2-methyltetrahydrofuran and placed in a 4-mm quartz tube. The solution was then degassed, sealed, and kept under liquid nitrogen.

Acknowledgment. The authors wish to thank Drs. V. P. Senthilnathan and B. B. Wright for technical assistance with the Curie Law measurements.

Registry No. **1a**, 62617-73-6; **1b**, 91424-03-2; **1c**, 91424-04-3; **1d**, 91424-05-4; **1e**, 91424-06-5; **1f**, 91424-07-6; **6**, 1729-99-3; **7**, 19310-98-6; **8b**, 91424-13-4; **8c**, 91424-08-7; **8d**, 91424-19-0; **9b**, 91424-14-5; **9c**, 91424-09-8; **9d**, 91424-20-3; **10b**, 91424-15-6; **10b** (tosylhydrazone), 91424-16-7; **10c**, 91424-10-1; **10c** (tosylhydrazone), 91424-11-2; **10d**, 91424-21-4; **10d** (tosylhydrazone), 91424-22-5; **11b**, 91424-17-8; **11c**, 91424-12-3; **11d**, 91424-23-6; **12**, 91424-25-8; **13**, 91424-26-9; **14**, 91424-27-0; **15**, 91424-28-1; **15** (tosylhydrazone), 91424-29-2; **16**, 91424-30-5; **17**, 91424-31-6; **18**, 91424-32-7; **18** (tosylhydrazone), 91424-33-8; **19**, 91424-34-9; 5-(iodomercurio)-8-methyl-1-naphthoic acid, 91424-18-9; 5-bromo-8-methyl-1-naphthoyl chloride, 91424-24-7; cuprous phenymercaptide, 1192-40-1.

On the Conjugative Isomerizations of β,γ-Unsaturated Esters. Stereochemical Generalizations and Predictions for 1,3-Prototropic Shifts under Basic Conditions

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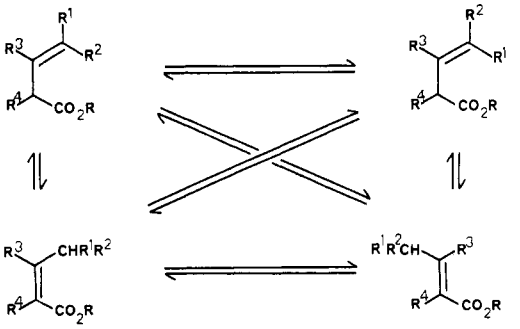
An investigation of the base-catalyzed conjugative isomerization of a series of β,γ-unsaturated esters to their corresponding α,β-unsaturated esters was performed. It was found that, with sodium hydride in THF, methyl 3-butenoate isomerized initially to a 5:1 ratio of (*Z*)- to (*E*)-methyl 2-butenoates; the *Z*:*E* ratio is time dependent, and after several days, the thermodynamic ratio 1:23 = *Z*:*E* was obtained. The isomerization appears to be catalytic in NaH, as it proceeds with less than 1 molar equiv of base, no hydrogen evolution is observed, and the reaction rate is approximately first order in NaH and zero order in ester. Under the same conditions (*Z*)-methyl 3-hexenoate isomerized stereoselectively to (*E*)-methyl 2-hexenoate while (*E*)-methyl 3-hexenoate isomerized to a 2:1 mixture of (*Z*)- and (*E*)-methyl 2-hexenoates. These product ratios are far from the isomeric compositions obtained under equilibrating conditions. To investigate further the stereochemical outcome of these isomerizations, three isomeric β,γ-unsaturated methyl esters were studied: (a) methyl 3-ethyl-3-butenoate isomerized exclusively to (*E*)-methyl 3-methyl-2-pentenoate; (b) (*E*)-methyl 3-methyl-3-pentenoate isomerzied exclusively to (*Z*)-methyl 3-methyl-2-pentenoate; (c) (*Z*)-methyl 3-methyl-3-pentenoate isomerized exclusively to (*E*)-methyl 3-methyl-2-pentenoate. In the latter three cases, dimerization was not observed presumably due to steric effects. Related results were observed for a smaller series of β,γ-unsaturated amide isomerizations. Examination of the literature on olefin isomerizations reveals a general trend that the current results exemplify. Thus, in the absence of severe steric factors or cation–anion complexation, deprotonation at allylic positions kinetically preferentially forms the anion possessing a cisoid crotyl subunit (if available) regardless of initial substrate conformation. The stereochemical consequences of this results in $E \rightarrow Z$ and $Z \rightarrow E$ geometry conversions in kinetic 1,2-transpositions of olefins. This generalization can also be applied to the stereochemical results of ketone, ester, and hydrazone enolate formation, base-catalyzed exchange in polysubstituted aromatics and heteroaromatics, and other reactions involving the formation of allylic or benzylic anions.

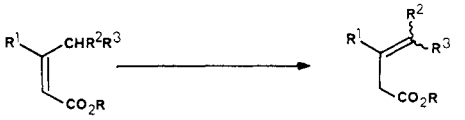
α,β- and β,γ-unsaturated esters play important roles in organic chemistry. The reactivity of these groups to both nucleophiles and electrophiles under a variety of reaction conditions has made them ideal precursors in many organic chemical syntheses, and numerous natural products possess these structural subunits.

While it is well-known that α,β- and β,γ-unsaturated esters can readily isomerize to each other under a variety of conditions,[1-3] there are significant gaps in our full understanding of the mechanistic basis of these reactions and also in our ability to control the course of the isomerizations. Most of the studies published to date,[2-4] and certainly the bulk of the early investigations,[1] deal with the *thermodynamic* equilibrium of these unsaturated esters

Scheme I



Scheme II



(1) (a) Pines, H.; Stalick, W. M. "Base Catalyzed Reactions of Hydrocarbons and Related Compounds"; Academic Press: New York; 1977. (b) Pines, H. "Chemistry of Catalytic Hydrocarbon Conversions"; Academic Press: London; 1981. (c) Yanovksaya, L. A.; Shakhidayatov, K. *Russ. Chem. Rev. (Engl. Transl.)* **1970**, *39*, 859.

(2) For leading references, see: (a) Rhoads, S. J.; Chattopadhyay, J. K.; Waali, E. E. *J. Org. Chem.* **1970**, *35*, 3352. (b) Hine, J.; Kanagasabapathy, V. M.; Ng, P. *J. Org. Chem.* **1982**, *47*, 2745. (c) Hine, J.; Flachskam, N. W. *J. Am. Chem. Soc.* **1973**, *95*, 1179.

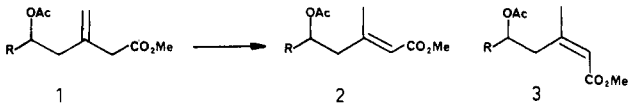
(3) Sakai, M.; Nishikawa, S.; Koike, H.; Sakakibara, Y.; Uchino, N. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2970. Sakai, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1232. For thermal isomerization, see: McGreer, D. E.; Chiu, N. W. K. *Can. J. Chem.* **1968**, *46*, 2225. For photochemical isomerizations, see: Skinner, I. A.; Weedon, A. C. *Tetrahedron Lett.* **1983**, 4299. Lewis, F. D.; Oxman, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 7345.

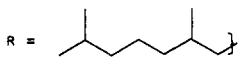
(4) Rathke, M. W.; Sullivan, D. *Tetrahedron Lett.* **1972**, 4249.

0022-3263/85/1950-3526$01.50/0

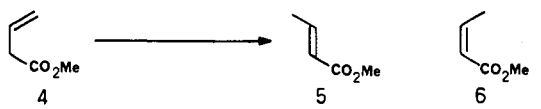
Scheme III

Scheme IV





Scheme V



(Scheme I). Since the pioneering studies of Rathke[4] and Schlessinger,[5] the regiochemistry and (less frequently) stereochemistry of deprotonation followed by kinetic protonation,[6] alkylation,[7] and acylation[8] of α,β-unsaturated esters to the β,γ-counterparts have been widely studied (Scheme II). To date, very little is known regarding kinetic *conjugative* isomerizations of β,γ-unsaturated esters to α,β-unsaturated esters (Scheme III).

In this paper, we will present our recent experimental results and mechanistic arguments with the aim of filling some of this void. The stereochemical consequences of this conjugative isomerization will then be discussed and related isomerization of β,γ-unsaturated amides will be considered. Evidence for the reaction process under study being a catalytic, surface phenomenon will be presented also. Finally, we will propose a unified generalization for the stereochemistry of the isomerization of substituted olefins under kinetic, anionic conditions.

Results

Kinetic deconjugation of α,β-unsaturated esters to their β,γ-unsaturated counterparts involves the formation of a molar equivalent of an enolate anion which is subsequently quenched to the corresponding β,γ-unsaturated ester.[4-8] The inverse, kinetic conjugative process also formally involves an anionic intermediate. For both of these counterpart isomerizations to be experimentally attainable they must pass through different reaction surfaces. Only then can directional differentiation be obtained.

Our survey of the available literature suggested one reaction system for consideration as a candidate for a kinetic conjugative process. Cardillo[9] had previously reported the stereochemical consequences of conjugation of

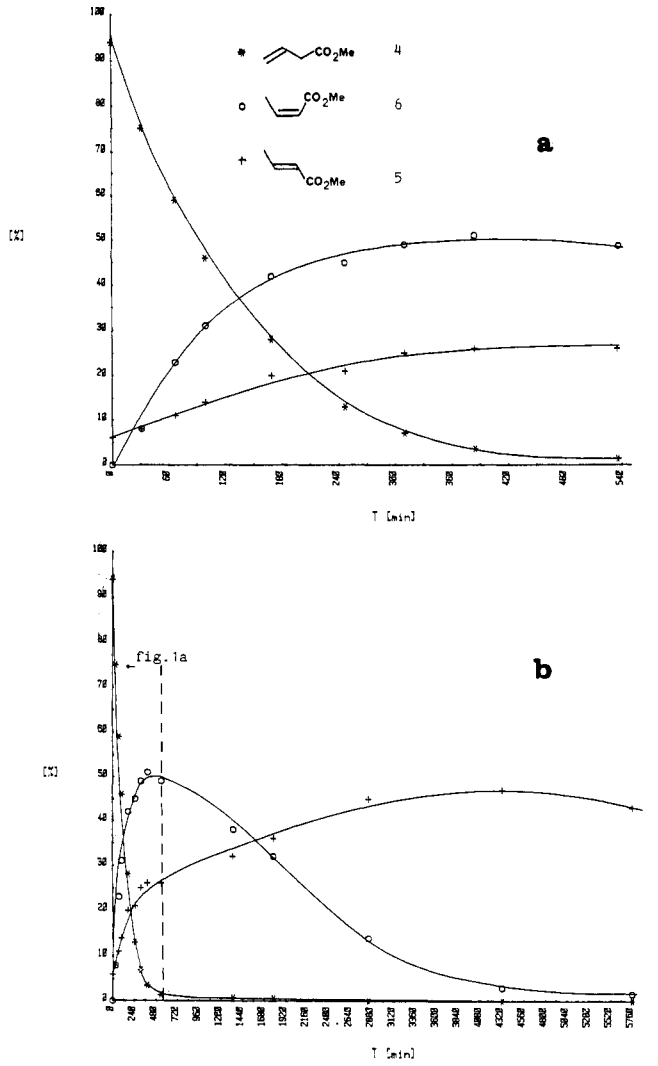


Figure 1. Comparative rates of formation of **4**, **5**, and **6**. Experimentally obtained equilibrium ratios for this system (K = [5]/[6]) are as follows K(200–500 °C; gas phase) = 4.5, K(195 °C; liquid phase) = 7.0; K(117 °C; NaOMe, HMPA) = 6.3, K(77 °C; NBS, CCl_4) = 10.[2a] Extrapolation of these values to 20 °C leads to an equilibrium distribution of K = 10–30.

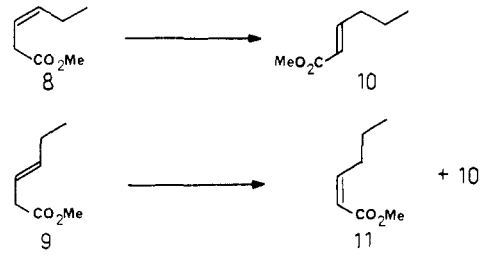
the 3-methylene ester **1** with a range of bases (Scheme IV). While most reagents led to mixtures of *E* and *Z* α,β-unsaturated products **2** and **3**, respectively, sodium hydride was unique in promoting stereoselective rearrangements to the *E* α,β-unsaturated ester **2**.[10] It must be stressed that while the *E* product would be expected to predominate in any thermodynamically controlled conjugation,[1] its sole formation is indicative of the absence of rapid equilibration among **1–3**. The most obvious feature of the sodium hydride system (Scheme III) which distinguishes it from the other bases used for conjugation or deconjugation (Scheme II) is its heterogeneity. We anticipated that with this reagent, there was reason to propose the formation of an anionic intermediate different from that existing in the cases of deconjugation.

In order to test the validity of our assumptions, it was decided to investigate the effects of sodium hydride on the conversion of methyl 3-butenoate to (*E*)- or (*Z*)-methyl 2-butenoates (Scheme V).

Evidence both theoretical and experimental, exists which indicates that the cisoid crotyl anion system is more stable than the transoid arrangement.[11] This has been proposed

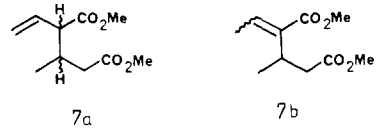
(5) Herrmann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433.
(6) Harris, F. L.; Weiler, L. *Tetrahedron Lett.* **1984**, 1333.
(7) Koyama, H.; Kogure, K.; Mori, K.; Matsui, M. *Agric. Biol. Chem.* **1972**, *36*, 793. Zimmerman, M. P. *Synth. Commun.* **1977**, *7*, 189. Kende, A. S.; Constantinides, D.; Lee, S. J.; Liebeskind, L. *Tetrahedron Lett.* **1975**, 405. Ortiz de Montellano, P. R.; Hsu, C. K. *Tetrahedron Lett.* **1976**, 4215. Katzenellenbogen, J. A.; Crumrine, A. L. *J. Am. Chem. Soc.* **1974**, *96*, 5662. For reactivity of γ,δ-unsaturated β-oxo esters via their dianions, see: van den Goorgergh, J. A. M.; van der Gen, A. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 393 and references cited therein.
(8) Kajikawa, A.; Morisaki, M.; Ikekawa, N. *Tetrahedron Lett.* **1975**, 4135. While acylation frequently occurs at the γ-position, see the work of Hudlicky for α-reactivity in the Reformatsky reaction: Short, R. P.; Revol, J.-M.; Ranu, B. C.; Hudlicky, T. *J. Org. Chem.* **1983**, *48*, 4453.
(9) Cardillo, G.; Contento, M.; Sandri, S.; Panunzio, M. *J. Chem. Soc., Perkin Trans 1*, **1979**, 1729.
(10) Mialhe, Y.; Vessiere, R. *Bull. Chim. Soc. Fr.* **1968**, 4181.

Scheme VI



to be due to hyperconjugative involvement of the *Z* substituent to form a six-electron cyclic delocalized system, although this electronic effect may in some cases be overwhelmed by secondary steric factors.[12] The 3-butenoate system was chosen so that, in initial studies, these additional steric effects would be absent.

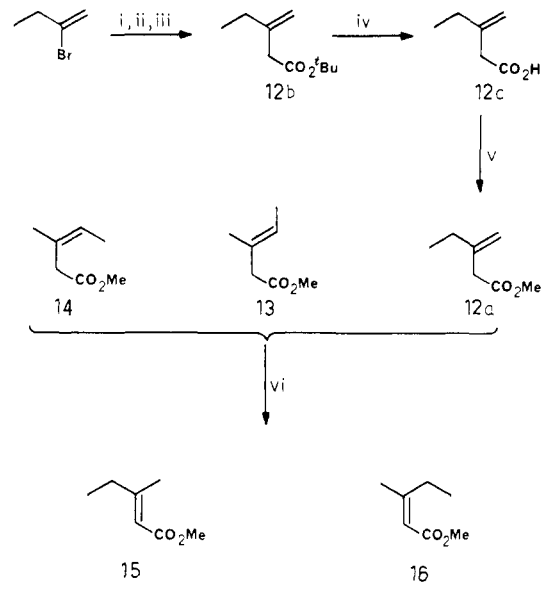
The reaction of methyl 3-butenoate **4** with sodium hydride could be followed conveniently by capillary GC analysis of aliquots of the reaction mixture. In the early stages of reaction the *Z*-isomer **6** was formed at roughly 5 times the rate of the *E* isomer (Figure 1a). After this time the *E* isomer continued to increase at the expense of the *Z* isomer to give a final product mixture ratio of 23:1 (*E*)-5-(*Z*)-6 after several days (Figure 1b). The time dependence of the product ratios indicated that the system was not operating under purely kinetic conditions and that significant conclusions regarding the stereochemistry of the kinetic rearrangement could be drawn only from the early stages of reaction. During the course of reaction, substantial material loss occurred which was found to be due to saponification of the esters and dimer **7a,b** formation, the latter process being more important.



Several pertinent features of the reaction should be stressed. It was found that the *E*:*Z* ratio of products at a given conversion was largely independent of the quantity of sodium hydride used (0.3–10.0 equiv), but the reaction rate was found to be close to first order in concentration in NaH and zero order in ester **4** concentration. No hydrogen evolution could be observed during the course of the reaction, and direct analysis of the clear supernatant obtained after allowing the mixture to settle gave the same GC profiles as those obtained following aqueous quenching of the total mixture. The reaction also demonstrated an induction period that was critically dependent upon the means of preparation of the sodium hydride and varied from 15 min to 6 h. We interprete these observations as implying a surface reaction with sodium hydride playing a catalytic role. Such a mechanistic dichotomy might explain the different stereochemical outcome of reactions involving sodium hydride and the other homogeneous conjugative or deconjugative processes.

The observation of an initial, more rapid formation of the *Z*-conjugated ester in this case led us to address the question of stereochemical transfer using the (*Z*)- and

Scheme VII[a]



[a] Reagents: (i) $NiBr_2$ *n*-BuLi, THF, −78 °C; (ii) $LiCH_2CO_2$-*t*-Bu, −78 → 20 °C; (iii) H_3O^+; (iv) TFA, 1 h, 20 °C; (v) MeI, K_2CO_3, $Me_2C{=}O$, 18 h, 20 °C; (vi) NaH, Et_2O, 20 °C.

(*E*)-3-hexenoate esters **8** and **9** (Scheme VI). Esters **8** and **9** and other substrates to be discussed subsequently are important extensions of this work in that the β,γ-double bond possesses stereochemical features not present in the compounds studied by Cardillo[9] (e.g., **1**) or in **4**. As shown in Scheme VI, the starting ester possessing *Z* double bond configuration gave totally *E*-conjugated product **10** but the *E* β,γ-unsaturated ester gave a ratio of *E*:*Z* products of 7.0:3.8. The low stereoselectivity in the isomerization of *E* starting material, giving a rearranged product mixture in which the major constituent had retained initial double bond stereochemistry, has to be interpreted in the light of the much slower rate of isomerization of the *Z* isomer (20 h) compared with the *E* isomer (3 h) and with the subsequent increase in *Z* → *E* isomerization of the products. Indeed it should be noted that neither isomerization gives a product mixture that represents the equilibrium ratio of the (*E*)- and (*Z*)-2-hexenoate system (K[**10**]/[**11**] > 20 at 59 °C based on methyl pentenoate equilibrations[2b]). Additionally, the preponderance of dimerization with these substrates makes any rigorous stereochemical interpretation difficult.

In order to investigate the stereochemical course of such double bond transpositions and obtain unambiguous results it was thus necessary to design and examine substrates whose primary reaction products were less susceptible to further reaction, either isomerization or dimerization. To this end we chose to study the three isomeric β,γ-unsaturated esters **12a**, **13**, and **14** (Scheme VII) all of which on conjugation would lead to the same pair of α,β-unsaturated esters **15** and **16**. Ester **12a** was prepared via Rathke condensation[13] of *tert*-butyl α-lithioacetate with 2-bromo-1-butene followed by hydrolysis of the *tert*-butyl ester **12b** to the acid **12c** and methylation with MeI/K_2CO_3 in acetone (Scheme VII).

The literature methods were followed for the preparation of substrate esters **13** and **14**[14a] and the mixture of conju-

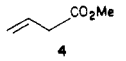
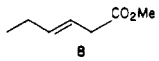
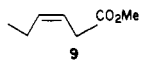
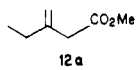
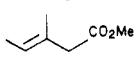
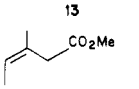
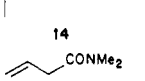
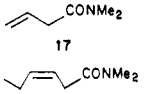
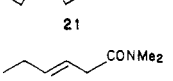
(11) (a) Houk, K. N.; Strozier, R. W.; Rondan, N. G.; Fraser, R. R.; Chauqui-Offermanns, N. *J. Am. Chem. Soc.* **1980**, *102*, 1426. (b) Hoffman, R.; Olofson, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 943. (c) Bartmess, J. E.; Hehre, W. J.; McIver, R. T.; Overman, L. E. *J. Am. Chem. Soc.* **1977**, *99*, 1976. (d) David, V.; Hartmann, J.; Schloser, M. *Helv. Chim. Acta* **1974**, *57*, 1567. (e) Hartmann, J.; Schlosser, M. *J. Am. Chem. Soc.* **1976**, *98*, 4674.

(12) Dill, J. D.; Hehre, W. J.; Pople, J. A.; Schleyer, P. v. R. *Tetrahedron* **1977**, *33*, 2497 and references cited therein.

(13) Millard, A. A.; Rathke, M. W. *J. Am. Chem. Soc.* **1977**, *99*, 4833.

(14) (a) Cornforth, D. A.; Opara, A. E.; Read, G. *J. Chem. Soc. C* **1969**, 2799. (b) Zimmerman, H. E.; Robbins, J. D.; McKelvey, R. D.; Samuel, C. J.; Sousa, L. R. *J. Am. Chem. Soc.* **1974**, *96*, 4630.

Table I. Summary of Kinetic Conjugative Experiments for Highest Yield of Monomeric Conjugated Products

β,γ-unsaturated substrate	equiv of NaH	reacn time for highest conversion to conjugated products, min	mixture composition, %			ratio E/Z
			starting material	E product	Z product	
 4	0.96	384		26	51	0.50
 8	1.80	1224	49	4	7	0.57
 9	1.90	225	21	7		a
 12a	10.00	960		70[b]		a
 13	5.00[c]	1200	38	9	30	0.30
 14	5.00[c]	1080	28	41	5	8.20
 17	0.89[c]	10	15[d]	6	24	0.25
 21	6.60	160	55	40		a
 23	5.5	1070	43	4	6	0.66

[a] Only one conjugated isomer detected. [b] Isolated yield. [c] THF used as solvent. [d] Yields estimated by NMR due to inability to separate starting material from Z-conjugated product by GC.

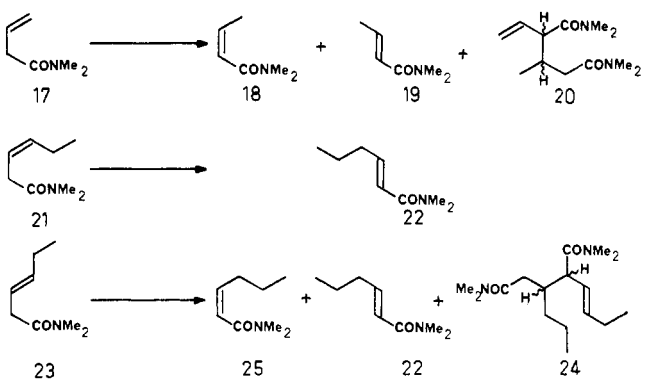
gated esters **15** and **16**[14b] (**15:16** = 2.3:1).

It was hoped that the substitution pattern of the products would lower their propensity for Michael addition and therefore resultant dimerization. As a series, the three β,γ-unsaturated esters possess a substitution pattern about the double bond which might permit an estimation of the effect of increasing steric factors opposing any electronic effects in the rearrangement. The reactions were performed by using a large excess of sodium hydride in light in the previous observations that the amount of sodium hydride affected the rate of isomerization but not the isomer ratio. It was felt that shorter reaction times might further reduce the amount of dimerization occurring. The configurations of esters **13–16** were confirmed by the appropriate NOE difference experiments. The thermodynamic ratio of **15:16** at room temperature was determined (2.3:1) by the action of methanolic sodium methoxide on the esters.

The ester **12a**, possessing the *exo*-methylene unit, rearranged to give exclusively the *E*-product **15**. Gratifyingly, no dimerization was observed during the course of the reaction. Treatment of **13** with sodium hydride gave only the thermodynamically less stable *Z*-isomer **16** (after 24 h). This is entirely in accord with the results using methyl (*E*)-3-hexenoate **8**, as **13** can be considered to be a "buttressed" *E* β,γ-unsaturated ester. With longer reaction periods some *Z* → *E* isomerization of the product occurred, but no dimerization was observed. Crucially, the *Z*-isomer **14** yielded exclusively the *E*-product **15**. The three reactions in Scheme VII together form a complementary set of stereospecific conjugative isomerizations with regard to transfer of double-bond stereochemistry. The rate of isomerization is strikingly substituent dependent, the order of reactivity being **12a** ≫ **14** > **13**.

We briefly examined the scope of these isomerizations by considering the related properties of β,γ-unsaturated amides. As shown (Scheme VIII), *N,N*-dimethyl 3-butenamide (**17**) isomerizes under the NaH/THF conditions

Scheme VIII



to a 4:1 mixture of **18–19**. This kinetic stereoselectivity in favor of the *Z* isomer is directly analogous to the results found for methyl 3-butenoate (Scheme V). Dimer formation became dominant at longer reaction times with **17**, with NMR analysis suggesting the structure **20** for this dimer. Scheme VIII also summarizes the results for the more highly substituted. β,γ-unsaturated amides which we have examined. The (*Z*)-hexenamide **21** isomerized relatively rapidly to the *E* α,β-unsaturated amide **22** in modest yield, while the (*E*)-hexenamide **23** reacted sluggishly to yield mostly dimer **24** and a low percentage of α,β-unsaturated amides **22** and **25** with the *Z* isomer in a 2:1 predominance. We tentatively conclude that, as in the examples of Schemes VI and VII, the reaction stereochemistry follows the *E* → *Z* and *Z* → *E* course observed in the ester series. The low yields of conjugated amides and the high dimerization yields discouraged us from further studying these substrates from both a mechanistic and synthetic point of view. Table I summarizes the chromatographic yields and product composition at the time of highest observed concentration of the conjugated products resulting from sodium hydride treatment of the

β,γ-unsaturated substrates 4, 8, 9, 12–14, 17, 21, and 23.

Summary of Results

The results with regard to the ester and amide conjugative isomerizations can be summarized as follows:

1. The NaH/ether reaction condition results in the isomerization of a variety of β,γ-unsaturated esters to their α,β-unsaturated analogues. The stereochemical profile clearly indicates that the initial isomerization is kinetically controlled, but as the reaction time increases secondary processes can compete and, at long reaction times, a thermodynamic product ratio can be obtained. Increasing substitution decreases the relative rates of both secondary isomerization and side reactions. The isomerization products may be obtained without the need for an external quenching reagent, and while it is clear that the anionic intermediates are involved, it is also evident that the reaction intermediates do not resemble those obtained in the complementary α,β-unsaturated ester to β,γ-unsaturated ester isomerization.

2. For the methyl 3-butenoate system, the initial product is the (*Z*)-olefin, but for the analogous ethyl 3-ethyl-3-butenoate, the *E* product is obtained, a stereochemical result seemingly opposite to but actually identical with the unsubstituted methyl 3-butenoate case.

3. Stereoselective isomerizations are observed for substrates in which there is stereochemical labeling of the β,γ-double bond. Thus, *E* β,γ-unsaturated esters isomerize primarily to the *Z* α,β-unsaturated esters, whereas *Z* β,γ-unsaturated esters isomerize primarily to the *E* α,β-unsaturated esters. The stereoselective esters. The stereoselective β,γ- to α,β-unsaturated ester isomerizations observed in this work demonstrate that the intermediates involved in these two reactions are distinct both from each other, and also from the intermediates of the deconjugative process.

4. The NaH/THF conditions involve a catalytic isomerization process, as the isomerizations can frequently be carried out with <1 equiv of NaH; hydrogen gas is not evolved, and the NaH apparently is not consumed. Even with a large excess of NaH, analysis of the supernatant without prior quenching gives the same results as analysis after an aqueous citric acid quench.

5. A feature of reactions involving monosubstituted β,γ-unsaturated substrates or those lacking substitution at the β-position is the formation of dimeric material which may become the dominant process with slow rates of isomerization.

We tentatively suggest a sequence of events to account for the aforementioned features and the regiochemical disparity between this process and the more frequently encountered kinetic deconjugation proces.

During the initial induction period the β,γ-unsaturated substrate is absorbed onto the surface of the sodium hydride as the enolate until all available active sites of the catalyst become occupied. At this point the absorbed enolate may undergo protonation at the more basic γ-position by a further molecule of β,γ-unsaturated product and be replaced on the catalyst surface by the second molecule of substrate. This represents the commencement of reaction as detected by GC analysis. With increasing α,β-unsaturated material and decreasing β,γ-unsaturated material available in the supernatant the process of proton abstraction from β,γ-unsaturated starting material can be replaced by addition of the α,β-unsaturated product leading to dimerization. The eventual attainment, over long periods of time, of thermodynamic *E*:*Z* ratios of conjugated products is the result of the inevitable presence of small quantities of anionic material in solution. The area of the sodium hydride surface actively involved in this process can only represent a small proportion of the reagent present in the reaction due to the lack of need for quenching the reaction mixture to obtain the products even when large (10 equiv) excesses of sodium hydride are used. The fact that these isomerizations are stereoselective (*E* → *Z* and *Z* → *E*) poses a mechanistic challenge which will be addressed in the following section.

Mechanism for the Stereoselective Conjugative Isomerization of β,γ-Unsaturated Esters; Stereochemical Generalization and Prediction for Allylic Anion Formation

The stereoselective ester and amide isomerizations discussed in detail above serve as examples of the following phenomenon, frequently recognized in isolated cases but not previously generalized in the literature:

In a reaction that involves a formal 1,2-olefin shift, inversion of olefin configuration occurs with migration of the double bond. (In the specific case of substrates that are terminal olefins the product possessing *Z* configuration will be favored.) The stereoselective isomerizations of β,γ-unsaturated esters and amides discussed above are examples of this generalization. Further examples of this set of kinetically controlled stereoselective reactions can be found for a variety of substrate types including simple alkenes[11d,e] as well as α,β-unsaturated carboxylic acids,[15] α,β-unsaturated esters,[6,7] α,β-unsaturated thioethers,[16] and α,β-unsaturated sulfones[17] as shown in Table II.

We include in our considerations not only our results on unsaturated ester and amide conjugative isomerization but also other reactions in which the key step is the conversion of an allylic sp^3 moiety to an allylic anion. Included in this category are the "formal" 1,3-prototropic shifts already discussed, enolate formation (ketones,[24] esters,[25] and hydrazones[26]), and benzylic deprotonation of polyalkylated aromatic compounds.[27] We note that others[11,23] have presented similar mechanistic arguments for portions of the chemistry to be discussed below, but no report has discussed this related work in entirety. The following considerations are central to the stereo- and regiochemical consequences of these related processes:

i. The ease of formation and the conformational stability once formed of the anionic species.[11,28]

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(24) (a) Fataftah, Z. A.; Kopka, I. E.; Rathke, M. W. *J. Am. Chem. Soc.* **1980**, *102*, 3959. (b) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, 495.
(25) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. See also ref 24b for a commentary on this work. Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247.
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(27) (a) Klein, J.; Medlik-Balan, A. *J. Am. Chem. Soc.* **1977**, *99*, 1473. (b) Bassfield, R. L.; Houminer, Y. *J. Org. Chem.* **1983**, *48*, 2130. (c) Rizzi, G. P. *J. Org. Chem.* **1968**, *33*, 1333. (d) Houminer, Y. *J. Heterocycl. Chem.* **1981**, *18*, 445.
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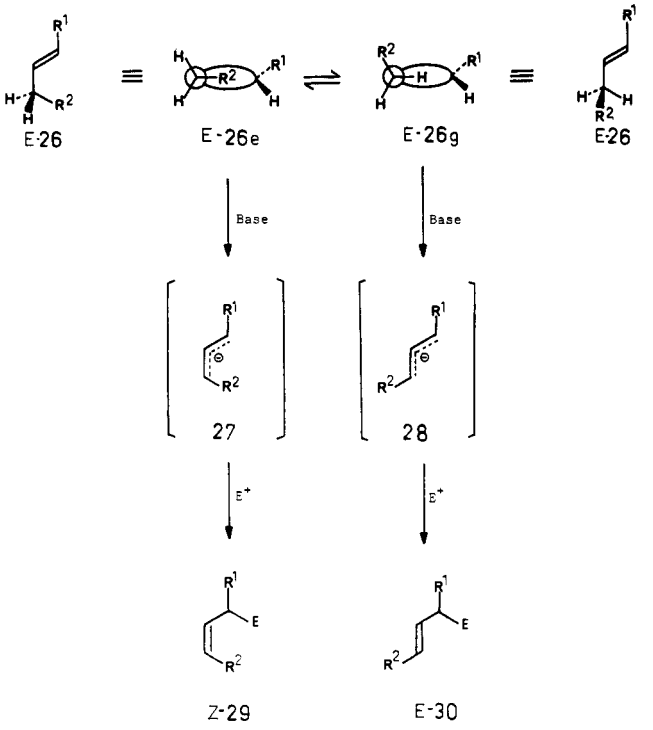
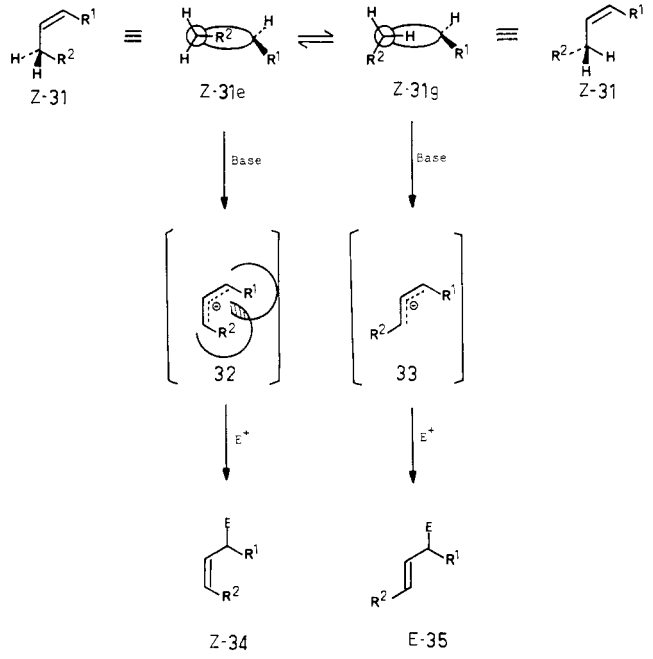
Scheme IX



Scheme X

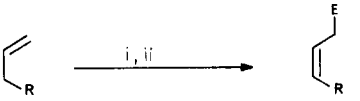


ii. The stabilizing consequence of a substituent R eclipsing the allylic anion to give a cisoid subunit.[11]

iii. The relative importance of destabilizing, compressive steric effects in the allylic anions or the transition state leading to them.[23]

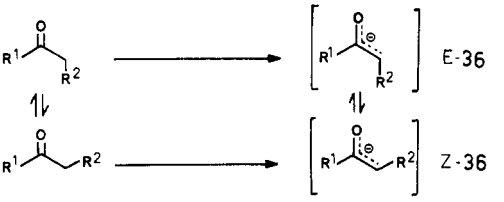
The basic stereochemical considerations for the $E \rightarrow Z$ and $Z \rightarrow E$ transformations are illustrated in Schemes IX and X, respectively. For Scheme IX, it is recognized that conformational energy minima for the disposition of allylic substituents occur when one substituent is eclipsing the double bond, (*E*)-**26e** and (*E*)-**26g**.[11,29] Ground-state

Scheme XI[a]



[a] Reagents: (i) base; (ii) E^+.

Scheme XII



control would predict (*E*)-**30** to be the major product, contrary to experimental observation. It is the eclipsed conformation (*E*)-**26e** that leads to the observed *Z* product. Thus, the relative Gibbs free energies of the transition states, leading to intermediates **27** and **28**, determine reaction stereoselectively.[30]

To explain this phenomenon, two opposing factors must be considered. The incipient allylic anion **27** will be stabilized by the cis substituent R^2 and will be destabilized by allylic $A^{1,3}$ strain.[31] When R^2 is small, the net effect is stabilization of the *Z*-intermediate **27** relative to the *E* intermediate **28**. The known greater stability of the *Z* isomer of the crotyl anion (**8**, R^1 = H; R^2 = CO_2R) over the *E* counterpart[11,28] supports the preferential formation of **27** and thus the *Z*-product (*Z*)-**29**. For a single $A^{1,3}$ interaction to override the benefits of *Z*-substituent stabilization, R^2 must be rather bulky.

For the $Z \rightarrow E$ transformation (Scheme X), the transition state leading to *Z*-product (*Z*)-**34** has two substituents, R^1 and R^2, which significantly destabilize it due to steric compression. For the alternative route, intermediate **33** may still profit from (*Z*)-allylic anion stabilization but more importantly lacks the $A^{1,3}$ strain present in **32** and is consequently more easily formed from (*Z*)-**31e** ↔ (*Z*)-**31g**. Thus, (*Z*)-**31** isomerizes stereospecifically to (*E*)-**35**.

Terminal monosubstituted olefins are a frequently observed special case of Scheme IX and X, where R^1 = H. In addn. to our results, the literature contains many examples in which these substrates isomerize stereoselectively to the (*Z*)-olefin (Scheme XI).[18,19] The absence of compressive steric effects coupled with *Z*-substituent stabilization in intermediate **27** (compared with **32**) and the transition state leading to it readily explains the stereochemical results.

These phenomena cohesively encompass other examples of chemical stereoselectivity. Consider the recently presented evidence for the stereoselective formation of (*Z*)-enolates of ketones,[24] esters,[25] and hydrazones[26] under thermodynamic conditions (Scheme XII). (*Z*)-**36** possesses the (*Z*)-allylic anion functionality and would be expected to be thermodynamically preferred over (*E*)-**36** on the basis of this alkyl–allyl anion stabilization. Further, the potential for overriding $A^{1,3}$ effect between R^1 and R^2 in (*E*)-**36** could further favor (*Z*)-**36**, in a manner strictly analogous to the destabilization of **27** (Scheme IX) and **32** (Scheme X) when R^1 and R^2 are bulky.

The above concepts are readily extended to aromatic systems. Consider kinetic acidity of benzylic protons,

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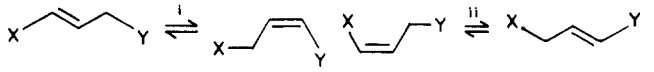
(30) For a discussion of the Curtin–Hammett principle, which relates ground state conformational equilibrium distribution to product stereoselectivities, see: Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

(31) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

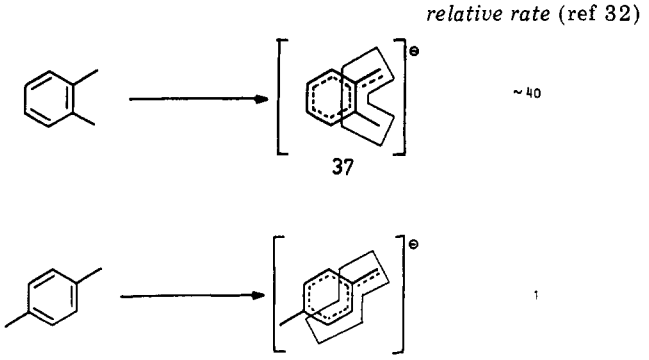
Table II. $E \rightarrow Z$ and $Z \rightarrow E$ Anionic, Kinetic Olefin Isomerizations



starting material structural class	substituents X	substituents Y	reacn conditions	reacn(s) obsd	ref
alkene	alkyl	alkyl	$LiNHCH_2CH_2NH_2/NH_2CH_2CH_2NH_2$	i, ii	18
	H	alkyl	MO-*t*-Bu/Me_2SO	i	19, 11d, 11e
	H	alkyl	RuO; CeO	i	20
	H	alkyl	various	i	1a
α,β-unsaturated carboxylic acid	CO_2H	alkyl	LDA, MeI	i, ii	21a, 21b
α,β-unsaturated carboxylic ester	CO_2R	alkyl	LDA/HMPA/DMF, aq HN_4Cl	i, ii	21b, 22, 23
β,γ-unsaturated carboxylic ester	alkyl	CO_2R	NaH/THF	i, ii	*a*
	H	CO_2H	NaH/THF	i	*a*
β,γ-unsaturated amide	H	$CONMe_2$	NaH/THF	i	*a*
	alkyl	$CONMe_2$	NaH/THF	i, ii	*a*
sulfide	S-*t*-Bu	CH_2OCH_3	*sec*-BuLi or LDA / RX	i, ii	16
	S-*t*-Bu	$CH(R)OCH_3$	*sec*-BuLi or LDA / RX	i, ii	
sulfone	SO_2CH_2Br	alkyl	KO-*t*-Bu	i, ii	17
	SO_2R	alkyl	KO-*t*-Bu	i, ii	

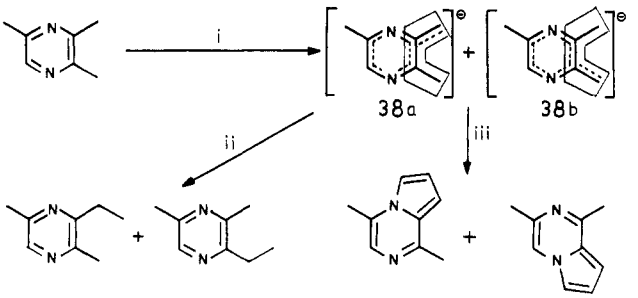
[a] This work.

Scheme XIII



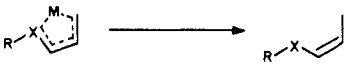
illustrated in Scheme XIII. The benzylic protons of *o*-xylene exchange ~40 times faster than those of *p*-xylene.[32] Note that *Z* stabilization is only possible in the *o*-xylyl anion **37** and the transition state leading to **37**. This phenomenon is similarly observed in the rates of metalation of polyalkylbenzenes,[27a] the equilibrium ion pair acidities of complex aromatic hydrocarbons,[12] and the rates of deuterium–hydrogen exchange in polyalkylpyrazines.[27b] Formation of the anions of trimethylpyrazine, presumably under themodynamic conditions, followed by alkylation with either dimethylsulfate[27c] or (*E*)-1,2-dichloroethene[27d] gave products shown in Scheme XIV. The observed regiochemistry is again explained by reaction from the *Z*-stabilized "allylic anions" **38a** and **38b** analogous to **37**. We note that the arguments presented above will be overridden when cation–anion association exists, giving rise to a cyclic intermediate or transition state, e.g., in the isomerization of allylic amides[33] or allylic esters[34] or the formation of ketone and ester enolates in the absence of HMPA (LDA/THF)[24b,35] (Scheme XV).

Scheme XIV [a]



[a] Reagents: (i) base; (ii) Me_2SO_4, (iii) ClCH=CHCl.

Scheme XV [a]



[a] M = metal; X = heteroatom.

We thus present a more inclusive generalization, based on the stereochemical consequences of β,γ-unsaturated ester and amide conjugative isomerizations described herein, on related olefin shifts (Table II), and on additional literature results cited above. *In the absence of the imposition of specific geometry requirements by severe steric crowding or cation–anion complexation, the kinetically formed anion from deprotonation at an allylic or benzylic position will possess a cisoid crotyl subunit, if one is available, regardless of initial substrate conformation. In the presence of steric crowding in the cisoid crotyl subunit, a transoid crotyl intermediate will be obtained* (Scheme XVI). This phenomenon will also hold if the intermediate anion(s) is formed under thermodynamic control. While individual cases have been explained in similar terms, we believe the above statement to be quite general and to have valuable predictive utility. We await further experimental results in order to evaluate the scope of these stereochemical generalizations and their sensitivity to secondary steric and electronic factors.

Experimental Section

Instruments and Techniques. Melting points were recorded with a Koffler heated stage microscope and are uncorrected.

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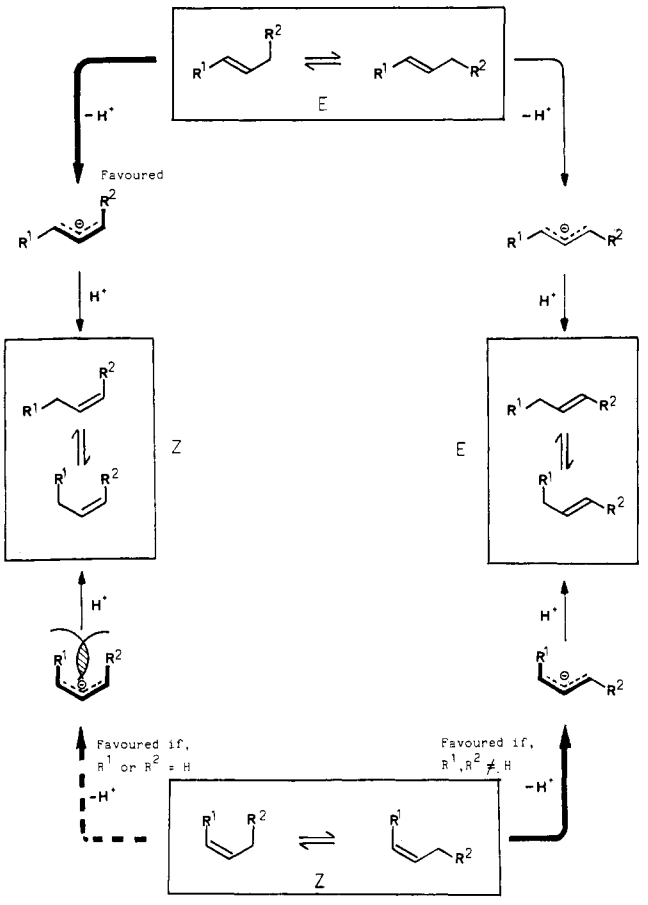
(33) Hassel, T.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 399. Biellmann, J.-F.; Ducep, J.-B. *Org. React.* (N.Y.) **1982**, *27*, 1.
(34) Price, C. C.; Snyder, W. H. *J. Am. Chem. Soc.* **1961**, *83*, 1773. Still, W. C.; Macdonald, T. L.; *J. Org. Chem.* **1976**, *41*, 3620.
(35) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

Scheme XVI



IR spectra were recorded on a Unicam SP3 200 or Perkin-Elmer 297 spectrometer as solutions in chloroform.

Proton NMR spectra were recorded in deuteriochloroform with a Bruker WH 300 operating at 300 MHz. Peak positions are recorded in δ relative to Me_4Si, and peak forms denoted s, d, t, q, dd, and m denoting singlet, doublet, triplet, quartet, double doublet, and multiplet, respectively.

Mass spectroscopic data were recorded on a VG-16F spectrometer with either electron impact or chemical ionization as stated. Accurate mass measurements were performed with a VG-ZAB-1F instrument.

GC analyses were performed on a Carlo Erba Fractovap Series 2150 gas chromatograph with bonded phase BP1 25 m × 0.33 mm capillary column, helium carrier gas, and flame-ionization detection. Peak areas were integrated with a Hewlett-Packard 3390 integrator.

Diethyl ether and tetrahydrofuran were distilled from sodium or potassium benzophenone ketyl, respectively.

General Isomerization Procedure for Kinetics Studies. The given amount of sodium hydride (50% dispersion in oil) was placed in a round-bottomed flask. The flask was then evacuated to 0.2 mbar and purged with nitrogen 3 times. The sodium hydride was freed from oil by trituration with dry diethyl ether (3 × 5 mL) and then suspended in ether (5 mL). The β,γ-unsaturated substrate dissolved in ether was finally added in one portion together with an internal standard (cyclooctane or cycloheptane). The reaction mixture was magnetically stirred at 20 °C under a 40 mbar overpressure of nitrogen. At given times 0.5-mL samples of the reaction mixture were removed and added to an excess of 0.2 mL aqueous citric acid. Hydrogen production was vigorous at this point. No hydrogen evolution was observed when this procedure was applied to a sample of the clear supernatant obtained by allowing the mixture to settle for 20 min before sampling. The separated ether solution was analyzed by gas chromatography. Composition and mass balance results were identical within the experimental error (2%) for equivalent samples of clear supernatant and heterogenous mixture. All reactions were run at least twice. The reaction was critically dependent upon the quality of the sodium hydride surface and reproducibility of separate reactions was not good enough for exact kinetic measurements. In addition to the gas chromatographic analysis, 300-MHz ^1H NMR spectra of several samples were taken. Integrations of suitable signals in the mixture confirmed the corresponding gas chromatographic results in all cases. In addition the structure of dimers was elucidated from the ^1H NMr spectra. In case of the *N,N*-dimethyl-3-butenamide (**17**) isomerization, gas chromatographic conditions could not be found which distinguished between starting material (**17**) and *Z* product (**18**) and for this reason the isomerization was investigated by ^1H NMR only.

Methyl 3-Butenoate (4). To a solution of 3-butenoic acid (10 g, 120 mmol, 90% Aldrich, main impurity (*E*)-2-butenoic acid) in methanol (80 mL) was added acetyl chloride (1.7 mL, 1.88 g, 24 mmol) in one portion. After 15 h at room temperature the solution was made alkaline with aqueous sodium carbonate, extracted with diethyl ether (4 × 10 mL), and dried ($MgSO_4$). The crude ester was purified by distillation [bp 106 °C (lit.[36] bp 108 °C)] to produce β,γ-unsaturated ester **4** in 98% purity: ^1H NMR δ 5.87 (tdd, *J* = 7, 10, 17 Hz, 1 H, $H_2C{=}CHCH_2$), 5.10 (m, 2 H), 3.61 (s, 3 H), 3.04 (td, *J* = 1.5, 7 Hz, 2 H).

(*Z*)-Methyl 2-butenoate (6) was prepared by treatment of (*Z*)-2-butenoic acid[37] with diazomethane. Distillation (bp 118–119 °C) gave the ester **6** (99% (*Z*)-**6**, 1% (*E*)-**5**): ^1H NMR δ 6.34 (dq, *J* = 11, 7 Hz, 1 H, $CH_3CH{=}CH$), 5.82 (dq, *J* = 11, 1.5 Hz, 1 H, $C{=}CHCO$), 3.72 (s, 3 H), 2.22 (dd, *J* = 7, 1.5 Hz, 3 H, $CH_3CH{=}$).

Dimethyl 2-Ethenyl-3-methylpentanedioate (7a) (1:1 mixture of diastereoisomers): ^1H NMR δ 5.84 and 5.82 (ddd, *J* = 10, 10, 17 Hz, 1 H, $CH_2{=}CHCH$), 5.23 and 5.21 (dd, *J* = 1.5, 10 Hz, 1 H, $CHCHH$), 5.18 and 5.15 (br d, *J* = 17 Hz, 1 H, $CH{=}CHH$), 2.99 and 2.90 (dd, *J* = 7, 10 Hz, and t, *J* = 9 Z, 1 H, ${=}CHCH(COR)CH$), 2.51 and 2.38 (dd, *J* = 5, 15 Hz, 1 H, $COCHHCH$), 2.40 (m, 1 H, $CH_2CH(CH_3)CH$), 2.19 and 2.08 (dd, *J* = 8, 15 Hz and *J* = 9, 15 Hz, 1 H, $COCHHCH$), 0.99 and 0.96 (d, *J* = 7 Hz, 3 H, $CHCH_3$).

Dimethyl 2-Ethylidene-3-methylpentanedioate (7b) (2:1 mixture of *E*–*Z* isomers): ^1H NMR δ 6.83 (q, *J* = 7 Hz, 1 H, (*E*) $CH_3CH{=}C$), 5.99 (q, *J* = 7 Hz, 1 H, (*Z*) $CH_3CH{=}$), 3.77 (s, 3 H, (*Z*) OCH_3), 3.72 (s, 3 H, (*E*) OCH_3), 3.66 (s, 3 H, (*Z*) OCH_3), 3.64 (s, 3 H, (E) OCH_3) 3.30 (sextet, *J* = 7 Hz, (*E*) $CH_2CH(CH_3)C{=}$), 3.05 (sextet, *J* = 7 Hz, (*Z*) $CH_2CH(CH_3)C{=}$), 2.75 (dd, *J* = 7, 15 Hz, (*E*) $COCHHCH$), 2.60 (dd, *J* = 7, 15 Hz, (*E*) $COCHHCH$), 2.58 (dd, *J* = 6, 15 Hz, (*Z*) $COCHHCH$), 2.36 (dd, *J* = 7, 15 Hz, (*Z*) $COCHHCH$), 2.91 (d, *J* = 7 Hz, 3 H (*Z*) $CH_3CH{=}$), 2.86 (d, *J* = 7 Hz, 3 H (*E*) $CH_3CH{=}$), 1.20 (d, *J* = 7 Hz, 3 H, (E) CH_3CH), 1.12 (d, *J* = 7 Hz, 3 H, (*Z*) $CH_3CH{=}$).

(*E*)-Methyl 3-hexenoate (8) was prepared by treatment of (*E*)-3-hexenoic acid (97% Aldrich) with diazomethane. The distilled product contained 98% **8** and 2% **10**: IR ν_{max} (neat liquid) 1740 cm^{-1}; ^1H NMR δ 5.61 (td, *J* = 7, 17 Hz, 1 H), 5.52 (td, *J* = 7, 17 Hz, 1 H), 3.70 (s, 3 H), 3.04 (d, *J* = 7 Hz, 2 H), 2.05 (quintet, *J* = 7 Hz, 2 H), 0.99 (t, *J* = 7 Hz, 3 H).

(*Z*)-Methyl 3-hexenoate (9) was prepared by the method of Frankel.[38] Gas chromatographic analysis of the distilled product indicated it was 96% **9**, 2% **10**, 1% **8**, and 1% anisole: IR ν_{max} (neat liquid) 1740 cm^{-1}; ^1H NMR δ 5.59 (dt, *J* = 11, 7 Hz, 1 H), 5.53 (dt, *J* = 11, 7 Hz, 1 H), 3.70 (s, 3 H), 3.10 (d, *J* = 7 Hz, 2 H), 2.06 (quintet, *J* = 7 Hz, 2 H), 0.99 (t, *J* = 7 Hz, 3 H).

(*E*)-Methyl 2-hexenoate (10) was prepared by esterification of (*E*)-2-hexenoic acid (99% Aldrich) with excess CH_3OH containing 5% H_2SO_4 at room temperature overnight. The purity of the distilled product was higher than 99% as judged by GC: ^1H NMR δ 7.97 (dt, *J* = 17, 7 Hz, 1 H), 5.82 (dt, *J* = 17, 1.7 Hz, 1 H), 3.72 (s, 3 H), 2.28 (qd, *J* = 7, 1.7 Hz, 2 H), 1.49 (sextet, *J* = 7, 2 H), 0.93 (t, *J* = 7 Hz, 3 H).

(*Z*)-Methyl 2-Hexenoate (11). (*Z*)-2-Hexenoic acid[39] was esterified with excess CH_3OH containing 5% H_2SO_4 for 15 h at

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(39) Rappe, C.; Adestrome, R. *Acta Chem. Scand.* **1965**, *19*, 383.

room temperature. The purity of the distilled product was greater than 95% (NMR): ^{1}H NMR δ 6.23 (dt, J = 12, 7 Hz, 1 H), 5.79 (dt, J = 12, 1.5 Hz, 1 H), 3.71 (s, 3 H), 2.63 (qd, J = 7, 1.5 Hz, 2 H), 1.47 (sextet, J = 7 Hz, 2 H), 0.95 (t, J = 7 Hz, 3 H).

***tert*-Butyl 3-Ethyl-3-butenoate (12b).** A 100-mL round-bottomed flask equipped with septum inlet, magnetic stirring, and positive nitrogen pressure was charged with anhydrous nickel(II) bromide (2.18 g, 10 mmol) and THF (10 mL). The flask was immersed in a dry ice/acetone bath and *n*-butyllithium (1.3 mL, 2 mmol; a 1.6 M solution in hexane) was injected. The resultant black suspension was stirred for 5 min, and 2-bromo-1-butene (1.35 g, 10 mmol) was injected followed by a solution of *tert*-butyl lithioacetate (10 mL of a 1 M solution prepared by addition of *tert*-butyl acetate to a solution of LDA in THF at −78 °C). The solution was allowed to reach room temperature and stirred for 30 min. The cooling bath was reapplied and the reaction mixture quenched by addition of hydrochloric acid (6 mL; 6 N solution). The mixture was stirred with *n*-pentane. The organic layer was separated and dried (K_2CO_3) and the solvent removed under reduced pressure. The crude product was distilled to give *tert*-butyl 3-ethyl-3-butenoate (**12b**) (1.2 g, 71%), bp 74–76 °C (10 mmHg). Anal. Found: C, 70.65; H, 10.58. Calcd for $C_{12}H_{18}O_2$: C, 70.55; H, 10.66). IR ν_{max} (neat liquid) 2975, 1730, 1650 cm^{-1}; ^{1}H NMR δ 1.04 (t, J = 7.5 Hz, 3 H, CH_3CH_2), 1.44 (9 H, s, CMe_3), 2.11 (q, J = 7.5 Hz, 2 H, CH_3CH_2), 2.94 (s, 2 H, CH_2CO_2), 4.85 (d, J = 1.1 Hz, 1 H, olefinic), 4.88 (d, J = 1.6, 1 H, olefinic); MS, m/z (relative intensity) 170 (M$^+$, 11), 114 (37), 97 (23), 69 (37), 57 (100), 39 (43), 37 (15).

Methyl 3-Ethyl-3-butenoate (12a). The *tert*-butyl ester **12b** (1 g, 5.9 mmol) was dissolved in trifluoroacetic acid (~10 mL), and this mixture was left for 1 h at room temperature. The excess reagent was removed under reduced pressure, the crude product was dissolved in ether (10 mL), and the solution was extracted with saturated aqueous sodium hydrogen carbonate (10 mL). The aqueous phase was acidified and the acid **24** extracted with ethyl acetate (2 × 25 mL), which was subsequently dried (Na_2SO_4) and evaporated off to yield 3-ethyl-3-butenoic acid (**12c**) (0.61 g, 91%): IR ν_{max} (neat film) 2980, 1710 cm^{-1}; ^{1}H NMR δ 0.99 (J = 7.5 Hz, 3 H, CH_3CH_2), 2.10 (q, J = 7.5 Hz, 2 H, CH_3CH_2), 3.03 (s, 2 H, HO_2CCH_2), 4.83 (d, J = 1.1 Hz, 1 H, olefinic), 4.87 (d, J = 1.3 Hz, 1 H, olefinic); MS, m/z (relative intensity) 114 (M$^+$, 32), 69 (37), 57 (100), 39 (43). A solution of the acid **12c** (0.6 g, 5.3 mmol) in acetone (10 mL) was stirred magnetically with methyl iodide (5 mL) and potassium carbonate (5 g) for 18 h at room temperature. Brine was then added and the mixture (10 mL) extracted with ether (3 × 25 mL). The ethereal extracts were combined, dried ($MgSO_4$), and evaporated to yield methyl 3-ethyl-3-butenoate (**12a**) (0.5 g, 74%), bp 70 °C (10 mmHg). Anal. Found: C, 65.55; H, 9.18. Calcd for $C_7H_{12}O_2$: C, 65.6; H, 9.4. IR ν_{max} (neat film) 2950, 1690 cm^{-1}; ^{1}H NMR δ 1.03 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 2.10 (2 H, q, J = 7.4 Hz, CH_3CH_2), 3.05 (2 H, s, CH_2CO_2), 3.67 (3 H, s, Me), 4.86 (1 H, d, J = 1.1 Hz, olefinic), 4.90 (1 H, d, J = 1.3 Hz, olefinic); MS, m/z (relative intensity) 128 (M$^+$, 22), 96 (41), 69 (100), 68 (70), 59 (28), 41 (99).

(*E*)-Methyl 3-methyl-3-pentenoate (13) was prepared by the method of Cornforth.[40] The purity of the product was 99% (GC). The reaction sequence, after the separation of the intermediate β-lactones, was stereospecific within the limits of detection (^{1}H NMR, 300 MHz): ^{1}H NMR δ 5.36 (qq, J = 1.1, 6.6 Hz, 1 H), 3.68 (s, 3 H), 2.99 (br s, 2 H), 1.68 (t, J = 1.1 Hz, 3 H), 1.62 (qd, J = 1.1, 6.6 Hz, 3 H).

(*Z*)-Methyl 3-methyl-3-pentenoate (14) was prepared by the method of Cornforth.[40] The composition of the product was 97% **14** with 3% **13** (the separation of the intermediate β-lactones gave within experimental error the same relative composition): ^{1}H NMR δ 5.44 (br q, J = 7 Hz, 1 H), 3.69 (s, 3 H), 3.06 (br s, 2 H), 1.77 (quintet, J = 1 Hz, 3 H), 1.61 (br d, J = 7 Hz, 3 H). NOE experiments with **13** and **14** confirmed the assignment of Cornforth.[40]

Preparation of (*E*)-Methyl 3-Methyl-2-pentenoate (15). Into a 100-mL round-bottomed flask equipped with a septum inlet and magnetic stirring was placed a 50% dispersion of sodium hydride in oil (0.48 g, 10 mmol). The oil was removed by addition of *n*-pentane followed by rapid magnetic stirring, then allowing the sodium hydride to settle, and syringing off the *n*-pentane. This procedure was repeated 3 times, and the remaining pentane was removed at reduced presure. Anhydrous ether (20 mL) was added to the sodium hydride, and the flask was flushed with nitrogen and then maintained under positive nitrogen pressure. The methyl ester **12a** (128 mg, 1 mmol) in ether (5 mL) was syringed into the flask. The reaction mixture was stirred at room temperature (16 h) and quenched by the addition of water (10 mL). The ethereal layer was separated, dried ($MgSO_4$), and evaporated off to give (*E*)-methyl 3-methyl-2-pentenoate (**15**) (90 mg, 70%). Anal. Found: C, 65.4; H, 9.4. Calcd for $C_7H_{12}O_2$: C, 65.6; H, 9.4. IR ν_{max} (neat film) 2985, 1720, 1650 cm^{-1}; ^{1}H NMR δ 1.03 (t, J = 7.5 Hz, 3 H, CH_3CH_2), 2.13 (q, J = 7.5 Hz, 2 H, CH_3CH_2), 2.14 (d, J = 0.75 Hz, 3 H, CH_3), 3.65 (3 H, s, CH_3), 5.63 (d, J = 2.5 Hz, 1 H, =CH); MS, m/z (relative intensity) (M$^+$, 78), 97 (100), 60 (24), 59 (18), 4 (96).

***N*,*N*-Dimethyl-3-butenamide (17)** was prepared by reaction of 3-butenoyl chloride (5.0 g, 48 mmol) in dioxane (100 mL) with dimethylamine gas for 15 min. Acidification with HCl, removal of dioxane under reduced pressure, extraction with CH_2Cl_2, drying with $MgSO_4$, and distillation [bp 78 °C (8 mbar)] gave amide **17** (4.5 g, 83%) containing 97% **17** and 3% **18**. Anal. Found: C, 60.90; H, 9.90; N, 11.80. Calculated for $C_6H_{11}NO{\cdot}0.25H_2O$: C, 61.25; H, 9.85; N, 11.90. IR ν_{max} (neat liquid) 3050, 2940, 1640, 1498, 1400, 1160, 998, 922 cm^{-1}; ^{1}H NMR δ 5.93 (tdd, J = 6.6, 10.2, 16.8 Hz, 1 H), 5.14 (dddd, J = 1.4, 1.5, 1.9, 10.2 Hz, 1 H), 5.10 (dddd, J = 1.4, 1.5, 1.9, 16.8 Hz, 1 H), 3.13 (ddd, J = 1.4, 1.5, 6.6 Hz, 2 H), 2.99 (s, 3 H), 2.93 (s, 3 H).

***N*,*N*-Dimethyl-2-butenamide (Mixture of (*Z*)-18 and (*E*)-19).** (*Z*)-2-Butenoic acid (1 g)[37] was treated with benzoyl chloride (3 g) at 120 °C. The first 0.1 g of product distilled directly from the reaction was dissolved in diethyl ether and reacted with dimethylamine gas. After the usual workup the product was distilled and the first 30 mg of the low-boiling fraction taken in an attempt to obtain a sample enriched in *Z*-amide **18**, which was analyzed by gas chromatography and ^{1}H NMR. The product was a mixture of 79% *Z*-amide **18** and 21% E-amide **19**: ^{1}H NMR δ 6.86 (dq, J = 15, 7 Hz, **19** 1 H), 6.25 (dq, J = 15, 1 Hz, **19** 1 H), 5.99 (m, **18** 2 H), 3.06 (s, **19** 3 H), 3.02 (s, **19** 3 H), 2.99 (s, **18** 6 H), 1.89 (dd, J = 7, 1 Hz, **18** 3 H), 1.88 (dd, J = 7, 1 Hz, **19** 3 H).

***N*,*N*,*N*′,*N*′-Tetramethyl-2-ethenyl-3-methylpentanediamide (20) (Mixture of Diastereoisomers).** *N*,*N*-Dimethyl-3-butenamide (**17**) was treated for 3.5 h with NaH (0.89 equiv) as described above. ^{1}H NMR analysis of the reaction product gave 88% dimer **20**, 9% **19**, and 3% **18**: ^{1}H NMR δ 5.76 (ddd, J = 9, 10, 17 Hz, 1 H, $CHCHCH_2$), 5.07 (dd, J = 1.5, 10 Hz, 1 H = CH=CHH), 5.00 (br d, J = 17 Hz, 1 H, CH=CHH), 3.37 (dd, J = 7, 10 Hz, 1 H, minor isomer $CHCH(COR)CH$=), 3.32 (dd, J = 7, 10 Hz, 1 H, major isomer $CHCH(COR)CH$=), 2.65 (dd, J = 4, 17 Hz, 1 H, $COCHHCH$), 2.45 (m, 1 H, $CH_3CH(CH_2)CH$), 2.05 (dd, J = 8, 17 Hz, 1 H, $COCHHCH$), 1.01 (d, J = 7 Hz, 3 H, major isomer CH_3CH), 0.98 (d, J = 7 Hz, 3 H, minor isomer CH_3CH). Irradiation at δ 2.45 caused collapse of peaks at δ 3.32, 2.65, 2.05, 1.01, and 0.98; irradiation at δ 1.00 simplified the signal at δ 2.45.

(*Z*)-*N*,*N*-Dimethyl-3-hexenamide (21). To a solution of KOH (2.9 g) in aqueous methanol (50 mL, $MeOH/H_2O$ = 1/1) was added (*Z*)-methyl-3-hexenoate (**9**) (3.9 g).[41] The reaction mixture was left 16 h at room temperature, extracted with diethyl ether (2 × 20 mL), acidified with HCl, and extracted again with diethyl ether (3 × 50 mL). After the extract was dried over $MgSO_4$, distillation [bp 118 °C (29 mbar)] gave 2.2 g (63%) of acid (93% (*Z*)-3-hexenoic acid, 5% (*E*)-2-hexenoic acid, and 2% (*E*)-3-hexenoic acid by ^{1}H NMR). This mixture (1.5 g) was treated with $SOCl_2$ (2.3 g, 1.5 equiv). Distillation gave 1.4 g (83%) of (*Z*)-3-hexenoyl chloride, which was dissolved in dioxane (20 mL) and treated with dimethylamine gas. The usual workup and distillation gave the amide **21** (1.2 g, 80%):[42] 93% **21**, 5% **22**, and 2% **23** (by GC); ^{1}H NMR δ 5.56 (td, J = 5.5, 11 Hz, 1 H), 5.53 (td, J = 5.5, 11 Hz, 1 H), 3.12 (d, J = 5.5 Hz, 2 H), 3.00 (s, 3 H), 2.95 (s, 3 H), 2.07 (tq, J = 5.5, 7 Hz, 2 H), 0.99 (t, J = 7 Hz, 3 H).

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(*E*)-*N*,*N*-Dimethyl-3-hexenamide (23)[42] was prepared from (*E*)-3-hexenoic acid (97% Aldrich, 10.0 g) as described for amide **21** (53% yield): ^{1}H NMR δ 5.59 (td, *J* = 5, 17 Hz, 1 H), 5.52 (td, *J* = 5, 17 Hz, 1 H), 3.08 (d, *J* = 5 Hz, 2 H), 2.98 (br s, 6 H), 2.06 (tq, *J* = 5, 7 Hz, 2 H), 0.99 (t, *J* = 7 Hz, 3 H).

***N*,*N*-Dimethyl-2-hexenamide (Mixture of (*E*)-22 and *Z* Isomer 25).** (*Z*)-2-Hexenoic acid (1.0 g)[37,39] was treated with $SOCl_2$ (1.4 g) for 15 min at room temperature and then distilled during 10 min to give 2-hexenoyl chloride (0.85 g, 75%). The chloride was dissolved in dioxane (20 mL) and treated with dimethylamine gas for 30 min. After workup and distillation as detailed for **21** the amide mixture (0.61 g, 66%) was analyzed by gas chromatography and ^{1}H NMR, giving a product composition of 80% *Z*-amide **25** and 20% *E*-amide **22**. Anal. Found: C, 65.69; H, 10.80; N, 9.54. Calcd for $C_8H_{15}NO{\cdot}0.25H_2O$: C, 65.94; H, 10.72; N, 9.61. ^{1}H NMR δ 6.87 (td, *J* = 7, 15 Hz, 1 H, **22** CH_2CH=CH), 6.24 (br d, *J* = 15 Hz, 1 H, **22** CH=C*H*CO), 5.98 (br d, *J* = 12 Hz, 1 H, **25** CH=C*H*CO), 5.90 (td, *J* = 7, 12 Hz, 1 H, **25** CH_2CH=CH), 2.99 (br s, 6 H, **22** and **25** NCH_3), 2.31 (q, *J* = 7 Hz, 2 H, **25** CH_2CH_2CH=), 2.18 (q, *J* = 7 Hz, 2 H, **22** CH_2CH_2CH=), 1.49 (sextet, *J* = 7 Hz, 2 H, **22** $CH_3CH_2CH_2$), 1.44 (sextet, *J* = 7 Hz, 2 H, **25** $CH_3CH_2CH_2$), 0.93 (t, *J* = 7 Hz, 3 H, **22** CH_3CH_2), 0.92 (t, *J* = 7 Hz, 3 H, **25** CH_3CH_2).

***N*,*N*,*N*′,*N*′-Tetramethyl-2-((*Z*)-1-butenyl)-3-propylpentanediamide (24)**: by dimerization of **21** (mixture of diastereoisomers); ^{1}H NMR δ 5.49 (m, 2 H, CH_2CH=C*H*CH), 3.94 and 3.89 (dd, *J* = 5, 9 Hz, 1 H, CH=C*H*(COR)CH), 3.00 (m, 12 H), 2.63 (dd, *J* = 3, 16 Hz, 1 H, RCOC*H*HCH), 2.03 (sextet, *J* = 7 Hz, CH_3CH=CH), 0.95 (m, 6 H, CH_3CH_2). Irradiation at δ 2.03 simplified absorptions at δ 0.95 to br s and δ 5.49 to 5.53 (br d, *J* = 11 Hz, (*Z*) CH_2CH=CH) and 5.45 (major isomer) and 5.41 (minor isomer) (dd, *J* = 3.5, 11 Hz, 1 H, (*Z*) CH=C*H*CH)).

***N*,*N*,*N*′,*N*′-Tetramethyl-2-((*E*)-1-butenyl)-3-propylpentanediamide (24b)**: by dimerization of **23**; ^{1}H NMR δ 5.50 (m, 2 H, CH*CH*=*CH*CH_2), 3.49 (m, 1 H, CH*CH*(COR)CH=), 2.65 (dd, *J* = 4, 16 Hz, 1 H, COC*H*HCH), 2.31 (m, 2 H, COCH*HCH*), 2.07 (m, 2 H, =CHCH_2CH_3), 1.27 (m, 4 H, $CH_2CH_2CH_3$), 0.99 (m, 3 H, =CHCH_2CH_3), 0.90 (m, 3 H, CH_3). Irradiation at δ 3.49 simplified absorptions at δ 5.50 to 5.54 (br d, *J* = 16 Hz, 1 H, (*E*) CH*CH*=CH) and 5.45 (dt, *J* = 15, 5.5 Hz, 1 H, (*E*) CH=*CH*CH_2). Irradiation at δ 2.07 simplified absorptions at δ 5.50 to 5.54 (dd, *J* = 7, 16 Hz, 1 H, CH*CH*=CH) and 5.45 (br d, *J* = 15 Hz, 1 H, CH=*CH*CH_2).

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Registry No. **4**, 3724-55-8; **4** (acid), 625-38-7; **4** (acid chloride), 1470-91-3; **5**, 623-43-8; **6**, 4358-59-2; **6** (acid), 503-64-0; (*E*)-**7a**, 16657-04-8; (*Z*)-**7a**, 16657-03-7; (*R**,*R**)-**7b**, 97253-79-7; (*R**,*S**)-**7b**, 97253-78-6; **8**, 13894-61-6; **8** (acid), 1775-43-5; **8** (acid chloride), 97253-82-2; **9**, 13894-62-7; **9** (acid), 1577-18-0; **10**, 13894-63-8; **10** (acid), 13419-69-7; **11**, 13894-64-9; **11** (acid), 1577-28-2; **12a**, 89897-27-8; **12b**, 97253-80-0; **12c**, 21962-25-4; **13**, 41654-12-0; **14**, 56728-17-7; **15**, 17447-01-7; **16**, 17447-00-6; **17**, 97253-74-2; **18**, 97253-76-4; **19**, 14064-75-6; (*R**,*R**)-**20**, 97253-85-5; (*R**,*S**)-**20**, 97253-81-1; **21**, 72178-91-7; **22**, 97253-75-3; **23**, 72178-90-6; (*R**,*R**)-**24**, 97253-86-6; (*R**,*S**)-**24**, 97253-83-3; (*R**,*R**)-**24b**, 97277-61-7; (*R**,*S**)-**24b**, 97253-84-4; **25**, 97253-77-5; CH_2=C(Br)CH_2CH_3, 23074-36-4; $LiCH_2CO_2Bu$-*t*, 53503-61-0; Me_2NH, 124-40-3; C_6H_5COCl, 98-88-4; $CH_3(CH_2)_2CH$=CHCOCl, 18802-95-4.

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Benzobicyclo[3.1.0]hexene Derivatives from Benzosemibullvalene. CO_2- and CO-Bridged Naphthalenes

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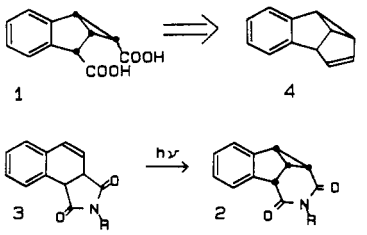
Transformation of benzosemibullvalene to various benzobicyclo[3.1.0]hexene derivatives is described. Reductive ozonolysis of benzosemibullvalene gave diol **9** which was oxidized with Fetizon's reagent to a mixture of lactones **10** and **11**. Lactone **11** was stereoselectively methylated via a protection–deprotection sequence. Hydrolysis and oxidation of methylated lactone **17** gave the target *cis-diendo*-diacid **18**. The diacid was cyclized to anhydride **19**. *trans*-Diacid **21**, generated on oxidation of acid alcohol **13**, was further oxidized to keto acid **23**. The ketone was reacted with 2 equiv of methyllithium and cyclized to yield lactone **25**. Anhydride **19** represents a novel "naphthalene + CO_2 + CO" system and lactone **25** is a "naphthalene + CO_2" system. Irradiation of anhydride **19** at 254 nm gives mainly lactone **25**. This result contrasts previous investigations of anhydride photolyses where decarboxylation predominates and suggests a different mechanism for decomposition. Irradiation of lactone **25** at 254 nm cleanly gives 1-methylnaphthalene. Preparations of several other benzobicyclo[3.1.0]hexene derivatives are detailed.

In the course of mechanistic studies of high-energy precursors to aromatic compounds,[1] centering on the bicyclo[3.1.0]hexene ring system, we required the *cis*-diacid **1**. The presence of four contiguous asymmetric centers in **1** presents a formidable synthetic challenge. To our knowledge, the only reported analogous ring system with similar substitution is imide **2**.[2] Unfortunately, **2** is only a very minor photoproduct of **3** in a complicated mixture, and is thus an unappealing starting point.



We felt that **1** might be synthesized from benzosemibullvalene (**4**), which has the required carbon framework endowed with the necessary stereochemistry. Interestingly, although **4** has been known for some years,[3] reports of its reactivity seem to only include photolysis,[3] thermolysis,[4]

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