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(10) NMR ($CDCl_3$) δ 5.78 (ddd, 1 H, J = 1, 5, 10 Hz), 5.48 (dt, 1 H, J = 3, 10 Hz), 4.08 (m, 1 H), 3.67 (dd, 1 H, J = 3.5, 7 Hz), 1.40–3.15 (complex, 11 H); IR 1683 cm^{-1}.
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(12) We thank Professor L. Mandell for the IR spectra of **10** and **14** for comparison with our synthetic materials. The picrate of **10** melted at 229–231 °C (lit.[11] mp 226–228 °C).
(13) Reaction of divinylcarbinol with triethyl orthoacetate in the presence of propionic acid afforded ethyl 4,6-heptadienoate (85%) which could be converted into 4,6-heptadienoyl chloride by sequential hydrolysis (LiOH, MeOH) and treatment of the intermediate lithium carboxylate with 1 equiv of thionyl chloride in benzene.
(14) **12a:** NMR ($CDCl_3$) δ 5.57 (complex, 2 H), 4.32 (m, 1 H), 3.39 (dd, 1 H, J = 5.5, 9 Hz), 1.35–3.15 (complex, 13 H); IR 1620 cm^{-1}. **13a:** NMR ($CDCl_3$) δ 5.88 (ddd, 1 H, J = 2, 5, 10 Hz), 5.31 (br dd, 1 H, J = 2, 10 Hz), 4.79 (m, 1 H), 3.56 (br d, 1 H, J = 6 Hz), 1.25–2.95 (complex, 13 H); IR 1612 cm^{-1}.
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(17) NMR ($CDCl_3$) δ 5.65 (ddt, 1 H, J = 2, 5, 10 Hz), 5.39 (dt, 1 H, J = 3, 10 Hz), 4.05 (m, 1 H), 3.19 (d, J = 7 Hz), 1.00–3.05 (complex, 12 H), 0.88 (t, 3 H, J = 7 Hz); IR 1689 cm^{-1}.
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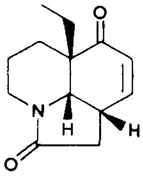
(22) An ~20% yield of an isomeric enone which appears to be i was also obtained.



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(23) We thank Professor G. Stork for a generous sample of **16**.

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Direct Calculation of Equilibrium Constants for Isotopic Exchange Reactions by Ab Initio Molecular Orbital Theory

Sir:

Equilibrium constants for isotopic exchange reactions may be obtained either by direct measurement or indirectly by the methods of statistical mechanics, in the harmonic approximation, in terms of the normal mode vibrational frequencies of the molecules involved.[1] Because slight errors in observed frequencies lead to large variations in isotope effect, the usual practice has been to fit the experimental spectral data for isotopically substituted molecules to force fields, and from these to calculate the needed frequencies. In principle, frequencies obtained from force fields calculated a priori by molecular orbital theory may be substituted for the quantities derived from spectroscopic measurements. Until recently, however, theoretical force fields of sufficient accuracy were unavailable for any but the smallest molecular species.[2]

We communicate here preliminary results of our investigations into the performance of simple levels of molecular orbital theory with regard to the calculation of equilibrium constants of isotope exchange processes. Three levels of ab initio molecular orbital theory have been surveyed. The first two are single-determinant Hartree–Fock methods utilizing the 3-21G split-valence[3] and 6-31G* polarization[4] basis sets, respectively. The third and computationally the most complex method also utilizes the 6-31G* basis set[4] but allows for partial account of electron correlation by way of Møller–Plesset perturbation theory terminated at second order.[5] Equilibrium geometries have been obtained for all species at each of the three levels of calculation. These have already been reported elsewhere.[3,5e] Fundamental vibrational frequencies have been evaluated according to Wilson's FG matrix procedure[6] utilizing force constants obtained in massless symmetry coordinates by numerical second differentation. Full details will be presented elsewhere.[7]

The equilibrium constant for an isotopic exchange equilibrium

$$\mathrm{A} + \mathrm{B}^* \underset{}{\overset{k_{\mathrm{eq}}}{\rightleftharpoons}} \mathrm{A}^* + \mathrm{B} \qquad (1)$$

may be written in terms of the ratio of the reduced isotopic partition function ratios for A and B

$$k_{\mathrm{eq}} = (s_2/s_1)f[\mathrm{A}^*/\mathrm{A}]/(s_2/s_1)f[\mathrm{B}^*/\mathrm{B}]$$

where the $(s_2/s_1)f$'s are expressed in terms of the complete set of normal mode frequencies, ν_i:[1]

$$(s_2/s_1)f[\mathrm{A}^*/\mathrm{A}] = \prod_i \frac{u_i(\mathrm{A}^*)}{u_i(\mathrm{A})} \frac{1 - \mathrm{e}^{-u_i(\mathrm{A})}}{1 - \mathrm{e}^{-u_i(\mathrm{A}^*)}} \mathrm{e}^{[u_i(\mathrm{A}) - u_i(\mathrm{A}^*)]/2}$$

$$u_i = \frac{h\nu_i}{kT}$$

By convention A* refers to the heavy isotopically substituted molecule. The effect of symmetry numbers, which is of no particular interest, is omitted here from K_{eq}.[1]

Reduced isotopic partition function ratios for hydrogen and for a number of one- and two-heavy-atom hydrides obtained from theoretical harmonic force constants are compared with the corresponding ratios derived from spectroscopic data in Table I. The latter quantities are obtained in one of two ways: (a) by fitting observed frequencies, corrected for anharmonicity, to harmonic force fields (designated "harmonic" in the tables) and (b) by fitting observed uncorrected frequencies to harmonic force fields (designated "anharmonic"). Details concerning the evaluation of these force fields and the calculation of frequencies will be discussed elsewhere.[8]

Table II compares theoretical and spectroscopic equilibrium constants for reactions

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Table I. Comparison of Theoretical and Spectroscopic Reduced Isotopic Partition Function Ratios $(s_2/s_1)f$ (300 K)

	HF/3-21G	HF/6-31G*	MP2/6-31G*	spectroscopic[a] harmonic	spectroscopic[a] anharmonic
HD	3.86	3.85	3.71	3.56	3.32
LiD	1.76	1.76	1.74	1.74	1.71
BeHD	3.55	3.56	3.54		
BH_2D	6.55	6.85	6.76		
CH_3D	14.04	13.81	12.44	11.63	10.09
NH_2D	15.89	17.23	14.65	13.65	11.60
HDO	15.76	16.39	13.22	13.23	11.50
DF	10.61	12.85	10.40	11.11	10.01
CHCD	12.20	11.63	9.35	9.02	8.30
CH_2CHD	14.49	14.19	12.53		10.19
CH_3CH_2D	15.71	15.25	13.64		11.01
CH_2DNH_2[b]	15.95	14.80	13.70		
CH_2DOH[b]	16.63	16.53	14.00		
DCN	13.25	11.81	9.31	8.89	8.10
DHCO	13.07	12.94	10.75		
H_2DCF	17.31	15.91	13.17	13.60	11.86

[a] Harmonic values derived from force constants obtained by fitting experimentally observed frequencies which have been corrected for anharmonicity. Anharmonic values derived from force constants obtained by fitting experimentally observed (uncorrected) frequencies. For details see ref 8. [b] Theoretical values averaged for gauche and trans CH bonds.

Table II. Equilibrium Constants[a] for Isotope Exchange Reactions $X\text{-}H + HD \rightarrow X\text{-}D + H_2$ (300 K)

X-H	HF/3-21G	HF/6-31G*	MP2/6-31G*	spectroscopic[b] harmonic	spectroscopic[b] anharmonic
LiH	0.46	0.46	0.47	0.49	0.51
BeH_2	0.93	0.95	0.98		
BH_3	1.8	1.8	1.8		
CH_4	3.6	3.6	3.4	3.3	3.0
NH_3	4.1	4.5	4.0	3.8	3.5
H_2O	4.1	4.3	3.6	3.7	3.5
HF	2.7	3.3	2.8	3.1	3.0

[a] Symmetry number effects are omitted. [b] See footnote *a* in Table I.

Table III. Equilibrium Constants[a] for Isotope Exchange Reactions $X\text{-}H + CH_3D \rightarrow X\text{-}D + CH_4$ (300 K)

X-H	HF/3-21G	HF/6-31G*	MP2/6-31G*	spectroscopic[b] harmonic	spectroscopic[b] anharmonic
C_2H_6	1.12	1.10	1.10		1.09
CH_3NH_2[c]	1.14	1.07	1.10		
CH_3OH[c]	1.18	1.20	1.13		
CH_3F	1.23	1.15	1.06	1.17	1.18
C_2H_4	1.03	1.03	1.01		1.01
H_2CO	0.93	0.94	0.86		
C_2H_2	0.87	0.84	0.75	0.78	0.82
HCN	0.94	0.86	0.75	0.76	0.80

[a] See footnote *a* Table II. [b] See footnote *a* in Table I. [c] D substitution is in methyl group.

$$XH + HD \rightleftharpoons XD + H_2 \quad (2)$$

where XH is a first-row hydride. Agreement between each of the three theoretical levels and spectroscopically derived values is remarkable over the entire range of equilibrium constants studied (experimentally from 0.49 for the LiH/H_2 exchange to 3.8 for NH_3/H_2). Overall, the MP2/6-31G* calculations fare best, although the performance of the two Hartree-Fock levels is not much inferior. The performance of the HF/3-21G method is particularly encouraging, in that the results here are of comparable quality with those obtained at the computationally more expensive HF/6-31G* level. Calculations using the 3-21G basis set are relatively inexpensive and may be performed on quite large systems.

Theoretical and spectroscopic equilibrium constants for exchange reactions

$$XH + CH_3D \rightleftharpoons XD + CH_4 \quad (3)$$

involving CH bond cleavage are compared in Table III. The effects here are smaller than those previously considered, spectroscopically derived values ranging from 0.76 for the HCN/CH_4 exchange to 1.17 for the process involving CH_3F and CH_4. As before, all three levels of theory reproduce the spectroscopic equilibrium constants reasonably well. The MP2/6-31G* calculations do the best overall, although the performance of the two Hartree-Fock levels is not much poorer.

In conclusion, the present work demonstrates the ability of simple levels of ab initio molecular orbital theory to describe with reasonable accuracy the energetics of isotopic exchange processes. It should also be noted that increased computational efficiency will result when the numerical methods for force constant evaluation are replaced by analytical schemes, making possible routine applications to larger systems. We suggest that theoretical techniques may become a viable and efficient alternative to experiment for surveying entire classes of chemical reactions in search of processes which might be of practical import to isotope separation.

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(9) National Science Foundation predoctoral fellow.

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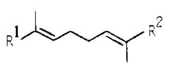
Palladium-Catalyzed Cross-Coupling Reaction of Homoallylic or Homopropargylic Organozincs with Alkenyl Halides as a New Selective Route to 1,5-Dienes and 1,5-Enynes

Sir:

The construction of 1,5-diene units present in various natural products of terpenoid origin,[1] such as **1** and **2**, via cross-coupling has been achieved in most cases by the Biellmann and related allyl-allyl coupling reactions.[2] While these reactions appear well suited for synthesizing 1,5-dienes represented by **1**, their application to the synthesis of **2** is often complicated by regiochemical scrambling and other side reactions.[3] Our recent development of a highly stereoselective method for converting terminal acetylenes into various (*E*)-β-methyl-1-alkenyl derivatives[4] prompted us to synthesize 1,5-dienes, especially those represented by **2**, via alkenyl-homoallyl or alkenyl-homopropargyl coupling. As the reaction of alkenyllithiums or the corresponding Grignand reagents with homoallylic halides leads mainly to the β-elimination of the halides,[5] the possibility of applying the palladium-catalyzed cross-coupling[6] to the synthesis of 1,5-dienes was explored. If the palladium-catalyzed cross-coupling reaction of alkenyl halides with alkyl metals containing β-carbon-bound hydrogen atoms should proceed via oxidative addition-transmetalation-reductive elimination sequence,[7] it could be competed by the well-known β-elimination reaction[8] of the hypothetical diorganopalladium intermediate **3** (Scheme I). It was therefore of interest to find out what factors affect the relative extents to which the two competing elimination processes, i.e., paths A and B, occur.



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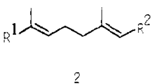


2

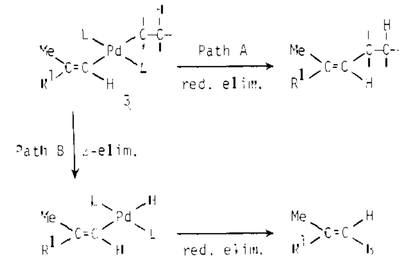
We first examined the reaction of (*E*)-1-iodo-2-methyl-1-hexene (**4**) with *n*-, *sec*, and *tert*-butylzinc chlorides and the corresponding magnesium derivatives and found that, while the *tert*-butyl metals react nearly exclusively (>90%) via β-elimination (path B), both *n*- and *sec*-butylzinc chlorides can undergo predominantly the cross-coupling reaction[9] (Table I). Far more exciting, however, were the results obtained in the corresponding reactions of homoallylzinc chloride and the trimethylsilyl derivative of homopropargylzinc chloride with **4** which proceeded at least as well as that of *n*-butylzinc chloride. Despite the presence of allylic or propargylic β-hydrogen atoms, the extent of β-elimination as judged by the amount of the deiodinated alkene was less than 1-2% (Table I). In light of the widely known β-elimination of alkylpalladium species,[8] these results are unexpected. Should these reactions proceed as shown in Scheme I, the observed results then indicate that *reductive elimination can proceed far faster than β-elimination even in cases where the latter process involves removal of an allylic or propargylic hydrogen atom.*

Table I. Pd-Catalyzed Reaction of (*E*)-1-Iodo-2-methyl-1-hexene with Alkylzinc and Alkylmagnesium Reagents[a]

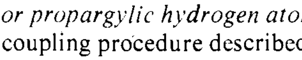
organometallic reagent[b]	time, h	product yield,[c] % cross-coupled	deiodo	homo-coupled[d]
n-BuZnCl	2	76	2	8
n-BuMgBr	2	25	51	8
sec-BuZnCl	16	68[e]	15	5
sec-BuMgBr	16	40[f]	35	1
$CH_2{=}CH(CH_2)_2ZnCl$	16	81	trace	8
$CH_2{=}CH(CH_2)_2MgBr$	16	21	37	11
$Me_3SiC{\equiv}C(CH_2)_2ZnCl$	2	91	trace	5

[a] All reactions were carried out in THF-ether at 20-25 °C under an atmosphere of nitrogen. [b] The organozinc reagents were prepared by treating the corresponding Grignard reagents with anhydrons $ZnCl_2$. [c] Yields were obtained by GLC (SE-30). [d] The homo-coupled product refers to 5,8-dimethyl-5,7-dodecadiene. [e] A 60:40 mixture of the *sec*-butyl and isomerized *n*-butyl derivatives. [f] A 40:60 mixture of the *sec*-butyl and *n*-butyl derivatives.

Scheme I



The cross-coupling procedure described above provides an expeditious and selective route to 1,5-dienes of terpenoid origin. To demonstrate its synthetic utility, we chose to synthesize (*E,E*)-farnesol (**5**) and a tetraenol, **6**, which has recently been synthesized and converted into mokupalide (**7**) by Sum and Weiler.[10]



7

2-Methylhept-2-en-6-yne (**8**) was obtained in 71% yield from 6-methyl-5-hepten-2-one by a procedure developed by us recently,[11] which consists of sequential treatment of the methyl ketone with lithium 2,2,6,6-tetramethylpiperidide (LTMP) (1.05 equiv, −78 °C, 1 h), $ClPO(OEt)_2$ (1.15 equiv, −78 °C to room temperature), LTMP (2.25 equiv, −78 °C to room temperature), and aqueous NH_4Cl (excess). The enyne **8** was converted into **9** (bp 54-55 °C, 0.55 mmHg) in 75% yield by a procedure which was developed by us recently[12] (procedure i, Scheme II). The trimethylsilyl derivative of homopropargylzinc chloride **10** was prepared by trimethylsil-

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