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SELECTIVITY IN THE DESIGN OF THE TOTAL SYNTHESIS OF NATURAL PRODUCTS

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Abstract - The synthesis of complex natural products requires the development of selective methods to create molecular architecture. The utilization of palladium complexes as templates to achieve such selectivity is discussed in terms of effecting substitutions at allylic positions. The chemo-, regio-, and stereocontrol exhibited by such reactions is outlined. The facilitation of synthetic strategy is considered. Synthetic targets include steroids, macrolides, amino acids, and alkaloids and the total synthesis of representatives of each of these classes is presented.

INTRODUCTION

The synthesis of complex natural products involves proceeding from readily available starting materials to the target molecule via the most efficient route. To facilitate such approaches requires the continuing development of new methodology that achieves selectivity. Chart 1 summarizes the main types of selectivity that should be addressed. In this account, I want to outline the development and application of new methodology for improving synthetic strategy in the general area of natural products.

CHART 1. Classification of Selectivity

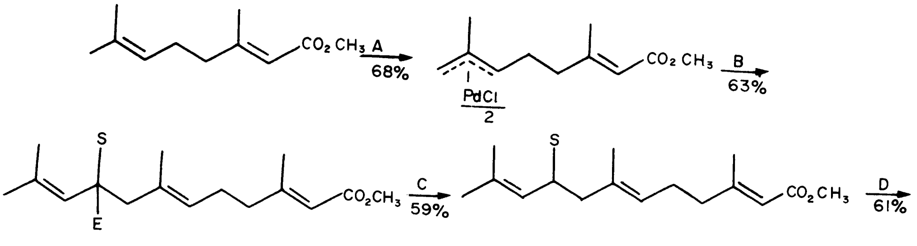
1. Chemoselectivity
2. Regioselectivity
3. Stereocontrol
    a. Relative
        (1) Stereoselective
        (2) Stereospecific
    b. Absolute

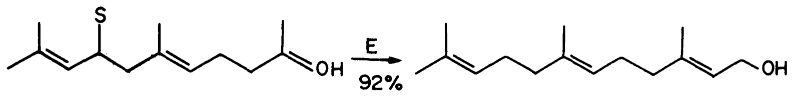
General Features of Allylic Alkylation via Organopalladium Chemistry

The tremendous synthetic utility of a carbonyl group stems from the chemoselective addition of nucleophiles to the carbonyl carbon and the chemoselective replacement of an α-hydrogen by an alkyl or heteroatom substituent via the intermediacy of enols or enolates. The π-isoelectronic olefinic linkage has not enjoyed as widespread applications - particularly because of the difficulty of effecting chemoselective substitution at the allylic position.

The formation of π-allylpalladium complexes from olefins has allowed a net allylic alkylation (1). Scheme 1 illustrates a prenylation sequence based upon this concept (2). One key feature of this approach is the functional group compatibility. Thus, methyl

Scheme 1. Direct Prenylation of Olefins

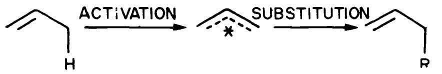




$E = CO_2CH_3$ $S = PhSO_2$

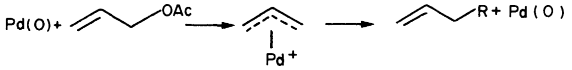
(a) $PdCl_2$, $CuCl_2$, NaCl, NaOAc, HOAc (b) $(CH_3)_2C \overset{\ominus}{=\!=} CHC(SO_2Ph)CO_2CH_3$, Na^+, HMPA, THF (c) $LiI \cdot 3H_2O$, NaCN, DMF (d) DIBAL, $PhCH_3$-hexane, -40°→0° (e) Li, $C_2H_5NH_2$, -78°

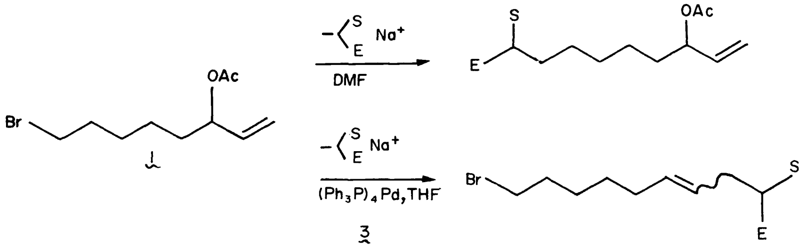
geraniate, which normally reacts at the conjugated ester end, can be selectively activated at the isolated olefin end due to the electronic preference of palladium for the less polarized unsaturation. The disadvantage of this approach is the stoichiometric palladium requirement. While for the synthesis of fine organics, such a procedure is satisfactory since the palladium can be easily recycled, a more desirable approach would employ a reaction catalytic in palladium. In viewing the process of allylic alkylation as an activation step



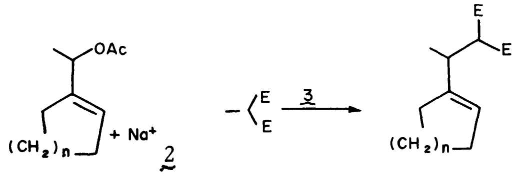
followed by a substitution step, we turned our attention to a catalytic process for the substitution stage with the anticipation that ultimately an overall catalytic process will evolve.

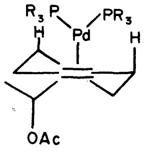
This process employs an allylic alcohol derivative such as an allylic acetate which undergoes oxidative addition with a palladium(0) species, such as tetrakis(triphenylphos-





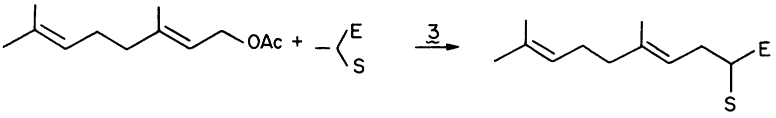
phine)palladium (3) to give a π-allylpalladium cationic complex which subsequently reacts with a nucleophile to give the substitution product and regenerate the palladium(0) catalyst (3,4). Thus, palladium activation can reverse the normal reactivity of a substrate such as 1 which undergoes alkylation at the reactive halide end with methyl benzenesodioacetate but reacts exclusively at the allylic acetate end in the presence of a palladium catalyst (5). A delightful chemoselectivity is seen as witnessed by the ring size effects. Allylic acetate 2 undergoes smooth alkylation with malonate anion in refluxing THF in 12 hrs for n=1 and 44 hrs for n=3 but not at all for n=2 (5,6). The latter requires a more reactive solvent system such as DMSO where alkylation proceeds normally. This chemoselectivity can be attributed to the conformational rigidity of the cyclohexenyl ring relative to the cyclopentenyl and cycloheptenyl systems. The steric interactions of the axial hydrogens with



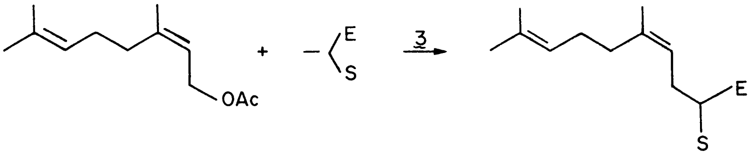


the bulky palladium reagent hamper its approach in the six membered ring case. In the five and seven membered rings sufficient flexibility allows minimization of such effects.

The stereochemistry of the olefinic linkage in the product normally reflects the stereochemistry of the olefin of the starting material as reflected in eq 1 and 2 when dealing with trisubstituted olefins (3b). Disubstituted olefins do give some loss of olefin geometry in some cases in the intermolecular alkylation (5).

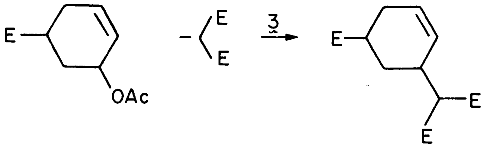


Eq 1

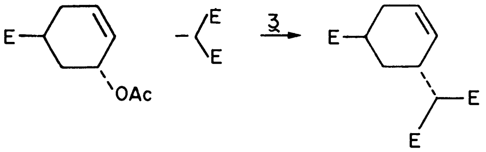


Eq 2

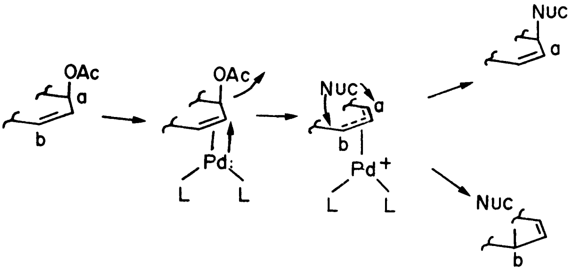
The most fascinating aspect of this approach is the stereochemistry of substitution at the allylic carbon bearing the acetate. As illustrated in eq 3 and 4, this process allows the equivalent of a S_N2 displacement with net retention of configuration (3b). This at first startling observation results from a double inversion as illustrated in eq 5. This representation for the reaction also reiterates the fact that the regiochemistry of the alkylation is not determined by the starting allylic acetate but is a consequence of the structural features associated with the attack of the nucleophile on the π-allylpalladium intermediate.



Eq 3



Eq 4



Eq 5

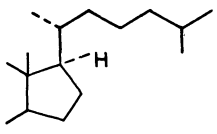
Nature of the Catalyst

For these reactions, tetrakis(triphenylphosphine)palladium has been extensively exploited as the catalyst. Other palladium(0) catalysts such as bis(triphenylphosphine)(ethylene)-palladium are also effective. Alternatively, the catalyst can be generated in situ by reduction of palladium chloride or bis(triphenylphosphine)palladium chloride with DIBAL or diethylethoxyaluminum in the presence of varying amounts of triphenylphosphine.

An interesting variation is a catalyst supported on a resin. Phosphinylated polystyrene crosslinked with 2% divinylbenzene and phosphinylated large pore silica gel (8-12 mesh) form palladium complexes which are excellent catalysts (7). The polystyrene catalyst has approximately 0.14 mmol of palladium per gram. They allow easy recovery and direct reuse of the catalyst and have also allowed development of a flow system. This catalyst has the remarkable property of retaining activity after exposure to air. Whereas the normal palladium(0) complexes decompose rapidly upon exposure to air; these catalysts retain their activity up to three months. Enhanced selectivity is also seen as outlined below.

Use of Carbon Nucleophiles

The stereocontrolled formation of C-C bonds led to consideration of introduction of acyclic side chains as found in steroids. The ready availability of 17-keto steroids (6) suggested the use of such substrates to form the cholesteryl (4) (3a) and ecdysone (5) (8) side chains. Conversion of 7 to the allylic acetate 8 took advantage of the stereocontrolled formation of the Z-olefin in the Wittig reaction and the preferential attack of the peracid on the sterically less hindered α face. The stereochemistry of 7 requires the formation of the C-C bond with retention of configuration, exactly as performed by the palladium catalyst. Indeed, substitution proceeds smoothly and in high yield with the tetrakis catalyst 3 to give a single epimer at C(20) although a mixture at C(21). Catalytic hydrogenation and alkylation produce 10.



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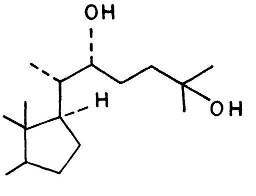

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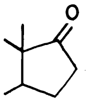

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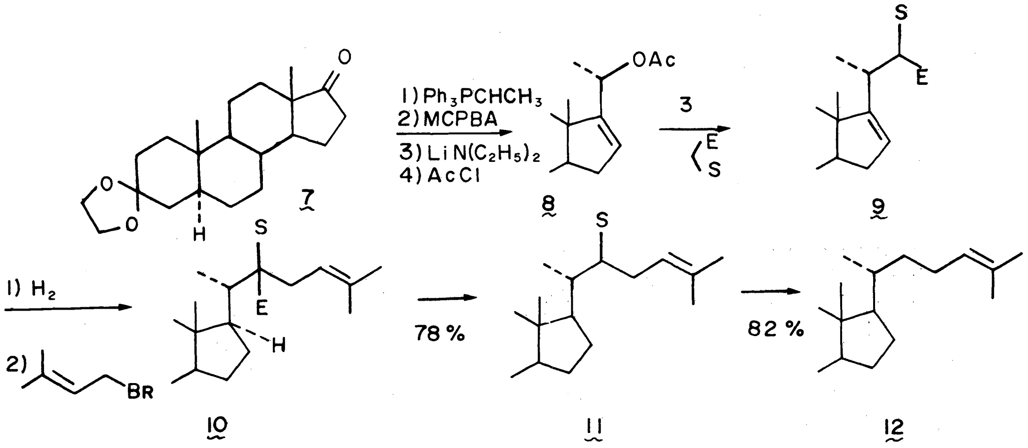
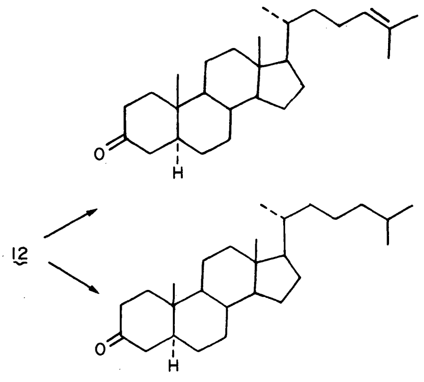
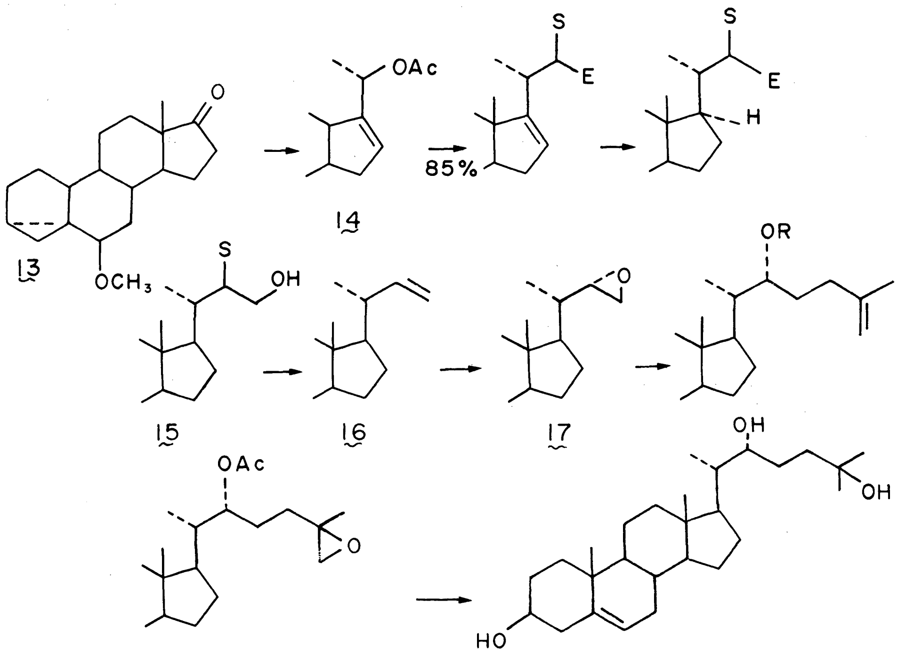


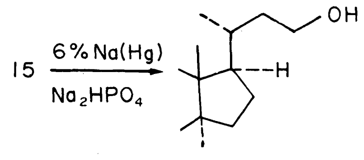
The choice of the anion of methyl benzenesulfonylacetate as the nucleophile provides great flexibility as illustrated in the further transformations. Decarbomethoxylation employs tetramethylammonium acetate in hot HMPA to give the sulfone 11 which can be smoothly desulfonylated with 6% Na(Hg) in the presence of an acid phosphate buffer to 12 (9). To confirm the stereochemistry, 12 was converted to 5α-cholest-24-en-3-one and 5α-cholestan-3-



one, the latter identical by rotation $[\alpha]_D^{CHCl_3}$ + 40.5° (C 0.850), mixture melting point (126.5-128°), chromatography, ir, ^{1}H and ^{13}C nmr with an authentic sample.

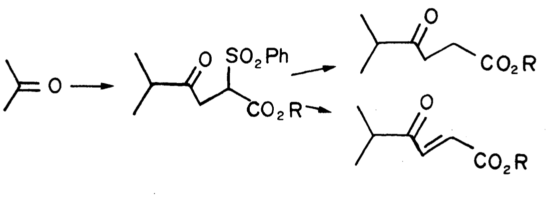
For the ecdysone side chain, ketosteroid 13 was converted to allylic acetate 14 in an identical fashion to the above. Alkylation also as above led to an 85% yield of the desired alkylation product. In this case, the sulfone ester serves as a vinyl substituent. Catalytic hydrogenation (5% Pd on BaCO$_3$) and ester reduction (LAH) created a β-hydroxysulfone 15 which upon subjection to 6% Na(Hg) led to the desired olefin 16. It is interesting to note that





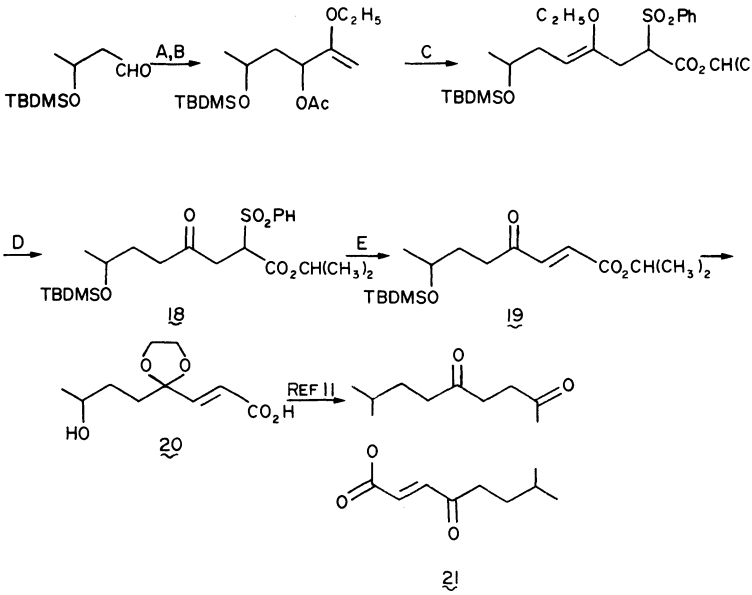
when a buffered reduction was employed, a simple desulfonylation ensued. Epoxidation through formation of an iodohydrin followed by base created the desired 22S epoxide 17; whereas, direct epoxidation with a peracid gave predominantly the 22R epoxide. Confirmation of the stereochemical assignments derived from correlation of both epimeric series with the 22-hydroxycholesterols whose stereochemistry has been well established. With the chiral centers all intact, the remaining structural elaboration followed more standard chemistry to create the 22R,25-dihydroxycholesterol. Since the cholesterol nucleus has been converted into the ecdysone nucleus, this approach can be considered a synthesis of the commercially important insect hormone, ecdysone.

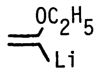
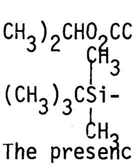
Functionalization of the allylic system increases the versatility of the process. For example, a four carbon chain extension sequence from a carbonyl group has evolved as outlined in eq 6 (10). For this sequence, the silyl ether of aldol was treated with 1-ethoxy-



Eq 6

Scheme 2. An Approach to Pyrenophorin (21)



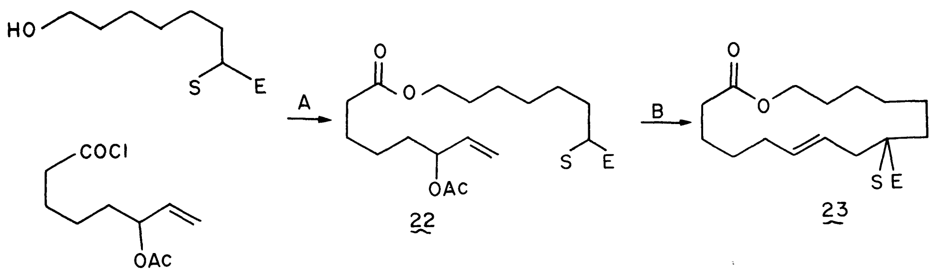
(a) , THF, -78° (b) Ac_2O (c) DBU, $(CH_3)_2CHO_2CCH_2SO_2PH$, $PhCH_3$, $(Ph_3P)_4Pd$ (d) H_2SO_4, H_2O, ether (e) $(C_2H_5)_3N$, TBDMS =  $(CH_3)_3C\overset{CH_3}{\underset{CH_3}{Si}}-$

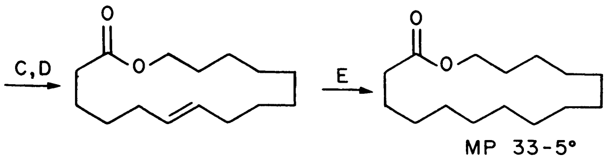
1-lithioethylene and the resultant alcohol capped with acetate. The presence of an ethoxy substituent on the double bond was anticipated to retard the palladium reaction since the olefin palladium complex, whose stability depends in part upon back donation of electron density from palladium to the π orbitals, would be destabilized due to the raising of the energy of the antibonding orbitals by the ethoxy substituent. While the traditional methods for effecting the palladium reaction gave less than satisfactory results, the use of DBU as the base in toluene as the solvent led to an excellent alkylation. Special note should be taken of the fact that a single stereoisomer of the enol ether results. There are few stereocontrolled syntheses of enol ethers which gives this method special merit. Unmasking the ketone sets up the sulfone for easy elimination to create the desired enedione system. In this particular case, conversion of 19 to the hydroxyacid 20 which already has been converted to pyrenephorin 21 by standard hydrolytic and ketalization methods (11) would complete the synthesis. The saturated γ-ketoester is potentially equally accessible from 18 by direct reductive desulfonylation.

Macrolide Formation

In exploring the potential of this transition metal template for directing reactions, the formation of rings, especially containing more than seven members becomes an important target. The growing number of natural products of high biological interest possessing such a structure led us to consider whether this approach to carbon-carbon bond formation occurred in an intramolecular sense. The importance of macrolides and the ease of formation of the requisite substrates led us to specifically examine this class (12). Scheme 3 outlines this convergent approach. The key step is the cyclization of allylic acetate 22 using

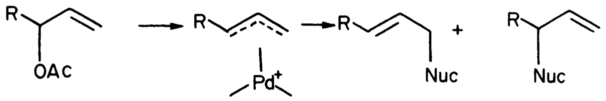
Scheme 3. Exaltolide Synthesis





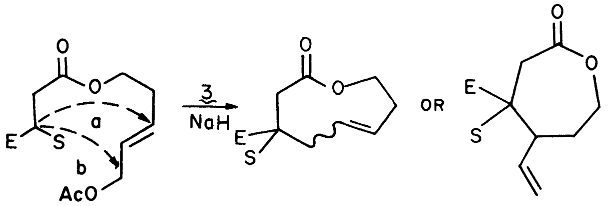
(a) $(C_2H_5)_3N$, ether, 50° (b) NaH, $(Ph_3P)_4Pd$, THF, reflux (c) $(CH_3)_4NOAc$, HMPA, 100° (d) 6% Na(Hg), Na_2HPO_4, C_2H_5OH, THF, -20° (e) H_2, $Pd/BaCO_3$

3.5 mole percent of the palladium(0) catalyst 3 to give macrolide 23 in 69% isolated yield. In addition to the delightfully high yield of macrocyclization, the regio- and stereoselectivity exhibited by this reaction is quite noteworthy. As illustrated in eq 7, intermolecular versions of this reaction normally lead to mixtures of stereo- and regioisomers in contrast to the intramolecular reaction. For the synthesis of exaltolide, the removal of the carbomethoxy and sulfone substituents by the methods outlined above and which have become routine in our laboratories followed by double bond reduction gave crystalline exaltolide.



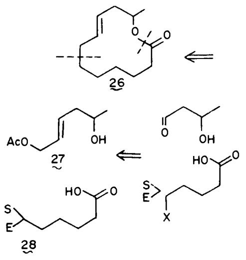
Eq 7

A spectacular illustration of this regioselectivity is the case of substrate 24 where cyclization can lead to either a seven membered ring (via "a") or nine membered ring (via "b"). The disfavorability for formation of a nine membered ring normally leads to the expectation that only seven membered ring formation would be observed in such a competition. In contrast to that expectation, the only cyclization product is the octolide 25.

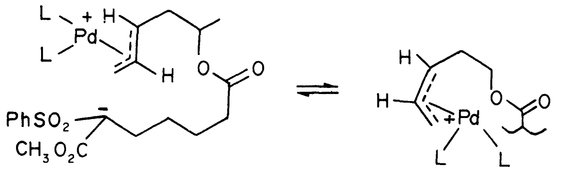


24 25

The preparation of lactones via C-C bond formation rather than the more conventional lactonization routes potentially provides a greater degree of flexibility in allowing the synthesis of the alcohol and acid portions independently. The synthesis of the naturally occurring macrolide, recifeiolide (26), isolated from the fungus Cephalosporium recifei, illustrates this principle (13). In a retrosynthetic analysis, cleavage at the ester linkage and the allylic carbon constitute the "natural" cleavages using our strategy. The resultant alcohol 27 originates from a two carbon chain extension of aldol, among the simplest building blocks. The acid 28 would originate from the commercially available 5-bromopentanoic acid and methyl benzenesulfonylacetate. Thus, this analysis allows rapid simplification to easily available starting materials. Scheme 4 summarizes the realization of this analysis. In this case, the macrocyclization step proceeded in 78% yield to give a stereo- (with

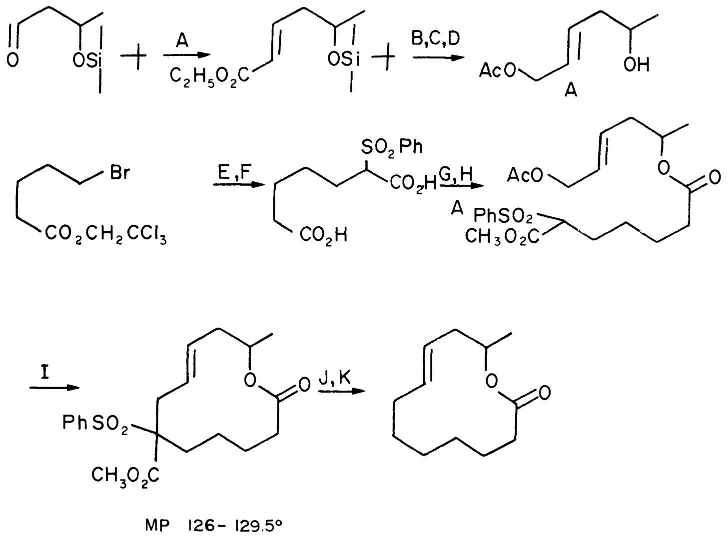


respect to the double bond) and regiohomogeneous product. The retention of the pure E olefin in the product means that the potential equilibration represented by eq 8 is slow relative



Eq 8

Scheme 4. Synthesis of Recifeiolide

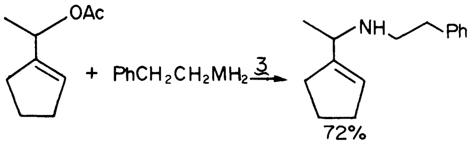


(a) $(C_2H_5O)_2P(O)\cdot CH_2CO_2C_2H_5$, NaH, THF, -78° → 0° (b) DIBAL, $PhCH_3$, 0°
(c) AcCl, pyridine, CH_2Cl_2, 0° (d) $HClO_4$, THF-H_2O, RT (e) $PhSO_2CH_2CO_2CH_3$, NaH, DMSO, 50° (f) Zn, DMF, 0° (g) $SOCl_2$ (h) A, ether, pyridine, 0°
(i) NaH, THF, then $(Ph_3P)_4Pd$ (9 mol %) (j) $(CH_3)_4NOAc$, HMPA, 95° (k) 6% Na(Hg), Na_2HPO_4, C_2H_5OH - THF, -20°

to the cyclization. The completion of the synthesis utilizes our standard conversion of the sulfone ester to a methylene group. (±) Recifeiolide was identical to an authentic sample of the racemic natural product obtained from Dr. Gerlach.

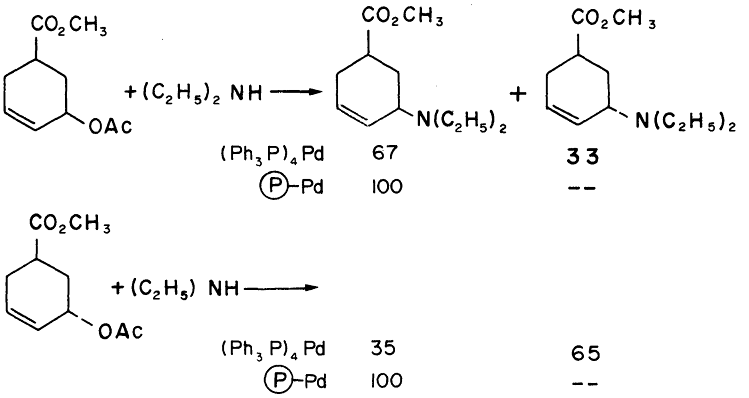
Amines as Nucleophiles

Heteroatom nucleophiles also participate in these reactions. From the point of view of natural product synthesis, the most interesting heteroatom nucleophile is nitrogen. Like in the case of carbon, primary and secondary amines participate in this reaction (14). Primary amines alkylate with little tendency for polyalkylation. The stereochemistry of the

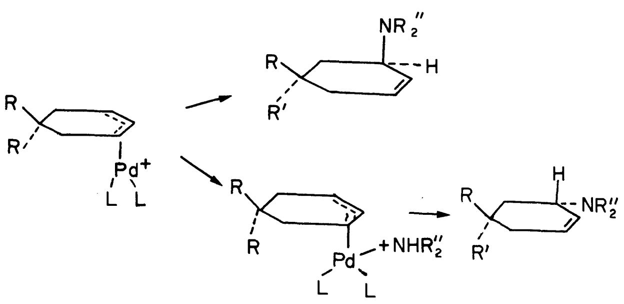


reaction is more complex as summarized in Scheme 5. Whereas, the soluble catalyst gives some loss of stereochemistry (15), the polymer supported catalyst gives only the product of retained stereochemistry (7). It appears that with amines there is a competition between

Scheme 5. Stereochemistry of Amine Alkylation

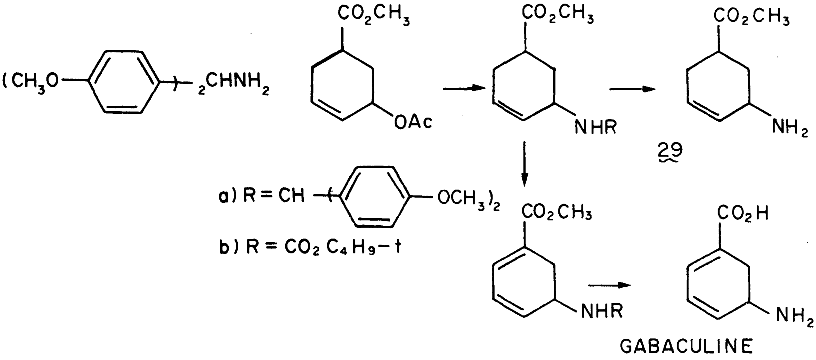


the nucleophile directly attacking carbon of the π-allylpalladium complex to give the normal net stereochemical retention (see eq 9) and attack at palladium followed reductive elimination



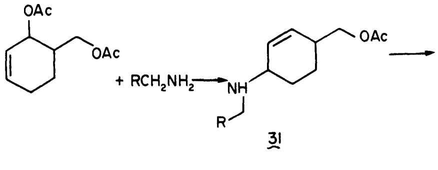
Eq 9

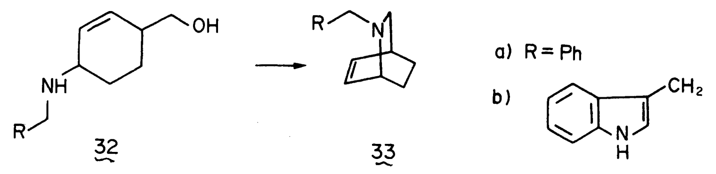
to give the product of stereochemical inversion. This observation can extend to a synthesis of the methyl ester of dihydrogabaculine 29 or extended, via the procedure of iodination -



dehydroiodination (16) to a synthesis of the naturally occurring amino acid gabaculine, a compound of biochemical interest as an inhibitor of γ-aminobutyrate aminotransferase.

The increased selectivity offered by the polymeric supported catalyst made available a useful synthesis of isoquinuclidines (7). The diacetate 30 undergoes regio- and stereospecific allylic amination with both benzyl amine and tryptamine to give 31. Hydrolysis and

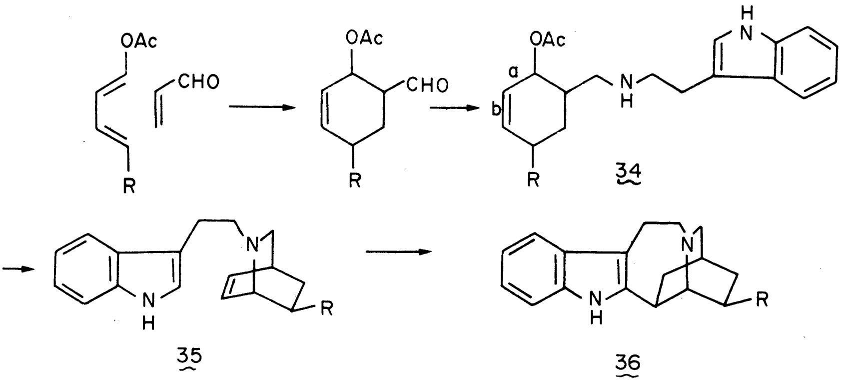


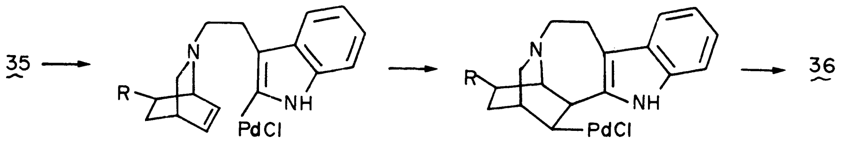


cyclization of the aminoalcohol 32 with triphenylbromophosphonium bromide completes this short synthesis of isoquinuclidines.

An alternative approach to isoquinuclidines takes advantage of the endo specificity of the Diels-Alder reaction (14). The Diels-Alder adduct of acetoxybutadiene and acrolein, formed in the presence of boron trifluoroide-etherate, undergoes imine formation and reduction to generate an amino acetate (see Scheme 6). Cyclization of this substrate requires the replacement of the allylic acetate by nitrogen on the same face of the allyl system. Keeping in mind that since these palladium catalyzed reactions involve π-allyl intermediates, attack of nitrogen can occur at either site "a" or "b" of 34. Experimentally, reaction occurs at site "b" to give the isoquinuclidine 35 rather than at site "a" to give the azetidine. The facile formation of such isoquinuclidines immediately raises the question of the applicability of this process to the synthesis of the iboga alkaloids since 35 (R=H) is an isomer of desethylibogamine. Indeed, palladium achieves this final cyclization as well. Treatment of 35 with palladium chloride in refluxing acetonitrile containing triethylamine followed by sodium borohydride forms (±) desethylibogamine, identical with an authentic sample. This reaction apparently involves a palladation of the indole nucleus at C(2), a cis addition to the olefin in a Heck type reaction, and subsequent reductive depalladation (see eq 10).

Scheme 6. Iboga Alkaloid Synthesis

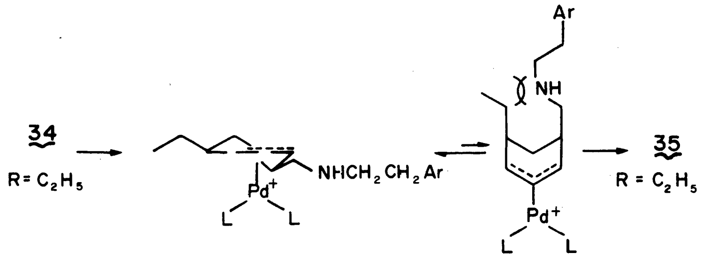




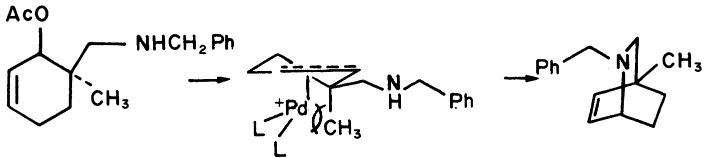
Eq 10

Since 33b is identical to 34 R=H, that approach as well constitutes an alternative route to the iboga system.

Ibogamine, 36 R = C_2H_5, can be examined from the point of view of this strategy where the key new structural feature is of the ethyl group (17). In tracing this back, it ultimately translates into the structure of the starting diene where 1-acetoxy-E,E-1,4-hexadiene is required for the Diels-Alder reaction. Indeed, the Diels-Alder reaction proceeds with equal regio- and stereocontrol as in the parent system as determined by careful analysis of the 270 MHz NMR spectrum. Reductive amination affords the requisite cyclization substrate. In this case, the cyclization must pass through a twist boat conformation 37 in which the



two ring substituents must encounter severe steric interactions of a 1,3-diaxial variety. Thus, it is not a foregone conclusion that this analog of the original cyclization would proceed without complications. Previously, we had encountered a severe rate retardation in the case of 38 which presumably arises because of unfavorable steric interactions, in this



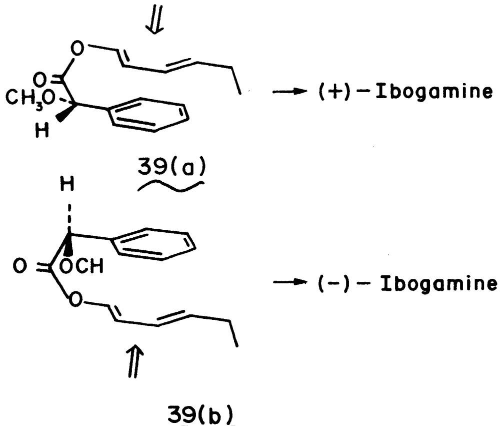
38

case between the palladium and the pseudoaxial quaternary methyl group.

Nevertheless, the cyclization of 34 (R=C$_2$H$_5$) proceeded well (45%) to give the desired isoquinuclidine 35 (R = C$_2$H$_5$). Subjection of the latter to a modified cyclization reaction in which silver fluoroborate is used as a cocatalyst led to (±)-ibogamine in 40-45% yields. Thus, ibogamine is available in 17% overall yield in four steps from readily available starting materials.

In carrying out any natural product synthesis, equal concern must be given to the question of absolute stereochemistry. In the present case, it can be seen that the absolute stereochemistry is created in the very first step where achiral starting materials are transformed into a chiral cyclohexene. The Diels-Alder reaction is one of the few reactions that lends itself to the possibility of asymmetric induction with the anticipation of a reasonable level of induction.

We chose to consider the use of the mandelate diene 39. One could envision in such a

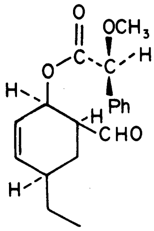


39(a)

39(b)

case a favorable π-stacking interaction leading to conformers 39a and 39b for this diene in which the benzene ring of the mandelate shields the opposite enantiotopic faces of the diene. Since the dienophile is forced to approach from the top face of the 39a, the ultimate product should lead to the (+) iboga series; whereas, for conformer 39b approach from the bottom face of the diene should lead to (-) series. The difference between these conformers lies in the orientation of the methoxy group with respect to the diene. Since this substituent is projected away from the diene and thus in the sterically less congested region in 39a this conformer might be anticipated to be the preferred one. An additional advantage of the mandelate unit resides in the ability to utilize nmr spectroscopy to directly read the optical purity of the product as shown by Mislow and Mosher.

Repetition of the synthetic sequence with diene 39 of approximately 97% optical purity



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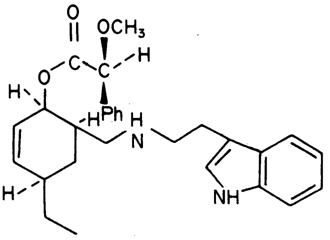

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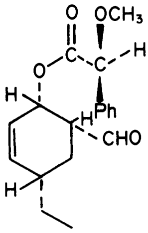


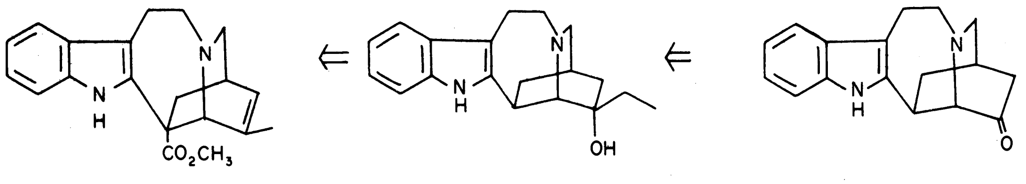
42

passes through synthetic intermediates 40 and 41. The nmr spectrum of 40 reveals two aldehydes (δ 9.56 and 9.07) and two methoxy groups (δ 4.58 and 4.59) in the ratio of 80:20. The minor compound corresponds to the stereoiosomer 42 which is epimeric at each asymmetric cyclohexyl carbon. Thus, 40 and 42 will lead to the opposite enantiomers of the final product and that ratio should be 80:20. Considering that no attempt has been made to optimize the asymmetric induction, this high enantiomeric excess is quite delightful.

At this point, we do not know what the absolute configuration of the major or minor adduct is. This point requires completion of the synthesis. Subjection of 41 to the first palladium cyclization produces the isoquinuclidine 35 (R = C_2H_5) with $[\alpha]_D^{25}$ +17.4° (c 2.48 $CHCl_3$) and subjection of optically active 35 to the second palladium cyclization produces ibogamine with $[\alpha]_D^{25}$ +31.4° (c 0.45 CH_3OH). Correcting this rotation for the optical purity of the starting diene (97%) and comparing this rotation to that for optically pure (+) ibogamine (+52.7°) leads to a ratio of (+) and (-) ibogamine of 81:19 in full accord with the nmr results on the initial adduct. Thus, the observed absolute configuration agrees with that predicted from our model. Since most work to date has employed only asymmetric dienophiles, the present approach of using an asymmetric diene appears to have great potential.

While most of the naturally occurring ibogamine belongs to the opposite enantiomeric series, both enantiomers do occur in nature. Of course, utilization of R-mandelate would provide (-)-ibogamine. More importantly, catharanthine, a most exciting target because of its potential use in a practical partial synthesis of the clinically important antitumor agents vinblastine and vincristine, belongs to the enantiomeric series corresponding to (+)-ibogamine.

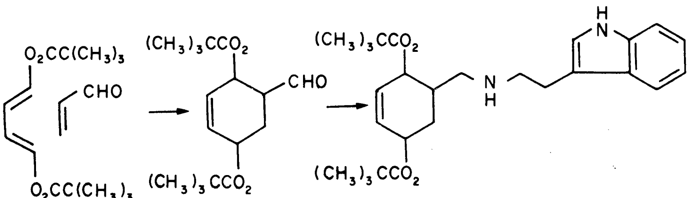
Application of this synthetic strategy to catheranthine 43 also appears quite feasible. Büchi has already converted the alcohol 44 into catharanthine (18) involving an elegant oxidative cyanation technique for introduction of the missing carbon. Since the alcohol 44



43 44 45

should be available from the ketone 45, we undertook an investigation of the synthesis of this compound as outlined in Scheme 7 (19). An important aspect of this synthesis is the chemoselectivity for the initial palladium cyclization in which two allylic carboxylates are present. Consideration of a conformational drawing of the initial olefin-palladium(0)

Scheme 7. Approach to Catharanthine.



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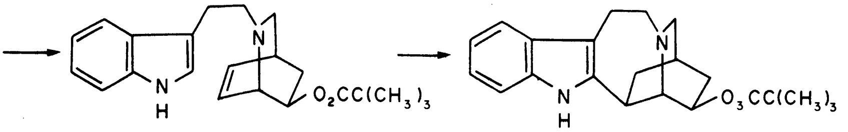
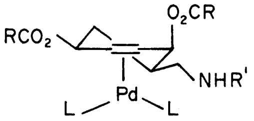


48 49

complex 47 derived from the dipivalate 46 would lead to the expectation of preferential



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ionization of the pseudoaxial pivalate which would produce the desired isoquinuclidine. Indeed, the latter was isolated in 40-50% yields, quite comparable to that observed for the ibogamine precursor 35 (R = C_2H_5). Since the cyclization of 46 to 48 suffers from the same unfavorable steric interactions as in the iboga case, the comparable yields are quite satisfying. Delightfully, the mildness of the second palladium cyclization proceeds unhampered by the pivalate. Preliminary experiments have indicated that methyllithium removes the pivalate from 49 and that a modified Moffatt oxidation employing pyridine-sulfur trioxide, pyridinium chloride, and triethylamine in DMSO provides the desired ketone 45. In contrast to Büchi's lactam which failed to add ethylmagnesium bromide, the ketone 45 adds the ethyl group nicely to give the Büchi intermediate 44 and consequently a catharanthine synthesis. Thus, this strategy provides a general entry to the iboga alkaloids and, unlike many other methods, appears adaptable to their chiral synthesis.

CONCLUSIONS

The use of palladium as a transition metal template provides an extraordinary degree of selectivity of all types as listed in Chart 1. Synthetic applications of a broad array of natural products ranging from steroids, other terpenes, and macrolides to unusual amino acids and alkaloids are feasible. Surely, other applications will follow. The efficiency of several of these syntheses attests to the value that new methodology plays in the area of total synthesis. Approaching older but important target molecules with new methods frequently will streamline synthesis. Molecules of a complexity that formerly were not approachable are now reasonable goals. The real key for utility for new methodology is whether it provides a selectivity that previously did not exist. Clearly, transition metal chemistry does just that. The above contributes to just one aspect of this fascinating area.

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REFERENCES

1. (a) B. M. Trost, P. E. Strege, L. Weber, T. J. Fullerton, and T.J. Dietsche, J. Am. Chem. Soc., 100, 3407 (1978) and references therein. (b) B. M. Trost, L. Weber, P. E. Strege, T. J. Fullerton, and T. J. Dietsche, ibid., 100, 3416 (1978).
2. B. M. Trost, L. Weber, P. Strege, T. J. Fullerton, and T. J. Dietsche, ibid., 100, 3426 (1978).
3. (a) B. M. Trost and T. R. Verhoeven, J. Am. Chem. Soc., 100, 3435 (1978); (b) B. M. Trost and T. R. Verhoeven, J. Org. Chem., 41, 3215 (1976).
4. K. E. Atkins, W. E. Walker, and R. M. Manyik, Tetrahedron Lett., 3821 (1970); K. Takahashi, A. Miyaki, and G. Hata, Bull. Chem. Soc. Japan, 45, 230 (1972); H. Onoue, I. Moritani,

and S. F. Murahashi, Tetrahedron Lett., 121 (1973).
5. B. M. Trost and T. R. Verhoeven, unpublished results.
6. P. E. Strege, Ph.D. Thesis, University of Wisconsin, 1976.
7. B. M. Trost and E. Keinan, unpublished results.
8. B. M. Trost and Y. Matsumura, J. Org. Chem., 42, 2036 (1977).
9. B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, Tetrahedron Lett., 3477 (1976).
10. B. M. Trost, F. W. Gowland, unpublished results.
11. H. Gerlach, K. Oertle, and A. Thalmann, Helv. Chim. Acta, 60, 2860 (1978).
12. B. M. Trost and T. R. Verhoeven, J. Am. Chem. Soc., 99, 3867 (1977).
13. B. M. Trost and T. R. Verhoeven, Tetrahedron Lett., 2275 (1978).
14. B. M. Trost and J. P. Genet, J. Am. Chem. Soc., 98, 8516 (1976).
15. B. M. Trost and J. P. Genet, unpublished results.
16. S. P. Singer and K. B. Sharpless, J. Org. Chem., 43, 1448 (1978).
17. B. M. Trost, and S. Godleski, and J. P. Genet, J. Am. Chem. Soc., 100, 3930 (1978).
18. G. Büchi, P. Kulsa, K. Ogasawara, and R. L. Rosati, J. Am. Chem. Soc., 92, 999 (1970).
19. B. M. Trost, S. Godleski, and J. Belletire, unpublished results.