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DIASTEREOSELECTION IN RHODIUM-MEDIATED INTRAMOLECULAR C-H INSERTION: PREPARATION OF A TRANS-3,4 DIALKYL CYCLOPENTANE

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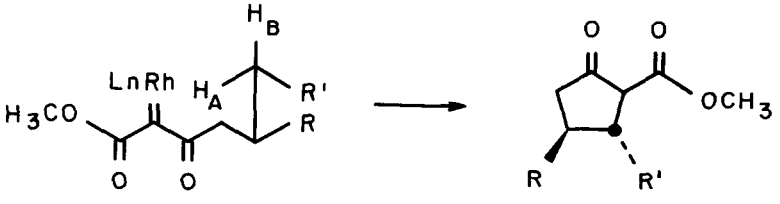
Summary: Transition state analysis suggests that substantial 1,2 asymmetric induction could be observed in the course of rhodium-mediated intramolecular C-H insertion. This analysis successfully predicts predominant formation of the trans 3,4-dialkyl cyclopentane when an α-diazo β-ketoester having a δ-phenyl substituent is cyclized.

One of the central challenges in synthetic organic chemistry is the development of new methods for the construction of carbocyclic rings. We recently reported[2,3] a general method for cyclopentane construction, based on rhodium-mediated[4] intramolecular C-H insertion. We now report that when there is an alkyl substituent on the 4-position of the incipient ring, substantial 1,2 asymmetric induction is observed. The predominant product is the trans-3,4 dialkyl cyclopentane 2.

This result is predicted by transition state analysis. We have postulated[3] that cyclization proceeds via a chair-like transition state, as in 1. The choice is between insertion into H_A, to give the trans product, or into H_B, to give the cis product. As insertion into H_B would make R' axial in the transition state, insertion into H_A seemed more likely. The trans-3,4 diastereomer should therefore be the major product from the cyclization.



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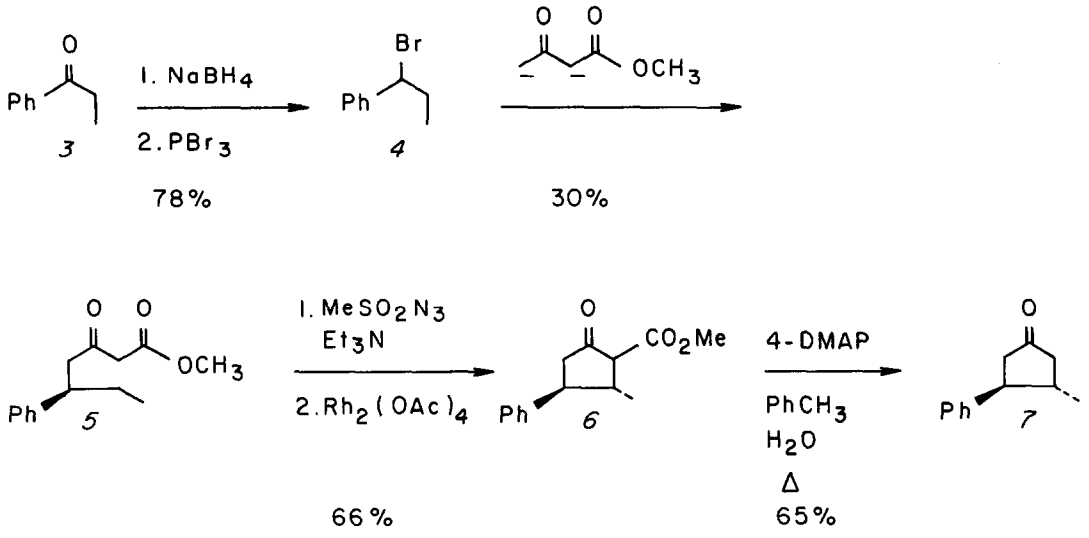
SCHEME I



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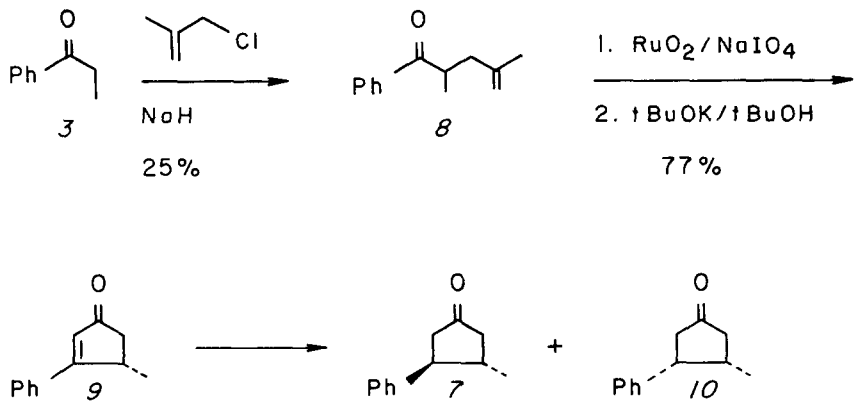

We chose to employ R= phenyl, to take advantage of the significant upfield NMR shift[5] to be expected for the cis diastereomer 10. The starting point for the project was thus β-ketoester 5, prepared by alkylation of the dianion[6] of methyl acetoacetate with bromide 4[7]. In the event, exposure of the derived[8] α-diazo β-ketoester to a catalytic amount of rhodium acetate in CH_2Cl_2 at room temperature led smoothly to a single product 6[9]. Observation of a methyl doublet at 1.06 δ led to the structural assignment shown.

To confirm this assignment independent syntheses of the decarbomethoxylated[10] ketone 7 (^1H NMR = 1.05 δ) and its cis diastereomer 10 were undertaken. Thus, cleavage[11] of 8[12] followed by cyclization gave enone 9. Dissolving metal reduction gave an equal mixture of 7, identical with the previously prepared material, and 10, which, as expected, showed a methyl doublet further upfield (^1H NMR = 0.73 δ). Catalytic hydrogenation of 9 gave 10 and 7 in a ratio of 95:5.[13]

There is much yet to learn about transition metal-mediated intramolecular C-H insertion. The result reported herein was predicted from simple consideration of molecular mechanics, without any real reference to the structure of the diacyl metallocarbene. In that carbene, the carbonyls could be syn, as drawn, or anti.[14] The carbene-stabilizing metal could be bonded to carbon, as shown, or bonded to oxygen. These fundamental questions are being addressed in ongoing investigations.

In addition to shedding some light on the transition state for rhodium-mediated intramolecular C-H insertion,[15] it should be noted that the overall process (5 → 6) described herein effects transformation of an open-chain precursor having a single ternary stereogenic[16] center diastereoselectively to a trans-3,4-dialkyl cyclopentane. As acyclic ternary centers of high optical purity are readily available,[17] this could represent a general strategy for enantioselective ring construction.

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References and Notes

1. Fellow of the Alfred P. Sloan Foundation, 1982-1987.

2. Taber, D. F.; Petty, E. H. J. Org. Chem. 1982, 47, 4808.

3. Taber, D. F.; Raman, K. J. Am. Chem. Soc. 1983, 105, 5935.

4. For other studies of Rh-mediated intramolecular C-H insertion see: a) Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; daSilva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. J. Org. Chem. 1982, 47, 3242. b) Cane, D.; Thomas, P. J. Am. Chem. Soc. 1984, 106, 5295.

5. McMurry, J. E.; von Beroldingen, L. A. Tetrahedron 1974, 30, 2027.

6. Huckin, S. N.; Weiler, L. J. Am. Chem. Soc. 1974, 96, 1082.

7. Levene, P. A.; Rothen, A.; Kuna, M. J. Biol. Chem. 1937, 120, 777.

8. Hendrickson, J. B.; Wolf, W. A. J. Org. Chem. 1968, 33, 3610.

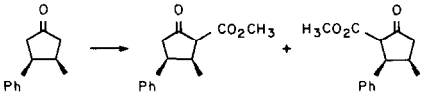
9. TLC R_f (20% EtOAc/hexane) = 0.33; IR: 2965, 1740, 1730, 1500, 1460, 1440, 1410, 1330, 1295, 1205, 1145, 1040, 695 cm^{-1}; ^1H NMR: 1.06, d, J = 6.1, 3H; 2.5-2.9, m, 4H; 3.05, d, J = 11.9, 1H; 3.8, s, 3H; 7.2-7.4, m, 5H; ^{13}C NMR: 16.7(q), 43.3(d), 47.3(t), 48.5(d), 52.5(q), 63.7(d), 127.3(d), 127.5(d,2), 128.9(d,2), 140.4(s), 169.3(s), 208.9(s); MS: 232(43), 217(9), 214(17), 201(11), 200(13), 173(11), 172(19), 132(15), 131(17), 104(100), 101(28), 91(15), 69(22). Calculated for $C_{14}H_{16}O_3$: 232.110, found 232.110.

10. This is a mild procedure for decarbalkoxylation of an enolizable β-ketoester recently developed by our research group: Taber, D. F.; Amedio, J. C., Jr. Manuscript in preparation.

11. Carlsen, H. J.; Katsuki, T., Martin, V. S.; Sharpless, K. B. J. Org. Chem. 1981, 46, 3936.

12. Ketone 8 was prepared by alkylation of propiophenone (1.5 eq. NaH, THF, 60°, 18h) with methallyl chloride: TLC (10% EtOAc/hexane) R_f = 0.56.

13. Pure 10 was carbomethoxylated (NaH/methyl carbonate) to give a mixture of 11 and 12. These esters co-chromatographed with 6 (TLC). From the ^1H NMR of crude 6, we can estimate that less than 5% of cis diastereomer 12 is formed in the cyclization.



10 11 12

14. Preliminary calculations (personal communication, K. N. Houk, U. Pittsburgh) indicate a preference for the syn conformer for singlet diacyl carbene.

15. The catalytic studies reported here are clearly relevant to stoichiometric studies of Rh-mediated C-H activation reported recently:
a) Periana, R. A.; Bergman, R. G. Organomet. 1984, 3, 508.
b) Jones, W. D.; Feher, F. J. J. Am. Chem. Soc. 1984, 106, 1650.

16. Mislow, K.; Siegel, J. J. Am. Chem. Soc. 1984, 106, 3319.

17. For a review, see Martin, S. F. Tetrahedron 1980, 36, 419.

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