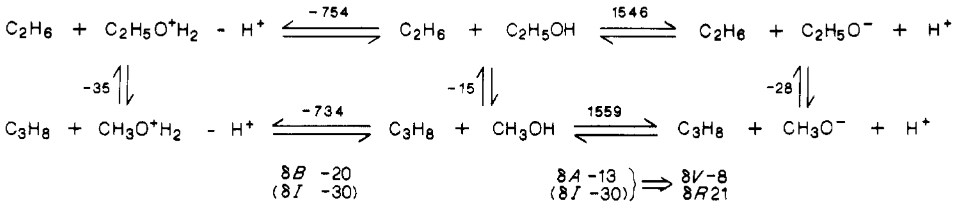
Chart III[a]



[a] Values in kJ mol^{-1}.

portant. In spite of some calculations,[1] the energy difference must be large. Also the charge redistribution could be poorly expressed by a unique polarizability, e.g., the same in both phenolate anion and cation. In organic chemistry terms the above theory neglects the mesomeric effects, while the inductive effects should be included in δV. The core ionization as a vertical process can be affected only by the latter effect, but ionization equilibrium is affected by both. Hence the two quantities δA and δI cannot be directly compared. Inherent approximations of the model remain in its quantum chemical verification[1] which follows the same reasoning and calculates δV and δR from the potentials at the hydrogen and oxygen atoms. However, for the acid-base equilibrium the energies of the whole molecules are deciding. Their quantum chemical calculation would also be possible, but it could give nothing more than replacing the experimental quantities in Chart I by calculated ones.

We tested still the above model by extending it to basicities[10] (acetic acid relative to acetone, Chart I, left). Now the changes of charge due to addition of proton or to removal of a 1s electron are equal, but the pertinent energies are not (28 and 37 kJ, respectively). Substituent effects on basicities and on core ionization energies are generally not equal[11] and it is not warranted to assume a closer similarity in the case of acidities. A further test was application to the pair ethanol-methanol (Chart III), where assumptions of the theory should be met much better since the differences both in acidity and basicity are due mainly to polarizability effects.[12] From the experimental[3,13] δA and δI one gets $\delta V = -8$ kJ and $\delta R = 21$ kJ, confirming the view that the greater polarizability in the ethanolate anion is decisive. However, even here the agreement of δI with δB is quite poor. The stabilization energies of the anion and cation are rather similar, in agreement with the view[12] that the polarizability of the methyl group stabilizes both the anion and the cation equally well.

Regardless of the better or worse approximation of the electrostatic model it follows from the above examples that the energy content of the anion is the controlling factor in most cases while that of the acid controls in some other cases. This will depend on the structure of the examined acid and of the reference compound. In a similar approach[14] acidities of substituted phenols were evaluated with reference to phenol, using STO-3G calculated energies instead of experimental $\Delta G_f{}^\circ{}_{298}$. The observed effects were smaller than in this paper, and the stability of the anion was the controlling factor in most cases but not in all (substituent 4-F). Returning to carboxylic acids and phenols we may state that the title question cannot be answered in a simple way. All available experimental facts have to be taken into account and a decomposition into various "effects", as inductive or mesomeric, must be largely artificial. Nevertheless, the terms energy content of the acid and of the anion have a physical meaning, and for their evaluation the thermodynamic quantities are deciding. Hence it is, in my opinion, experimentally proven that the acidity of carboxylic acids and phenols—as compared to alcohols—is conditioned by a low energy content of their anions.

Acknowledgment. I thank to Professor T. Darrah Thomas for a fair and valuable discussion, although a complete agreement was not reached.

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[11] Brown, R. S.; Tse, A. *J. Am. Chem. Soc.* **1980**, *102*, 5222-5226.

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Isodesmic Reaction Energies and the Relative Acidities of Carboxylic Acids and Alcohols

T. Darrah Thomas,* Thomas X. Carroll,[1a] and
Michele R. F. Siggel[1b]

Department of Chemistry and Center for Advanced Materials Research, Oregon State University, Corvallis, Oregon 97331

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The greater acidity of carboxylic acids relative to alcohols has traditionally[2] been explained as being due to extra stability of the carboxylate anion, which is enhanced by resonance delocalization of the negative charge over the two oxygens of the carboxylate group. Similar stabilization has been thought to be of little importance in alcohols because such resonance forms cannot be drawn for the alkoxide anion.

This traditional view has been challenged by Siggel and Thomas,[3] who have used comparisons of oxygen core-ionization energies with gas-phase acidities as well as theoretical calculations to show that the differential stabilization of the carboxylate anion relative to the alkoxide anion is not the major factor responsible for the greater acidity of carboxylic acids relative to alcohols. Rather this arises primarily because of differences in the charge distribution in the neutral molecules, which lead to a potential at the acidic proton of the carboxyl group that is more positive than the potential at the hydroxyl hydrogen in alcohols. These conclusions receive further support from calculations[4] of charge distributions in formic acid and ethanol and of the charge flow when the hydroxyl proton

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[1] (a) Current address: Natural Sciences, Keuka College, Keuka Park, NY 14478. (b) Current address: Department of Chemistry, University of California, Berkeley, CA 94720.

[2] (a) Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 5th ed.; Allyn and Bacon: Boston, MA, 1987; p 836. (b) Ferguson, L. N. *Electron Structures of Organic Molecules*; Prentice-Hall: New York, 1952; p 190.

[3] Siggel, M. R.; Thomas, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 4360.

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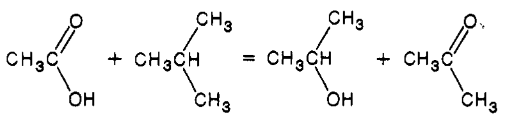
is removed from these molecules.

The Traditional View: Anion Stabilization

Although the interpretation presented by Siggel and Thomas is based on firm theoretical and experimental grounds, it is important to consider arguments that appear to support the traditional view. Among these is an analysis of energies for isodesmic reactions presented by Exner.[5a] A similar analysis of theoretically calculated energies for substituted phenols and their anions has been made by Pross, Radom, and Taft.[5b] In both cases it was concluded that the differences in acidities among these compounds are determined by the energies of the anions.

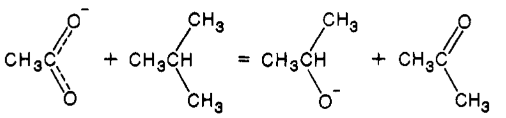
In the discussion presented by Exner, the gas-phase acidities of acetic acid and isopropyl alcohol are compared by considering two isodesmic reactions. The first involves the neutral species (eq I), with ΔH_I equal to 77 kJ/mol.[6]



(I)

This energy can be considered to represent the stabilization of acetic acid because of the interaction of the carbonyl oxygen with the hydroxyl group; this interaction does not occur in the molecules on the right-hand side of eq I.

The second reaction involves the anions of the two species of interest (eq II), with ΔH_{II} equal to 184 kJ/mol.[7]



(II)

This energy can be interpreted as being due to stabilization of the carboxylate anion because of the interaction of the two oxygens in the molecule; as above, this interaction is not possible on the right-hand side of the equation.

The difference between the two energies is just the difference between the gas-phase acidities of acetic acid and isopropyl alcohol. ΔH_{II} has been derived from ΔH_I by adding this energy difference, in accordance with Hess' law. That the energy change for eq II is greater than that for eq I has been interpreted as evidence for an extra stabilization of the carboxylate anion because of resonance delocalization in this anion.[5a]

We would, however, like to point out that the difference between ΔH_I and ΔH_{II} can also be accounted for by a model that is the complete antithesis of this traditional view and that, in fact, the energies of these reactions do not provide any insight at all into the reason for the higher acidity of carboxylic acids relative to alcohols.

A Point-Charge Model Supporting the Nontraditional View

The traditional view emphasizes the rearrangement or relaxation of electrons in response to the removal of a proton and ignores the effects that are due to the initial-state charge distribution of the neutral molecule. To illustrate these effects, we take an opposite point of view, that is, one that focuses on fixed charges and ignores the effects of relaxation. Reality lies somewhere between these two extreme models.

Since eq I is isodesmic, we expect that to first approximation ΔH_I will be zero. However, this view ignores the electrostatic interaction between the two polar bonds (carbonyl and carbon–hydroxyl). This interaction will be present in acetic acid, but not in the two molecules on the right-hand side of eq I (assuming that the polarization of the methyl–carbon bond is negligible). For a simple model to represent this interaction, we assign charge $-q_O$ to the carbonyl oxygen and $-q_{OH}$ to the hydroxyl group. The counter charges needed to preserve charge neutrality in the neutral molecule are assigned to the carbon to which the oxygen is attached.

Within the framework of this model, the change in energy for eq I is given in eq 1, where the r's represent average distances between the carbonyl oxygen and the central carbon (r_{CO}), between the hydroxyl group and the central carbon (r_{COH}), and between the hydroxyl group and the carbonyl oxygen (r_{OOH}).

$$\Delta H_I = [-q_O^2/r_{CO} - q_{OH}^2/r_{COH}] - [(q_O + q_{OH})(-q_O/r_{CO} - q_{OH}/r_{COH}) + q_O q_{OH}/r_{OOH} + F] \qquad (1)$$

The first term in square brackets describes the Coulomb interactions in the two separated molecules on the right-hand side of eq I, and the second term describes these for acetic acid. The term F in the second set of square brackets represents the energy cost (unknown) of assembling the two positive charges, q_O and q_{OH}, which are on different molecules in the species on the right-hand side, onto the central carbon atom of acetic acid. Equation 1 simplifies to eq 2. Equation 2

$$\Delta H_I = q_O q_{OH}(1/r_{CO} + 1/r_{COH} - 1/r_{OOH}) - F \qquad (2)$$

shows explicitly why ΔH_I is not zero. Static Coulomb interactions exist between the two polar bonds in the carboxylic acid but are absent or very small in the molecules on the right-hand side of eq I.

For a similar analysis of eq II, we change the charge on the hydroxyl group to $-q_{OH} - 1$ to account for the removal of the proton. No rearrangement of charge is allowed, since we are interested in the consequences of an extreme static model. The resulting change in energy for eq II is given by eq 3. The terms containing q_O on the right-hand side

$$\Delta H_{II} = \Delta H_I + q_O(1/r_{COH} - 1/r_{OOH}) \qquad (3)$$

of eq 3 account for the interactions of the acidic proton with the positively charged carbon and negatively charged oxygen of the carbonyl bond. These interactions are present on the left-hand side of eq I and absent in eq II. The overall effect of these terms is repulsive and with reasonable values[8] for q_O and appropriate values of the distances is equal to about 125 kJ/mol—about the same as the difference between the values of ΔH for the isodesmic reactions I and II and the difference in gas-phase acidity between acetic acid and isopropyl alcohol. The acidic proton in the carboxylic acid is, therefore, subject to a potential that is more positive than that of the acidic proton in the alcohol. The energy needed to remove the hydroxyl proton from the carboxylic acid is lower than the corresponding energy for the alcohol by an amount equal to the energy of the repulsive interaction between the carboxylic acid proton and the polar carbonyl group.

From the foregoing discussion, we see that the energies for the isodesmic reactions are consistent with either of two extreme views: the traditional view that resonance

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[6] Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data for Organic Compounds*, 2nd ed.; Chapman and Hall; New York, 1986.

[7] Calculated from ΔH_I and the gas-phase acidities of acetic acid and isopropyl alcohol. Bartmess, J. E.; McIver, R. T., Jr. *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic: New York, 1979; Vol. 2, pp 98, 101.

[8] Thomas, Siggel, and Streitwieser (ref 4), using integrated charge distributions, have found that the charge to be associated with the carbonyl oxygen in formic acid is about −1.0. We assume this value for acetic acid.

Table I. ΔH for the Isodesmic Reaction III, with R = CH_3, for Different Choices of the Substituent X (Values in kJ/mol)

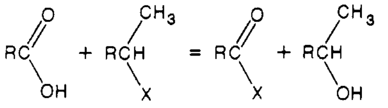
subst	ΔH_{III}[a]	electronegativity[b]	subst	ΔH_{III}[a]	electronegativity[b]
H	98.6	2.20	F	11.4	4.10
CH_3	76.9	2.50	NH_2	5.5	3.07
Cl	62.1	2.83	OH	0.0	3.50
SH	61.1	2.44			

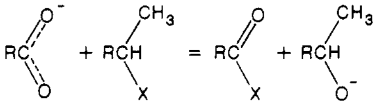
[a] Data from ref 6. [b] Allred-Rochow values taken from: Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 3rd ed.; Interscience: New York, 1972; p 114.

delocalization imparts extra stabilization to the anion and a contrary view that considers only the Coulomb interactions in a static charge distribution. The real situation involves contributions from both the static charge distribution and the relaxation of charges in response to removal of the proton. It is, however, impossible from these reaction energies alone to determine the contributions of these to the overall relative acidities. We will, however, show that a consideration of a series of isodesmic reactions, such as eq I, does provide some insight into various contributions to the energies of the species involved.

Related Isodesmic Reactions

Reactions I and II are examples of a general class of reactions that can be written as reactions III and IV, with


(III)


(IV)

both R and X being CH_3 for the reactions considered so far. While it seems perfectly plausible to make the choice of CH_3 for X, there is no a priori reason to do so, and there are good reasons to consider other choices. In particular, as has been noted above, there are static Coulomb interactions between the polar bonds in the carboxylic acid or in its anion, on the left-hand side, that are not present on the right-hand side. These interactions may play a major role in establishing the value of ΔH for eq I and II. To provide some insight into the relative importance of these static interactions versus other effects, such as electron rearrangement, it is instructive to consider values of ΔH_{III} for reactions in which X is an electronegative substituent, and, in particular, a substituent with about the same electronegativity as OH. Table I shows the results of such an analysis.

It is apparent from Table I that there is a wide variation of values of ΔH_{III} and that these roughly correlate with the electronegativity of the substituent, X. It is important to note that the carboxylic acid and the alcohol that are being compared remain the same throughout this series of reactions. Only the reference compounds are being changed. We see that the absolute value of ΔH_{III} for the isodesmic reactions depends critically on the reference compounds chosen. This result is not surprising, since the energy of acetyl fluoride will include static Coulombic contributions that are similar to those found in acetic acid but quite different from those found in acetone. This overall variation of ΔH_{III} with the electronegativity of X is, therefore, generally consistent with the idea outlined above that the static Coulomb interaction plays a major role in determining these reaction energies.

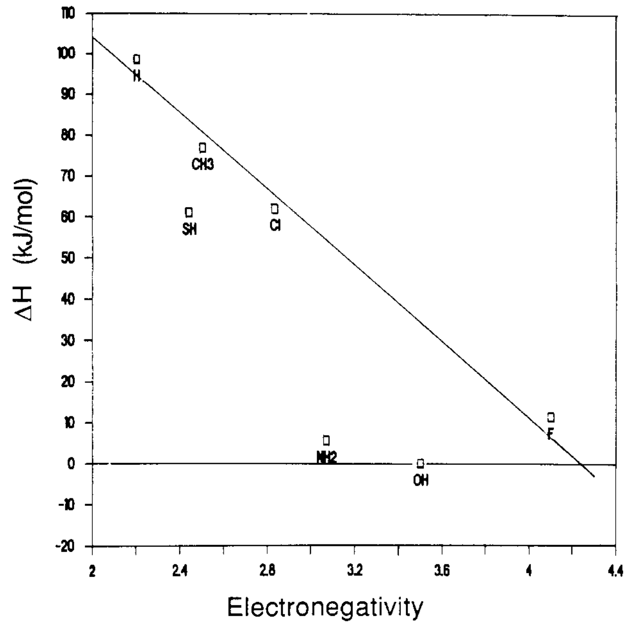
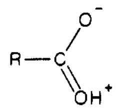


Figure 1. Enthalpy changes for reaction III plotted against electronegativity of the substituent X.

Figure 1, which shows the values of ΔH_{III} plotted against the electronegativity of X, illustrates the trend that has been described. It also illustrates some significant deviations from the trend. In particular, we note that the points for X = H, CH_3, Cl, and F fall approximately along a straight line, whereas those for SH, NH_2, and OH fall significantly below this line. For example, the point for OH is about 35 kJ/mol below the line. We interpret these deviations as being evidence for extra stability associated with these species beyond that due to the static Coulomb interactions. The extra stability might arise from contributions to the neutral molecule from resonance structures such as



and similar species for SH and NH_2 or from hydrogen bonding between the hydroxyl hydrogen and the carbonyl group.

A similar figure for eq IV would be identical with Figure 1, except that the points would be shifted vertically upward by 107 kJ/mol, which is the acidity difference between acetic acid and isopropyl alcohol. No additional information is contained in the reaction energies for eq IV.

Conclusions

A comparison of the energy changes in isodesmic reactions that involve carboxylic acids and alcohols with those for reactions involving the corresponding anions does not provide an explanation for the higher acidity of the carboxylic acid. Although these energies are consistent with the traditional idea of resonance stabilization of the anion, they are also consistent with a contrary view. This is that the higher acidity of the carboxylic acid arises because of a repulsive interaction between the hydroxyl group and the carbonyl group of the acid. This interaction is not present in any of the anions or in the alcohol.

Sets of isodesmic reactions, such as eq I and eq II or eq III and IV, may *seem* to provide explanations for acidity differences between alcohols and carboxylic acids. However, these explanations are critically dependent on the assumptions involved. If one believes a priori that the higher acidity of carboxylic acids is due solely to resonance stabilization of the anion, then the difference between ΔH_I and ΔH_{II} will be assigned to this stabilization energy. However, the fact that there is an energy difference does not provide evidence that the initial assumption is correct. Because of Hess' law, ΔH_{II} is greater than ΔH_I by the amount of the difference in acidity between acetic acid and isopropyl alcohol, regardless of the reason for this difference.

Once we recognize that both initial- and final-state effects influence the acidities of carboxylic acids,[9] then we need a model that can account for both effects. The use of isodesmic reactions does *not* provide information that can separate the two effects. Such separation can come only from comparisons of experimental and/or theoretical results that are sensitive in different ways to initial- and final-state effects.

However, consideration of a series of isodesmic reactions in which carboxylic acids and alcohols are compared with compounds having substituents of different electronegativities does provide some insight into the interaction between a carbonyl oxygen and a hydroxyl group attached to the same carbon atom. Such a configuration appears to be about 35 kJ/mol more stable than would be expected from electronegativity considerations alone. This result suggests that there is some special stabilization of the carboxylic acid because of this interaction.

Acknowledgment. We would like to thank Professor Otto Exner for sharing his thoughts on isodesmic reactions with us prior to publication. This work was supported by the National Science Foundation.

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(9) The idea that the initial-state effect is important is not new, but was well recognized in early treatments of the subject. (See, for instance: Wheland, G. W. *The Theory of Resonance and Its Application to Organic Chemistry*; Wiley: New York, 1944; pp 167–172. Also see: *Resonance in Organic Chemistry*; Wiley: New York, 1955; pp 340–345.) It is only more recently that the greater acidity of carboxylic acids has been attributed almost exclusively to resonance stabilization of the anion (ref 2).

Tristrimethylsilylation of Phenol and Related Reactions

Anthony G. M. Barrett*

Department of Chemistry, Northwestern University, Evanston, Illinois 60208

Ian A. O'Neil

Department of Chemistry, Imperial College, London SW7 2AY, England

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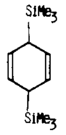
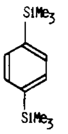
In 1962 Weyenberg and Toporcer reported that benzene was reduced by the use of lithium and chlorotrimethylsilane in THF to produce 3,6-bis(trimethylsilyl)-1,4-cyclohexadiene (1) (40%) and 1,4-bis(trimethylsilyl)benzene (2) (15%).[1] This silyl Birch reduction chemistry was extended to toluene and anisole to produce the corresponding 1,4-cyclohexadiene systems (30–50%). Laguerre et al. subsequently optimized the preparation of 1 (85%), observed that air oxidation was particularly effective in the aromatization of 1, and extended the chemistry to a series of alkylbenzene derivatives.[2] Recently we have utilized this methodology for the conversion of indole (**3a**) into 1,4-bis(trimethylsilyl)indole (**3b**) and subsequently 4-(trimethylsilyl)indole (**3c**). Thus reaction of **3a** or **3d** with lithium metal and chlorotrimethylsilane under ultrasonication gave **3b** (50%, 55% respectively) on oxidation of the intermediate dihydroindole derivative with *p*-benzoquinone.[3] Subsequent methanolysis of **3b** gave **3c** (98%). 4-(Trimethylsilyl)indole (**3c**) was found to be useful in the preparation of 4-acylindoles via ipso Friedel–Crafts acylation. In addition to indole (**3a**), both pyridine and quinoline were converted into the corresponding C-4 trimethylsilyl derivatives **4** (42%) and **5** (35%).



1



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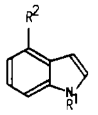
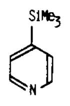


3

a $R^1=R^2=H$
b $R^1=R^2=Me_3Si$
c $R^1=H$, $R^2=Me_3Si$
d $R^1=Me_3Si$, $R^2=H$



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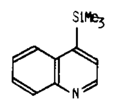

5

Herein we report the extension of the silyl Birch reduction to phenol and its derivatives. Reduction of phenol by use of lithium in the presence of chlorotrimethylsilane proceeded efficiently providing that the reaction mixture was ultrasonicated.[4] Without ultrasonication the reaction was much slower and proceeded in poor yield. The 1,4-cyclohexadiene product was not isolated. Direct oxidation by reflux in air gave the trisilyl product **6a** (72%). In the same way *m*- and *p*-cresol were converted into **7a** (39%) and **8a** (58%). Since aerobic oxidation of the intermediate **9a** was very slow, *p*-benzoquinone was used to restore aromaticity. Anisole was converted into **9b** by use of the silyl Birch reduction. Again this material was readily air oxidized to produce **6b** (63% overall). Finally 4-methoxytoluene was converted into **8b** (64%). The trisilyl derivatives **6a**–**8a** were smoothly and cleanly monodesilylated by reaction with tetrabutylammonium fluoride in THF to provide the corresponding phenols **6c**, **7b**, and **8c** (87–92%). It is clear from these experiments that simple oxygenated benzene derivatives may be readily converted into the *p*-bis(trimethylsilyl) aromatic systems with retention of the oxygen substituent. This is in contrast to the naphthalene derivatives **10a** and **10b** which have been reported to be converted respectively into **10c** and **10d** on silyl Birch reduction.[5] Additionally it is clear that the regioselectivity of the reaction follows directly the known mechanism of the Birch reduction.[6]

We have briefly examined the reaction of **6b** with electrophiles.[7] Bromination of **6b** with *N*-bromosuccinimide (−30 °C) or bromine (25 °C), respectively, gave **11** (82%) and **12** (84%). In contrast to these reactions **6b** gave **13** (67%) on Friedel–Crafts acylation. Presumably the electrophile in this case is too bulky to ipso substitute the

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(4) For further examples of the use of ultrasonication in synthesis, see: Suslik, K. S. "Ultrasound in Synthesis" In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1986; Vol 4, pp 2–60.

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(6) Birch, A. J. *Q. Rev. Chem. Soc.* **1950**, *4*, 69. Birch, A. J.; Smith, H. *Ibid.* **1958**, *12*, 17.

(7) For related ipso aromatic substitution reactions, see: Félix, G.; Dunoguès, J.; Calas, R. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 402. Félix, G.; Laguerre, M.; Dunoguès, J.; Calas, R. *J. Chem. Res. Synop.* **1980**, 236. Eaborn, C. *J. Organomet. Chem.* **1975**, *100*, 43 and references therein. Wilbur, D. S.; Stone, W. E.; Anderson, K. W. *J. Org. Chem.* **1983**, *48*, 1542.

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