multichannel analyzer equipped with a fast-gated (20 ns) image intensifier.

Acknowledgment. We thank the Association for International Cancer Research (U.K.) and the National Foundation for Cancer Research (U.S.A.) for partial support of this work. We also thank Dr. J. C. Scaiano for the use of his laser flash photolysis system and Chris Evans for permission to use some of his unpublished results. E.G.J. and Y.K. also acknowledge funding from the Natural Sciences and Engineering Research Council of Canada for the EPR/ENDOR spectrometer and ENDOR photolysis cavity. We also thank two anonymous referees for their helpful comments and suggestions.

Registry No. **1a**, 10191-41-0; **3a**, 85460-71-5; **3a** (radical), 114996-40-6; **3a** (acetate), 85460-72-6; **3b**, 101836-19-5; **3b** (radical), 114996-41-7; **3c**, 101836-18-4; **3d**, 101836-17-3; **3d** (radical), 114996-42-8; **3e**, 107697-39-2; **4b**, 101836-19-5; **4b** (radical), 114996-43-9; **5**, 40316-60-7; **6**, 2054-35-5; **7**, 114996-51-9; **8b** (radical), 114996-44-0; **8c** (radical), 114996-45-1; **8d**, 114996-49-5; **8e** (radical), 114996-46-2; **9c** (radical), 114996-47-3; **9d** (radical), 114996-48-4; **10**, 85979-45-9; **11**, 107697-42-7; **12**, 107697-43-8; **13**, 107697-41-6; **14**, 114996-50-8; AIBN, 78-67-1; styrene, 100-42-5; cumene, 98-82-8; 2,3,5-trimethyl-4-hydroxybenzenethiol, 85460-73-7; phytol, 150-86-7; isophytol, 505-32-8; thiochroman-4-one, 3528-17-4.

Reaction of Dilithiated Carboxylic Acids with Iodine: Evidence for the Formation of a Radical Anion Intermediate

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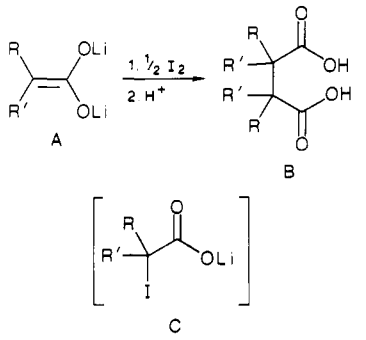
Received December 30, 1987

The mechanism for oxidative dimerization of carboxylic acid dianions involves single electron transfer to iodine, producing an organic anion radical. Rearrangement of this species was observed with suitable substrates at a rate competitive with intermolecular reactions. The radical anion can dimerize or react with iodine. The iodide thus generated can be isolated (reaction with excess of iodine) or can participate in a polar S_N2-type reaction sequence leading to dimeric products (reaction with $^1/_2$ equiv of iodine). The interference by free amines (liberated during the metalation with lithium amides) is rationalized by the formation of a charge-transfer complex with iodine which decomposes, liberating protons.

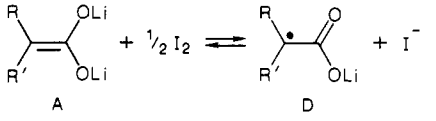
Introduction

Carboxylic acid dianions are very useful reagents in preparative organic chemistry.[1] Their highly electron-rich character renders them particularly susceptible to reactions proceeding by electron transfer. Early studies by Ivanoff[2] have shown that the dianions of carboxylic acids react with bromine to give dimeric products. Recently Belletire et al.[3] have reported a method for the synthesis of succinic acid derivatives B via oxidative coupling of a dilithiated carboxylic acid A (Scheme I). In these studies, iodine was used as the oxidant, and a route involving the formation of the iodide C, followed by a nucleophilic displacement with the dianion A, was suggested. This mechanism was proposed, for instance, for the dimerization of ester enolates induced by treatment with iodine.[4] However, the possibility that electron transfer was involved was also considered.[5] In this work we have used electrochemical techniques and the characteristic ring-opening or ring-forming reactivity of radicals to obtain further information about the mechanism of the oxidative dimerization of dilithiated carboxylic acids.

Scheme I. Preparation of Succinic Acid Derivatives



Scheme II. Electron Transfer between Dilithiated Carboxylic Acids and Iodine



Results and Discussion

Oxidation Potentials. The standard free energy for electron transfer between a carboxylic acid dianion and iodine (Scheme II) can be estimated by the difference between the oxidation potentials of the dianion and the I^-/I_2 couple. Such a simple calculation has proved to be successful, for example, in predicting whether the addition of an organic cuprate to an α,β-unsaturated carbonyl compound could proceed via an initial electron transfer.[6] A more elaborate treatment, based on Marcus theory, has been developed by Eberson for analogous electron transfers involving organic donors and acceptors.[7] In practice, this method suffers, however, from the requirement that the

(1) Petragnani, N.; Yonashiro, M. *Synthesis* **1982**, 521.
(2) Ivanoff, D.; Spassoff, A. *Bull. Soc. Chim. Fr.* **1935**, *2*, 76.
(3) (a) Belletire, J. L.; Spletzer, E. G.; Pinhas, A. R. *Tetrahedron Lett.* **1984**, *25*, 5969. (b) Belletire, J. L.; Fremont, S. L.; *Tetrahedron Lett.* **1986**, *27*, 127. (c) Belletire, J. L.; Spletzer, E. G. *Synth. Commun.* **1986**, *16*, 575. (d) Spletzer, E. G. Ph.D. Dissertation, University of Cincinnati, 1986.
(4) Brocksom, T. J.; Petragnani, N.; Rodrigues, R.; La Scala, H. *Synthesis* **1975**, *396*.
(5) Belletire, J. L.; Fry, D. F. *J. Org. Chem.* **1987**, *52*, 2549.
(6) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.
(7) Eberson, L. *Acta Chem. Scand., Ser. B38* **1984**, 439.

0022-3263/88/1953-3745$01.50/0

Table I. Oxidation Potentials ($E_{1/2}$) of Several Carboxylic Acid Dianions and Estimated Free Energies (ΔG) for Their Reaction with Iodine[a]

carboxylic acid	$E_{ox.}$(dianion), vs SCE (±0.05 V)	$\Delta G°$ [kcal/mol][c]
phenylacetic acid (1)	−0.62	−20.9
2-phenylpropanoic acid (2)	−0.68	−22.5
diphenylacetic acid (3)	−0.67	−21.9
phenylthioacetic acid (4)	−0.34	−14.5
tert-butylacetic acid (5)	+0.41[d]	

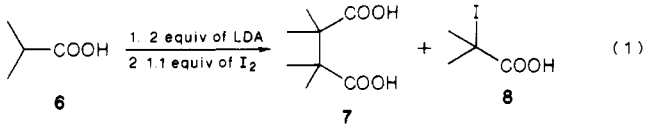
[a] $E_{red.}$(iodine) = +0.294 V vs SCE.[9] [b] In THF/HMPA (7:3), 0.2 M $LiClO_4$. Oxidation peak potentials (E_p) in cyclic voltammetry experiment. [c] $\Delta G = -23.06[E_{red.}(I_2) - E_{ox.}(\text{dianion})]$. [d] Rough approximation for $E_{1/2}$ because of the very broad shape of the peak.

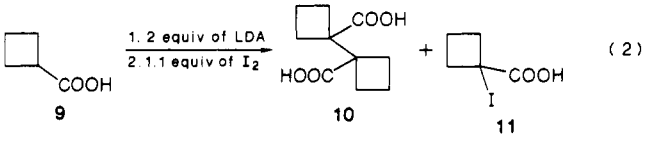
reorganization free energies and the redox potentials of the reagents be known. In many cases, they are unknown and are particularly difficult to estimate.

The oxidation potentials of some carboxylic acid dianions have been measured.[8] These are reported, together with the estimated $\Delta G°$ values, in Table I. In each of these examples, single electron transfer is thermodynamically favorable ($\Delta G° < -10$ kcal/mol).

In general, alkanoic acid dianions fail to show any well-defined cyclic voltammetric oxidation peaks. Dilithiated *tert*-butylacetic acid displays an oxidation peak, but it is too broad for a useful estimation of $\Delta G°$. This poor voltammetric behavior was attributed to slow charge transfer at the electrode surface, which would not be encountered in a homogeneous reaction with iodine. The absence of an oxidative cyclic voltammetric wave was also reported for $Me_4Cu_2Li_2$ by House,[6] but this compound proved to be capable of transferring an electron to fluorenone or benzophenone in homogeneous solution.

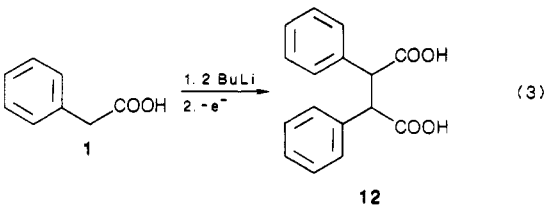
Dianion Coupling Products. Iodination of Disubstituted Acetic Acid Dianions. Dilithiated isobutyric acid (6) and cyclobutanecarboxylic acid (9), when treated with an excess of iodine (1.1 equiv) at −78 °C, gave respectively tetramethylsuccinic acid (7) (38% yield, eq 1)





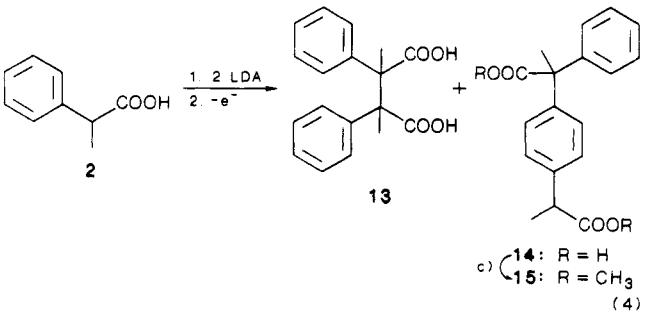
and [1,1′-bicyclobutyl]-1,1′-dicarboxylic acid (10) (16% yield, eq 2) besides the iodides 8 and 11. The formation of dimeric product by reaction of the dianion with the product iodide is unlikely, since the dimerization reaction is much faster than nucleophilic substitution under the reaction conditions (−78 °C for about 2 min before quenching). Indeed, dimer 10 was formed in less than 10% yield when a homogeneous mixture (THF/HMPA) of dilithiated 9 and lithium 1-iodocyclobutanecarboxylate was stirred for 10 min at −78 °C. The faster reaction with iodine is thus permissive of a radical coupling for the formation of 7 and 10.

Dimerization of Phenylacetic Acid Derivatives. The feasibility of dimerization of radical anions D could be more clearly tested with a substrate exhibiting better voltammetric behavior. Accordingly, we have electrochemically oxidized[10] dilithiated phenylacetic acid (eq 3),

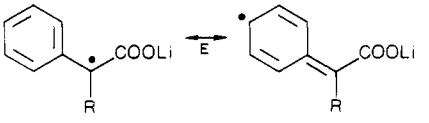


forming 2,3-diphenylsuccinic acid (12) as a *dl*/meso (2:1) mixture of diastereomers (30–40% yield). The major diastereomer (*dl*) is identical with that observed when the reaction is performed with iodine as the oxidizing agent[3a] (*dl*/meso 11:1, 90% yield). Although the Coulombic takeup reached nearly 90% theoretical (1 F/mol), the yield of this reaction never exceeded 40%. This low yield is probably caused by competing hydrogen abstraction from the solvent since the electrolysis is most conveniently performed at low current density (~30 mA/cm²). (Charge repulsion should slow the radical anion coupling relative to hydrogen abstraction.) This competing reaction is even more important with the radical anion derived from dilithiated α-phenylthioacetic acid (4), where only traces of dimer are detected (1 F/mol is consumed).

A sterically more hindered radical was generated from 2-phenylpropanoic acid (2) (eq 4) in order to slow the hydrogen abstraction. Less than 20% of the starting



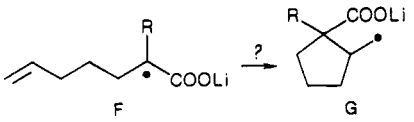
material was recovered after electrolysis, but in addition to the expected 2,3-dimethyl-2,3-diphenylsuccinic acid (13) (16% yield), the α, para-dimer 14, characterized as its dimethyl ester 15 (40%), was also isolated. When iodine[11] is used to perform the same reaction, a similar product distribution is observed: 23% 13 and 38% 15. Para coupling has previously been reported in the dimerization of radicals E: for example, triphenylmethyl radical[12] and



some diphenylmethyl radicals[13] are known to give α,-para-dimers. Steric hindrance apparently governs the

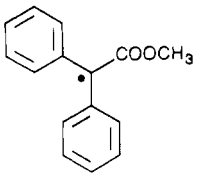
(8) Fox, M. A.; Renaud, P. *J. Am. Chem. Soc.*, in press.
(9) Bard, A. J.; Faulkner, L. R. In *Electrochemical Methods*; John Wiley & Sons: New York, 1980; p 700.
(10) The large difference in oxidation potential of anions and radicals allows us to oxidize selectively anions to radicals by performing the oxidation at a constant potential. Wayner, D. D. M.; Griller, D. *J. Am. Chem. Soc.* **1985**, *107*, 7764.
(11) This reaction has been described previously by Belletire et al. (see ref 3a and 3d); however, they did not mention the formation of the α,α-dimer.
(12) Lankamp, H.; Nauta, W. T.; MacLean, C. *Tetrahedron Lett.* **1968**, 249.
(13) Neumann, W. P.; Stapel, R. In *Substituent Effects in Radical Chemistry*; Viehe, H. G., et al., Eds.; D. Reidel Publishing Co.: New York, 1986; pp 219–222.

Scheme III. Proposed Cyclization of a Hexenyl Radical Anion



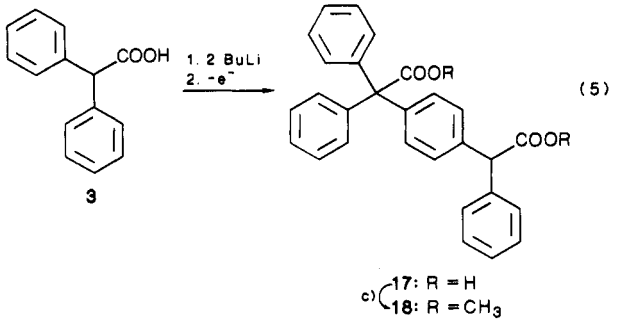
orientation of the dimerization. The preferential formation of dimer **14** can thus be rationalized by the large size of the solvated carboxylate group, as well as by electrostatic factors.

Since the coupling of carbomethoxydiphenylmethyl radical (**16**) is known to give exclusively the α,para-dimer **18**, we investigated the oxidation of dilithiated di-



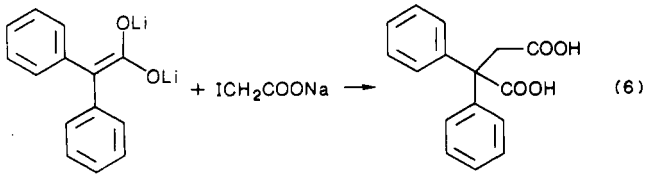
16

phenylacetic acid (**3**) with iodine and at a poised anode (eq 5). The two methods gave only the α,para-dimer **17** in



(5)

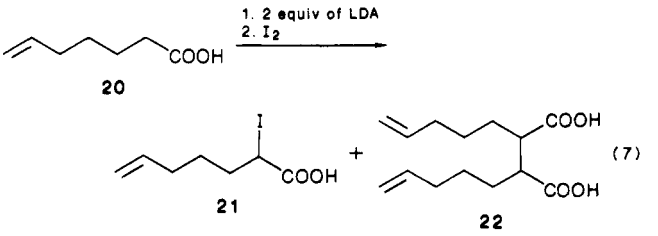
60% and 72% yield, respectively. Traces of the α,α-dimer, as the anhydride, were sometimes detrected, but irreproducibly, during the electrolysis. Benzophenone (<5% yield) was observed in both reactions as a side product. Although the formation of α,para-dimer by an ionic mechanism cannot be ruled out unambiguously, the alkylation of diphenylacetic acid dianion with sodium iodoacetate led exclusively to 2,2-diphenylsuccinic acid (**19**) (eq 6).



(6)

Another possible mechanism, the addition of a radical anion (E) to the starting dianion followed by oxidation, is inconsistent with the absence of cross-product during the electrolysis of dilithiated phenylacetic acid (**1**) in the presence of the acetic acid dianion. This electrolysis, which was performed at 0.0 V (vs SCE), a potential where only diphenylacetic acid dianion was oxidized, gave only dimer **12**.

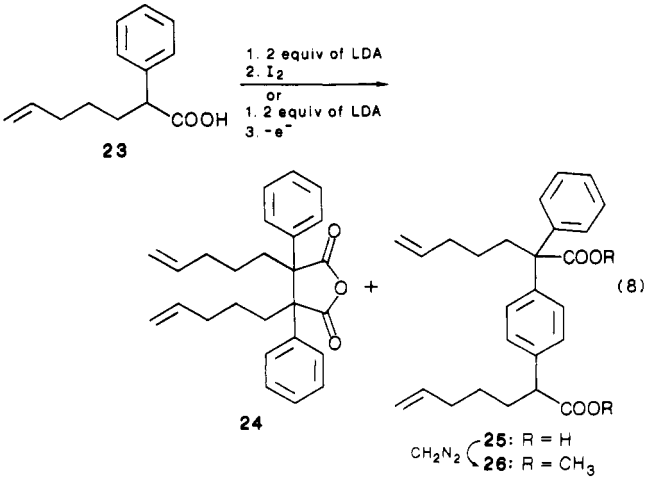
Radical Anion Rearrangement. An intramolecular trap for the radical anion intermediate (based on the well-documented ability of 5-hexenyl radicals to cyclize to cyclopentylmethyl radicals) was proposed (F → G, Scheme III). The dianion of 6-heptenoic acid (**20**) is stable at room temperature, and treatment with iodine (1 equiv) gave the iodide **21** (70% yield) and dimeric product **22** (12% yield) (eq 7). No product derived from the cyclopentylmethyl



(7)

radical was detected. The direct electrochemical oxidation of **20** could not be obtained because of the impossibility of oxidizing the corresponding dianion electrochemically. Without electrolysis or iodination, unrearranged acids were recovered upon quenching in all cases.

In order to determine whether radical anions F do indeed cyclize, the dianion of 2-phenyl-6-heptenoic acid (**23**) was examined. Preparative electrolysis of dilithiated **23** gave the α,α-dimer **24** (8% yield) and the α,para-dimer **26** (32% yield) (eq 8). No cyclized product was observed even

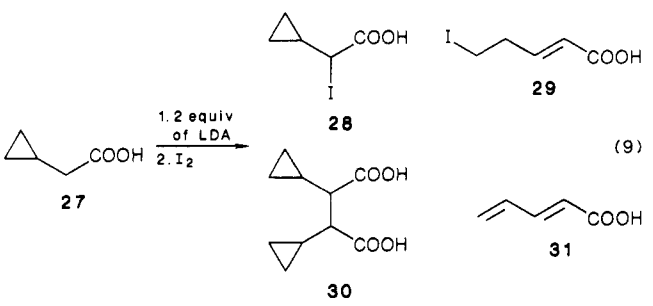


(8)

when the electrolysis was performed at very low current density (5 mA/cm^2). Oxidation of the same dianion with iodine leads to a similar product distribution (**24**, 26% and **26**, 36%). The radical anion rearrangement F → G (Scheme III) apparently does not occur at a rate competitive with dimerization. Presumably the slower cyclization rate of F than in the 1-hexenyl radical can be attributed to resonance stabilization of F.

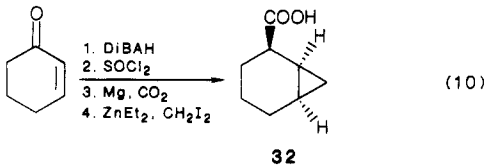
An alternate radical rearrangement involves the cyclopropylmethyl ring opening reaction H → I (Scheme IV). Cyclopropylacetic acid[14] (**27**), prepared by cyclopropanation of vinylacetic acid, was treated with 2 equiv of LDA, producing, after evaporation of the solvent, a dianion stable at room temperature. Treatment of this dianion with iodine (1.1 equiv) yielded, respectively, a 5:1 mixture of the iodides **28** and **29** (eq 9). The dimer **30** was also isolated in a small quantity. The product distribution was independent of the reaction temperature between −100 and −20 °C. When $^1/_2$ equiv of iodine was used, the reaction gave the dimer **30** (50% yield), starting material (30%), and *trans*-2,4-pentadienoic acid (**31**) (10% yield). Three hypotheses can explain the relatively small amount of rearranged iodide **29**: (1) a radical anion H rearranges more slowly than it couples; (2) the rearrangement of H

(14) The iodination and electrochemical oxidation of dilithiated 1-(phenylthio)-1-cyclopropylacetic acid were also studied. In both cases, a complex mixture of oligomeric products was formed. Proton NMR spectra show clearly that partial opening of the cyclopropyl rings had occurred.

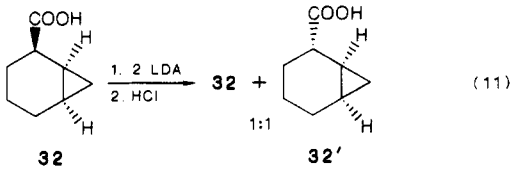


is fast, but an equilibrium between H and I exists; or (3) an ionic reaction between the dianion and iodine competes with the radical pathway. Although the relative yields of **28** and **30** with varying concentrations of I_2 make hypotheses (1) and (3) less likely, they do not provide compelling support for hypothesis (2) since the mixtures are complex.

Irrespective of which hypothesis is correct, the formation of the rearranged product should be favored by increasing ring strain within the cyclopropyl moiety. Therefore we have prepared *cis*-bicyclo[4.1.0]heptane-2-carboxylic acid (**32**) (eq 10). The cyclopropanation reaction (step d) was

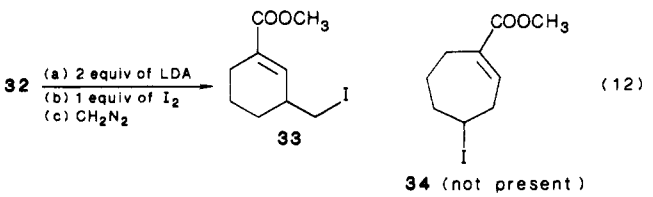


over 98% diastereoselective. In order to ascertain the stereochemical assignment of **32** by NOE measurements, we prepared a 1:1 mixture of the two diastereomers (**32**/**32′**) by dilithiation of **32** followed by protonation with 1 N HCl (eq 11). Saturation of the proton in the position



α to the carboxyl group was accompanied by a positive enhancement of the signal of the endo proton in position 7 of the isomer **32′** only. This observation is in accordance with, respectively, cis and trans configurations for **32** and **32′** (see Figure 1).[15]

Treatment of **32** with LDA gave a stable dianion, which upon reaction with iodine and esterification of the crude material with diazomethane gave the iodide **33** (75% yield) as the only identified product (eq 12). No trace of the cycloheptenyl iodide **34** could be detected.



The exclusive formation of the radical K by rearrangement of J can be explained by stereoelectronic effects (Scheme V). A similar explanation has been advanced for the ring opening of a 2-hydroxy-2-bicyclo[4.1.0]heptyl radical.[16] The nearly parallel arrangement of the singly

(15) The cyclopropanation of 2-cyclohexen-1-ol is also known to give exclusively the cis diastereomer: Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468.

(16) Dauben, W. G.; Schutte, L.; Wolf, R. E.; Deviny, E. J. *J. Org. Chem.* **1969**, *34*, 2512.

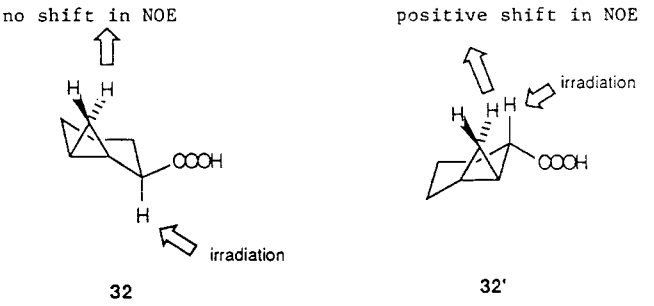
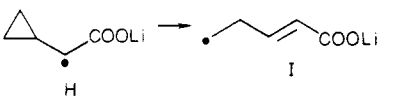
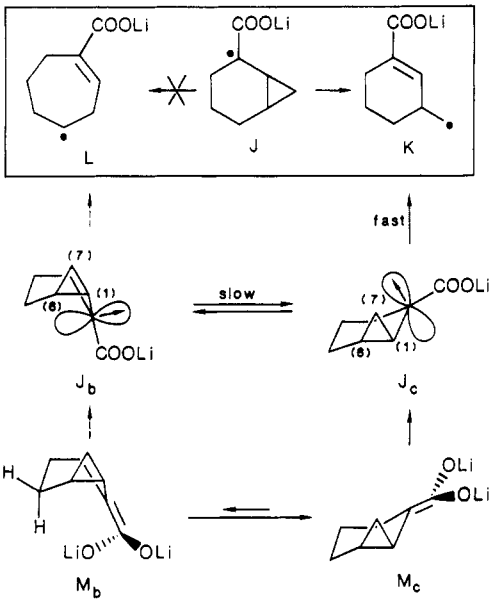


Figure 1. Determination of the relative configuration of **32** by measurement of NOE differential spectra.

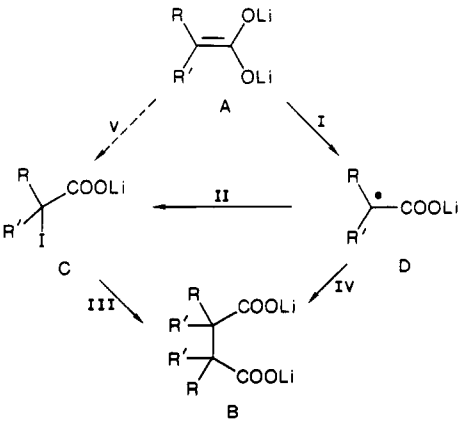
Scheme IV. Proposed Ring Opening of a Cyclopropyl Radical Anion



Scheme V. Stereoelectronic Control in the Ring Opening of a Cyclopropylcarbinyl Radical Anion



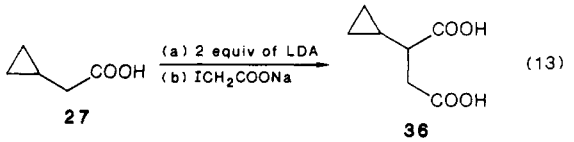
Scheme VI. General Mechanism for the Dimerization of Dilithiated Carboxylic Acid with Iodine



occupied orbital (p orbital) with the C_1–C_7 bond in the chairlike conformation of J (J_c) leads to the formation of K. Similar considerations imply that the radical L should be formed by the rearrangement of J in a boatlike form (J_b). The ratio of boat- and chair-like conformers is determined by the preferred conformation of dilithiated **32**, since at −78 °C the radical rearrangement is much faster

than conformational equilibration. The chair form (M_c) of the dianion is believed to be much more stable than the boat form (M_b) since the enolate should be considered as a very bulky group because of solvation, counter ion, and aggregation effects.

Possible Cross-Coupling: Alkylation of Dilithiated Carboxylic Acids with α-Iodo Carboxylates. A single electron transfer (SET) could, in principle, be operative during the reaction of dilithiated carboxylic acids with α-iodo carboxylates. None of the experiments we have run, however, support this possibility. For instance, the alkylation of cyclopropylacetic acid (**27**) with sodium iodoacetate (eq 13) gave exclusively the unrearranged diacid



27 36 (13)

36. Even when the sterically more hindered lithium 1-iodocyclobutanecarboxylate was used as electrophile, no trace of olefinic protons was found in the ^1H NMR spectrum of the crude product. Presumably, S_N2 reactions of the dianion with alkyl iodides are faster than electron-transfer/coupling routes.

Effect of Amines. Much lower yields were obtained in the oxidative coupling of dilithiated carboxylic acids when an amine was present in the reaction medium.[3a,d] For example, the 90% yield obtained in the electrooxidative dimerization of the phenylacetic acid dianion generated from butyllithium fell to 30% when LDA was used for the deprotonation. Diisopropylamine does not act as a hydrogen donor, since the electrochemical dimerization of dilithiophenylacetic acid is not perturbed by a 5-fold excess of amine. It does however react with iodine to form a charge-transfer complex (a deep green color appears during the addition of iodine) which decomposes rapidly, liberating protons.[17] The use of lithium hexamethyldisilazide (LiHMDS) as a base slows charge-transfer complex formation for steric and electronic reasons. (In THF, diisopropylamine has an oxidation potential $E_{1/2} \sim +1.2$ V vs SCE, a value much less positive than that of hexamethyldisilazane, $E_{1/2} \sim 1.6$ V vs SCE). By employing this base, we obtain a greater than 90% yield for the dimerization of phenylacetic acid. Nevertheless, the use of LiHMDS, instead of LDA, is not always feasible since many alkanoic acids are not sufficiently acidic[18] to be deprotonated by this base.

Conclusions

The formation of symmetrical dimers by oxidation of dilithiated carboxylic acids with iodine occurs by the mechanism shown in Scheme III. The dianion A reacts with iodine by single electron transfer to give the anion radical D (path I). This anion radical may react with iodine[19] to give the iodide C (path II) which can be displaced in an SN_2-type reaction by the dianion A still present in solution (path III). There is no indication for the involvement of SET in this reaction step. The anion radical D can also directly give the dimer B by radical coupling (path IV), a route that is particularly important with sterically hindered anion radicals in which S_N2 reactivity is blocked. The formation of the iodide C by an ionic mechanism (path V) is neither supported nor excluded by our experimental results.

Experimental Section

General. ^1H NMR spectra were obtained on a Nicolet NT-360 (360 MHz), a General Electric QE-300 (300 MHz), or a Varian EM-390 (90 MHz) spectrometer and are reported in parts per million from TMS (0 ppm) as internal standard. ^{13}C NMR spectra were recorded on a Nicolet NT-360 (90 MHz) or a General Electric QE-300 (75 MHz) spectrometer. Broad band decoupled spectra are reported; chemical shifts are given in ppm from TMS (0 ppm) as an internal reference. The observed splitting in off-resonance spectra is reported when required for the identification of the compound. In the NOE experiment, a General Electric GN-500 spectrometer was used.[20] The samples were carefully degassed prior to the measurement (sealed tube). High resolution mass spectra were recorded on a DuPont (CEC) 21-110 instrument. Flash chromatography was performed on silica gel 60 (230–400 mesh, Macherey-Nagel). Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Metalation reactions were performed under argon by using syringes and cannula for the transfer of reagents and solvents. The following abbreviations are used: EtOAc (ethyl acetate); Et_2O (diethyl ether); HMPA (hexamethylphosphoramide); BuLi (*n*-butyllithium); DiBAH (diisobutylaluminium hydride).

Chemicals. Commercially available chemicals were used without further purification unless described. THF was distilled under argon over potassium. HMPA was heated at 180 °C for 4 h over CaH_2 under argon before being distilled at reduced pressure. Diisopropylamine and 1,1,1,3,3,3-hexamethyldisilazane were distilled from CaH_2. BuLi (1.6 to 2.5 M in hexane) was titrated with 2,5-dimethoxybenzyl alcohol.[21]

Electrolyses. A divided cell (2 × 10 mL, medium fritted glass) with a silver wire as pseudo-reference electrode, a platinum net (1.5 cm^2) as counterelectrode, and a mercury pool[22] (1 cm^2) as working electrode were used. A Model 173 potentiostat coupled with a Model 179 digital coulometer (Princeton Applied Research) or a Model 415 potentiostat controller and a Model 640 digital coulometer (The Electrosynthesis Company) were used for the electrolyses.

Preparation of Dilithiated Carboxylic Acids (Method a).[1,23] The acid (10 mmol) dissolved in THF was added to a 1 M LDA solution (20 mL, 20 mmol) diluted with 12 mL of THF. The reaction mixture was stirred at room temperature for 3 to 5 h, at which time a homogeneous solution had formed. In some cases, the dianion was isolated as a powder after removal of the solvent under high vacuum.

Reaction of Dilithiated Carboxylic Acids with Iodine (Method b).[3] Iodine (5–11 mmol) in THF (6 mL) was added at −78 °C over 3 min to a solution of the dianion (10 mmol) in THF (20 mL). The iodine color disappeared immediately after the addition of the first 7 mmol of iodine. The reaction mixture was acidified with 1 N HCl and extracted with EtOAc (3×). The organic phases were washed with small portions of a sodium bisulfite solution (until complete disappearance of the iodine color occurred) and brine. After drying over sodium sulfate, the solvent was removed under reduced pressure (without heating).

Electrochemical Oxidation of Dilithiated Carboxylic Acids (Method c). In both compartments of the electrochemical cell, $LiClO_4$ (200 mg, 1.9 mmol) and HMPA (1 mL) were introduced. The anodic compartment was then filled with the dianion solution (8 mL) and THF (8 mL) was introduced into the cathodic compartment. The electrolysis was performed at a constant potential. About 90% of the theoretical charge (1 F/mol) was taken up. Typically a current of 40 mA flowed through the cell. In the cathode, a blue solution of electrons was formed and some lithium was deposited on the cathode. After electrolysis, the

(17) See Hassel and Romming (Hassel, O.; Romming, C. *Q. Rev. Chem. Soc.* **1962**, *16*, 1) for charge-transfer complexes between iodine and amines and Bohme and Krause (Bohme, H.; Krause, W. *Chem. Ber.* **1951**, *84*, 170) for the reaction of amines with iodine.

(18) Renaud, P.; Fox, M. A. *J. Am. Chem. Soc.*, in press.

(19) Or any other species like I_3^- or $I_2^{\bullet-}$ which may be present in solution. See Fornier de Violet (Fornier de Violet, P. *Rev. Chem. Int.* **1981**, *4*, 121) for a discussion of the occurrence of polyhalide radical anions.

(20) We thank Dr. B. Shoulders and S. Sorey for performing the nuclear Overhauser effect (NOE) measurements.

(21) Winkle, M. R.; Lasinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

(22) A stirred Hg pool allowed us to avoid problems caused by coating of the electrode surface: Tokuda, M.; Shigei, T.; Itoh, M. *Tetrahedron Lett.* **1975**, 621.

(23) Creger, P. L. *J. Am. Chem. Soc.* **1967**, *89*, 2500.

(24) Varma, P. S.; Menon, V. T. S. *J. Ind. Chem. Soc.* **1933**, *10*, 591.

content of the anode compartment was poured into 1 N HCl and extracted (3×) with EtOAc. After washing (brine) and driving (Na_2SO_4) of the organic phase, the solvent was evaporated to give the crude product.

Reaction of Dilithiated Isobutyric Acid with Iodine (eq 1). Isobutyric acid (0.93 mL, 10 mmol) was deprotonated according to method a. The resulting slightly yellow powder was dissolved in THF (20 mL). This solution was treated with iodine (2.8 g, 11 mmol) according to method b. The reaction mixture was stirred for 1 min at −78 °C before workup. A brown oil was triturated with CH_2Cl_2/pentane (1:1), producing tetramethylsuccinic acid (**7**) (330 mg, 38%) as a white solid, mp 178–180 °C (lit.[3d] mp 177–178 °C).

From the filtrate 2-iodoisobutyric acid (**8**) (920 mg, 43%) was isolated after crystallization from Et_2O/pentane, mp 70–72 °C (lit.[23] mp 73.5 °C).

Reaction of Dilithiated Cyclobutanecarboxylic Acid with Iodine (eq 2). Cyclobutanecarboxylic acid (**9**) (0.96 mL, 10 mmol) was deprotonated via method a. The yellowish powder that was obtained was dissolved in THF (20 mL). This solution was treated with iodine (2.8 g, 11 mmol) according to method b. The reaction mixture was stirred for 1 min at −78 °C before workup. A brown oil was obtained. Trituration with Et_iO gave [1,1′-bicyclobutyl]-1,1′-dicarboxylic acid (**10**) (185 mg, 16%) as a white solid, mp 168–170 °C: ^{1}H NMR (360 MHz, $CDCl_3$/DMSO-d_6) 1.62 (m, 2 H), 1.95 (m, 2 H), 2.15 (m, 8 H); ^{13}C NMR (90 MHz) 15.36 (t), 26.49 (t), 50.95 (s), 178.48 (s); high resolution MS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0657.

The filtrate was evaporated, yielding a brown oil. Recrystallization from Et_2O/pentane gave crystals of 1-iodocyclobutanecarboxylic acid (**11**) (1.62 g, 72%), mp 48–50 °C: ^{1}H NMR (360 MHz, $CDCl_3$) 1.95 (m, 1 H), 2.22 (m, 1 H), 2.63 (m, 2 H), 2.90 (m, 2 H), 9.3 (br, 1 H); ^{13}C NMR (90 MHz) 18.42 (t), 27.86 (t), 39.33 (s), 178.88 (s); high resolution MS calcd for $C_5H_7IO_2$ 225.9491, found 225.9484.

Reaction of Dilithiated Cyclobutanecarboxylic Acid with 1-Iodocyclobutanecarboxylate. A solution of dilithiated cyclobutanecarboxylic acid (5 mL, 2.5 mmol) in THF, prepared as above, was added at −78 °C to a solution of lithium 1-iodocyclobutanecarboxylate (2.5 mmol) in THF (10 mL), prepared by deprotonation of the free acid **11** at −78 °C with a 1 M LDA solution (2.5 mmol). After 2 min of stirring at −78 °C, the reaction mixture was quenched with acetic acid. Workup according to (b) gave the diacid **10** (<10% yield) beside starting materials **9** and **11**.

Electrolysis of Dilithiated Phenylacetic Acid (eq 3). Dilithiated phenylacetic acid was prepared by treatment of the acid **1** (272 mg, 2 mmol) in THF (8 mL) with *n*-butyllithium (2.33 mL, 4 mmol) at −78 °C. Electrolysis of this solution (8 mL, 1.5 mmol) was performed via method c (at E = 0.0 V, 132 C were consumed). The crude solid obtained was suspended in CH_2Cl_2/pentane (1:1). The insoluble part consisted of 2,3-diphenylsuccinic acid (**12**)[3a,25] (71 mg, 35%) as a *dl*/meso 10:3 mixture of diastereomers.[3a,25] The filtrate contained almost exclusively starting material **1**: ^{1}H NMR of **12**(*d,l*) (90 MHz, $CDCl_3$/DMSO-d_6) 4.22 (s, 2 H), 7.18 (m, 10 H), 10.0 (br, 2 H); **12**(meso) 4.35 (s, 2 H), 7.18 (m, 10 H), 10.0 (br, 2 H).

Electrolysis of Dilithiated Phenylacetic Acid in the Presence of Dilithiated Acetic Acid. A solution of dilithiated phenylacetic acid (1 mmol) and acetic acid (2 mmol) was electrolyzed via method c (0.0 V, 90 C were consumed). Workup gave 2,3-diphenylsuccinic acid (**12**) (40%) as a single dimer.

Electrolysis of Dilithiated 2-Phenylpropanoic Acid (eq 4). 2-Phenylpropanoic acid (**2**) (0.75 g, 5 mmol) was deprotonated via method a. The yellow solid dianion was dissolved in THF (27 mL). Electrolysis of this solution (8 mL, 1.5 mmol) was performed via method c (at E = −0.2 V, 118 C were consumed). The crude product was triturated with CH_2Cl_2/pentane (1:1). The insoluble part consisted of 2,3-dimethyl-2,3-diphenylsuccinic acid (**13**) (35 mg, 16%) as one single diastereomer, mp 216 °C subl lit.[3d] mp 178 °C): ^{1}H NMR (360 MHz, $CDCl_3$/DMSO-d_6) 1.67 (s, 6 H), 5.4 (br, water and COOH), 7.02 (m, 4 H), 7.23 (m, 6 H); ^{13}C NMR (90 MHz) 23.06 (q), 56.50 (s), 126.65 (d), 126.85 (d), 128.71 (d), 140.55 (s), 177.59 (s); high resolution MS calcd for $C_{18}H_{16}O_3$ ($M^+ - H_2O$) 280.1099, found 280.1102.

(25) Wren, H.; Still, C. J. *J. Chem. Soc.* **1915**, *107*, 444.

Concentration of the filtrate gave a viscous oil which was dissolved in methanol (2 mL) and esterified with diazomethane.[26] After evaporation of the solvent, the residue was chromatographed with pentane/Et_2O (9:1) to give methyl 2-phenyl-2-[4′-(methylcarbomethoxymethyl)phenyl]propanoate (**15**) (95 mg, 40%) as a colorless oil: ^{1}H NMR (360 MHz, $CDCl_3$) 1.49 (d, J = 7 Hz, 3 H), 1.91 (s, 3 H), 3.66 (s, 3 H), 3.69 (q, J = 7 Hz, 1 H), 3.72 (s, 3 H), 7.12–7.35 (m, 9 H); ^{13}C NMR (90 MHz) 18.47 (q), 27.07 (q), 45.01 (d), 51.85 (q), 52.29 (q), 56.38 (s), 126.78 (d), 127.14 (d), 127.95 (d), 128.05 (d), 128.27 (d), 138.99 (s), 143.27 (s), 144.41 (s), 174.82 (s), 175.45 (s); high resolution MS calcd for $C_{20}H_{22}O_4$ 326.1518, found 326.1528.

Reaction of Dilithiated 2-Phenylpropanoic Acid with Iodine (eq 4). The isolated dilithiated 2-phenylpropanoic acid **2** (4 mmol) prepared via method a was treated with iodine (504 mg, 2 mmol) via method b. The reaction mixture was allowed to warm up to room temperature before workup. The crude product was treated as in the preceding electrolysis, producing **13** (140 mg, 23%) and **15** (250 mg, 38%).

Electrolysis of Dilithiated Diphenylacetic Acid (eq 5). Diphenylacetic acid (1.06 g, 5 mmol) in THF (20 mL) was deprotonated at 0 °C with *n*-butyllithium (5.75 mL, 10 mmol). Electrolysis of this solution (8 mL, 1.5 mmol) was performed via method c (at E = −0.4 V, 128 C). The crude product (white solid) was chromatographed. Elution with CH_2Cl_2 and EtOAc gave benzophenone (40 mg, 4%) and (4′-(phenylcarboxymethyl)-phenyl]diphenylacetic acid (**17**) (227 mg, 72%) which was characterized after reaction with diazomethane[26] as its dimethyl ester **18**, mp 140–142 °C; ^{1}H NMR (360 MHz, $CDCl_3$) 3.72 (s, 3 H), 3.78 (s, 3 H), 5.01 (s, 1 H), 7.08–7.38 (m, 19 H); ^{13}C NMR (90 MHz) 52.21 (q), 52.54 (q), 56.70 (d), 67.30 (s), 126.94 (d), 127.33 (d), 127.72 (d), 127.87 (d), 128.61 (d), 128.71 (d), 130.25 (d), 130.56 (d), 137.29 (s), 138.51 (s), 141.86 (s), 149.89 (2 × d), 172.81 (s), 174.08 (s). (The first run also gave traces of tetraphenylsuccinic anhydride.)

Reaction of Dilithiated Diphenylacetic Acid with Iodine (eq 5). Diphenylacetic acid (**3**) (1.06 g, 5 mmol) in THF (20 mL) was deprotonated at 0 °C with *n*-butyllithium (5.75 mL, 10 mmol). This solution was treated with iodine (635 mg, 2.5 mmol) via method b. The reaction mixture was allowed to warm up to rt before workup. The crude product was treated as before, producing **17** (631 mg, 60%). Benzophenone (25 mg, 3%) was also isolated.

Reaction of Dilithiated Diphenylacetic Acid with Sodium Iodoacetate (eq 6). A solution of dilithiated **3** (18 mL, 3.5 mmol) prepared as previously described was added at −78 °C to a suspension of sodium iodoacetate (830 mg, 4 mmol) in THF (10 mL). The reaction mixture was allowed to warm up to room temperature overnight. The resulting white suspension was poured into 1 N HCl. Extraction with EtOAc, drying, and evaporation of solvent gave 2,2-diphenylsuccinic acid (**19**) (850 mg, 89%) as a white solid, mp 173–175 °C: ^{1}H NMR (360 MHz, $CDCl_3$/DMSO-d_6) 3.40 (s, 2 H), 4.50 (br, 2 H), 7.05–7.30 (m, 10 H); high resolution MS calcd for $C_{16}H_{12}O_3$ ($M^+ - H_2O$) 252.0786, found 252.0783.

Reaction of Dilithiated 6-Heptenoic Acid with Iodine (eq 7). 6-Heptenoic acid (0.68 mL, 5 mmol) was deprotonated via method a. The white powder obtained after evaporation of the solvent was dissolved in THF (20 mL) and treated with iodine (1.27 g, 5 mmol) via method b (15 min of stirring at −78 °C before workup). Upon trituration with CH_2Cl_2/pentane, the crude product gave 2,3-di-4′-pentenylsuccinic acid (**22**) (80 mg, 12%) as a white insoluble powder (mixture of diastereomers), mp 130–131 °C: ^{1}H NMR (300 MHz, $CDCl_3$/DMSO-d_6) 1.10–1.35 (m, 4 H), 1.80 (m, 2 H), 2.13–2.24 (m, 1 H), 4.75 (m, 2 H), 5.60 (m, 1 H), 11.4 (br, 1 H); ^{13}C NMR (75 MHz, minor diastereomer in parentheses) 26.09 (25.69), 29.76 (27.78), 32.92 (32.97), 47.70 (45.92), 114.08 (114.18), 137.85, 137.81, 175.84 (176.21); high resolution MS calcd for $C_{14}H_{20}O_3$ ($M^+ - H_2O$) 236.1412, found 236.1421.

Evaporation of the filtrate gave 2-iodo-6-heptenoic acid (**21**) (892 mg, 70%) as a white solid: ^{1}H NMR ($CDCl_3$) 1.30–2.15 (m, 6 H), 4.32 (t, J = 9 Hz, 1 H), 4.90–5.10 (m, 2 H), 5.70–5.90 (m, 1 H), 11.2–11.6 (br, 1 H); ^{13}C NMR 19.80, 28.41, 32.62, 35.05,

(26) DeBoer, T. J.; Baker, H. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. 4, p 250.

115.37, 137.47, 177.76; high resolution MS calcd for $C_7H_{11}IO_2$ 253.9803, found 253.9799.

Preparation of 2-Phenyl-6-heptenoic Acid (23). 5-Bromo-1-pentene (3 mL, 25 mmol) was added at −78 °C to a solution of dilithiated phenylacetic acid (20 mmol) in 30 mL of THF prepared as previously described (eq 3). The reaction mixture was stirred for 2 h at room temperature. The usual workup and chromatography with Et_2O/pentane (1:1) gave **23** (3.88 g, 95%) as a colorless liquid: high resolution MS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1152.

Oxidation of Dilithiated 2-Phenyl-6-heptenoic Acid (eq 8). 2-Phenyl-6-heptenoic acid (**23**) (1.02 g, 5 mmol) was deprotonated via method a and the solid dianion was dissolved in THF (25 mL).

Electrolysis. The dianion solution (8 mL, 1.6 mmol) was electrolyzed via method c (0.0 V, 131 C were consumed). Chromatography of the crude product with Et_2O/pentane (1:1) gave 2,3-diphenyl-2,3-di-4′-pentenylsuccinic anhydride (**24**) (25 mg, 8%) as a colorless liquid: ^1H NMR (360 MHz, $CDCl_3$, mixture of diastereomers) 1.00–2.35 (m, 12 H), 4.80 and 5.00 (m, 4 H), 5.50 and 5.72 (m, 2 H), 6.62–7.39 (m, 10 H); ^{13}C NMR (90 MHz) 23.37 (t), 23.95 (t), 31.84 (t), 33.31 (t), 33.85 (t), 37.84 (t), 62.34 (s), 64.45 (s), 115.32 (t), 115.38 (t), 127.72 (d), 128.03 (d), 128.17 (d), 128.29 (d), 128.87 (2 × d), 132.57 (s), 134.64 (s), 137.21 (d), 137.62 (d), 171.71 (s), 172.36 (s); high resolution MS calcd for $C_{26}H_{28}O_3$ 388.2038, found 388.2020.

The residue of the chromatography was eluted with Et_2O and esterified with diazomethane.[26] Chromatography (Et_2O/pentane, 1:25 to 1:9) gave **26** (112 mg, 32%) as a colorless viscous oil: ^1H NMR (360 MHz, $CDCl_3$) 1.09–1.45 (m, 4 H), 1.77–2.33 (m, 8 H), 3.53 (t, J = 8 Hz, 1 H), 3.68 (2 × s, 6 H), 4.85–5.02 (m, 4 H), 5.73 (m, 2 H), 7.10–7.35 (m, 9 H); ^{13}C NMR (90 MHz) 24.53 (t), 26.91 (t), 33.03 (t), 33.36 (t), 33.98 (t), 37.67 (t), 51.12 (d), 51.81 (q), 52.16 (q), 60.16 (s), 114.62 (t), 114.72 (t), 126.67 (d), 127.31 (d), 127.81 (d), 128.80 (d), 129.08 (d), 137.54 (s), 138.23 (d), 138.37 (d), 141.80 (s), 142.93 (s), 174.36 (s, 174.72 (s); high resolution MS calcd for $C_{28}H_{34}O_4$ 434.2457, found 434.2444.

With Iodine. The solution of the dianion (12 mL, 2.4 mmol) was treated with iodine (305 mg, 1.2 mmol) via method b. The reaction mixture was allowed to warm up to room temperature overnight. Purification of the crude product as described in the previous electrolysis experiment gave **24** (120 mg, 26%) and **26** (195 mg, 36%).

Preparation of Cyclopropylacetic Acid (27). Vinylacetic acid (4.25 mL, 50 mmol) was added at 0 °C to a 1.5 M solution of Et_3Zn in toluene (60 mL, 96 mmol), before CH_2I_2 (6 mL, 75 mmol) was added dropwise. The reaction mixture was stirred at room temperature overnight and poured into 1 N HCl. Extraction with Et_2O, drying (Na_2SO_4), and evaporation of the solent gave crude **27**. Distillation gave pure **27** (3.78 g, 75%), bp 92–96 °C/15 mmHg (lit.[27] bp 90 °C/15 mmHg): ^1H NMR (90 MHz, $CDCl_3$) 0.20 (m, 2 H), 0.60 (m, 2 H), 1.10 (m, 1 H), 2.30 (d, J = 6 Hz, 2 H), 11.0 (br, 1 H).

Reaction of Dilithiated Cyclopropylacetic Acid (eq 9). Cyclopropylacetic acid (0.30 g, 3 mmol) was deprotonated via method a. The dianion (white powder) was dissolved in THF (10 mL) and treated at −78 °C with iodine (761 mg, 3mmol) via method b. The reaction mixture was stirred for 15 min at −78 °C before workup. Careful chromatography of the crude material (Et_2O/pentane 1:1.5) gave 2-iodocyclopropylacetic acid (**28**) (223 mg, 33%), mp 56–60 °C: ^1H NMR (90 MHz) 0.50–1.30 (m, 4 H), 1.60 (m, 1 H), 3.70 (d, J = 10 Hz, 1 H), 9.80 (br); high resolution MS calcd for $C_5H_7IO_2$ 225.9490, found 225.9485.

5-Iodo-2-pentenoic acid (**29**) (37 mg, 5%) was isolated as a white solid, mp 123–125 °C after recrystallization from Et_2O/pentane: ^1H NMR (360 MHz, $CDCl_3$) 2.835 (dt, J = 1.2 and 7.0 Hz, 2 H), 3.223 (t, J = 7.0, 2 H), 5.91 (dt, J = 1.2 and 15.6 Hz, 1 H), 6.967 (dt, J = 15.6 and 6.9 Hz), 9.0 (br, 1 H) [The trans configuration was assigned from the coupling constant (J = 15.6 Hz) of the olefinic protons.]; high resolution MS calcd for $C_5H_7IO_2$ 225.9490, found 225.9493.

2,3-Dicyclopropylsuccinic acid (**30**) (41 mg, 14%) as a white solid, mp 190–192 °C subl: ^1H NMR (360 MHz, $CDCl_3$/DMSO-d_8) 0.05–0.32 (m, 8 H), 0.75 (m, 2 H), 1.725 (m, 2 H); ^{13}C NMR (90 MHz) 4.64 (t), 11.83 (d), 52.90 (d), 176.03 (s); high resolution MS calcd for $C_{10}H_{12}O_3$ ($M^+ - H_2O$) 180.0786, found 180.0780.

The same reaction was also run at −100 °C and −20 °C. No significant change of the product distribution was observed in the crude NMR spectrum. The reaction was also run under exactly the same conditions (−78 °C to room temperature) with 0.5 equiv of iodine (380 mg, 1.5 mmol). Examination of the crude ^1H NMR spectrum showed the presence of starting material **27** (~30%) together with **30** (~50%, 3:1 mixture of diastereomers).

trans-Pentadienoic acid (**31**) (~10%) was isolated by chromatography (Et_2O/pentane), mp 70–72 °C (lit.[28] trans 72 °C; cis 41 °C): ^1H NMR (360 MHz, $CDCl_3$) 5.56 (d, J = 9.2 Hz, 1 H), 5.67 (d, J = 16.5 Hz, 1 H), 5.93 (d, J = 14.7 Hz, 1 H), 6.49 (dt, J = 16.5 and 10.2 Hz, 1 H), 7.35 (dd, J = 11.0 and 14.7 Hz, 2 H), 10.0 (br, 1 H).

Preparation of *cis*-Bicyclo[4.1.0]heptane-2-carboxylic Acid (32, eq 10). A solution of 1 M DiBAH (in CH_2Cl_2) (70 mL) was added dropwise at 0 °C to a solution of 2-cyclohexenone (4.8 mL, 50 mmol) in Et_2O (100 mL). The mixture was stirred for 1 h at 0 °C, poured into 1 N HCl, and extracted with Et_2O. Distillation of the crude product gave pure 2-cyclohexenol (4.20 g, 85%), bp 85 °C/15 mmHg. 2-Cyclohexenol (2.4 g, 25 mmol) was added to thionyl chloride (2.0 mL, 2.8 mmol) in Et_2O (30 mL). The reaction mixture was stirred for 2 h at room temperature and the solvent was removed under vacuum. Distillation of the residue gave 3-chloro-1-cyclohexene (2.14 g, 73%), bp 58–60 °C/15 mmHg. 3-Chloro-1-cyclohexene in THF (5 mL) was added slowly at −10 °C to Mg turnings in THF (10 mL). The reaction mixture was stirred overnight at room temperature. The solution was cooled to −60 °C; solid CO_2 (excess) was added and the resulting solution was allowed to warm to room temperature before being poured into 1 N KOH. The aqueous phase was washed with Et_2O, acidified with 1 N HCl, and extracted with CH_2Cl_2. Evaporated of the solvent gave 2-cyclohexene-1-carboxylic acid (0.76 g, 32%) as a colorless liquid. The acid (407 mg, 3.23 mmol) in benzene (5 mL) was added to a 1.6 M solution of Et_2Zn in toluene (4 mL, 6.4 mmol) at 0 °C followed by the addition of CH_2I_2 (0.64 mL, 8 mmol). The solution was stirred at room temperature overnight as a white precipitate appeared. The reaction mixture was poured into 1 N HCl and extracted with Et_2O (3×). The organic phase was extracted with 1 N KOH. The aqueous phase was then acidified with 1 N HCl and extracted with dichloromethane. Evaporation of the solvent gave **32** (380 mg, 84%) as a white solid; only one diastereomer was detectable by ^1H NMR, mp 50–52 °C: ^1H NMR (360 MHz, $CDCl_3$) 0.22 (q, J = 5.5 Hz, 1 H, H-C(7), endo), 0.62 (dt, J = 4.7 and 9.4 Hz, 1 H, H-C(7), exo), 1.02 (m, 1 H), 1.10–1.95 (m, 7 H), 2.90 (dt, J = 9.4 and 5.0 Hz, 1 H), 11.5 (br, 1 H); high resolution MS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0834.

Epimerization (eq 11). The acid **32** (1 mmol) was deprotonated via method a. Quenching of the dianion with 1 N HCl at −78 °C gave after the usual workup **32**/**32′** as a 1:1 mixture. ^1H NMR of **32′**: (500 MHz, $CDCl_3$) 2.60 (dd, 1 H, H-C(2)), 0.67 (dt, 1 H, H-C(7), exo), 0.06 (q, H-C(7), endo).

Differential NOE Spectra. Compound **32**: No positive signal for H-C(7) (0.20 and 0.67 ppm) was observed when H-C(2) (2.88 ppm) was irradiated. Compound **32′**: A strong positive signal was observed for H-C(7) endo (0.06 ppm) when H-C(2) (2.60 ppm) was irradiated.

Reaction of Dilithiated *cis*-Bicyclo[4.1.0]heptane-2-carboxylic Acid with Iodine (eq 12). The acid **32** (140 mg, 1.2 mmol) was deprotonated via method a. The yellowish dianion powder was dissolved in THF (5 mL) and treated with iodine 340 mg, 1.3 mmol) via method b. The reaction mixture was stirred for 15 min at −78 °C before workup. The crude product was esterified with diaomethane[26] and chromatographed (Et_2O/pentane, 1:10) to give methyl 3-(iodomethyl)-1-cyclohexene-1-carboxylate (**33**) (180 mg, 74%) as a colorless liquid: ^1H NMR (360 MHz, $CDCl_3$) 1.32–1.43 (m, 1 H), 1.50–1.63 (m, 1 H), 1.77–1.95 (m, 2 H), 2.07–2.20 (m, 1 H), 2.28–2.37 (m, 1 H), 2.53 (m, 1 H), 3.20 (m, 2 H), 3.75 (s, 3 H), 6.81 (s, 1 H); ^{13}C NMR ($CDCl_3$) 11.39, 20.74, 24.40, 28.74, 38.05, 51.71, 131.96, 140.49, 167.63; high resolution MS calcd for $C_9H_{13}IO_2$ 279.9960, found 279.9955.

Alkylation of Dilithiated Cyclopropylacetic Acid (eq 13). Cyclopropylacetic acid (300 mg, 3 mmol) was deprotonated via method a. The dianion was not isolated, but the resulting solution

(27) Turnbull, J. H.; Wallis, E. S. *J. Org. Chem.* **1956**, *21*, 663.

(28) Kirmse, W.; Lechte, H. *Liebigs Ann. Chem.* **1970**, *739*, 235.

was added at −78 °C to a solution of sodium iodoacetate (624 mg, 3 mmol) in THF (10 mL). Workup by method b gave 2-cyclopropylsuccinic acid (**36**) (440 mg, 93%) as a white solid, mp 135–137 °C. No olefinic protons were detected in the crude ^{1}H NMR spectrum. ^{1}H NMR (360 MHz, $CDCl_3$/DMSO-d_6): −0.02 (m, 1 H), 0.22 (m, 1 H), 0.30 (m, 2 H), 0.70 (m, 1 H), 1.80 (dt, J = 5.0 and 10.0 Hz, 1 H), 2.29 (dd, J = 5.0 and 16.3 Hz, 1 H), 2.57 (dd, J = 10.0 and 16.3 Hz, 1 H), 8.0 (br). High resolution MS calcd for $C_7H_8O_3$ ($M^+ - H_2O$), 140.0473; found, 140.0472.

The reaction was repeated with lithium 1-iodocyclobutanecarboxylic acid (prepared in situ by treatment of the free acid with 1 equiv LDA at −78 °C). No ring-opened product could be detected in the ^{1}H NMR spectrum of the crude product.

Electrolysis of Dilithiated Phenylacetic Acid in the Presence of Diisopropylamine. The electrolyses were carried out exactly as described previously (eq 3). Before the electrolysis, diisopropylamine (1 to 5 equiv) was added to the anodic compartment. The composition of the crude product was determined by ^{1}H NMR. Dimer **12** was formed in 30 to 40% yield, irrespective of the amount of amine present.

Reaction of Dilithiated Phenylacetic Acid Generated with LiHMDS with Iodine. Phenylacetic acid (4 mmol, 545 mg) in THF (3 mL) was added at 0 °C to a solution of lithium hexamethyldisilazide [prepared at 0 °C from 1,1,1,3,3,3-hexamethyldisilazane (8 mmol) and butyllithium (8 mmol) in THF (16 mL)]. After 2 h of stirring at room temperature, the clear yellow solution was treated with iodine (508 mg, 2 mmol) by method b. The mixture was allowed to warm up to room temperature overnight before workup. The crude product consisted only of the dimer **12**; less than 2% of phenylacetic acid could be detected in the ^{1}H NMR spectrum of the crude product.

Acknowledgment. We are grateful to the National Science Foundation and to the Robert A. Welch Foundation for support of this work.

Meerwein–Ponndorf–Verley-Type Reduction of Dicarbonyl Compounds to Hydroxy Carbonyl Compounds and α,β-Unsaturated Carbonyl Compounds to Allylic Alcohols Catalyzed by Zirconocene and Hafnocene Complexes

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Received January 6, 1988

Group IVA metallocene complexes such as bis(η^5-cyclopentadienyl)zirconium dihydrides, Cp_2ZrH_2 (**1**), and hafnium dihydrides, Cp_2HfH_2 (**8**), catalyze the chemoselective reduction of polycarbonyl compounds to hydroxy carbonyl compounds. For instance, the reduction of keto aldehydes 3-ketobutanal (**2g**) and 2-phenyl-2-ketoethanal (**2h**) proceeded selectively at aldehyde group to provide the corresponding hydroxy ketones **3g** and **3h** in 91% and 93% yields, respectively. Under similar conditions, however, cyclohexanediones were easily aromatized to benzenediols. On the other hand, **1** and **8** also catalyze the selective 1,2-reduction of various types of α,β-unsaturated carbonyl compounds, giving the corresponding allylic alcohols in good to excellent yields. Thus, steroidal dicarbonyl compounds, having an enone framework in their molecules Δ^4-androstene-3,17-dione (**11a**) and Δ^4-progestene-3,20-dione (**11b**) were reduced by **1** to 17-hydroxy-Δ^4-androsten-3-one (**12a**) and 20-hydroxy-Δ^4-progest-3-one (**12b**), which are essential human hormones, in 80% and 67% yields, respectively.

Recently we reported that bis(η^5-cyclopentadienyl)zirconium dihydride, Cp_2ZrH_2 (**1**), catalyzed the hydrogen-transfer reaction of alcohols to carbonyl compounds.[1-4] Thus, the Meerwein–Ponndorf–Verley-type (MPV-type) reduction of carbonyl compounds and the Oppenauer-type (OPP-type) oxidation of alcohols proceed simultaneously under the influence of catalytic amount of **1**. Simple carbonyl compounds can be readily reduced by **1** in 2-propanol to give the corresponding alcohols in good yields.[1] In the above reduction, the ease with which zirconocene catalyzed MPV-type reduction occurred decreased in the order aldehydes > aromatic > alicyclic > aliphatic ketones. Therefore, in the reduction of compounds containing multiple carbonyl groups, a particular carbonyl group will be expected to be reduced preferentially by this method.

Hydroxy carbonyl derivatives derived from the reduction of dicarbonyl compounds are often used as valuable precursors in synthetic organic chemistry.[5,6] Usually the selective reduction of dicarbonyl compounds to hydroxy carbonyl compounds has been achieved by using special reducing agents.[7] Therefore, the preferential reduction to hydroxy carbonyl compounds of dicarbonyl compounds **2** and **4** catalyzed by zirconocene complexes offer an attractive route to the valuable products **3** and **5** (eq 1 and 2).

Table I. Reduction of 3-Ketobutanal (2g) in 2-Propanol Catalyzed by Some Group IVA Metallocene Complexes[a]

run	catalyst	**3g**, %[b]	others, %[c]
1	Cp_2ZrH_2	94 (56)	trace
2	Cp_2HfH_2	91 (95)	trace
3	Cp_2TiCl_2	11 (7)	38
4	Cp_2ZrCl_2	43 (32)	26
5	Cp_2HfCl_2	92 (90)	4
6	$Cp_2Ti(O\text{-}i\text{-}Pr)_2$	42 (26)	25
7	$Cp_2Zr(O\text{-}i\text{-}Pr)_2$	94 (95)	trace
8	$Cp_2Hf(O\text{-}i\text{-}Pr)_2$	93 (84)	trace

[a] A mixture of **2i** (10 mmol) and 2-propanol (50 mL) was allowed to react in the presence of catalyst (0.2 mmol) at 130 °C for 8 h. [b] Determined by VPC. Parentheses indicate the yield at 80 °C. [c] Condensation products were included.

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(1) Ishii, Y.; Nakano, T.; Inada, A.; Kishigami, Y.; Sakurai, K.; Ogawa, M. *J. Org. Chem.* **1986**, *51*, 240.
(2) Nakano, T.; Terada, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1986**, 774.
(3) Nakano, T.; Ando, J.; Ishii, Y.; Ogawa, M. *Tech. Rep. Kansai Univ.* **1987**, *29*, 69.
(4) Chemoselective oxidation of allylic alcohols by Cp_2ZrH_2: Nakano, T.; Ishii, Y.; Ogawa, M. *J. Org. Chem.* **1987**, *52*, 4855.
(5) Weinshenker, N. M.; Crosby, G. A.; Wong, J. Y. *J. Org. Chem.* **1975**, *40*, 1966.

0022-3263/88/1953-3752$01.50/0