of SiO_2, EtOAc eluant) afforded 4 (7 mg, 9.6 mg theoretical, 73%) as a light yellow solid: mp 215–217 °C ($CHCl_3$–MeOH); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.52–7.29 (m, 6 H, ArH), 7.11–6.98 (m, 3 H, ArH), 3.18 (br s, 2 H, NH_2), 1.92 (s, 3 H, CH_3); ^{13}C NMR (CD_3OD, 600 MHz) δ 161.9, 154.5, 144.5, 133.5, 130.5, 130.2, 129.7, 129.5, 129.4, 127.1, 126.5, 126.0, 123.0, 120.5, 116.5, 13.5; IR (KBr) ν_{max} 3060, 1612, 1528, 1496, 1450, 1372, 1342, 1288, 1238, 752, 700 cm^{-1}; UV (MeOH) λ_{max} 282 (4800), 360 nm (6200); EIMS *m/e* (relative intensity) 292 (M^+, base), 275 (16), 104 (38), 77 (56); EIHRMS *m/e* 292.1205 ($C_{18}H_{16}N_2O_2$ requires 292.1212).

Similarly the aminophenol 14 (1 mg, 0.0033 mmol) was treated with 47.5% aqueous hydrogen bromide (0.1 mL), and the resulting reaction mixture was warmed at 105 °C for 1 h in a resealable Kontes vial. After being cooled to 25 °C, the reaction mixture was diluted with water (5 mL), neutralized with saturated aqueous $NaHCO_3$, and extracted with EtOAc (8 mL). The organic extract was washed with saturated aqueous NaCl (4 mL) and dried (Na_2SO_4). Removal of the solvent in vacuo and purification of the residue by flash chromatography (1 × 5 cm SiO_2, EtOAc eluant) afforded 4 (0.4 mg, 0.96 mg theoretical, 42%).

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Supplementary Material Available: ^1H NMR spectra of 4, 11, 13–14 (4 pages). Ordering information is given on any current masthead page.

Improved Radical Stabilization Energies

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Considerable effort has been expended in the studies of how various functional groups interact with a radical center and to determine quantitatively the stabilization by a substituent.[1] As accurate experimental stabilization energies are difficult to obtain, theoretical values have been widely used. Previous calculations of radical stabilization energies (RSE) of monosubstituted methyl radicals have used unrestricted (UHF) or restricted open-shell Hartree–Fock (ROHF) methods.[2,3] The UHF method produces wave functions that are not eigenfunctions of the S^2 operator and all UHF wave functions show some degree of spin contamination from higher multiplets. In many cases the spin contamination is negligible, but in systems where the odd electron can be delocalized, the problem can be severe (see, e.g., Table I). By using an ROHF wave function, the spin contamination can be eliminated entirely; however, ROHF wave functions are not readily amenable to subsequent introduction of electron correlation via a perturbation expansion. In any case it is desirable to determine what level of theory is necessary for obtaining accurate results.

Recently a new method for decreasing spin contamination in UHF wave functions has been introduced where the first spin contaminant is annihilated self-consistently during the SCF procedure.[4] The procedure has been labeled AUHF, and the corresponding wave function can be used as a reference for a Møller–Plesset (MP) perturbation expansion,[5] giving rise to the acronym AUMP.[6] A series of calculations have recently been presented by Baker, from which it appears that the AUMP method is operationally equivalent to performing MP calculations using an ROHF reference wave function.[6] We here present improved estimates of RSE's for a number of substituents attached to methyl and allyl radicals using the AUMP method.

Table I. $\langle S^2 \rangle$ **Values for the Radicals in Reactions 1–3**

	$\dot{C}H_2X$		$\dot{X}CHCHCH_22$		$\dot{C}H_2CXCH_2$	
X	UHF[a]	AUHF[b]	UHF[a]	AUHF[b]	UHF[a]	AUHF[b]
H	0.761	0.754	0.975	0.782	0.975	0.782
F	0.759	0.753	0.967	0.781	0.963	0.781
OH	0.759	0.754	0.955	0.778	0.960	0.777
CH	0.972	0.759	1.156	0.779	1.125	0.787
NH_2	0.759	0.754	0.945	0.777	0.960	0.781
BH_2	0.756	0.753	0.962	0.775	1.000	0.788
CHO	1.005	0.758	1.271	0.778	1.250	0.778
CH_3	0.762	0.754	0.971	0.781	0.978	0.782

[a] 3-21G basis set. [b] 6-31G* basis set.

The RSE's are defined by the following isodesmic reactions,[3,7] positive values indicate a stabilizing interaction:

$$\cdot CH_2X + CH_4 \rightarrow CH_3X + \cdot CH_3 \tag{1}$$

$$\cdot CH_2CHCHX + CH_4 \rightarrow CH_3X + \cdot CH_2CHCH_2 \tag{2}$$

$$\cdot CH_2CXCH_2 + CH_4 \rightarrow CH_3X + \cdot CH_2CHCH_2 \tag{3}$$

All geometries have been fully optimized at the ROHF/3-21G level for methyl radicals, at the UHF/3-21G level for allyl radicals, and at the RHF/3-21G level for all closed shell molecules.[8] The UHF method was used for allyl radicals due to the symmetry breaking problems associated with ROHF methods.[9] Only the trans isomers in reaction 2 have been considered; the differences between cis and trans isomers are on the order of a few kcal/mol.

Previous calculations of RSE's for reaction 1 at the ROHF/4-31G level[2] give almost the same results as our AUHF/6-31G* calculations (Table II), indicating little basis set effect. Calculations at the UHF/3-21G level[3] show similar results for the systems with X = F, OH, NH_2, BH_2, and CH_3. For the CN, CHO, and $CHCH_2$ substituents, however, quite large differences appear, and Table I shows that this is due to spin contamination. Including electron correlation increases all RSE's by 1–3 kcal/mol, and the AUMP4 results are almost identical with those at the AUMP2 level. Experimental data are scarce, but kinetic studies show RSE values for cyano of 5–7 kcal/mol,[10] for vinyl of 9–14 kcal/mol,[11] for hydroxy of 8–11

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[1] For a discussion of substituent effects on the chemistry and properties of radicals, see: *Subtituent Effects In Radical Chemistry*; Viehe, H. G., Janousek, Z., Merenyi, R., Eds.; NATO ASI Series C, Vol. 189; D, Reidel: Dordrecht, 1986.

[2] Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062.

[3] Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley Interscience: New York, 1986.

[4] Baker, J. *Chem. Phys. Lett.* **1988**, *152*, 227.

[5] Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

[6] Baker, J. *J. Chem. Phys.* **1989**, *91*, 1789.

[7] Dewar, M. J. S.; Fox, M. A.; Nelson, D. J. *J. Organomet. Chem.* **1980**, *185*, 157.

[8] All calculations have been done by using the Gaussian-86 program package: Frisch, M. J.; Binkely, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fleuder, E. M.; Pople, J. A. Carnegi-Mellon Quantum Chemistry Publishing Unit: Pittsburgh PA, 1984. Basis sets: 3-21G: Binkely, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939. 6-31G*: Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257. Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comp. Chem.* **1983**, *4*, 294.

[9] Davidson, E. R.: Borden, W. T. *J. Phys. Chem.* **1983**, *87*, 4783. Attempts of performing ROHF calculations on substituted allyl radicals were largely unsuccesful due to severe SCF convergency problems.

0022-3263/91/1956-0884$02.50/0

Table II. Calculated Methyl Radical Stabilization Energies, Defined by Isodesmic Reaction 1 (in kcal/mol)

X	ROHF[a]	ROHF[b]	UHF[c]	AUHF[d]	AUMP2[d]	AUMP3[d]	AUMP4[d]
H	0.0	0.0	0	0.0	0.0	0.0	0.0
CH_3	2.3	3.3	2	2.9	2.9	3.1	3.2
F	3.4	1.8	3	2.6	4.8	3.0	5.0
CN	4.6	5.3	11	4.8	6.1	6.1	6.7
OH	6.5	5.8	6	6.4	8.8	8.0	8.9
CHO	6.7	7.7	4	8.6	9.2	9.2	9.5
NH_2	10.0	10.3	10	7.8	11.5	10.5	11.1
$CHCH_2$	6.6	7.8	21	7.9	11.0	10.6	12.6
BH_2	12.1	11.7	11	12.5	12.8	12.9	13.0

[a] 3-21G basis set. [b] 4-31G basis set (ref 2). [c] 3-21G basis set (ref 3). [d] 6-31G* basis set.

Table III. Calculated Radical Stabilization Energies for Trans 1-Substituted Allyl Radicals Defined by Isodesmic Reaction 2 (in kcal/mol)

X	UHF[a]	AUHF[b]	AUMP2[b]
H	0.0	0.0	0.0
CH_3	3.2	3.6	5.6
F	7.7	5.2	8.3
CN	8.1	4.3	9.9
CHO	15.7	4.8	11.7
OH	9.5	9.0	12.8
NH_2	10.5	8.6	13.7
BH_2	10.3	12.4	15.1

[a] 3-21G basis set. [b] 6-31G* basis set.

Table IV. Calculated Radical Stabilization Energies for 2-Substituted Allyl Radicals Defined by Isodesmic Reaction 3 (in kcal/mol)

X	UHF[a]	AUHF[d]	AUMP2[b]
H	0.0	0.0	0.0
CN	2.5	-0.6	3.0
CH_3	1.8	1.8	4.3
BH_2	5.4	3.8	5.2
NH_2	9.4	6.1	9.4
F	11.4	8.8	11.0
CHO	9.8	4.8	11.6
OH	10.9	10.1	12.6

[a] 3-21G basis set. [b] 6-31G* basis set.

kcal/mol,[12] and for amino of 9–10 kcal/mol.[13] The AUMP values compare favorably with these data. Accepting the AUMP4 values as the reference, it is seen that the ROHF method gives quite acceptable results exept for the vinyl group.

We have also calculated RSE's for allyl radicals where spin contamination is substantial for all substituents. For reaction 2 we again observe a large effect upon going from the UHF to the AUHF level for the CN and CHO substitutents (Table III). The effects for the other substitutents are smaller, which is due to the fact that RSE's are relative energies, and these species contain similar amounts of spin contamination. Adding electron correlation again increases all RSE's. Similar trends are found for reaction 3 (Table IV).

For 1-substituted allyl radicals, the stabilizing order of the substituents is the same as for the methyl system, with the exception of the switch between OH and CHO, although the effects are somewhat larger. The RSE's for the cross-conjugated 2-substituted allyl radicals show no correlation with those for the 1-substituted system. At the 2-position especially the polar substituents F and OH have large RSE's, but also CHO is a good stabilizing group.

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(10) (a) Luckraft, D. A.; Robinson, P. J. *Int. J. Chem. Kinet.* **1973**, *5*, 137. (b) Sarner, S. F.; Gale, D. M.; Hall, H. K., Jr.; Richmond, A. B. *J. Phys. Chem.* **1972**, *76*, 2817. (c) King, K. D.; Goddard, R. D. *Int. J. Chem. Kinet.* **1973**, *7*, 109. (d) Bellus, D.; Rist, G. *Helv. Chim. Acta* **1974**, *57*, 194. (e) Doering, W. v. E.; Horowitz, G.; Sachdev, K. *Tetrahedron* **1977**, *33*, 273. (f) King, K. D.; Goddard, R. D. *Int. J. Chem. Kinet.* **1978**, *10*, 453. (g) King, K. D.; Goddard, R. D. *Int. J. Chem. Kinet.* **1975**, *7*, 837. (h) King, K. D.; Goddard, R. D. *J. Am. Chem. Soc.* **1975**, *97*, 4504. (i) King, K. D.; Goddard, R. D. *J. Phys. Chem.* **1976**, *80*, 546.

(11) (a) Golden, D. M.; Rodgers, A. S.; Benson, S. W. *J. Am. Chem. Soc.* **1966**, *88*, 3196. (b) Rossi, M.; Golden, D. M. *J. Am. Chem. Soc.* **1979**, *101*, 1230. (c) Korth, H.-G.; Trill, H.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483. (d) Golden, D. M.; Gac, N. A.; Benson, S. W. *J. Am. Chem. Soc.* **1969**, *91*, 2136. (e) Doering, W. v. E.; Beadley, G. H. *Tetrahedron* **1973**, *29*, 2231.

(12) Cruickshank, F. R.; Benson, S. W. *J. Phys. Chem.* **1969**, *73*, 733.

(13) (a) Colussi, A. J.; Benson, S. W. *Int. J. Chem. Kinet.* **1977**, *9*, 307. (b) Griller, D.; Lossing, F. P. *J. Am. Chem. Soc.* **1981**, *103*, 1586.

Enantiomerically Pure Acetals in Organic Synthesis. 3. A Synthesis of (*R*)-Mevalonic Acid Lactone

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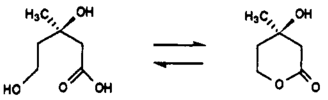
(*R*)-Mevalonic acid is the acetate-derived biosynthetic precursor of the terpene family of natural products.[1,2] The ubiquity of terpenes in nature together with the preeminent position of (*R*)-mevalonic acid in the biosynthetic pathway have prompted the development of syntheses of (*R*)-mevalonic acid lactone (1).[3]



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Recently we reported an enantioselective approach to carbohydrates and their derivatives via a general chromatographic resolution of diastereomeric furanoside and pyranoside acetals derived from α-hydroxy esters.[4] We believed that this approach could complement the established practice of synthesizing rare or unavailable carbohydrates and their derivatives from other carbohydrates available in the "chiral pool"[5] and could be especially useful for syntheses of deoxy, branched, and heteroatom-containing sugars. Since from a synthetic perspective (*R*)-mevalonic acid lactone can be considered an example of a highly deoxygenated, branched pentopyranose, we set

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