enhance reactions in systems in which the unsubstituted analogs perform in mediocre fashion.

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Supplementary Material Available: Spectral data and experimental procedures for the preparation of **1a/b, 7a/b, 8, 10, 11**; ^1H and ^{13}C NMR spectra of **1a/b** (and their bromocyclopropane precursors), **7a/b, 8, 10, 11**, and **21a**; experimental procedures for the competition experiments; and summaries of NOE data for **1a/b** and their bromocyclopropane precursors (31 pages). Ordering information is given on any current masthead page.

Transmetalation Reactions of Alkylzirconocenes: Copper-Catalyzed Conjugate Addition to Enones

Peter Wipf* and Jacqueline H. Smitrovich

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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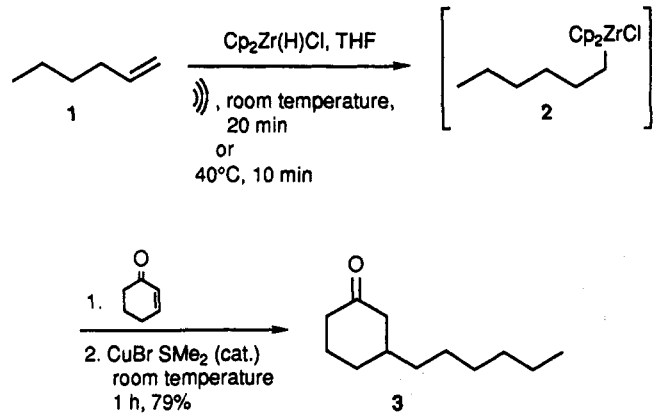
Summary: Rapid hydrozirconation of alkenes by zirconocene hydrochloride, followed by addition of 1 equiv of enone and catalytic amounts of Cu(I) salts, led to the corresponding 1,4-addition products in moderate to high yields and provided the first protocol for in situ preparation of alkyl cuprates from alkenes.

Organocuprates are among the most versatile organometallic derivatives applied in organic synthesis. However, most of the ligands that are transferred via both higher and lower order cuprates originate from organolithium or organomagnesium species.[1] The involvement of highly reactive and strongly basic first- and second-column derivatives in the preparation of cuprates complicates the experimental protocol and limits the range of functionality that is tolerated in the starting material. Therefore, alternative preparations of copper complexes that do not originate in alkyl or alkenyl halides considerably extend the synthetic scope of organocopper chemistry beyond present limitations. In a preliminary study, we have shown that *alkenyl* alanes undergo an in situ exchange process with a bisalkynylcopper complex.[2] As precursors to *alkyl* cuprates, however, we considered zirconium derivatives, because alkylzirconocenes are easily prepared by treatment of alkenes with zirconocene hydrochloride ($Cp_2Zr(H)Cl$,[3] Schwartz Reagent).[4,5]

Contrary to previous observations,[5a,6] addition of 0.10 equiv of $CuBr \cdot SMe_2$ to a solution of 1 equiv of 1-hexylzirconocene (**2**) and 2-cyclohexenone in THF led to rapid 1,4-addition. After the reactants were stirred at room temperature for 1 h, product **3** was isolated in 79% yield. Commercially available[7] $Cp_2Zr(H)Cl$ was used for the preparation of zirconocene reagent **2** from 1-hexene (**1**). Sonication or warming of the reaction mixture to 40 °C considerably increased the rate of hydrozirconation of alkenes.[8,9]

Scheme I



Besides $CuBr \cdot SMe_2$, other Cu(I) and Cu(II) salts such as CuBr, CuI, CuCN, $(C_4H_9C_2)_2CuCNLi_2$, $Cu(acac)_2$, and $Cu(OTf)_2$[10] catalyzed the 1,4-addition of zirconocene **2** to cyclohexenone, presumably via a transmetalation process related to the Cu(I) catalyzed 1,4-addition of Grignard reagents to α,β-unsaturated carbonyl compounds.[11,12]

Table I shows the results of the initial investigation of the scope of this novel in situ transmetalation and conjugate addition process.[13,14] As expected,[3] hydrozirconation

(1) (a) Posner, G. H. *Org. React.* **1972**, *19*, 1. (b) Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980 (c) Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947. (d) Lipshutz, B. H. *Synthesis* **1987**, 325. (e) Chapdelaine, M. J.; Hulce, M. *Org. React.* **1990**, *38*, 225.

(2) (a) Ireland, R. E.; Wipf, P. *J. Org. Chem.* **1990**, *55*, 1425. (b) Wipf, P.; Moon, C.-W.; Smitrovich, J. H. Manuscript in preparation.

(3) Hart, D. W.; Schwartz, J. *J. Am. Chem. Soc.* **1974**, *96*, 8115.

(4) Cardin, D. J.; Lappert, M. F.; Raston, C. L. *Chemistry of Organo-Zirconium and -Hafnium Compounds*; Ellis Horwood Ltd.: New York, 1986.

(5) For preparation and use of *alkenyl*zirconocenes, see: (a) Yoshifuji, M.; Loots, M.; Schwartz, J. *Tetrahedron Lett.* **1977**, 1303. (b) Loots, M. J.; Schwartz, J. *J. Am. Chem. Soc.* **1977**, *99*, 8045. (c) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486. (d) Negishi, E.; Swanson, D. R.; Miller, S. R. *Tetrahedron Lett.* **1988**, *29*, 1631. (e) Lipshutz, B. H.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 7440. (f) Babiak, K. A.; Behling, J. R.; Dygos, J. H.; McLaughlin, T. K.; Ng, J. S.; Kalish, V. J.; Kramer, S. W.; Shone, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 7441.

(6) *Alkyl* groups did not transmetalate from Zr to Cu(I) under the conditions reported by Schwartz and co-workers for *alkenyl*zirconocenes.[5a] The significant decrease in reactivity from alkenyl- to alkylzirconocenes is likely due to the superior bridging capabilities of systems with π-bonds adjacent to the metal–carbon bond, which increase transferability; see: (a) Negishi, E. I. *Pure Appl. Chem.* **1981**, *53*, 2333. (b) Zweifel, G.; Miller, J. A. *Org. React.* **1984**, *32*, 375. (c) Alexakis, A.; Hanaizi, J.; Jachiet, D.; Normant, J.-F.; Toupet, L. *Tetrahedron Lett.* **1990**, *31*, 1271.

(7) Aldrich Co., Milwaukee, WI, and Alfa Products, Ward Hill, MA. Material from several different batches of Schwartz's reagent obtained from these companies was used and gave consistent results throughout this study.

(8) Bremner, D. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Ed.; J. Wiley & Sons: New York, 1989; Vol. 5, p 3.

(9) Hydrozirconation of unfunctionalized alkenes with $Cp_2Zr(H)Cl$ proceeds slowly at room temperature in aprotic solvents: Carr, D. B.; Schwartz, J. *J. Am. Chem. Soc.* **1977**, *99*, 638.

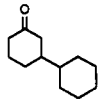
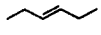
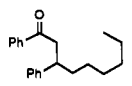
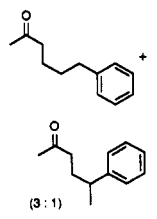
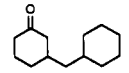
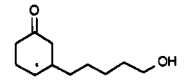
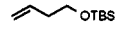
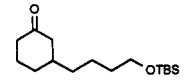
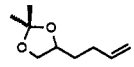
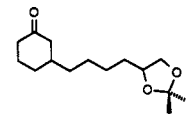
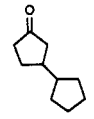
(10) At present time, we are unable to decide if indeed it is Cu(II) that catalyzes this process (see, for example: Sakata, H.; Aoki, Y.; Kuwajima, I. *Tetrahedron Lett.* **1990**, *31*, 1161), or if, more likely, the Cu(II) salt is rapidely reduced to Cu(I) by excess alkylzirconocene.

(11) Beard, C.; Wilson, J. M.; Budzikiewicz, H.; Djerassi, C. *J. Am. Chem. Soc.* **1964**, *86*, 269.

(12) In the absence of copper salts, no reaction between alkylzirconocene and enone was detected.

0022-3263/91/1956-6494$02.50/0

Table I. In Situ Hydrozirconation and Cu(I)-Catalyzed Conjugate Addition of Alkenes[a]

entry	alkene	ketone	product[b]	yield (%)[c]
1				70
2				51
3				61
4				66
5				85[d]
6				76
7				78
8				48

[a] All operations were performed under argon gas in Schlenk glassware. [b] All new compounds were fully characterized by ^1H NMR, ^{13}C NMR, IR, MS, and HRMS. [c] Yields are based on equimolar amounts of alkene and ketone and isolated products; an excess of alkylzirconocene reagent led to nearly quantitative formation of addition products. [d] Based on the reaction of dihydropyran with 2 equiv of zirconocene hydrochloride.

of (*E*)-3-hexene led to the formation of the least substituted, terminal alkylzirconocene (entry 2). No elimination of terminal or internal ether functionalities of acyclic derivatives was observed (entries 6, 7).[15] Hydrozirconation of styrene (entry 3) gave a mixture of straight-chain and branched products in a 3:1 ratio, rather than the 85:15 ratio found in the hydrozirconation of styrene in hydrocarbon solvents.[16] Interestingly, the hydrozirconation of 3,4-dihydro-2*H*-pyran led to the isolation of a straight-chain alcohol derivative (entry 5). To the best of our knowledge, this represents the first example of a tandem hydrozirconation–β-elimination–hydrozirconation sequence of a cyclic ether.[15]

The reactions presented in Table I were performed with commercially obtained zirconocene hydrochloride. Following a recent protocol,[17] $Cp_2Zr(H)Cl$ was also prepared in situ by treatment of Cp_2ZrCl_2 with $LiEt_3BH$ in THF. Whereas the hydrozirconation of olefins with this procedure proceeded readily, no subsequent Cu(I)-catalyzed conjugate addition to enones was observed. Triethylborane, a side product of the reduction of Cp_2ZrCl_2 with $LiEt_3BH$, did not interfere in the transmetalation, as was demonstrated by addition of Et_3B to the reaction mixture from commercial Schwartz reagent.

Commercial Cp_2ZrCl_2 contains significant amounts of the dihydride Cp_2ZrH_2 due to overreduction in the manufacturing process. However, experiments with this material and the oxo-bridged complexes $[Cp_2ZrCl]_2O$ and $[Cp_2ZrH]_2O{\cdot}Cp_2ZrH_2$ did not reveal any catalytic activity of these species.[18] Because we were unable to rationalize the difference in reactivity of alkylzirconocenes **2** obtained via in situ prepared or commercially available $Cp_2Zr(H)Cl$, we investigated alternative protocols for the laboratory preparation of Schwartz reagent.[19] Reduction of zirconocene dichloride with ^{t}BuMgCl,[19d,e] followed by addition of 1-hexene, led to the formation of yellow alkylzirconocene **2**. However, no 1,4-addition product could be detected upon addition of cyclohexenone and Cu(I) salts. In contrast, alkylzirconocene from Schwartz reagent prepared by $LiAl(O^tBu)_3H$ reduction[19a] of Cp_2ZrCl_2 proved to be "active" and gave the desired cyclohexenone addition product **3** in 72% yield![20]

In summary, the methodology presented in this report allows the in situ preparation of alkyl cuprates from alkenes via hydrozirconation. Only catalytic amounts of Cu(I) or Cu(II) salts are necessary, and subsequent 1,4-addition to enones appears to be further catalyzed by side products in commercial Schwartz reagent. Since most recently reported transmetalation protocols for cuprates involve the transfer of kinetically labile alkenyl groups, this example of *alkyl* transfer via relatively stable, easily ac-

(13) Addition of 2 equiv of TMS-Cl to the reaction mixture did not influence the course of the reaction. Especially, no change in the rate of transmetalation and conjugate addition and no change in the yield of isolated product was observed (for chlorosilane-accelerated conjugate addition of catalytic and stoichiometric organocopper reagents, see: Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, *45*, 349 and references cited herein).

(14) A representative procedure for the preparation of 3-hexylcyclohexan-1-one is as follows: A solution of 200 mg (2.38 mmol) of 1-hexene in 5 mL of THF was treated at room temperature with 674 mg (2.61 mmol, 1.1 equiv) of zirconocene hydrochloride and stirred at 40 °C for 10 min. After the mixture was cooled to room temperature, 228 mg (2.38 mmol) of 2-cyclohexenone and 50 mg (0.24 mmol, 0.10 equiv) of copper(I) bromide–dimethyl sulfide complex were added. The reaction mixture was stirred at 40 °C for 10 min, quenched with 25 mL of wet Et_2O, and extracted with a saturated aqueous solution of $NaHCO_3$ (2×). The organic layer was dried (Na_2SO_4), filtered through silica gel, and concentrated. The residue was purified by chromatography on silica gel (10% AcOEt in hexanes) to afford 344 mg (79%) of 3-hexylcyclohexan-1-one as a colorless oil: IR (neat) 2975, 2945, 2875, 1717, 1465, 1452, 1230 cm^{-1}; ^1H NMR δ 0.85 (t, 3 H, J = 6.9 Hz), 1.2–1.3 (m, 11 H), 1.55–1.8 (m, 2 H), 1.85–2.5 (m, 3 H), 2.2–2.4 (m, 3 H); ^{13}C NMR δ 14.0, 22.6, 25.3, 26.6, 29.3, 31.3, 31.7, 36.6, 39.1, 41.5, 48.2, 212.2; MS (EI) m/z (relative intensity) 182 (M^+, 6), 139 (7), 97 (100), 74 (25), 69 (20), 59 (40), 55 (30); HRMS (EI) m/z calcd for $C_{12}H_{22}O$ 182.1671, found 182.1671.

(15) Compare with: Karlsson, S.; Hallberg, A.; Gronowitz, S. *J. Organomet. Chem.* **1991**, *403*, 133.

(16) Nelson, J. E.; Bercaw, J. E.; Labinger, J. A. *Organometallics* **1989**, *8*, 2484.

(17) Lipshutz, B. H.; Keil, R.; Ellsworth, E. L. *Tetrahedron Lett.* **1990**, *31*, 7257.

(18) For the preparation of Cp_2ZrH_2, $[Cp_2ZrCl]_2O$, and $[Cp_2ZrH]_2O{\cdot}Cp_2ZrH_2$, see: Wailes, P. C.; Weigold, H. *J. Organomet. Chem.* **1970**, *24*, 405.

(19) (a) Wailes, P. C.; Weigold, H. *Inorg. Synth.* **1979**, *XIX*, 223. (b) Carr, D. B.; Schwartz, J. *J. Am. Chem. Soc.* **1979**, *101*, 3521. (c) Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B.; Watson, B. T.; King, S. M. *Tetrahedron Lett.* **1987**, *28*, 3895. (d) Negishi, E. I.; Miller, J. A.; Yoshida, T. *Tetrahedron Lett.* **1984**, *25*, 3407. (e) Swanson, D. R.; Nguyen, T.; Noda, Y.; Negishi, E. *J. Org. Chem.* **1991**, *56*, 2590.

(20) Interestingly, addition of 0.2 equiv of methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD: Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573) to "inactive" solution of alkylzirconocene, cyclohexenone, and CuBr did indeed lead to the formation of 1,4-addition product, however, rather sluggishly and only in ca. 10% yield. Addition of 1–2 equiv of MAD to the reaction mixture led to even lower yields of isolated product.

cessible zirconocene derivatives represents a distinct breakthrough in transmetalation methodology. Further applications of this process are actively being investigated.

Supplementary Material Available: Experimental details and spectroscopic data for all new compounds (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Accurate Determination of Small Splitting Constants for Organic Radicals by NMR

Peter A. Petillo, James De Felippis, and Stephen F. Nelsen*

S. M. McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin—Madison, Madison, Wisconsin 53706

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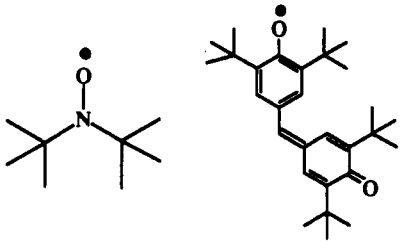
Summary: FT-NMR spectra of the radicals di-*tert*-butyl nitroxide (1) and glavinoxyl (2) are reported. Earlier CW NMR work using internal referencing gave inconsistent results for ESR splitting constants because the concentration dependence of the paramagnetic chemical shift $\Delta\delta$ was unaccounted for. This technique is a viable alternative to ENDOR and uses standard NMR equipment.

We report the use of ^1H and ^{13}C NMR to determine small ESR hyperfine coupling constants (hfcs) of 1 and 2.[1] These studies are the first using FT-NMR technology and represent, to our knowledge, the first reports of direct NMR determinations of ^1H and ^{13}C hfcs in nearly 10 years.[2] Early determinations hfcs via NMR were plagued by sensitivity, referencing, and reproducibility problems which ultimately led to the method's disrepute. For example, previous studies on 1 failed to arrive at a consistent hfc for the *tert*-butyl protons.[3] The inconsistencies plaguing the early investigations have now been resolved, allowing easy access to small hfcs for stable paramagnetic species.



1

2

NMR-observed $\Delta\delta$s are related to hfcs by eq 1, where X corresponds to the nucleus under observation.[4] The $\Delta\delta$s are given as the chemical shift difference of the paramagnetic resonance and an appropriate diamagnetic reference. The sign of the $\Delta\delta$ reveals the sign of the ESR hfc. When eq 1 is solved at a temperature of 300 K for ^1H and ^{13}C, respectively, the relationships in eqs 2 and 3 are obtained.[3a] These equations fail to explicitly account

$$\Delta\delta_X = \Delta H/H_0 = -a_X\gamma_E^2\hbar/4\gamma_X kT \quad \text{gauss/gauss} \quad (1)$$

$$\Delta\delta_H(300\text{ K})/-a_H = 73.76 \quad \text{ppm/gauss} \quad (2)$$

$$\Delta\delta_C(300\text{ K})/-a_C = 293.3 \quad \text{ppm/gauss} \quad (3)$$

for changes in bulk sample magnetic susceptibility as a function of the paramagnetic sample concentration. A clear concentration dependence of 1's ^1H contact chemical shift, $\Delta\delta_H$, is demonstrated in Figure 1.[5-7] Equations 1-3 only apply when the $\Delta\delta$s are extrapolated to infinite dilution, which for 1 yields an $a(18\text{ H}) = -0.077$ G (Figure 2).[8] *Failure to account for the concentration dependence has resulted in incorrect and variable determinations of hfcs.*[3] For instance, if the $\Delta\delta$ was obtained for 1 at a concentration of 1.26 M, the calculated ^1H hfc using eq 2 would be exactly zero. The negative sign of the hfc is clear from an extrapolated $\Delta\delta$ upfield of external tetramethylsilane. We have been unable to obtain data below a radical concentration of 5 mM due to broadening of the ^1H resonances. Figure 1 also demonstrates the futility of internal chemical shift referencing, since the resonance frequency of the internal standard (i.e. TMS) also changes as a

(1) For reviews of earlier paramagnetic NMR experiments, see: (a) Orrell, K. G. N.M.R. of Paramagnetic Species in *Nuclear Magnetic Resonance* (Specialists Periodical Reports); Webb, G. A., Ed.; The Royal Society of Chemistry: London; 1989; Vol 18, p 369. (b) *NMR of Paramagnetic Molecules: Principles and Applications*; La Mar, G. N., Horrocks, W., Jr., Holm, J. R., Eds. Academic Press: New York, 1973.

(2) (a) Pearson, G. A.; Walter, R. I. *J. Am. Chem. Soc.* **1977**, *99*, 5262. (b) Linkletter, S. J. G.; Pearson, G. A.; Walter, R. I. *J. Am. Chem. Soc.* **1977**, *99*, 5269. (c) Neugebauer, F. A.; Fischer, H.; Brunner, H. *Tetrahedron* **1981**, *37*, 1391. (d) Neugebauer, F. A.; Fischer, H. *J. Chem. Soc., Perkin Trans. II* **1981**, 896.

(3) Previous NMR studies on 1 have been performed. (a) $a(18\text{ H}) = -0.107$ G: Hausser, K. H.; Brunner, H.; Jochims, J. C. *Mol. Phys.* **1965**, *10*, 253. (b) $a(18\text{ H}) = +0.15$ G: Kreilick, R. W. *J. Chem. Phys.*, **1966**, *45*(6), 1922. (c) $a(18\text{ H}) = +0.30$ G: Stehlik, D.; Hausser, K. H. *Z. Naturforsch.* **1967**, *22a*, 914. (d) $a(18\text{ H}) = -0.092$ G: Faber, R. J.; Markley, F. W.; Weil, J. A. *J. Chem. Phys.* **1967**, *46*(5), 1652, via personal communication from R. W. Kreilick. ESR studies have also been reported. (e) $a(18\text{ H}) = 0.12$ G: Faber, R. J.; Markley, F. W.; Weil, J. A. *J. Chem. Phys.* **1967**, *46*(5), 1652. (f) $a(18\text{ H}) = 0.10$ G, $a(18\text{ H}) = 0.20$ G: Poggi, G.; Johnson, S. *J. Magn. Reson.* **1970**, *3*, 436. (g) a (18 H) = 0.10 G: Kotake, Y.; Kuwata, K. *Chem. Lett.* **1984**, 83.

(4) Brown, T. H.; Anderson, D. H.; Gutowsky, H. S. *J. Chem. Phys.* **1960**, *33*, 720.

(5) The contact chemical shift, $\Delta\delta_f$ is the difference between the chemical shift of the paramagnetic sample and that of an appropriate diamagnetic reference. Reduction products were used as diamagnetic references. For di-*tert*-butylhydroxylamine, $\delta(^1H, CDCl_3) = 1.10$ ppm, $\delta(^{13}C(q), CDCl_3) = 63.0$ ppm, $\delta(^{13}C(Me), CDCl_3) = 29.0$ ppm. For the phenol derived from 2, $\delta(^tBu, CDCl_3) = 1.47$ ppm.

(6) All ^1H experiments were performed on either a Bruker AM-500 or a Varian UNITY-300 spectrophotometer at a constant temperature of 300 ± 0.1 K in $CDCl_3$. ^{13}C experiments were performed on the Varian UNITY-300 instrument at the same temperature. Titration experiments were performed by titrating 1 and 2 into a solution of $CDCl_3$ (low concentration points) or $CDCl_3$ into neat 1 (high concentration). Spectra were obtained unlocked (with the field sweep disabled) and referenced externally. Roughly 60° pulse widths were used and long relaxation delays (relative to T_2) were employed (ca, 0.25-1.0 s).

(7) It is not clear that small changes in the ESR hfcs do not occur as a function of concentration.

(8) The NMR-derived splitting reported for 1 is smaller than the reported ESR splittings (ref 3), but the ^1H hyperfine was not directly observable by ESR; a(H) was estimated from the width of the envelope of the unresolved lines and from spectral simulation. In addition, ESR does not directly give the sign of an hfc. A TRIPLE experiment is often performed if the sign is desired. See ref 9 for more information on TRIPLE experiments.

(9) (a) Kurreck, H.; Kirste, B.; Lubitz, W. *Electron Nuclear Double Resonance Spectroscopy of Radicals in Solution: Application to Organic and Biological Chemistry*; Marchand, A. P., Ed.; VCH: New York, 1988. (b) Biehl, R.; Plato, M.; Möbius, K. *J. Chem. Phys.* **1975**, *63*(8), 3515-3522.

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