

Figure 1. Correlation of combined data in Tables I and II using eq 3.

a simple "master equation" for heterolytic bond energies to produce resonance-stabilized ions in an inert polar medium

$$\Delta H_{\text{het}} = ApK_{R^+} + BpK_a + C \quad (1)$$

where the heterolytic bond energy (ΔH_{het}) is the negative of the measured heat of reaction between the carbocation whose free energy of formation from its carbinol in water is $2.303RT$ (i.e., $1.36pK_{R^+}$) and the carbanion whose free energy of formation from a precursor carbon acid in Me_2SO at 25°C is $1.36pK_a$ and A , B , and C are constants.

Tables I and II test such a relationship using ΔH_{het} for reaction of a variety of resonance-stabilized carbocations and carbanions in two solvents. Despite the variety of the ionic species and conditions, eq 1 has good correlative and predictive power for a given series of compounds. This implies at once quantitative validation of the simple approach to predicting heterolytic bond strengths in terms of the stabilities of the formed ions.

When both sets of data from Tables I and II are combined, one obtains eq 2: a master equation for all of the carbocation-

$$\Delta H_{\text{het}} = 11.98 - 1.178pK_{R^+} + 1.176pK_a \quad (2)$$

carbanion reactions we have studied so far. This equation was derived by a standard multiple regression analysis program for which the standard deviations of the constants are respectively in order: ± 0.5383 , ± 0.0651 , and ± 0.0536 with a correlation coefficient $r = 0.9981$.

Comparison of the third and fourth columns of Table I shows that this equation reproduces the measured heats of reaction with an average difference of 0.79 kcal/mol even though most of the data from which 2 is derived were taken from the systems in Table II.

These results may be presented graphically with a single correlation line on Figure 1 by recasting 1:⁸

$$\Delta H_{\text{het}} = A + D(pK_a - pK_{R^+}) \quad (3)$$

Although there are clearly small differences between lines generated by each of the three data sets, it is remarkable that such a good correlation holds over such a wide range of structures and

energies. It is quite possible that a fortuitous cancellation of solvation and resonance effects is responsible for the extraordinary correlation of Figure 1 and it will be interesting to see how well this simple treatment holds up when a wider variety of ionic combinations are brought into reaction.

There is increasing interest in developing low-temperature processes for the cleavage of carbon-carbon bonds in macromolecules⁹⁻¹³ especially as applied to the fossil fuel industries, where pyrolytic processes waste thermal energy and lead to tars. Heterolysis by treatment with strong acids or bases to yield ionic products are a promising alternative. The approach presented here may provide useful guidelines for predicting the most easily cleaved bonds in complex macromolecules.

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Intramolecular C-H Insertion: Synthesis of (\pm)-Pentalenolactone E Methyl Ester

Douglass F. Taber*¹ and Jonathan L. Schuchardt

Department of Chemistry, University of Delaware
Newark, Delaware 19716

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We recently reported a general route to highly functionalized cyclopentanes, based on rhodium-mediated intramolecular C-H insertion.² There was some concern as to whether this reaction, facile with open-chain systems, would be as effective in sterically more constrained situations. Among other considerations, theoretical calculations³ lead to the prediction that the activation energy for the insertion process will depend on the angle of approach of the intermediate Rh complex to the target C-H bond. We now report a simple route to the sesquiterpene antibiotic pentalenolactone E methyl ester (**1**) (Scheme I),^{4,5} the key step of which is a rhodium-mediated intramolecular C-H insertion via a sterically constrained transition state.

Previous routes to **1**⁵ (Scheme I) have dissected the angular lactone at "a", leading to a substituted bicyclo[3.3.0]octan-3-one such as **2**. An alternative analysis leads to a potentially more effective dissection, scission at "b". While **1** has three asymmetric centers, **3** has only one. Further, **3** should be readily available by spiroannulation of the symmetrical 4,4-dimethylcyclohexanone **4**, followed by carbonyl extrusion. Clearly, the key to such a retrosynthetic analysis lies in the *synthetic* step in which the

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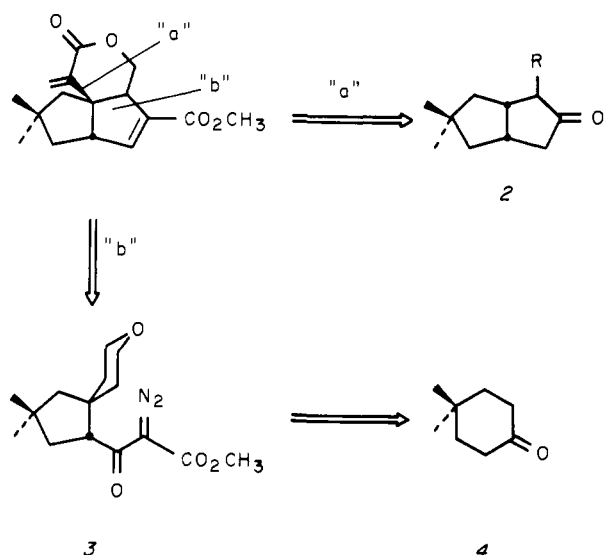
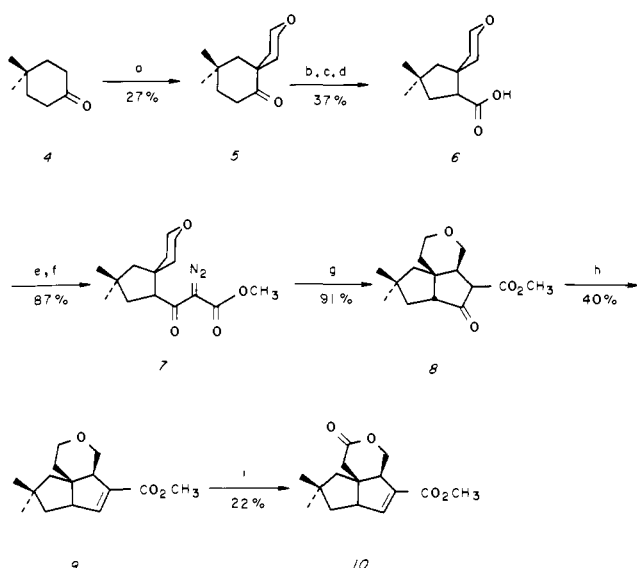
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Scheme I

Scheme II^a

^a (a) $(\text{ICH}_2\text{CH}_2)_2\text{O}$, NaH, THF, Δ ; (b) trisyl azide, KOH, PhCH_3 , PTC; (c) MeOH, $h\nu$; (d) LiOH, DME, Δ ; (e) oxalyl chloride, $\text{LiCH}_2\text{COOMe}$; (f) TsN_3 , Et_3N ; (g) $\text{Rh}_2(\text{OAc})_4$, CH_2Cl_2 , room temperature; (h) NaBH_4 , MeOH, 0°C , dicyclohexylcarbodiimide, Cu_2Cl_2 , THF, Δ ; (i) CrO_3 , HOAc, CH_2Cl_2 , room temperature.

molecular complexity of **1** is assembled by forming the carbon-carbon bond at "b". We have found that rhodium-mediated intramolecular C-H insertion is particularly effective in this application.

The starting point for the synthesis (Scheme II) is the readily available⁶ 4,4-dimethylcyclohexanone (**4**). Spiroannulation with bis(2-iodoethyl) ether⁷ proceeded smoothly to give **5**. Diazo transfer by the method of Mander⁸ followed by photolysis in methanol and saponification then gave the crystalline acid **6**, which was homologated to **7** by the method of Rathke.⁹ This set the stage for the anticipated C-H insertion.

We were gratified to observe that exposure of α -diazo- β -keto ester **7** to catalytic $\text{Rh}_2(\text{OAc})_4$ in CH_2Cl_2 at room temperature led to smooth conversion to a single substance, shown by subsequent transformation to be the desired tricyclic ether **8**. Reduction

and dehydration¹⁰ of **8** gave **9**, which was regioselectively oxidized¹¹ to the previously prepared⁵ lactone **10**. The alternative lactone, from oxidation of the more hindered methylene, was observed as a minor product from the oxidation. Methylation of **10** to give pentalenolactone E methyl ester (**1**) has been demonstrated by previous investigators.⁵

The synthetic utility of intramolecular C-H insertion is apparent. Unlike most methods for ring construction, in which two functionalized carbon atoms are joined, intramolecular C-H insertion allows bond formation to an unfunctionalized carbon atom, generating a striking increase in molecular complexity¹² in a single step. Further investigations of the scope and limitations of this reaction are under way.¹³

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Supplementary Material Available: Full experimental details for the preparation of **1-10** (10 pages). Ordering information is given on any current masthead page.

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Dynamic Intermolecular Tautomerism of 3,5-Dimethylpyrazole in the Solid State by ¹³C CP/MAS NMR Spectroscopy and X-ray Crystallography

André Baldy,[†] José Elguero,^{*†} Robert Faure,[§] Marcel Pierrot,[†] and Emile-Jean Vincent[§]

Service de Cristallographie, Faculté des Sciences et Techniques, 13397 Marseille, France
Instituto de Química Médica, CSIC Juan de la Cierva 3, 28006 Madrid, Spain
Laboratoire de Chimie Organique Physique Université d'Aix-Marseille III 13397 Marseille, France

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The combined use of CP/MAS carbon-13 NMR spectroscopy and X-ray crystallography is giving new insights on the dynamic phenomena in the solid state. Among the dynamic phenomena that have interested the chemist, prototropic tautomerism is one of the most elusive, due to the sensitivity of the activation energy to environmental effects (concentration, nature of the solvent, water traces, etc.). Heterocyclic prototropic tautomerism¹ in the solid state concerns almost exclusively static studies, i.e., the structure of the most abundant tautomer.^{1a} Up to now the only dynamic study of heterocyclic tautomerism in a crystal concerns

[†] Faculté des Sciences et Techniques.

[‡] Instituto de Química Médica.

[§] Université d'Aix-Marseille III.

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