establish a three-proton exchange process (H_b,H_1,H_2, $\Delta G^{\ddagger}$ = 9.2 kcal/mol) via methyl group rotation and a five-proton exchange process (H_b,H_1,H_2,H_3,H_4, $\Delta G^{\ddagger}$ = 13.4 kcal/mol) consistent with formation of the ethylene hydride **12** accompanied by ethylene rotation.[13]   Treatment of **10a** with $P(OMe)_3$ results in displacement of the C–H bridge and formation of **13**, a reaction typical of M–H–C systems.[14]   Similarly, treatment of **10a** with ethylene should yield **14**, an alkyl(alkene) analogue of **10a**. If alkyl migration is rapid as postulated, **10a**, should catalyze ethylene polymerization by successive migratory insertion reactions. In fact, treatment of **10a** under ethylene pressure yields *linear* polyethylene (–7 °C, CH_2Cl_2, 40 psi C_2H_4, 850 turnovers in 70 h with catalyst remaining active).

Following this ethylene polymerization by ^1H NMR (3 equiv of C_2H_4, CD_2Cl_2, –40 °C), in spite of the spectroscopic complexity, is quite informative. As **10a** disappears with ethylene consumption, no ethylene ethyl complex **14** could be detected. Instead, three new resonances assigned to new bridging hydride species appear at δ –11.8, –12.9, and –13.1 in the ratio 8:12:80, respectively. As polymerization proceeds the methylene resonance at δ 1.2 intensifies but the three briding hydride signals remain essentially unchanged in intensity and relative ratios. The δ 3.2–1.6 region is quite complex.

Scheme I is consistent with our experimental observations. The three new hydride signals have been assigned (see below) to mono-*n*-alkyl substituted isomers of **10a** retaining the bridging hydride structures, i.e., **16a–c** (R = alkyl with R = ethyl the first-formed homologue). These must result from ethyl (or subsequently *n*-butyl, *n*-hexyl, etc.) migration (**14 → 15**) followed by bridging of the β-hydrogen of the new alkyl ligand to the metal center. Operation of the exchange processes delineated for **10a** results in scrambling the alkyl group to the three observed positions.

To support these assignments, equilibrating complexes **16a–c**

R=methyl,ethyl   **16 a,b,c**   alkyl = methyl,ethyl
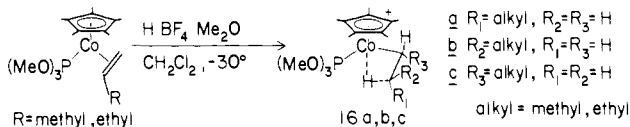
have been independently generated by protonation of $(C_5Me_5)(P(OMe)_3)Co(CH_2=CHR)$, where R = Me or Et.[15] ^1H and ^{13}C NMR spectra are simplified in that the mixture of homologues arising from differing numbers of ethylene insertions are not present. A key observation is that for R = ethyl there are three bridging hydride signals whose chemical shifts and ratios are identical with those observed in the ethylene polymerization studies. The isomer ratios and chemical shifts of the R = methyl isomers are nearly identical with those of the R = ethyl complexes; thus the positions of the bridging hydride signals appear insensitive to alkyl chain length. For R = CH_3, complete assignments for ^1H and ^{13}C resonances were obtained.[12] Spin saturation transfer experiments confirm the dynamic processes that interconvert the various structural isomers[12] and prove that for (propyl)-$(Me_5C_5)Co(P(OMe)_3)^+$ the two predominant isomers have the methyl group attached to C_β (**16a,b**) with the methyl bound to C_α in the minor isomer, **16c**.

Following the polymerization by ^{13}C NMR confirms Scheme I. Monitoring the ratios of **10a**:**16**(alkyl = $-C_2H_5$):**16** (alkyl =

C_4H_9, C_6H_{13}, etc.) shows that the first insertion (**10a → 16** (alkyl = ethyl)) is *slower* than subsequent insertions.

Three further aspects of this scheme are noted: (1) since under our experimental conditions no alkyl alkene complexes (e.g., **14**) were directly observed, bridged structures **16** are the "resting state" of the catalyst, (2) independent entry into **14** (reaction of $P(OMe)_3$ with **10**, L = C_2H_4) leads initially to **10a** and ethylene which suggests the migration step **14 → 15** is rate determining, and (3) only linear polyethylene forms so only (*n*-alkyl)(ethylene) complexes ultimately undergo migratory insertion even though branched alkyl substituents could arise from reaction of **16c** with ethylene. Although more complex mechanisms[1,7,8] for the insertion reaction cannot be ruled out by these experiments, we favor migratory insertion as the simplest most reasonable mechanism particularly in view of our initial hypothesis.

The principles outlined here are being applied to identify and investigate other alkene polymerization catalysts and carbon–carbon bond forming reactions in metal alkyl polyene complexes.

Supplementary Material Available: Dynamic NMR of **10a** and ^1H and ^{13}C NMR characterization of **16a–c** (R = methyl, ethyl) and C_5Me_5 $(P(OMe)_3)(C_2H_3R)$ (R = H, CH_3, C_2H_5) (5 pages). Ordering information is given on any current masthead page.


Penem Synthesis through C3–N Ring Closure of a β-Lactam Precursor

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The search for β-lactam antibiotics possessing enhanced activity, satisfactory stability, and resistance to β-lactamases has generated continuing strong interest in methods of preparing the penem system.[1]   The early Woodward procedure for constructing this framework made use of an intramolecular Wittig reaction for forming the C_2-C_3 bond[2] (**1 → 2**) and this has remained the
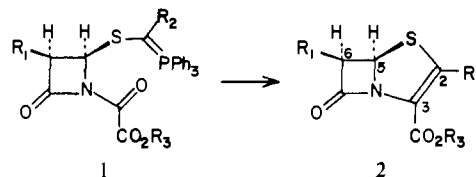

principal method for fusing the five-membered ring to the β-lactam nucleus in the formation of **2**.

Unlike the results obtained in the carbapenem series, the route to penems through C_3-N bond formation has, up to the present, not shown promise. Thus, recent approaches to **2** starting from precursors **3**,[2a] **4**,[3] and **5**[4] have all failed to give C_3-N ring closure.[5]

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(12) **10a** (prepared via $HBF_4\cdot Me_2O$ reaction with C_5Me_5 $(P(OMe)_3)Co$-(C_2H_4) at –30 °C, CH_2Cl_2): ^1H NMR (–70 °C, CD_2Cl_2) δ –12.1 (m, H_b), –0.3 (m, H_1 or H_2), –0.2 (m, H_1 or H_2), 1.9 (m, H_4 or H_5), 2.5 (m, H_4 or H_5); ^{13}C NMR (–90 °C, CD_2Cl_2) δ –5.8 (t d, J_{CH} = 152, J_{CH} = 61 Hz, C_2), 8.3 (q, J = 129 Hz, C_5Me_5), 26.5 (t, J = 160 Hz, C_1), 52.0 (q, J = 147 Hz, OMe), 96.8 (s, C_5Me_5).

(13) For details see supplementary material.

(14) **13**: ^1H NMR (–10 °C, CD_2Cl_2) δ 0.95 (t, J = 6 Hz, CH_3), 1.34 (tt, J = 6, J_{HP} = 5 Hz, CH_2), 1.55 (t, J = 3 Hz, C_5Me_5), 3.73 (t, J = 5 Hz, OMe); $^{13}C[^1H]$ NMR (–50 °C, CD_2Cl_2) δ 7.0 (t, J_{CP} = 25 Hz, C_1), 9.2 (s, C_5Me_5), 18.5 (s, CH_2CH_3), 52.8 (s, OMe), 99.3 (s, C_5Me_5).

(15) Prepared by reaction of $C_5Me_5Co(CH_2CHR)_2$ with $P(OMe)_3$ in analogy with preparations of $C_5Me_5(L)Co(C_2H_4)$: Beevor, R. G.; Frith, S. A.; Spencer, J. L. *J. Organomet. Chem.* **1978**, *221*, C25.

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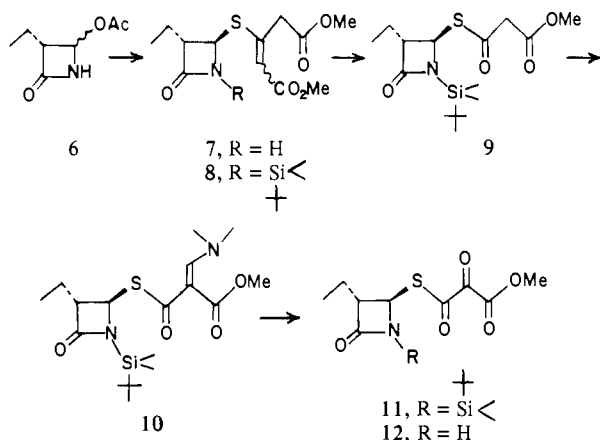
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Communications to the Editor

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3   4   5
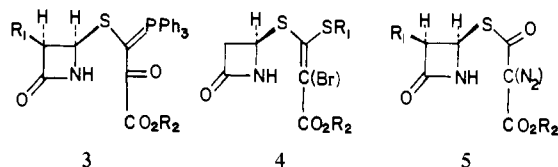
In earlier work on the photooxidative generation of carbonyl groups from enamines, we have shown that the carbacepham and carbapenam systems can be formed by addition of the β-lactam NH to the highly reactive central carbonyl function of a vicinal tricarbonyl unit.[11] Since this reaction sequence has provided a convenient pathway to carbapenems, we sought to apply this procedure to the formation of the penem system. We now report that this route can successfully be used to effect C_3-N coupling in precursors leading to penems. A noteworthy feature of this synthesis is that, unlike penem-forming reactions involving thermal processes,[6] the ring closure to the precursor takes place under conditions mild enough to preserve the stereochemistry at C_5.

Azetidinone 6 prepared from N-chlorosulfonyl isocyanate and ethylvinyl acetate as described by Kametani[7] was allowed to react with dimethylthioacetone dicarboxylate and sodium bicarbonate yielding 7 (60%).[8] Protection of the NH group in 7 (t-BuMe$_2$SiCl, DMF, Et$_3$N, DMAP) afforded 8 (90%), which was ozonized in CH_2Cl_2 at -78 °C followed by reductive workup with dimethyl sulfide to form 9 (46%). Treatment of 9 with N,N-dimethylformamide dimethyl acetal (2.5 equiv, 25 °C) gave the enamino derivative 10 (84%).

6   7, R = H   8, R = Si<   9

10   11, R = Si<   12, R = H

The enamine 10 was subjected to photooxidation in CDCl$_3$ (BANT sensitizer, 19 °C) for 2 days, affording the mostly hy-

drated vicinal tricarbonyl 11 (76% after silica gel chromatography). Desilylation with HF–pyridine (CH$_3$CN, 25 °C) led directly to the formation of the bicyclic system 13, through the desilylated product 12. The trans stereochemical relationship between the C_6 ethyl substituent and the C_5–S bond was completely preserved. Compound 13, obtained as a mixture of isomers differing in the hydroxyl orientation at the 3-position (54% overall from 11), could be reduced by conversion of OH to Cl with thionyl chloride/pyridine, followed by treatment with zinc–acetic acid–water to form 14 (51% from 13).[9]

On treating 14 with diazomethane (CH$_2$Cl$_2$, Et$_2$O), the penem 15 was obtained (56%) as colorless crystals along with isomer 16 (26%). Enol ether 15 showed UV, IR, NMR, and mass spectra

13   14

15   +   16
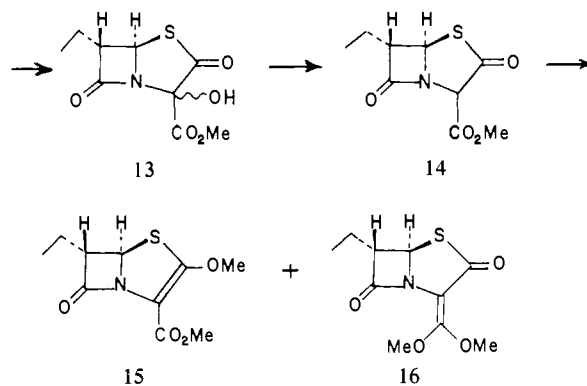
consistent with its structure. The assignment of this penem structure to our synthetic product was fully confirmed by an independent synthesis of 15 through an established route[10] starting with the acetoxy azetidinone 6 as outlined below.

Treatment of 6 with sodium allyl sulfide according to Cooke's method[10] yielded the allyl sulfide 17 (38%). This β-lactam was then alkylated with methyl bromoacetate to afford 18 (82%). With 2.5 equiv of lithium hexamethyldisilazide and methyl chlorothionoformate, 18 was converted to 19, which was then oxidized with MCPBA to yield the sulfoxide 20 (64%). Thermolysis of 20 in dioxane (20 min) yielded 21 (trans) (62%). Treatment of 21 with PPh$_3$ in refluxing dioxane (20 min) gave rise to a mixture of 15 and the cis isomer, 22 (3:2). The penem 15 separated from

17, R = H   18, R = CH$_2$COOMe   19

20   21

15 +   22
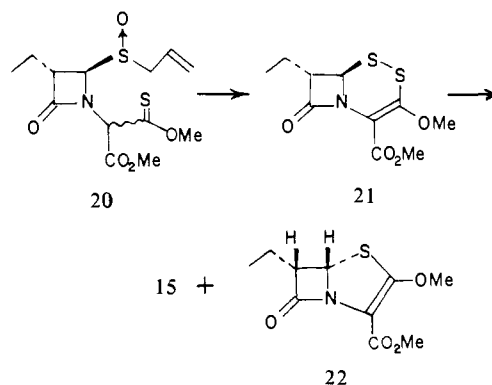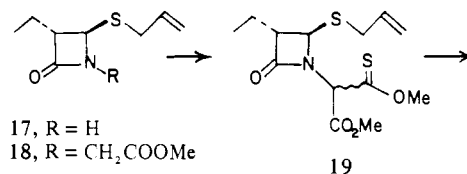
the mixtures by silica gel chromatography followed by fractional recrystallization (CH$_2$Cl$_2$/ether/hexanes), was identical in all respects (mp, IR, NMR) with the product synthesized above through the vicinal tricarbonyl route.[12]

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We are currently studying the formation of other hetero analogues of carbapenems through the C_3–N coupling route.

Dynamic NMR and Molecular Mechanics Study of the Rotation of a 1-Adamantyl, a 1-Bicyclooctyl, a 1-Norbornyl, and a *tert*-Butyl Group. The Relative Size of an Adamantyl Group. The Dilemma of Calculated Barriers to Rotation

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The particularities of the bridgehead position in bicyclic molecules have long interested organic chemists. Some unusual property of a substituent attached to the bridgehead is usually related to differences between the bridgehead and a *tert*-butyl quaternary carbon, the obvious acyclic analogue. As the geometry around the bridgehead changes, both the character of the bond attaching the substituent and the steric interactions experienced by the substituent change.

We now report an investigation that concentrates on the steric interactions. We have introduced a suitably large group $C(Me)_2Cl$ at the bridgehead in a series of compounds and have measured the barrier to its rotation by dynamic NMR spectroscopy. The results[1,2] in these compounds and in other compounds of interest[4,5] are shown in Chart I.

The barrier to rotation in the *tert*-butyl compound **4** is higher than for any of the bridged compound **1–3**, so in that sense the bicyclic compounds appear smaller to a bridgehead substituent than does a *tert*-butyl group.

Interestingly high rotational barriers are found in the more flexible molecules, the *tert*-butyl **4**, and the bicyclooctyl **2**.[6] This suggests that flexibility in attaining a stable rotational ground state may be as important as any transition state effects in determining the relative magnitudes of barriers.

The bicycloheptane system has smaller endocyclic bond angles[7] at the bridgehead. In a sense, the bridges are pinned back more, and so interactions during rotation are less. The low barrier agrees
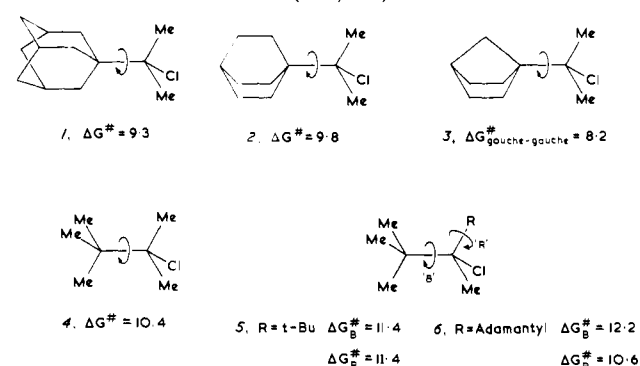
Chart I. Barriers to Rotation (kcal/mol)

1, $\Delta G^\# = 9.3$ *2*, $\Delta G^\# = 9.8$ *3*, $\Delta G^\#_{gauche\text{-}gauche} = 8.2$

4, $\Delta G^\# = 10.4$ *5*, R = t-Bu $\Delta G^\#_B = 11.4$ *6*, R = Adamantyl $\Delta G^\#_B = 12.2$

$\Delta G^\#_R = 11.4$ $\Delta G^\#_R = 10.6$

Table I. Calculations and Experimental Barriers (kcal/mol) for $R–C(Me)_2Cl$

R	$\Delta H^\#$		exptl $\Delta G^\#$
	MM2	MM2OS	
4, *tert*-butyl	7.1	10.2	10.4
1, 1-adamantyl	7.3	10.5	9.3
2, 1-bicyclooctyl	8.2	10.7	9.8
3, 1-bicycloheptyl			
gauche-gauche	6.4	9.6	8.2
gauche-anti	6.5	9.7	

with this. The barrier corresponds here to interconversion of gauche conformations, i.e., **7**, with its enantiomer **7′**. Such a

7   *8*
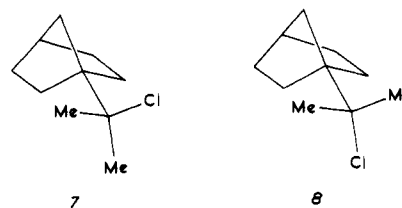
conformation is more stable than the anti one **8**, by at least 0.7 kcal/mol, since no signals are seen for the latter conformation when rotation **7** ⇌ **7′** is slow on the NMR timescale.[2]

The adamantyl rotational barrier is about 1 kcal/mol lower than the *tert*-butyl barrier, both in **1** vs. **4** and in **6R** vs. **5R**.[8] In contrast to this, when these groups are acting only as substituents on an ethane bond (see **5B** and **6B**) rather than forming one end of it (as in **1** and **4**), the adamantyl group hinders rotation more than the *tert*-butyl group. Thus the relative "size" of *tert*-butyl and adamantyl groups depends on the context.

Empirical force field calculations have been used with much success in predicting the structures of bicyclic and suchlike molecules.[9–11] They predict rotational barriers less satisfactorily, giving values markedly lower than experiment, particularly in more crowded molecules. Osawa[12] has recently proposed new values for some of the parameters[13] for MM2, chosen to produce calculated rotational barriers that are more consonant with those determined experimentally. Table I compares experimental barriers for **1** to **4** with ones calculated by using MM2 and also by using Osawa's modification (MM2OS).

Both parameter sets put the bicyclic compounds in the correct order of increasing barrier, but MM2OS predicts values greater than

(1) Barriers were determined from a full line-shape analysis of changes in the NMR spectrum around the coalescence temperature, and free energies of activation quoted in the scheme are for these temperatures (see supplementary material).

(2) Our search for anti conformations of **3** was based on the assumption that a signal 5% or more of such a conformation would be detected at around −125 °C, when limiting low temperatures are observed. No such signals were located, but there is evidence for some very small amount of an anti conformation (<5%) in that the C–H and C–Cl signals broaden around −100 °C and then sharpen at lower temperatures, compared with the C-quat and CH_2-7 signals. None of these four signals should be affected by the observed gauche-gauche interconversion. Application of the Anet and Basus equations[3] to these observations is not possible in the absence of reasonable chemical shift values.

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