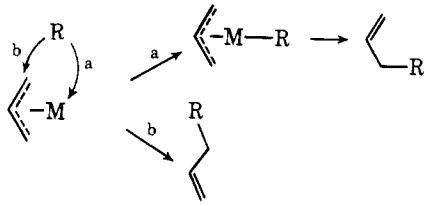
## New Synthetic Reactions. Stereochemistry of Allylic Alkylation

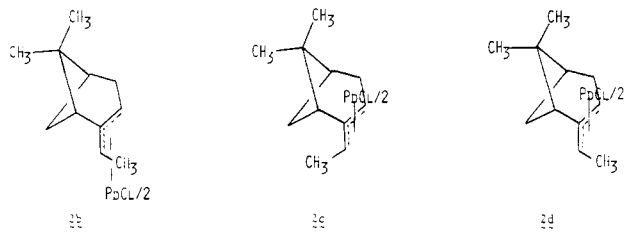
*Sir:*

The synthetic utility of the allylic alkylation procedure previously reported increases greatly if it provides stereochemical control in an absolute and relative sense.[1] Furthermore, the mechanism of carbon–carbon bond formation via $\pi$-allyl complexes has not been determined.[2-6] In particular, the question of whether bonding of the attacking reagent occurs initially at the metal (path a) with subsequent migration to carbon or directly at carbon (path b) remains

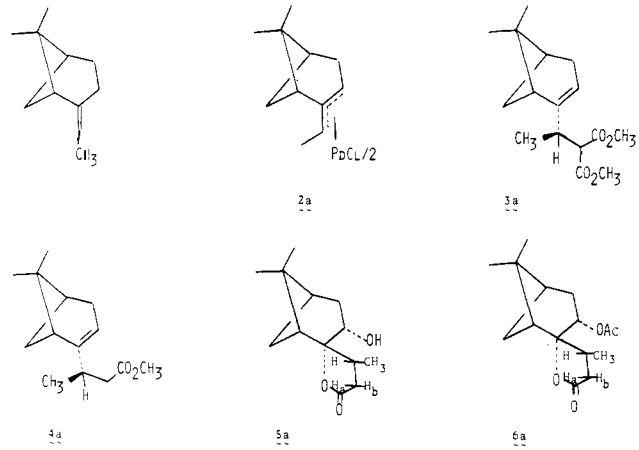


unanswered. To probe these points we undertook an examination of the stereochemistry of the reaction of nucleophiles with $\pi$-allyl palladium complexes.

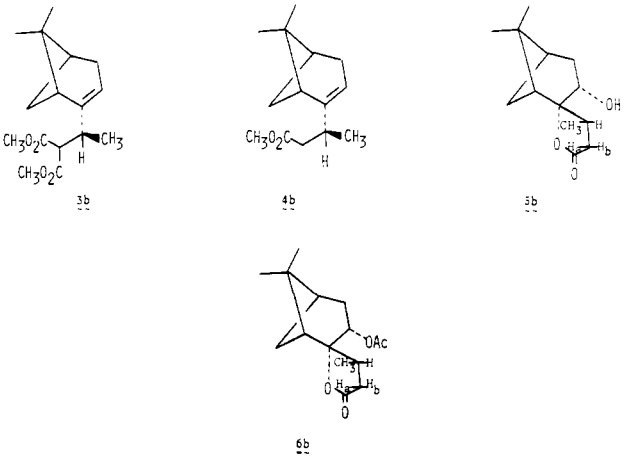
The single stereochemically homogeneous $\pi$-allyl complex (**1**) (found: C, 45.34; H, 5.94; Cl, 12.22) is obtained from an *E,Z* mixture of 2-ethylidenenopinane[7] ($PdCl_2$, NaCl, $CuCl_2$, NaOAc, HOAc, 60°, 75 min, 55%), the latter available from nopinone by the Wittig reaction. Examination of the crude reaction mixture by NMR spectroscopy reveals the absence of any other $\pi$-allyl complexes. The structure of the complex as **2a** (see Scheme I) rather than **2b, 2c,** or **2d** was based initially upon the NMR spectrum.[8,9] Of the two faces of the pinene (i.e., **2a–2b** vs. **2c–2d**), steric congestion on the face syn to the gem dimethyl bridge precludes isomers **2c–2d.** Indeed, virtually all additions to the pinene system are known to occur from the $\alpha$ face.[10-12] The NMR spectrum supports such a contention. The gem dimethyl groups should experience a differential shift in **2c–2d** relative to the pinenes as a result of the anisotropy of the palladium. In fact, the chemical shift difference of these groups in the complex ($\delta$ 0.93 and 1.36, $\Delta\delta$ = 0.43) is identical with this difference in $\alpha$-pinene ($\delta$ 0.84 and 1.27, $\Delta\delta$ = 0.43). The stereochemistry of the complex as *syn*-**2a** rather than *anti*-**2b** is also based upon the NMR spectrum,[8,9] in particular, a single doublet ($J$ = 6.7 Hz) at $\delta$ 1.14 for the allylic methyl group and a broad singlet at $\delta$ 3.81 and a quartet ($J$ = 6.7 Hz) at $\delta$ 3.71 for the $\pi$-allylic methines. These deductions leading to assignment of structure **2a** have been confirmed by a preliminary X-ray analysis.[9]



**Scheme I.** Alkylation of 2-Ethylidenenorpinane



Alkylation of **2a** (see Scheme I) with the anion of dimethyl malonate (DIPHOS, THF, room temperature, 16 hr, 69%) produces a single diastereomer **3a** or **3b** ($\delta$ 3.71, 2H, s; 3.66, 3 H, s; 3.43, 1 H, d, $J$ = 9.6 Hz; 0.99, 3 H, d, $J$ = 7 Hz). Decarbomethoxylation (LiI, NaCN, DMF, 120°, 10 hr, 80%) led to a stereochemically homogenous compound, **4** ($\delta$ 5.24, 1 H, bs; 3.63, 3 H, s; 1.00, 3 H, d, $J$ = 7 Hz).



In order to determine the stereochemistry at the newly formed chiral center, acyclic geometry was converted into cyclic geometry by hydroxylation ($OsO_4$, ether, pyridine, room temperature, 15 hr) of **4** on the $\alpha$ face[11] followed by lactonization (TsOH, benzene, reflux, 0.5 hr) to give **5a** or **5b** in 62% overall yield. The presence of the five-membered ring lactone was confirmed by ir spectroscopy (1780 $cm^{-1}$) and of a secondary alcohol by acetylation ($Ac_2O$, pyridine, room temperature 80%) (methine proton, $\delta$ 4.52, adjacent to alcohol shifts to $\delta$ 5.57 in acetate).

Europium(+3) induced shifts of **5** and **6** allow differentiation between the "a" and "b" series. One of the hydrogens $\alpha$ to the carbonyl group of the lactone in **6** appears as a doublet of doublets ($J$ = 17, 8 Hz) at $\delta$ 2.80 indicating it to be $H_a$ with $H_b$ appearing at $\delta$ 2.08 as a doublet of doublets ($J$ = 17, 2.5 Hz). Addition of 20 mol % $Eu^{3+}$ shifts the former 132 Hz and the latter 150 Hz confirming the assignment. In **5,** $H_a$ appears at $\delta$ 2.89 (dd, $J$ = 17.4, 8 Hz). Addition of 25 mol % $Eu^{3+}$ to the alcohol **5** should lead to preferential complexation at the hydroxyl group.[13] *Under these conditions, $H_a$ shifts by 164 Hz but the secondary methyl group on the lactone ring shifts by 237 Hz (from $\delta$ 1.23 to 3.60)*! This observation demands that this methyl group be closer to the hydroxyl group than $H_a$ and allows the stereochemistry depicted in the "a" series to be assigned.

The stereospecificity of allylic alkylation has potentially important consequences in the application of the method for the creation of stereochemistry in acyclic and macrocyclic systems. It is interesting to note that in this case high stereospecificity is achieved even though the nucleophile must approach the more congested face of the molecule. Further-

more, it establishes the fact that alkylation occurs on the face of the $\pi$-allyl unit opposite to that of the palladium.[2,4,5] This supports our earlier contention that $\pi$-allyl palladium cationic complexes are ambident electrophiles and that "soft" nucleophiles which attack directly at carbon are required for successful alkylation.[1a]

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## References and Notes

(1) (a) B. M. Trost and T. J. Fullerton, *J. Am. Chem. Soc.*, **95,** 292 (1973); (b) B. M. Trost and T. J. Dietsche, *ibid.*, **95,** 8200 (1973); (c) B. M. Trost, T. J. Dietsche, and T. J. Fullerton, *J. Org. Chem.*, **39,** 737 (1974).
(2) For reviews see J. Tsuji, *Acc. Chem. Res.*, **2,** 144 (1969); R. Baker, *Chem. Rev.*, **73,** 487 (1973); M. F. Semmelhack, *Org. React.*, **19,** 115 (1972).
(3) (a) H. Felkin and G. Swierczewski, *Tetrahedron Lett.*, 1433 (1972); (b) R. P. Hughes and J. Powell, *J. Am. Chem. Soc.*, **94,** 7723 (1972); (c) K. E. Atkins, W. E. Walker, and R. M. Manyik, *Tetrahedron Lett.*, 3821 (1970); (d) J. Tsuji, H. Takahashi, and M. Morikawa, *ibid.*, 4387 (1965); (e) H. Onoue, I. Moritani, and S. I. Murahashi, *ibid.*, 121 (1973); (f) G. Hata, K. Takahashi, and A. Miyake, *Chem. Commun.*, 1392 (1970); (g) K. Takahashi, A. Miyake, and G. Hata, *Bull. Chem. Soc. Jpn.*, **45,** 230 (1972).
(4) For suggestions that such reactions proceed by migration from metal to carbon, see ref 2 and Y. Takahashi, S. Sakai, and Y. Ishii, *Chem. Commun.*, 1092 (1967); Y. Takahashi, K. Tsukiyama, S. Sakai, and Y. Ishii, Tetrahedron Lett., 1913 (1970).
(5) For related condensations of dienes and active methylene compounds believed to involve transfer of allyl group from palladium to carbon see R. Baker, D. E. Halliday, and T. N. Smith, *J. Organomet. Chem.*, **35,** C61 (1972); G. Hata, K. Takahashi, and A. Miyake, *J. Org. Chem.*, **36,** 2116 (1971); K. Takahashi, A. Miyake, and G. Hata, *Bull. Chem. Soc. Jpn.*, **45,** 1183 (1972); S. Watanabe, K. Suga, and T. Fujita, *Can. J. Chem.*, **51,** 848 (1973).
(6) For stereochemistry of palladium catalyzed alkylations of olefins see A. Kasahara, T. Izumi, K. Endo, T. Takeda, and M. Ookita, *Bull. Chem. Soc. Jpn.*, **47,** 1967 (1974); H. Horino, M. Arai, and N. Inoue, *Tetrahedron Lett.*, 647 (1974); A. Segnitz, P. M. Bailey, and P. M. Maitlis, *J. Chem. Soc., Chem. Commun.*, 698 (1973); J. K. Stille and D. B. Fox, *J. Am. Chem. Soc.*, **92,** 1274 (1970).
(7) B. M. Trost and P. E. Strege, *Tetrahedron Lett.*, 2603 (1974).
(8) H. C. Volger, *Recl. Trav. Chim. Pays-Bas*, **88,** 225 (1969); J. W. Faller, M. E. Thomsen, and M. J. Mattina, *J. Am. Chem. Soc.*, **93,** 2642 (1971). For a review see R. Hüttel, *Synthesis*, 225 (1970).
(9) A preliminary X-ray analysis has been performed by Dr. Joseph Calabrese.
(10) C. A. Brown, *J. Am. Chem. Soc.*, **91,** 5901 (1969); J. M. Coxon, E. Dansted, M. P. Hartshorn, and K. E. Richards, *Tetrahedron*, **24,** 1193 (1968); L. E. Grunewald and D. C. Johnson, *J. Org. Chem.*, **30,** 1673 (1965); J. M. Coxon, E. Dansted, and M. P. Hartshorn, *J. Chem. Eng. Data*, **15,** 336 (1970). See, however, A. I. Scott and A. D. Wrixon, *Tetrahedron*, **27,** 2339 (1971).
(11) N. Sakota and S. Tanaka, *Bull. Chem. Soc. Jpn.*, **44,** 485 (1971).
(12) The term $\alpha$ face refers to the side of the pinane system anti with respect to the bridge bearing the gem dimethyl group.
(13) I. Fleming, S. W. Hanson, and J. K. M. Sanders, *Tetrahedron Lett.*, 3733 (1971); J. C. Duggan, W. H. Vary, and J. Schaefer, *ibid.*, 4197 (1971); D. E. V. Ekong, J. I. Okogun, and M. Shok, *J. Chem. Soc., Perkin Trans. 1*, 653 (1972); J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Am. Chem. Soc.*, **94,** 5325 (1972). For reviews see A. F. Lockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, **73,** 553 (1973); B. C. Mayo, *Chem. Soc. Rev.*, **2,** 49 (1973).
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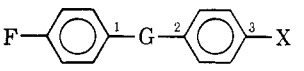
## Regarding $\pi$-Electron Transmission of Substituent Polar Effects on Fluorine Nuclear Magnetic Resonance Shielding[1]

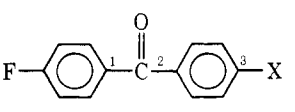
*Sir:*

Recent interest centers in the mode of transmission of the $\sigma_I$ effects of polar substituents[2] on the F NMR shifts of fluoroaromatics. Dewar and students have viewed[3] (and based their FMMF treatment[4]) upon these effects as arising predominantly from field transmission (electrostatic field theory). However, this view is poorly supported by the extremely small magnitude of substituent effects on the F NMR shifts for systems with saturated hydrocarbon molecular cavities.[5] Further, Stock et al.[6] have observed recently that relative to para-substituted fluorobenzenes there is a marked enhancement of the polar effects of 10-substituents in 9-fluoroanthracene. This enhancement was interpreted to mean that the $\pi$ electron framework connecting the meso positions of anthracene provides a more effective internal transmission of the effects of polar substituents than does that for the para positions of benzene. Dayal et al.[7] have studied extensively the effects of polar substituents, X, in structure I as a function of the variable molecular cavity, G. Greater than 25-fold increase in the effects of corresponding polar substituents was observed, for example, on going from G = $C(CF_3)OH$ to $C(CF_3)^+$. This and similar results led Dayal et al. to conclude that the marked enhancements of substituent polar effects *on the F NMR shifts* arise predominantly from the improved transmission through the $\pi$-electron system.[8]

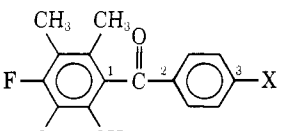


I

Comparison of the F NMR shielding effects of polar substituents (X) in ketones II and III and their complexes provides for a definitive decision regarding the relative importance of transmission of the polar effect through field or internal $\pi$-electron framework. The extension of $\pi$-electron framework beyond a phenyl ring is strongly subject to steric twisting influences.[9] Yet twisting of the phenyl rings of II and III alters but little the X-F distance. In consequence, corresponding polar effects on the F NMR shielding will be little altered in III relative to II if transmission is by field but will be substantially reduced if transmission is by the internal $\pi$-electron framework.



II



III

Table I. F NMR Substituent Shielding Effects for Ketones in Dilute Methylene Chloride Solutions[a]

| X | Series II[b] | Series III[c] |
|---|---|---|
| $NMe_2$ | 2.32 | 1.21 |
| OMe | 0.80 | 0.32 |
| Me | 0.46 | 0.23 |
| F | −0.16 | −0.28 |
| Cl | −0.51 | −0.44 |
| H | (0.00)[d] | (0.00)[e] |
| $CF_3$ | −1.29 | (−0.94) |
| CN | (−1.79)[f] | −1.21 |
| $NO_2$ | −2.00 | −1.38 |
| $-\rho_I$ | 2.55 | 1.82 |
| $-\rho_R$(BA) | 2.74 | 1.49 |
| $\lambda = \rho_R/\rho_I$ | 1.07 | 0.82 |
| SD | 0.12 | 0.06 |
| $f$ = SD/RMS | 0.091 | 0.064 |

[a] Shifts in ppm relative to unsubstituted (H) member. [b] Reference 7. [c] This work. [d] Shift of unsubstituted member relative to external reference of TCTFCB (60 wt % in $HCCl_3$) is −6.42. [e] Shift of unsubstituted member relative to external reference of TCTFCB (60 wt % in $HCCl_3$) is +5.73. [f] Calculated shift by DSP equation, ref 11b.