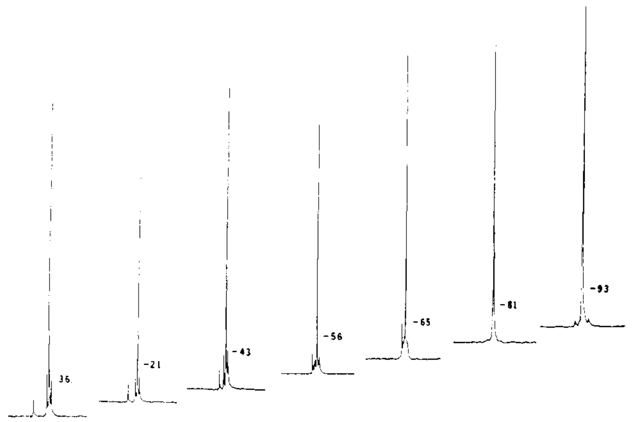

Figure 2. Variable-temperature $^{31}P\{^1H\}$ NMR spectra of $Pt(Se_2CN\text{-}i\text{-}Bu_2)_2PEt_3$ in $CDCl_3/CFCl_3$ (1:1). The small singlet is bisphosphine adduct impurity. ^{195}Pt satellites are not shown.

to the phosphorus. Since 7.58% of the selenium is NMR active, the total satellite intensity on the $^{31}P\{^1H\}$ signal is ~7.6%. At higher temperatures, but below temperatures which indicate loss of platinum to phosphorus coupling, the ^{77}Se satellite intensities on the $^{31}P\{^1H\}$ spectrum require the four selenium nuclei to appear coupled to the phosphorus with $^2J_{P\text{-}Se}$ ~25% of the low temperature value. (The trans $^2J_{P\text{-}Se}$ = 88 Hz and the two cis $^2J_{P\text{-}Se}$ ~ 5–10 Hz,[9] while, for the dangling Se, $^4J_{P\text{-}Se}$ = 0 Hz.)[14] The high intensity satellite doublet, $^2J_{P\text{-}Se}$ = 28 Hz, results since the percentage of molecules with two or more ^{77}Se on the same molecule is negligible. Intermolecular exchange, which happens at high temperatures, would lead to the complete loss of Pt–P and P–Se couplings. A similar intensity enhancement associated with intramolecular rearrangement was observed by Faller et al.[10] in $(\pi\text{-}C_5H_5)W(H)(CO)_3$.

Finally, it is to be noted that all four nonequivalent Se atoms become equivalent at higher temperatures without the detection of a two by two equivalence as expected for a static trigonal bipyramid species (eq 3). Hence, the activation energy to the formation of the five-coordinate intermediate or transition state required in an intramolecular rearrangement is larger than the barrier to the intramolecular five-coordinate rearrangement not involving bond rupture (such as the Berry pseudorotation[11]). In the absence of a five-coordinate pseudorotating intermediate a preferential loss of the ligand trans to phosphorus is expected. Since this also should lead to a two by two equivalence of the Se nuclei, the NMR data is best interpreted by assuming the existence of a rapidly rearranging five-coordinate intermediate along the pathway to chalcogenide ligand interchange.

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(13) The cis $^2J_{P\text{-}Se}$ of I at low temperature is apparently quite small since the satellites corresponding to such coupling could not be resolved from the major center peak, although some broadening (Figure 2) is noticed in the peak base at low temperatures. In $Pt(Se_2CNEt_2)PPh_3Cl$ the cis $^2J_{P\text{-}Se}$ is 10 Hz.[9] The corresponding satellites are barely observable in the inset of Figure 1.
(14) All $^2J_{P\text{-}Se}$ coupling constants are assumed to have the same sign.

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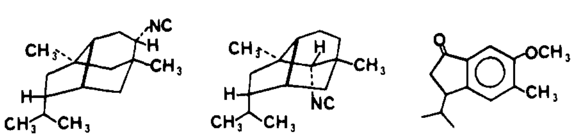
Total Synthesis of the Racemate of the Sesquiterpenoid Marine Allomone 9-Isocyanopupukeanane

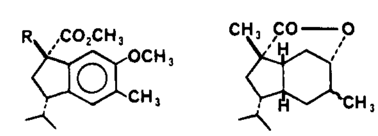
Sir:

The recent report[1] that a sponge (*Hymeniacidon sp.*) produces and transfers to the nudibranch *Phyllidia varicosa* the allomone 9-isocyanopupukeanane (formulated as **1**, or the mirror image)[2] has added a new member to the small but intriguing class of naturally synthesized isocyanides. In addition, it has subsequently been discovered that 2-isocyanopupukeanane (**2**) occurs admixed with **1** or, even exclusively, in individuals of the same species.[3] This communication describes a simple total synthesis of (±)-9-isocyanopupukeanane (**1**) by a route involving a bifunctional *cis*-hydrindan derivative which is also suitable as an intermediate for the synthesis of **2**.[4]

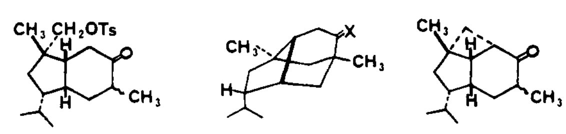
The hydrindanone **3**,[5] mp 64–65 °C, was readily prepared from methyl 3-(4-methoxy-3-methylphenyl)propenate, mp 72–73 °C,[6] in 80% overall yield by conjugate addition of isopropylmagnesium chloride–cuprous phenylmercaptide reagent in dry tetrahydrofuran (THF) at −15 °C for 40 min followed by isolation and cyclization of the resulting 3-isopropyl-3-



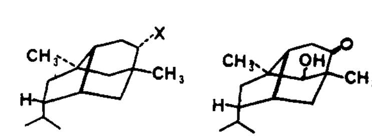
1 **2** **3**



4, R = H
5, R = CH_3
6



7
8, X = O
10, X = NOH
9



11, X = NH_2
12, X = NHCHO
13

arylpropionic ester using polyphosphoric acid first at 65 °C then at 91-93 °C for 8 h. Reaction of **3** in dry dimethoxyethane (DME) with potassium *tert*-butoxide and tosylmethyl isocyanide[7] at 0 °C for 20 min and 25 °C for 1 h followed by acidification with glacial acetate acid and isolation afforded the nitrile corresponding to **4** (as a mixture of two diastereomers) (52% yield) which was then transformed into the methyl ester **4** (as a mixture of diastereomers) by hydrolysis (KOH–H_2O_2–H_2O-ethanol[8]) to the acid and methylation (CH_2N_2). Methylation of the ester **4** was effected by deprotonation with 1 equiv of lithium diisopropylamide at −78 °C in THF followed by reaction with methyl iodide (4 equiv) and hexamethylphosphoric amide (1.3 equiv) at −78 °C for 3 h to give after chromatography on silica gel (8:1 pentane–ether) in 90% yield the ester **5** admixed with ~15% of the diastereomer (methyl and isopropyl cis) which could be removed conveniently at a later stage (intermediate **7**). The stereochemistry of **5** is assigned on the expectation that steric shielding by isopropyl will favor the formation of this geometry over the diastereomeric structure. Treatment of **5** with boron tribromide (2.1 equiv) in methylene chloride at −78 °C for 0.5 h and then at −10 ± 5 °C for an additional 4 h resulted in cleavage of the methyl ester and methyl ether functions to give the corresponding phenolic acid (82% after purification by rough chromatography on silica gel), which was then hydrogenated over Nishimura's catalyst[9] (20% by weight) in acetic acid containing 7% perchloric acid under 200 atm of hydrogen at 25 °C for 47 h to yield after chromatography on silica gel (25:1 hexane–ethylene acetate) the δ-lactone **6** as major product (IR max 1705 cm^{-1} in $CHCl_3$; R_f 0.48 on silica gel with 2:3 ether–petroleum ether as compared with starting phenolic acid R_f 0.41 with 100:20:1 benzene–dioxane–HOAc; yield 37%). The isolation of a saturated δ-lactone from the hydrogenation indicates that the aromatic ring has been fully reduced in the hydrogenation step to form the required cis fusion with a trans relationship between the hydrogens at the fusion atoms and the lactone bridge.

Reduction of the lactone **6** with lithium aluminum hydride in THF at 0 °C for 1 h produced a diol which, upon treatment with 1 equiv of tosyl chloride in pyridine at 0 °C for 2.5 h, isolation, and subsequent oxidation with pyridinium chlorochromate[10] (2 equiv) in methylene chloride at 25 °C for 2 h, furnished the keto tosylate **7** (68% overall). Addition of a solution of **7** in dry *tert*-butyl alcohol to a solution of potassium *tert*-butoxide in *tert*-butyl alcohol and reaction at 25 °C for ~30 min resulted in internal alkylation to form the desired tricyclic ketone **8** (70–75% isolated yield after chromatography on silica gel) along with an isomeric minor byproduct which is presumably **9**, the result of alkylation at the methylene α to carbonyl. Interestingly, this unexpected byproduct becomes the major cyclization product when lithium diisopropylamide in THF is used as the reagent, providing an unusual example of preferential formation of a four- rather than a six-membered ring by internal enolate alkylation.

The synthetic tricyclic ketone **8** was identical by spectral (IR, ^{1}H NMR, ^{13}C NMR, mass) and chromatographic comparison with a sample[11] of this constitution obtained as described previously[1] from naturally derived 9-isocyanopupukeanane. Reaction of **8** with hydroxylamine hydrochloride in pyridine–ethanol at 25 °C for 12 h yielded cleanly the corresponding oxime (**10**) which upon reduction with Nishimura's catalyst[9] and hydrogen (1 atm) in acetic acid afforded the amine **11**, further transformed in 80% overall yield into the formamide **12** by reaction with formic–acetic anhydride (−10 °C for 1.5 h). The ^{1}H NMR and IR spectra of synthetic **12** and naturally derived **12** were identical. Finally, reaction of the formamide **12** with methanesulfonyl chloride–pyridine[12] at 25 °C for 0.5 h produced synthetic (±)-9-isocyanopupukeanane (**1**), spectroscopically and chromatographically identical with naturally derived **1**.[13] Thus, the synthesis of this unusual natural product has been realized in a relatively simple way.

The lactone **6** has also been transformed (via an intramolecular aldol reaction) into the hydroxy ketone **13** and thence into **2**. Details of the synthesis of 2-isocyanopupukeanane (**2**) will be reported separately.[14,15]

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(15) We are grateful to the National Science Foundation for a research grant and to Dr. Stephen D. Hurt for experimental assistance.

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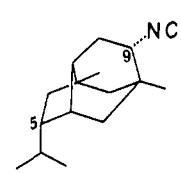
Total Synthesis of (±)-9-Isocyanopupukeanane

Sir:

An off-white sponge, *Hymeniacidon* sp., elaborates a novel sesquiterpene isocyanide, which is utilized by a nudibranch predator, *Phyllidia varicosa,* as a defensive secretion.[1] The structure of this marine invertebrate allomone was characterized recently by Scheuer and his collaborators as 1,3-dimethyl-9-isocyano-5-isopropyl[4.3.1.0^{3,7}]decane (**1**),[1] and this new ring system was named pupukeanane after the place where the mollusk and sponge were collected.[1] A highly stereose-



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lective synthesis of this unique compound is the subject of the present communication. The synthesis heavily depends on an intramolecular Diels–Alder reaction[2] as the skeleton-forming transformation.

The preparation of the key Diels–Alder substrate **2** was achieved as outlined in Scheme I. Reduction of commercially available 3,5-dimethyl-2-cyclohexen-1-one with diisobutyl-