.4345(5)	0.053(3)	C(14aB)	0.3474(9)	-0.0094(17)	0.5873(3)	0.048(4)
C(9aA)	0.9202(9)	0.3577(11)	0.4336(4) 0.4627(5)	0.054(4)	C(TB)	0.4836(8)	0.0644(18) 0.1420(20)	0.5871(7)	0.089(11) 0.107(14)
C(10A) C(11A)	1.0120(9)	0.3839(14) 0.3839(15)	0.4627(3) 0.4601(6)	0.060(5)	C(2'B) C(3'B)	0.5232(9) 0.5272(10)	0.1430(20) 0.1983(21)	0.6315(6)	0.107(14) 0.112(14)
C(12A)	$1 \cdot 0278(8)$	0.3408(16)	0.4284(6)	0.056(5)	C(4'B)	0.4903(10)	0.1762(18)	0.6515(8)	0.097(11)
C(13A)	0.9901(7)	0.3059(14)	0.3991(5)	0.051(4)	C(5'B)	0.4481(9)	0.1002(17)	0.6423(7)	0.078(8)
C(13aA)	0.9361(8)	0.3143(10)	0.4017(5)	0.049(3)	C(6'B)	0.4465(9)	0.0457(15)	0.6093(4)	0.073(8)
C(13bA)	0.8941(8)	0.2760(13)	0.3694(5)	0.045(3)	P(1B)	$0 \cdot 2012(3)$	0.0219(5)	0.4507(2)	0.035(3)
C(14A) C(14aA)	0.8967(9) 0.8410(9)	0.1992(13) 0.1834(13)	0.3408(4) 0.3245(5)	0.043(3) 0.040(3)	C(15B) C(16B)	0.2543(4) 0.3022(4)	-0.0644(12)	0.4528(2) 0.4780(4)	0.039(3)
C(1'A)	0.9586(9)	0.0452(19)	0.3423(6)	0.093(6)	C(10D) C(17B)	0.3429(5)	-0.1403(15)	0.4795(5)	0.044(4) 0.054(7)
C(2'A)	1.0039(10)	0.0005(23)	0.3299(7)	0.137(15)	C(18B)	0.3367(6)	-0.2305(13)	0.4561(5)	0.059(10)
C(3'A)	$1 \cdot 0322(11)$	0.0472(21)	0.3073(6)	0.150(22)	C(19B)	0.2892(7)	-0.2439(11)	0.4311(5)	0.056(8)
C(4'A)	$1 \cdot 0155(9)$	0.1442(25)	0.2959(7)	0.140(19)	C(20B)	0.2484(6)	-0.1682(9)	0.4294(4)	0.045(4)
C(5'A) C(6'A)	0.9711(8) 0.9436(9)	0.2002(20) 0.1465(14)	0.3056(6) 0.3202(4)	0.096(8)	C(21B) C(22B)	0.1409(4) 0.0036(4)	-0.0572(7) -0.0289(12)	0.4498(2) 0.4259(4)	0.038(3) 0.043(4)
P(1A)	0.6913(3)	0.4111(6)	0.3232(4) 0.2274(2)	0.033(3)	C(22B) C(23B)	0.0330(4) 0.0475(4)	-0.0239(12) -0.0896(15)	0.4252(5)	0.043(4) 0.051(9)
C(15A)	0.7437(4)	0.4747(7)	0.2605(3)	0.040(3)	C(24B)	0.0474(6)	-0.1796(13)	0.4483(5)	0.054(12)
C(16A)	0.7944(4)	0.4276(13)	0.2690(5)	0.055(6)	C(25B)	0.0942(7)	-0.2083(11)	0.4722(5)	0.049(9)
C(17A)	0.8345(5)	0.4765(17)	0.2944(5)	0.075(10)	C(26B)	0.1404(6)	-0.1479(9)	0.4729(4)	0.042(4)
C(18A) C(10A)	0.8250(7) 0.7748(8)	0.5733(16) 0.6208(14)	0.3119(4) 0.3035(5)	0.067(10)	C(27B) C(28B)	0.1854(3) 0.1653(8)	0.1951(8)	0.4058(3) 0.4030(4)	0.041(3) 0.058(7)
C(13A) C(20A)	0.7345(6)	0.0208(14) 0.5722(11)	0.3035(3) 0.2782(4)	0.007(5) 0.050(5)	C(28B) C(29B)	0.1033(8) 0.1532(9)	0.1351(10) 0.2465(14)	0.3685(5)	0.033(1) 0.077(11)
$\dot{C(21A)}$	0.6293(4)	0.4354(6)	0.2442(2)	0.037(3)	C(30B)	0.1609(7)	0.1932(16)	0.3361(4)	0.075(13)
C(22A)	0.6268(6)	$0 \cdot 4267(13)$	$0 \cdot 2822(3)$	0.040(4)	C(31B)	0.1808(8)	0.0878(17)	$0 \cdot 3385(3)$	0.062(13)
C(23A)	0.5793(7)	0.4453(15)	0.2950(4)	0.048(7)	C(32B)	0.1930(7)	0.0362(12)	0.3730(3)	0.048(7)
C(24A) C(25A)	0.5353(6) 0.5354(4)	0.4730(13) 0.4818(16)	0.2702(5) 0.2323(5)	0.059(10)	P(2B) C(33B)	0.2210(3) 0.2826(4)	0.2855(5) 0.3154(6)	0.5446(2) 0.5761(3)	0.040(3) 0.044(3)
C(26A)	0.5828(4)	0.4613(14) 0.4633(14)	0.2323(0) 0.2194(4)	0.047(4)	C(34B)	0.3316(4)	0.2787(13)	0.5684(4)	0.049(3)
C(27A)	0.6820(3)	0.4890(7)	0.1844(3)	0.037(3)	C(35B)	0.3788(4)	0.3017(16)	0.5926(5)	0.060(5)
C(28A)	0.6889(7)	0.6018(8)	0.1851(4)	0.047(5)	C(36B)	0.3782(6)	0.3617(14)	0.6250(5)	0.068(8)
C(29A)	0.6818(8)	0.6614(11)	0.1521(4)	0.058(9)	C(37B)	0.3297(7)	0.3985(15)	0.6329(4)	0.061(7)
C(30A) C(31A)	0.6606(8)	0.0098(14) 0.4978(15)	0.1178(4) 0.1168(3)	0.059(7) 0.055(5)	C(30B)	0.2824(3) 0.1712(4)	0.3737(13) 0.2736(6)	0.0087(3) 0.5745(3)	0.030(4) 0.045(3)
C(32A)	0.6677(7)	0.4379(11)	0.1497(3)	0.044(3)	C(40B)	0.1712(1) 0.1775(7)	0.1990(12)	0.6040(4)	0.056(3)
P(2A)	0.7213(3)	0.0370(6)	$0 \cdot 2160(2)$	0.040(3)	C(41B)	0.1393(8)	0.1900(15)	0.6269(4)	0.072(5)
C(33A)	0.7865(4)	-0.0213(7)	0.2325(2)	0.043(3)	C(42B)	0.0940(7)	0.2553(15)	0.6208(5)	0.075(8)
C(34A)	0.8325(4)	0.0426(12)	0.2360(5)	0.052(5)	C(43B)	0.0874(6)	0.3298(16)	0.5916(6)	0.067(9)
C(36A)	0.8825(4) 0.8876(6)	-0.0023(10) -0.1117(15)	0.2480(3) 0.2581(4)	0.060(7) 0.060(6)	C(44B) C(45B)	0.1255(5) 0.2079(4)	0.3390(13) 0.4030(8)	0.5080(5) 0.5144(3)	0.033(3) 0.043(3)
C(37A)	0.8420(6)	-0.1759(13)	0.2546(5)	0.057(6)	C(46B)	0.2426(6)	0.4920(9)	0.5186(4)	0.046(4)
C(38A)	0.7920(5)	-0.1314(9)	0.2420(5)	0.049(5)	C(47B)	0.2325(8)	0.5820(10)	0.4954(5)	0.053(8)
C(39A)	0.6811(4)	-0.0559(7)	0.2381(3)	0.045(3)	C(48B)	0.1875(8)	0.5853(11)	0.4675(4)	0.060(10)
C(40A)	0.6906(7)	-0.0700(13) 0.1412(15)	0.2769(3)	0.054(4)	C(49B) C(50P)	0.1528(8) 0.1627(6)	0.4973(13) 0.4071(11)	0.4631(4)	0.060(8)
C(41A) C(42A)	0.0398(8) 0.6188(7)	-0.2000(12)	0.2938(3) 0.2724(6)	0.009(0) 0.074(9)	C(9B')	0.1027(0) 0.3809(9)	-0.3692(9)	0.4802(4) 0.6026(5)	0.051(4) 0.065(6)
C(43A)	0.6091(7)	-0.1865(13)	0.2338(6)	0.065(9)	C(9aB')	0.4350(10)	-0.3417(8)	0.6078(6)	0.064(5)
C(44A)	0.6398(5)	-0.1154(11)	0.2167(4)	0.051(5)	C(10B')	0.4749(13)	-0.4168(19)	0.6171(11)	0.074(7)
C(45A)	0.7051(4)	0.0096(6)	$0 \cdot 1662(3)$	0.044(3)	C(11B')	0.5279(12)	-0.3844(24)	0.6219(14)	0.073(7)
C(46A)	0.7381(6)	-0.0563(12)	0.1486(3)	0.051(5)	C(12B') C(12P')	0.5412(9)	-0.2764(26)	0.6175(13)	0.067(6)
C(47A) C(48A)	0.7230(8) 0.6801(8)	-0.0327(14)	0.1103(4) 0.0892(3)	0.068(11)	C(13B') C(13aB')	0.3018(7) 0.4484(8)	-0.2003(21) -0.2329(16)	0.0082(9) 0.6033(5)	0.051(3) 0.057(4)
C(49A)	0.6471(7)	0.0329(16)	0.1064(3)	0.063(9)	C(2)	0.4409(34)	0.1033(63)	0.4800(21)	0.447(32)
$\dot{C(50A)}$	0.6594(6)	0.0540(13)	$0 \cdot 1445(3)$	0.051(5)	$\dot{C(1)}$	0.4733(29)	0.1897(62)	0.4804(22)	0.447(32)
Pd(1B)	0.2175(1)	0.1460(2)	0.5002(1)	0.034(1)	O(1)	0.4584(23)	0.2843(44)	0.4937(14)	0.447(32)
Br(1B)	0.2884(2)	0.2354(3)	0.4708(1)	0.072(1)	C(1')	0.4521(28)	0.3863(59)	0.5026(23)	0.447(32)
C(14bB) C(1B)	0.1049(9) 0.1102(0)	0.0692(12) 0.0847(14)	0.5252(5) 0.5140(5)	0+036(8)	$C(2^{\circ})$ C(4)	0.4973(37) 1.0154(31)	0.4263(59) 0.0537(78)	0.0005(25) 0.1817(31)	0.447(32) 0.511(48)
C(2B)	0.0720(9)	0.0294(16)	0.5320(6)	0.044(8)	C(3)	0.9678(29)	0.0387(60)	0.1684(31)	0.511(48)
$\dot{C(3B)}$	0.0912(10)	-0.0424(15)	0.5618(6)	0.046(7)	O(2)	0.9459(21)	0.1360(54)	0.1578(20)	0.511(48)
C(4B)	0.1461(10)	-0.0590(14)	0.5734(6)	0.045(7)	C(3')	0.8974(30)	0.1391(64)	0.1374(29)	0.511(48)
C(4aB)	0.1813(10)	-0.0036(13)	0.5552(5)	0.040(7)	C(4')	0.8883(34)	0.2258(75)	0.1385(32)	0.511(48)
O(SB)	u∙⊿3əð(b)	-0.0133(11)	u∙əb4ə(3)	0.042(4)					

Table 4. Final fractional atomic coordinates and equivalent isotropic displacement factors  $(Å^2)$  for (17), Cent Has BrNOp Po Pd Ca Hap O

Table 5. Bond lengths (Å) for (17),  $C_{61}H_{48}BrNO_2P_2Pd.C_4H_{10}O$ 

Atoms	Distance	Atoms	Distance		
Molecule	e A	Molecule	Molecule B		
Pd(1) - Br(1)	$2 \cdot 503(4)$	Pd(1)– $Br(1)$	$2 \cdot 498(4)$		
Pd(1)-C(14b)	1.978(20)	Pd(1)-C(14b)	1.978(20)		
Pd(1) - P(1)	$2 \cdot 340(7)$	Pd(1) - P(1)	$2 \cdot 334(7)$		
Pd(1)-P(2)	$2 \cdot 348(7)$	Pd(1)-P(2)	$2 \cdot 338(7)$		
Sel	lected distance	es constrained to be			
	equal for b	oth molecules			
C(14b)-C(1)	$1 \cdot 389(26)$	C(14b)-C(4a)	$1 \cdot 411(26)$		
C(1) - C(2)	$1 \cdot 431(26)$	C(2)-C(3)	$1 \cdot 412(28)$		
C(2) - C(3)	$1 \cdot 412(28)$	C(3)-C(4)	$1 \cdot 398(27)$		
C(4)-C(4a)	$1 \cdot 379(26)$	C(4a)-O(5)	$1 \cdot 369(23)$		
O(5) - C(6)	$1 \cdot 339(22)$	C(6) - O(6)	$1 \cdot 199(21)$		
C(6)-C(6a)	$1 \cdot 419(27)$	C(6a)-N(7)	$1 \cdot 378(24)$		
C(6a) - C(14a)	$1 \cdot 373(25)$	N(7)-C(8)	$1 \cdot 489(24)$		
N(7)-C(3b)	$1 \cdot 389(21)$	C(8) - C(9)	1.588(27)		
C(9)-C(9a)	$1 \cdot 394(24)$	C(9a) - C(10)	$1 \cdot 368(18)$		
C(9a) - C(13a)	$1 \cdot 394(14)$	C(10) - C(11)	$1 \cdot 383(18)$		
C(11) - C(12)	$1 \cdot 383(18)$	C(12) - C(13)	$1 \cdot 368(18)$		
C(13) - C(13a)	$1 \cdot 394(14)$	C(13a) - C(13b)	1.511(28)		
C(13b) - C(14)	$1 \cdot 412(23)$	C(14) - C(14a)	$1 \cdot 447(25)$		
C(14) - C(6')	$1 \cdot 478(29)$	C(1') - C(2')	$1 \cdot 415(23)$		
C(1') - C(6')	$1 \cdot 361(20)$	C(2')-C(3')	$1 \cdot 307(23)$		
C(3') - C(4')	$1 \cdot 307(23)$	C(4')-C(5')	$1 \cdot 415(23)$		
C(5') - C(6')	$1 \cdot 361(20)$	P(1) - C(15)	$1 \cdot 807(9)$		
P(1) - C(21)	$1 \cdot 807(9)$	P(1) - C(27)	1.807(9)		
$\dot{C(15)} - \dot{C(16)}$	$1 \cdot 395(7)$	C(15) - C(20)	$1 \cdot 395(7)$		
C(16) - C(17)	1.384(8)	C(17) - C(18)	1.386(8)		
C(18)-C(19)	1.386(8)	C(19)-C(20)	$1 \cdot 384(8)$		

conversion  $(4) \rightarrow (3)$  detract somewhat from the overall scheme. It will be necessary, therefore, to address this matter before a truly useful synthesis of the lamellarins can be realized by this sort of approach. The present work further highlights the need to design catalysts which can promote, in an efficient manner, the currently problematic *6-endo-trig*-type Heck cyclization reaction<sup>22</sup> as exemplified by the desired conversion (16)  $\rightarrow$  (3).

#### Experimental

Melting points were recorded with a Kofler hot-stage apparatus and are uncorrected. Proton (<sup>1</sup>H) and carbon (<sup>13</sup>C) n.m.r. spectra were recorded with a Varian Gemini 300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon. Unless otherwise stated, all such spectra were recorded in (D)chloroform (CDCl<sub>3</sub>) solution at 22°C. The protonicities of the carbon atoms observed in <sup>13</sup>C n.m.r. spectra were determined by attached proton test (a.p.t.) experiments. Infrared spectra ( $\nu_{max}$ ) were recorded with either a Perkin–Elmer 683G infrared spectrophotometer or a Perkin–Elmer 1800 Fourier-transform infrared

Table 6. Selected bond angles (degrees) for (17),  $C_{61}H_{48}BrNO_2P_2Pd.C_4H_{10}O$ 

Atoms	Molecule A	Molecule B
${ m Br}(1) - { m Pd}(1) - { m P}(1)$	$91 \cdot 8(2)$	$90 \cdot 3(2)$
Br(1) - Pd(1) - P(2)	$91 \cdot 6(2)$	$91 \cdot 6(2)$
C(14b) - Pd(1) - P(1)	$87 \cdot 4(2)$	$89 \cdot 8(3)$
C(14b) - Pd(1) - P(2)	$89 \cdot 2(2)$	$89 \cdot 0(2)$
Br(1) - Pd(1) - C(14b)	$179 \cdot 1(3)$	$176 \cdot 4(7)$
P(1) - Pd(1) - P(2)	$175 \cdot 4(3)$	$170 \cdot 3(3)$



Fig. 2. ORTEP derived from X-ray crystallographic structure analysis of compound (17).

spectrophotometer. Samples were analysed as potassium bromide disks. Low-resolution electron impact mass spectra (m/z)were recorded at 70 eV on a VG Micromass 7070F mass spectrometer. High-resolution mass spectra were recorded on the same instrument. High-pressure reactions were conducted by using a PSIKA 20 kbar high-pressure reactor. Diethyl ether and tetrahydrofuran were distilled under nitrogen from sodium benzophenone ketyl. Dichloromethane and hexane were each distilled from calcium hydride. N, N-Dimethylformamide was distilled from calcium hydride under reduced pressure (c. 25Torr) G.l.c./m.s. studies were conducted by using an HP 5890 gas chromatograph interfaced with an HP 5970 mass-selective detector. The gas chromatograph was fitted with a 12.5 m by 0.2 mm (i.d.) by  $0.33 \mu \text{m}$  HP-1 (cross-linked methyl silicone gum) capillary column. A carrier gas (helium) flow rate of c. 35 cm/s was used in conjunction with the following gradient temperature program: initial temperature of 200°C held for 2 min, then heating at 20°C/min to a final temperature of  $300^{\circ}$ C which was maintained for 10 min.

#### 2-(Trichloroacetyl)pyrrole (6)

Compound (6) was prepared from pyrrole ( $12 \cdot 5$  g, 186 mmol) and trichloroacetyl chloride ( $36 \cdot 5$  g, 200 mmol) according to the method of Bailey *et al.*<sup>12</sup> In this manner the title compound (6)<sup>12</sup> ( $31 \cdot 3$  g, 80%) was obtained as a cream solid, m.p. 73–74°C (lit.<sup>12</sup> m.p. 73–75°C). <sup>1</sup>H n.m.r.  $\delta$  9·30, broad s, 1H; 7·39, m, 1H; 7·17, m, 1H; 6·40, dt, *J* 3·9 and 2·4 Hz, 1H.

#### 4-Iodo-2-(trichloroacetyl)pyrrole (7)

The title compound was prepared from 2-(trichloroacetyl)pyrrole (6) according to the method of Bélanger.<sup>13</sup> Thus, iodine  $(12 \cdot 0 \text{ g}, 47 \cdot 2 \text{ mmol})$  was added portionwise (approximately 1 g per portion) over 0.17 h to a magnetically stirred mixture of silver trifluoroacetate  $(11 \cdot 0 \text{ g}, 49 \cdot 8 \text{ mmol})$  and 2-(trichloroacetyl)pyrrole  $(10 \cdot 0 \text{ g}, 47 \cdot 1 \text{ mmol})$  in dry chloroform (70 ml) maintained at  $0^{\circ}$ C (ice bath). After addition was complete the reaction mixture was allowed to warm to 18°C and stirred at this temperature for a further 2 h. The resultant suspension was filtered through a sintered glass funnel (No. 3) porosity) and the filtrate washed with  $Na_2S_2O_5$  (1×80 ml of 5% w/v aqueous solution) and water (2×80 ml), then dried  $(MgSO_4)$ , filtered and concentrated under reduced pressure. The solid residue thus obtained was treated with hexane/ether (50 ml of a 4:1 v/v mixture) and the resulting suspension stirred at  $18^{\circ}$ C for 5 h; then the solid was filtered off to give the title compound  $(7)^{13}$  (13.1 g, 82%) as a cream solid, m.p. 129–130°C (lit.<sup>13</sup> m.p. 128–130°C). <sup>1</sup>H n.m.r.  $\delta$  9.45, broad s, 1H; 7·44, dd, J 2·6 and 1·3 Hz, 1H; 7·19, dd, J 2·6 and 1·3 Hz, 1H.

#### 4-Iodopyrrole-2-carboxylic Acid (8)

 $K_2CO_3$  (100 ml of a 2 M aqueous solution) was added to a solution of 4-iodo-2-(trichloroacetyl)pyrrole (8.5 g, 2.5 mmol)in dimethyl sulfoxide (30 ml) and the resulting mixture stirred at  $18^{\circ}$ C for 3 h then diluted with H<sub>2</sub>O (200 ml). The solution thus obtained was washed with ethyl acetate  $(2 \times 100 \text{ ml})$ then acidified, by dropwise addition of HCl (2 M aqueous solution), to pH 3. The resulting slurry was extracted with ethyl acetate  $(3 \times 100 \text{ ml})$  and the combined organic fractions were dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to give the *title compound* (8)  $(5 \cdot 51 \text{ g}, 92\%)$  as a white solid, m.p. 200°C (Found:  $M^{+\bullet}$ , 236.9285. C<sub>5</sub>H<sub>4</sub>INO<sub>2</sub> requires M<sup>+•</sup>, 236·9287).  $\nu_{\rm max}$  (KBr) 3287, 3129, 3035, 1703, 1544, 1430, 1300, 1212, 1122 cm<sup>-1</sup>. <sup>1</sup>H n.m.r. [300 MHz, 3:1  $(CD_3)_2SO/CDCl_3 \delta 11.98$ , broad s, 1H; 6.98, t, J 1.5 Hz, 1H; 6.76, broadened s, 1H (resonance due to N-H not observed). <sup>13</sup>C n.m.r. [75.5 MHz, 3:1 (CD<sub>3</sub>)<sub>2</sub>SO/CDCl<sub>3</sub>]  $\delta$  159.0 (C), 126 · 0 (CH), 123 · 3 (C), 118 · 8 (CH), 59 · 0 (C). Mass spectrum m/z 237 (100%) (M<sup>+•</sup>); 219 (87) [(M - H<sub>2</sub>O)<sup>+•</sup>].

#### 2-Bromophenyl 4-Iodopyrrole-2-carboxylate (11)

Oxalyl chloride (203  $\mu$ l, 2.32 mmol) was added to a magnetically stirred suspension of 4-iodopyrrole-2-carboxylic acid (8) (500 mg,  $2 \cdot 11$  mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15  $\cdot 0$  ml) containing dimethylformamide (1 drop). After the resulting solution had been stirred at 18°C for 2 h it was added to a magnetically stirred solution of o-bromophenol (363 mg,  $2 \cdot 11$  mmol), triethylamine  $(660 \ \mu l, 4.73 \ mmol)$  and 4-(dimethylamino)pyridine (several crystals) in  $CH_2Cl_2$  (10 ml). After 1 h the reaction mixture was concentrated onto silica gel (5 g) and the residue subjected to flash chromatography (silica gel, 3:1 hexane/ether elution). Concentration of the appropriate fractions  $(R_{\rm F} \ 0.2)$  then gave the *title compound* (11) (761 mg, 92%) as a white crystalline solid, m.p. 126-127°C (Found: C, 33.9; H, 1.7; Br, 20.4; I, 32.4; N, 4.0. C<sub>11</sub>H<sub>7</sub>BrINO<sub>2</sub> requires C, 33.7; H, 1.8; Br, 20.4; I, 32.4; N, 3.6%).  $\nu_{\rm max}$  (KBr) 3383, 2969, 1709, 1580, 1541, 1472, 1444, 1377, 1312, 1218, 1169, 1133, 1043  ${\rm cm}^{-1}$  $^1\mathrm{H}$  n.m.r.  $\delta$  9.57, broad s, 1H; 7.65, dd, J 8.1 and 1.5 Hz, 1H; 7.37, td, J 8.1 and 1.5 Hz, 1H; 7.27, m, 2H; 7.18, td, J 8·1 and 1·5 Hz, 1H; 7·08, m, 1H.  $^{13}\mathrm{C}$  n.m.r.  $\delta$  158·0 (C), 148.3 (C), 134.0 (CH), 129.8 (CH), 129.1 (CH), 128.1 (CH), 124·4 (CH), 124·3 (CH), 123·6 (C), 116·9 (C), 62·9 (C). Mass spectrum m/z 393 (24%) 391 (22) (M<sup>+•</sup>); 220 (100)  $[(M - C_6 H_4 BrO)^{+\bullet}].$ 

#### 2-(2'-Bromophenyl)ethyl 4-Methylbenzenesulfonate (13)

A magnetically stirred solution of o-bromophenethyl alcohol (12) (5.00 g, 24.9 mmol, ex Aldrich) and 4-methylbenzenesulfonyl chloride  $(11 \cdot 20 \text{ g}, 59 \cdot 7 \text{ mmol})$  in diethyl ether (50 ml)was cooled to 0°C (ice bath) then treated with powdered KOH  $(3 \cdot 2 \text{ g}, 2 \cdot 4 \text{ mole equiv.})$ . The reaction mixture thus obtained was allowed to warm to 18°C, stirred at this temperature for  $2 \cdot 0$  h then diluted with water (100 ml). The separated organic phase was washed with water  $(1 \times 100 \text{ ml})$  then dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to give a white solid. Since this material contained residual 4-methylbenzenesulfonyl chloride it was dissolved in pyridine (75 ml) and the resulting solution stirred at  $18^\circ\mathrm{C}$  for  $0\cdot16$  h then diluted with water (500 ml) and extracted with diethyl ether  $(1 \times 500 \text{ ml})$ . The separated organic phase was washed with HCl  $(1 \times 250 \text{ ml of a 5 M aqueous solution})$  then sodium hydrogen carbonate  $(1 \times 250 \text{ ml of a } 0.5 \text{ M} \text{ aqueous solution})$ before being dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to give the title compound  $(13)^{23}$  (8.66 g,98%) as white crystalline masses, m.p. 39–39 $\cdot\,5^{\circ}\mathrm{C}$  (Found: C, 50.9; H, 4.2; Br, 22.6; S, 8.8. Calc. for C<sub>15</sub>H<sub>15</sub>BrO<sub>3</sub>S: C, 50·7; H, 4·3; Br, 22·5; S, 9·0%).  $\nu_{\rm max}$  (KBr) 1356, 1177, 1021, 980, 962, 895, 812, 769, 752, 665, 557 cm<sup>-1</sup>.  $^{1}$ H n.m.r.  $\delta$ 7·68, d, J8·3 Hz, 2H; 7·45, d, J7·7 Hz, 1H; 7·27, d, J8.3 Hz, 2H; 7.17, m, 2H; 7.07, m, 1H; 4.25, t, J 7.0 Hz, 2H; 3.09, t, J 7.0 Hz, 2H; 2.43, s, 3H. <sup>13</sup>C n.m.r.  $\delta$  144.5 (C), 135.3 (C), 132.7 (CH), 132.8 (C), 131.3 (CH), 129.7 (CH),  $128 \cdot 5$  (CH),  $127 \cdot 6$  (CH),  $127 \cdot 4$  (CH),  $124 \cdot 2$  (C),  $68 \cdot 6$  (CH<sub>2</sub>), 35.5 (CH<sub>2</sub>), 21.5 (CH<sub>3</sub>). Mass spectrum m/z 356 (0.7%) 354 (0.7) (M<sup>+•</sup>); 184 (98) 182 (100) [(M - H<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H)<sup>+•</sup>]; 171 (49) 169 (51); 155 (45); 103 (32); 91 (80)  $(C_7H_7^+)$ .

### 2-Bromophenyl 1-[2'-(2''-Bromophenyl)ethyl]-4-iodopyrrole-2-carboxylate (14)

Compound (13) (700 mg, 1.97 mmol), tetraethylammonium chloride (30 mg, 0.18 mmol) and K<sub>2</sub>CO<sub>3</sub> (278 mg, 2.0 mmol) were added to a solution of compound (11) (700 mg, 1.79 mmol) in dry dimethylformamide (30 ml) and the resultant slurry was stirred at 80°C for 2 h. The cooled reaction mixture was diluted with ethyl acetate (150 ml) and washed with water (3×150 ml). The separated organic phase was then dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure. The solid residue thus obtained was subjected to flash chromatography (silica gel, 4:1 hexane/ether elution) and concentration of the appropriate fractions ( $R_{\rm F}$  0.5, 3:1 hexane/ether elution) gave the *title* compound (14) (920 mg, 89%) as a white crystalline solid, m.p. 122–123°C (Found: C, 39.5; H, 2.1; Br, 27.6; I, 22.1; N, 2.3. C<sub>19</sub>H<sub>14</sub>Br<sub>2</sub>INO<sub>2</sub> requires C, 39.7; H, 2.5; Br, 27.8; I, 22.1; N, 2.4%).  $\nu_{\rm max}$  (KBr) 2949, 1716, 1517, 1468, 1438, 1411, 1374, 1326, 1232, 1216, 1191, 1055, 1028 cm<sup>-1</sup>. <sup>1</sup>H n.m.r.  $\delta$  7.65, dd, J 7.8 and 1.8 Hz, 1H; 7.55, dd, J 7.8 and 1.8 Hz, 1H; 7.37, m, 2H; 7.28–7.04, m, 5H; 6.70, d, J 2.1 Hz, 1H; 4.55, t, J 7.5 Hz, 2H; 3.20, t, J 7.5 Hz, 2H. <sup>13</sup>C n.m.r.  $\delta$  157.0 (C), 147.8 (C), 136.9 (C), 134.5 (CH), 133.3 (CH), 132.7 (CH), 131.2 (CH), 128.6 (CH), 128.4 (CH), 127.6 (CH), 127.3 (CH), 126.7 (CH), 124.4 (C), 124.0 (CH), 122.0 (C), 116.6 (C), 59.6 (C), 49.0 (CH<sub>2</sub>), 38.0 (CH<sub>2</sub>). Mass spectrum m/z 577 (1%) 575 (2) 573 (1) (M<sup>+</sup>•); 496 (10) 494 (11) [(M – Br•)<sup>+</sup>]; 404 (98) 402 (100) [(M – C<sub>6</sub>H<sub>4</sub>BrO•)<sup>+</sup>].

### 2-Bromophenyl 1-[2'-(2''-Bromophenyl)ethyl]-4-phenylpyrrole-2-carboxylate (4)

Phenylzinc chloride [prepared by the addition of anhydrous zinc chloride (540 mg, 3.96 mmol) to a solution of phenyllithium  $(2 \cdot 0 \text{ ml of a } 1 \cdot 8 \text{ M solution in cyclohexane/ether}, 3 \cdot 6 \text{ mmol})$ in tetrahydrofuran  $(4 \cdot 0 \text{ ml})$ ] was added dropwise, over 2 min, to a magnetically stirred solution of compound (14) (1.75)g, 3.04 mmol) and  $Pd(PPh_3)_2Cl_2$  (106 mg, 0.152 mmol) in dimethylformamide (15 ml). Stirring was continued at 18°C for 1 h then the reaction mixture was transferred to a separatory funnel, diluted with ethyl acetate (100 ml) and washed with  $NH_4Cl$  (100 ml of a saturated aqueous solution) then  $H_2O$  $(2 \times 100 \text{ ml})$ . The separated organic phase was dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to give a light-yellow oil which was subjected to flash chromatography (silica, 2:1 hexane/CH<sub>2</sub>Cl<sub>2</sub> elution). Concentration of the appropriate fractions  $(R_{\rm F} \ 0.5)$  gave the *title compound* (4) (1.52 g, 95%) as a microcrystalline solid, m.p.  $90-92^{\circ}\text{C}$  (Found: C, 57·1; H, 3·4; Br, 30·7; N, 2·5. C<sub>25</sub>H<sub>19</sub>Br<sub>2</sub>NO<sub>2</sub> requires C, 57·2; H, 3·7; Br, 30·4; N, 2·7%).  $\nu_{\rm max}$  (KBr) 2958, 2930, 1718,  $1603, 1580, 1562, 1472, 1397, 1215, 1196, 1066, 1024 \text{ cm}^{-1}.$  $^1\mathrm{H}$  n.m.r.  $\delta$  7+70, dd, J 8+0 and 1+5 Hz, 1H; 7+60–7+00, m, 14H; 4·63, t, J 6·9 Hz, 2H; 3·32, t, J 6·9 Hz, 2H.  $^{13}{\rm C}$  n.m.r.  $(75 \cdot 5 \text{ MHz}, \text{CDCl}_3) \delta 158 \cdot 4 \text{ (C)}, 148 \cdot 3 \text{ (C)}, 137 \cdot 5 \text{ (C)}, 134 \cdot 2$ (C), 133.5 (CH), 132.9 (C), 131.5 (CH), 128.9 (CH), 128.6(3) (CH), 128.6(1) (CH), 127.8 (CH), 127.4 (CH), 127.3 (CH), 126.5 (CH), 125.4 (CH), 124.8 (C), 124.6 (C), 124.4 (CH),  $120 \cdot 9$  (C),  $117 \cdot 5$  (CH),  $116 \cdot 9$  (C),  $49 \cdot 3$  (CH<sub>2</sub>),  $38 \cdot 2$  (CH<sub>2</sub>). Mass spectrum m/z 527 (3%) 525 (6) 523 (3) (M<sup>+•</sup>); 446 (12) 444 (11)  $[(M - Br^{\bullet})^+]$ ; 354 (100) 352 (96)  $[(M - C_6H_4BrO^{\bullet})^+]$ .

#### 14-Phenyl-8,9-dihydro-6H-[1]benzopyrano[4',3':4,5]pyrrolo-[2,1-a]isoquinolin-6-one (3)

 $Pd(OAc)_2$  (32 mg, 0.143 mmol) was added to a magnetically stirred solution of compound (4) (148 mg, 0.282 mmol), NaOAc  $(92 \cdot 7 \text{ mg}, 1 \cdot 13 \text{ mmol})$  and PPh<sub>3</sub>  $(74 \cdot 0 \text{ mg}, 0 \cdot 282 \text{ mmol})$  in dimethylformamide (2 ml) contained in a Schlenk tube. The resulting mixture was evacuated  $(1 \cdot 0 \text{ mmHg})$  and back-filled with  $N_2$  (gas) three times (to remove dissolved oxygen) then heated under nitrogen at 135°C for 6 h. The cooled reaction mixture was diluted with ether (25 ml) and washed with brine  $(2 \times 20 \text{ ml})$  then water (20 ml) before being dried (MgSO<sub>4</sub>), filtered and concentrated onto silica (2 g). The residue was subjected to flash chromatography (silica, 1:2, 1:1 then 2:1 $CH_2Cl_2$ /hexane elution) and the appropriate fractions ( $R_F \ 0.3$ , 2:1 CH<sub>2</sub>Cl<sub>2</sub>/hexane elution) were concentrated under reduced pressure to give the *title compound* (3) (16 mg, 16%) as cream-coloured microcrystals, m.p.  $259-260^{\circ}C$  (Found:  $M^{+\bullet}$ , 363.1257. C<sub>25</sub>H<sub>17</sub>NO<sub>2</sub> requires  $\dot{M}^{+\bullet}$ , 363.1259).  $\nu_{max}$  (KBr) 2925, 2853, 1708, 1449, 1420, 1396, 1339, 1281, 1241, 1198, 1151, 1133, 1106, 1085, 1047 cm<sup>-1</sup>. <sup>1</sup>H n.m.r.  $\delta$  7.58–7.55, m, 2H; 7.51-7.50, m, 2H; 7.40, dd, J 7.5 and 0.9 Hz, 1H; 7.32-7.18, m, 4H; 7.10, dd, J 7.8 and 1.2 Hz, 1H; 7.01-6.97,

m, 3H; 4·88, t, J 6·9 Hz, 2H; 3·21, t, J 6·9 Hz, 2H. <sup>13</sup>C n.m.r.  $\delta$  155·3 (C), 151·2 (C), 135·6 (C), 135·3 (C), 133·8 (C), 130·7 (CH), 129·4 (CH), 128·3 (CH), 128·1 (CH), 127·5 (C), 127·4 (CH), 126·9 (CH), 125·7 (CH), 123·7 (CH), 123·3 (CH), 118·2 (C), 117·5 (C), 117·1 (CH), 42·3 (CH<sub>2</sub>), 29·3 (CH<sub>2</sub>) (three peaks obscured or overlapping). Mass spectrum m/z 363 (100%) (M<sup>+•</sup>).

#### 2'-Bromophenyl 1-Phenyl-5,6-dihydropyrrolo[2,1-a]isoquinoline-3-carboxylate (16) and Bromo{2'-(1''-phenyl-5'',6''-dihydropyrrolo[2,1-a]isoquinolin-3''-ylcarbonyloxy)phenyl}bis(triphenylphosphine)palladium (17)

 $Pd(OAc)_2$  (197 mg, 0.88 mmol) was added to a solution of compound (4) (230 mg, 0.438 mmol), NaOAc (80 mg, 0.975 mmol) and PPh<sub>3</sub> (460 mg, 1.75 mmol) in dimethylformamide (20 ml). The solution was evacuated (1.0 mmHg) and back-filled with N<sub>2</sub> (gas) three times to remove dissolved oxygen and then heated under nitrogen at 110°C for 19 h. The cooled reaction mixture was diluted with ethyl acetate (25 ml) then washed with brine (2×20 ml) and water (1×20 ml). The separated organic phase was then dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure onto silica (2 g). Subjection of the resulting material to flash chromatography (silica, 1:2 then 1:1 CH<sub>2</sub>Cl<sub>2</sub>/hexane followed by 4:1 CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate elution) gave two fractions, A and B.

Concentration of fraction A ( $R_{\rm F}$  0.6, 2:1 CH<sub>2</sub>Cl<sub>2</sub>/hexane elution) afforded compound (16) (34 mg, 17%) as off-white crystalline masses, m.p. 130–131°C (Found: M<sup>+•</sup>, 443.0529. C<sub>25</sub>H<sub>18</sub><sup>79</sup>BrNO<sub>2</sub> requires M<sup>+•</sup>, 443.0521).  $\nu_{\rm max}$  (KBr) 2950, 1710, 1471, 1439, 1418, 1240, 1212, 1176, 1046 cm<sup>-1</sup>. <sup>1</sup>H n.m.r.  $\delta$  7.57, dd, J 8.1 and 1.5 Hz, 1H; 7.45–7.05, m, 12H; 6.95, br t, J 8.1 Hz, 1H; 4.57, t, J 6.3 Hz, 2H; 3.05, t, J 6.3 Hz, 2H. <sup>13</sup>C n.m.r.  $\delta$  158.5 (C), 148.1 (C), 136.1 (C), 133.4 (C), 133.3 (CH), 132.9 (C), 129.1 (CH), 128.6 (C), 128.4 (CH), 128.1 (C), 127.9 (CH), 127.7 (CH), 127.1 (CH), 126.9 (CH), 126.7 (CH), 125.5 (CH), 124.2 (CH), 123.5 (C), 121.3 (CH), 119.4 (C), 116.7 (C), 42.4 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>). Mass spectrum m/z 445 (10%) 443 (9) (M<sup>+•</sup>); 272 (100) [(M – C<sub>6</sub>H<sub>4</sub>BrO<sup>•</sup>)<sup>+</sup>].

Concentration of fraction B ( $R_{\rm F}$  0·1, CH<sub>2</sub>Cl<sub>2</sub> elution) afforded compound (17) (40 mg, 8·5%) as off-white crystalline masses, m.p. 159–162°C.  $\nu_{\rm max}$  (KBr) 3052, 2923, 1705, 1481, 1435, 1416, 1238, 1172, 1095, 1058, 1024 cm<sup>-1</sup>. <sup>1</sup>H n.m.r.  $\delta$ 7·65–7·40, m, 18H; 7·30–7·05, m, 22H; 6·58, m, 1H; 6·52, t, J 6·6 Hz, 1H; 6·39, m, 1H; 6·07, q, J 6·6 Hz, 1H; 4·73, m, 2H; 3·05, m, 2H. <sup>13</sup>C n.m.r.  $\delta$  159·2 (C), 151·8 (C), 138·3 (CH), 136·5 (C), 134·8 (CH), 133·2 (C), 131·8 (C), 131·5 (C), 131·0 (C), 129·9 (CH), 129·8 (CH), 129·5 (CH), 129·0 (CH), 128·7 (C), 127·8 (CH), 127·5 (CH), 127·2 (CH), 127·0 (CH), 121·1 (C), 120·5 (CH), 42·2 (CH<sub>2</sub>), 29·7 (CH<sub>2</sub>). Mass spectrum m/z 365 (6%) [(M – Pd(PPh<sub>3</sub>)<sub>2</sub>Br+H)<sup>+•</sup>]; 262 (100) (Ph<sub>3</sub>P<sup>+•</sup>).

### 1-Phenyl-5,6-dihydropyrrolo[2,1-a]isoquinoline (18) and 1-[2'-(2''-Bromophenyl)ethyl]-3-phenylpyrrole (19)

A solution of the dibromide (4) (13 mg, 25  $\mu$ mol), trans-di( $\mu$ -acetato)bis[o-(di-o-tolylphosphino)benzyl]dipalladium(II)<sup>16</sup> (2.5 mg, 2.5  $\mu$ mol) and anhydrous sodium acetate (6.2 mg, 75  $\mu$ mol) in degassed N,N-dimethylacetamide (0.25 ml) was heated, under nitrogen, at 140°C for 72 h. The cooled reaction mixture was then diluted with diethyl ether (5 ml) and the resulting solution washed with brine/water (3×5 ml of a 1:1 v/v mixture). The organic phase was then dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to give a light-yellow oil. Subjection of this material to flash chromatography (silica, 3:7 then 7:3 CH<sub>2</sub>Cl<sub>2</sub>/hexane elution) gave, after concentration of the appropriate fractions ( $R_F$  0.7, 3:7 CH<sub>2</sub>Cl<sub>2</sub>/hexane elution), a 1:3 mixture of compounds (18) and (19) (4 mg, 52% combined yield) as a light-yellow and unstable oil.  $\nu_{\text{max}}$  (KBr) 1705, 41 · 2, 1555, 1500, 1471, 1441, 1359, 1202, 1071, 1027, 751, 694, 655 cm<sup>-1</sup>. <sup>1</sup>H n.m.r.  $\delta$  [compound (19)] 7·60–6·95, complex m, 9H; 6·92, t, J 2·0 Hz, 1H, H 2; 6·63, t, J 1·6 Hz, 1H, H 5; 6·43, broadened t, J 2·3 Hz, 1H, H 4; 4·14, t, J 7·7 Hz, 2H; 3·22, t, J 7·7 Hz, 2H;  $\delta$  [compound (18)] 7·60–6·95, complex m, 9H; 6·73, d, J 2·7 Hz, 1H, H 3; 6·23, d, J 2·7 Hz, 1H, H 2; 4·08, t, J 7·7 Hz, 2H; 3·10, t, J 7·7 Hz, 2H. G.l.c./m.s. [compound (18)] ( $R_{\rm T}$  4·52 min) 245 (100%) (M<sup>+•</sup>), 167 (21), 149 (28), 120 (6); g.l.c./m.s. [compound (19)] ( $R_{\rm T}$  5·85 min) 327 (12%) 325 (12) (M<sup>+•</sup>), 246 (100) [(M – Br<sup>•</sup>)<sup>+</sup>].

#### Crystallography

#### Crystal Data

Compound (3). C<sub>25</sub>H<sub>17</sub>NO<sub>2</sub>, M 363·41, T 183(1) K, monoclinic, space group  $P 2_1/c$ ,  $a \ 11\cdot 063(4)$ ,  $b \ 11\cdot 316(3)$ ,  $c \ 28\cdot 688(3)$  Å,  $\beta \ 100\cdot 91(2)^{\circ}$ , V 3526(2) Å<sup>3</sup>,  $D_c(Z=8) \ 1\cdot 369$ g cm<sup>-3</sup>,  $F(000) \ 1520$ ,  $\mu$ (Cu K $\alpha$ )  $6\cdot 50 \ cm^{-1}$ , semiempirical absorption correction; 5577 unique data  $(2\theta_{\max} \ 120\cdot 4^{\circ})$ , 3294 with  $I > 3\sigma(I)$ ;  $R \ 0\cdot 049$ ,  $wR \ 0\cdot 051$ , goodness of fit  $2\cdot 37$ .

Compound (17). C<sub>61</sub>H<sub>48</sub>BrNO<sub>2</sub>P<sub>2</sub>Pd.C<sub>4</sub>H<sub>10</sub>O, *M* 1149·43, *T* 183(1) K, monoclinic, space group  $P_{21}/c$ , *a* 25·377(5), *b* 12·272(5), *c* 36·200(11) Å,  $\beta$  100·01(2)°, *V* 11102(6) Å<sup>3</sup>,  $D_c(Z = 8)$  1·375 g cm<sup>-3</sup>, *F*(000) 4720,  $\mu$ (Cu K $\alpha$ ) 44·46 cm<sup>-1</sup>. Other data are discussed below.

#### Structure Determination

Compound (3). Data were measured on a Rigaku AFC6R rotating-anode diffractometer (graphite crystal monochromator,  $\lambda 1.54180$  Å). The structure of compound (3) was solved by direct methods,<sup>24</sup> and refinement was by full-matrix least squares analysis on F with anisotropic thermal parameters on all non-hydrogen atoms. Hydrogen atoms were located from difference maps and included at idealized locations. The structure contains two molecules in the asymmetric unit, labelled A and B. All calculations were performed with the teXsan structure analysis software of Molecular Structure Corporation.<sup>25</sup>

Compound (17). Data were measured on a Rigaku AFC6R rotating-anode diffractometer (graphite crystal monochromator,  $\lambda 1.54180$  Å). The crystal was coated to prevent decay and data were corrected for absorption, A, by using the slowly moving empirical expression:

#### $\ln A = [\mathbf{h}, \mathbf{g}_1 \mathbf{h}] + [\mathbf{h}, \mathbf{g}_2 \mathbf{h}] / \mathbf{h} \cdot \mathbf{h}$

where **h** is the scattering vector and the  $[\mathbf{h}, \mathbf{g}_i \mathbf{h}]$  are quadratic forms each involving six variables. The trace of  $\mathbf{g}_2$  correlates with the scale constant and is not refined, and the trace of  $\mathbf{g}_1$ correlates with the overall temperature factor and is given a value estimated from the absorption correction of a sphere that approximates the crystal. For a monoclinic crystal only the 12 and 23 terms of  $\mathbf{g}_1$  do not correlate with an overall anisotropic thermal factor with the Laue symmetry of the crystal. This left seven parameters that could be meaningfully refined as part of the structure refinement. Data were subsequently corrected for absorption and merged before use in the final refinement.

The solid-state structure of compound (17) contained two formula units per asymmetric unit and one diethyl ether of crystallization per molecule. Only 3213 of the 11633 independent reflections collected were considered to be reliably observed ( $I > 3\sigma(I)$ ) and so the constrained refinement program RAELS<sup>26</sup> was used for structure refinement. Atoms in molecule A have labels that finish with A and atoms in molecule B have labels that finish in B or B'. Molecule A is ordered but part of molecule B [the planar fragment C(9), C(9a), C(10), C(11), C(12), C(13), C(13a)] is 0.75(2):0.25 disordered with the minor component denoted by B'. In the refinement the torsional angles N(7B)-C(8B)-C(9B)-C(9aB), final value  $45.5(11)^{\circ}$ , and N(7B)-C(8B)-C(9B')-C(9aB'), final value  $-46.6(14)^{\circ}$ , were

restrained to have opposite signs and approach equivalence with the torsional angle N(7A)-C(8A)-C(9A)-C(9aA), final value  $46 \cdot 7(16)^{\circ}$ . The Pd, Br and P atoms were refined as implicitly independent anisotropic atoms but the remaining atoms in the A and B molecules were refined with constraints imposed by using refinable local coordinates defined relative to refinable local orthonormal axial systems.  $^{27-29}$  Tabulated errors have implicit assumptions about the appropriateness of the constraints used. An ordered molecule was considered to contain 10 strictly planar fragments (local Z coordinates are 0.0, based on nine six-membered rings and one fivemembered ring. These fragments were constrained to be identical (i.e. reference the same refinable local coordinates) for both molecules. However, the molecules had independent thermal parameterizations. The origins of three phenyl rings attached to each phosphorus atom were constrained to coincide with the phosphorus atom and the local coordinates constrained to have the same refinable mm2 symmetry for all six phenyl rings per molecule, implying all P–C bonds are identical. The thermal motion of each of these phenyl rings was described by a TL model,<sup>27</sup> the Translational component being identical to the anisotropic thermal motion of the associated phosphorus atom, while the Librational component was centred on the phosphorus and was different for each ring. Thus, the four phosphorus and 72 carbon atoms were meaningfully described by just 54 positional and 96 thermal parameters. The origin of the six-membered ring attached to a palladium was constrained to coincide with the Pd position, implying the Pd is coplanar with the ring. The thermal parameters for these seven atoms were refined using a TL model centred on the palladium. The five-membered ring and the attached O(5), C(6), O(6) and C(8) atoms were considered a coplanar fragment, as were the seven-atom fragment C(9) to C(13a) (see earlier) and the phenyl ring C(1') to C(6'). A multiple axial system<sup>28</sup> in which these latter two rings are defined relative to the five-membered ring allowed the constraint that C(13b) and C(14) could be used as origins for the attached rings, implying C(13b) is coplanar with the first attached ring and C(14) is coplanar with the second. All these atoms were included in a single TL model centred on O(5) to describe their thermal motion. Further libration centred on C(14) was allowed for the phenyl ring C(1') to C(6'). Further restraints were used to relate the connections between fragments for the two molecules. O(5) was restrained to approach a position consistent with being included in the six-atom fragment attached to the palladium (i.e. zero angle out of plane and equal bond lengths and angles). Likewise, C(6') relative to the five-membered ring to which it is attached. Restraints on the C(13a) relative to the five-membered ring were not imposed because they were counterproductive and because of the implicit non-planarity of the six-membered ring N(7)-C(8)-C(9)-C(9a)-C(13a)-C(13b).

Hydrogen atoms were included in geometrically sensible positions which were updated in each refinement cycle. Their thermal parameters were determined by the rigid group thermal motion parameters pertaining to the atoms to which they were attached. The atoms of the two solvent molecules were poorly defined and simply fill up an available space. The refinement used 363 independent variables to describe 153 non-hydrogen atom positions and gave a final value of  $R_1$  0.073 for the 3213 reflections used in the refinement.

An uncorrelated 4% error in F was included along with counting statistic error in the evaluation of weights  $w = 1/(\sigma(F)^2 + (0.04F)^2)$ . A final value for the goodness of fit was 1.42 for the 3213 reflections used and 0.96 ( $R_1 = 0.69$ ) for the remaining 8420 reflections with  $I < 3\sigma(I)$ .

The two molecules in the asymmetric unit are approximately mirror-related; corresponding torsional angles are of opposite signs and approximately equal magnitude, e.g.  $129 \cdot 0(8)^{\circ}$  for C(14bA)–C(4aA)–O(5A)–C(6A) and  $-125 \cdot 0(8)^{\circ}$  for C(14bB)–C(4aB)–O(5B)–C(6B).

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