Gauman[42] by three successive treatments of 2-methylcyclohexanone with a 10% solution of DCl–D_3PO_4 in D_2O. Nmr analysis of the exchanged ketone indicated the deuterium content to be about 95% of that calculated for the d_3 compound.

6,6-d_2-1-Methoxy-2-methylcyclohexene (8a-d_2) and 1,3-d_2-2-Methoxy-3-methylcyclohexene (8b-d_2).—The enol ethers of the deuterated 2-methylcyclohexanone, prepared in the presence of methanol-d_1 by the method described earlier, were isolated by glpc trapping and identified by their spectral properties. Mass spectral analysis of **8b**-d_2 at low ionization voltage showed the deuterium distribution to be 78.8% d_2 species, 18.4% d_1 species, and 2.8% d_0 species after correction for natural isotopic contributions.[43] Moreover, analysis of a sample of **8b**-d_2 before and after glpc trapping showed that negligible amounts of exchange or fractionation occurred on the column.

Deuterium Exchange Experiment.—An equilibrium mixture of **8a**-d_2 and **8b**-d_2 was diluted with nonlabeled equilibrated ethers to give a sample with the deuterium distribution: d_2, 41.1%, d_1, 20.3%, and d_0, 38.6%. The mixture was then subjected to the conditions of the iodine catalyzed equilibrations. After 24 hr the mixture of isomers was isolated by glpc trapping and the deuterium distribution redetermined. The final distribution was d_2, 23.5%, d_1, 49.1%, and d_0, 27.4%, in close agreement with the statistical distribution of d_2, 26.8%, d_1, 48.8%, and d_0, 24.4%.

Registry No.—**1a**, 25662-28-6; **1b**, 2258-56-2; **2a**, 25662-30-0; **2b**, 25662-31-1; **3a**, 25662-32-2; **3b**, 25662-33-3; **4a**, 25662-34-4; **4b**, 25662-35-5; **5a**, 18448-47-0; **5b**, 25662-37-7; **6a**, 25662-38-8; **6b**, 25662-39-9; **7a**, 25662-40-2; **7b**, 25662-41-3; **8a**, 1728-38-7; **8b**, 1728-37-6; **9a** (*E*), 15790-88-2; **9a** (*Z*), 15790-87-1; **9b** (*E*), 20515-19-9; **10a** (*E*), 13168-99-5; **10a** (*Z*), 25665-54-7; **10b** (*E*), 13168-97-3; **10b** (*Z*), 13214-13-6; **11** (*E*), 623-43-8; **11** (*Z*), 4358-59-2; **12** (*E*), 4188-69-6; **12** (*Z*), 4188-68-5; **13** (*E*), 10034-13-6; **13** (*Z*), 10034-12-5; **14** (*E*), 5788-17-0; **14** (*Z*), 5739-81-1; methyl 5-methyl-1-cyclopentene-1-carboxylate, 25662-44-6.

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[42] J. Seibl and T. Gauman, *Helv. Chim. Acta*, **46**, 2857 (1963).

[43] K. Biemann, "Mass Spectrometry, Organic Chemical Application," McGraw-Hill, New York, N. Y., 1962, Chapter 5.

Double-Bond Isomerizations in Unsaturated Esters and Enol Ethers. II. Evaluation of Conjugative, Steric, and Polar Effects of Alkyl, Alkoxy, and Alkoxycarbonyl Substituents on Positional and Configurational Equilibria[1]

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Three carbon tautomeric equilibrium data for five- and six-membered cyclic olefinic systems bearing methyl, methoxy, and methoxycarbonyl substituents are analyzed in terms of stabilizing and destabilizing contributions to the observed free-energy changes. Stabilizing energies of 2.3, 6.8, and 2.6 kcal/mol are assigned to alkyl, OCH_3, and CO_2CH_3, respectively. Destabilizing *cis* interactions found for the six-membered ring and acyclic systems are CH_3 *vs.* CO_2CH_3, 1.4 kcal/mol; OCH_3 *vs.* CO_2CH_3, 3.5 kcal/mol; CH_3 *vs.* OCH_3, 0.1 kcal/mol. In the five-membered ring, the destabilizing *cis* interaction of OCH_3 *vs.* CO_2CH_3 amounts to 1.8 kcal/mol. A destabilizing interaction resulting from opposed alkyl–methoxy conjugation is assigned a value of 1.7 kcal/mol.

In 1952, in an analysis of the factors affecting the position of prototropic equilibrium in a number of open-chain unsaturated systems, de la Mare presented an empirical method for correlation of experimentally observed free-energy changes with the individual free-energy contributions of various substituent groups.[3] The group contributions were assessed from available heat of hydrogenation and equilibrium data. Pertinent to the present discussion are the values assigned to alkyl and ester groups, alone and in combination. Thus, a stabilizing value of 2.3 kcal/mol was assigned to each alkyl or substituted alkyl group in an ethylenic system and a stabilizing value of only 1.0 kcal/mol for each α- or β-alkyl substituent in an α,β-unsaturated acid derivative. It was further postulated that the effectiveness of any alkyl group is reduced by 0.5 kcal/mol for each cross- or opposed-hyperconjugation involving another alkyl group. A stabilizing, conjugative interaction of 3.8 kcal/mol was assigned to a carboxylate, ester, or nitrile function. de la Mare's calculated values for the free energy differences in a series of α,β–β,γ-unsaturated acid, ester, and nitrile systems were in reasonably good agreement with the experimental values. It may be noted, however, that the systems tested involved only open chain acid derivatives, most of them capable of configurational as well as positional isomerization, and that the substituent variation in these systems was limited to alkyl groups.

In the present paper, a similar analysis of five- and six-membered cyclic systems bearing methyl, methoxy, and methoxycarbonyl substituents is offered. In these cases, however, the introduction of a geometry-constraining ring and an additional polar group invalidates the simple treatment derived for alkylated acyclic acid derivatives. In order to restore the predictive power of the analysis, it has been necessary to evaluate the magnitude of such steric and polar effects and to include their contributions to the net free energy changes.

Results

The equilibrium data employed in this analysis are presented in the accompanying paper.[4] The free energy changes involved in the equilibrations of these systems will be interpreted according to the following postulates. (1) That the conjugative (or hyperconjugative) interaction of a double bond with an alkyl or substituted alkyl, methoxy, or methoxycarbonyl group stabilizes an ethylenic system. (2) That *cis* interactions

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[1] Abstracted in part from the Ph.D. dissertation of E. E. Waali, University of Wyoming, 1970. Financial support of this investigation under National Science Foundation Grants GP-1517 and GP-6375 is gratefully acknowledged.

[2] National Science Foundation Summer Research Fellow, 1967.

[3] P. B. D. de la Mare, *J. Chem. Soc.*, 1602 (1952).

[4] S. J. Rhoads, J. K. Chattopadhyay, and E. E. Waali, *J. Org. Chem.*, **35**, 3352 (1970).

(steric and polar) between two substituents on a double bond and opposing, conjugative interactions involving two alkyl groups or an alkyl group and a methoxy group contribute to the destabilization of an ethylenic system. (3) That these effects are additive.

The values adopted for the free-energy contributions of these various interactions are summarized in Table I.

TABLE I

FREE-ENERGY CONTRIBUTIONS TO DOUBLE-BOND STABILIZATION

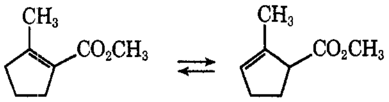
Stabilizing interactions (X)	$\Delta G°_X$, kcal/mol
Alkyl and substituted alkyl	−2.3
CO_2CH_3	−2.6
OCH_3	−6.8
Destabilizing interactions	$\Delta G°_X$, kcal/mol
cis Effects in Six-Membered Cyclic and Acyclic Systems	
CH_3, CO_2CH_3	+1.4
OCH_3, CO_2CH_3	+3.5
OCH_3, CH_3	+0.1
cis Effects in Five-Membered Cyclic System	
CH_3, CO_2CH_3	0.0
OCH_3, CO_2CH_3	+1.8
OCH_3, CH_3	0.0
Opposed Conjugation	
Alkyl, alkyl	+0.5
Alkyl, OCH_3	+1.7

A stabilizing value of 2.3 kcal/mol for alkyl and substituted alkyl groups reflects a representative value deduced from heats of hydrogenation of olefins,[3] calculated values of free energies of olefin isomerization,[5] and experimental values of the free energies of isomerization of methylpentenes reported by Schriesheim and Rowe.[6] Further refinement of this value in terms of primary, secondary, or tertiary structure,[7] or of substituted alkyl groups of the type $CH_2CO_2CH_3$ and CH_2OCH_3,[8] was not attempted. This value of 2.3 kcal/mol for each alkyl or substituted alkyl group is retained even when the group is a substituent in the α,β isomer. In this aspect of our treatment, we depart from the procedure of de la Mare outlined above. Our reason for this change is apparent from consideration of the following equilibria. The identity of the free energy changes for the systems **1ab** and **2ab** implies that alkyl substituents have the same power to stabilize a double bond whether it be isolated or conjugated with the ester function. Thus the α,β and β,γ isomers of system **2ab** are receiving an identical contribution from the β-methyl group so that the net change from the unsubstituted system, **1ab**, is zero.

1ab

$\Delta G^\circ_{100} = +2.1$ kcal/mol

and

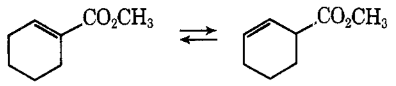


2ab

$\Delta G^\circ_{100} = +2.1$ kcal/mol

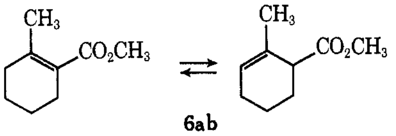
Viewed in this way, the observed free energy change of 2.1 kcal/mol in the systems **1ab** and **2ab** must be attributed entirely to the conjugative interaction of the double bond with the ester function since in both systems the α,β and β,γ isomers are receiving identical net contributions from the alkyl substituents (two in the system **1ab**, three in the system **2ab**). In these cyclic systems, one additional factor is involved in that an asymmetric center is present in the β,γ isomer. This isomer, then, is further favored by an entropy of mixing term (*R* ln 2)[9] which makes an additional free energy contribution of 0.5 kcal/mol at 100° (*RT* ln 2). Corrected for the latter, the conjugative stabilization energy of the ester function amounts to −2.6 kcal/mol, the value shown in Table I.

The system **5ab** is completely analogous to **1ab** and, again, is interpreted to reflect only the conjugative interaction of the double bond with the ester function, diminished by the mixing factor *RT* ln 2. On the other hand, the introduction of a methyl group at the β-carbon atom of the six-membered cyclic system does reduce the free energy change in **6ab** by 1.35 kcal/mol in comparison with its parent, **5ab**. This decrease in free energy is attributed to a *cis* steric destabilization energy of the coplanar methyl and ester groups in the α,β isomer. An independent check of the magnitude of this *cis* interaction is provided by the *cis–trans* equilibrium value for the acyclic methyl 2-butenoate system, **11ab**.



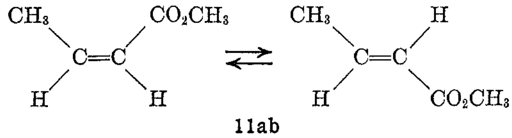
5ab

$\Delta G^\circ_{100} = +2.2$ kcal/mol



6ab

$\Delta G^\circ_{100} = +0.85$ kcal/mol



11ab

$\Delta G°_{117°} = -1.4$ kcal/mol

Comparison of the equilibrium values for the cyclopentene systems, **1ab** and **2ab**, with those of the cyclohexene derivatives, **5ab** and **6ab**, further reveals that the *cis* disposed groups in **2ab** are producing no detectable destabilizing interaction; *i.e.*, the free energy contribution of the *cis* effect of methyl and methoxycarbonyl is virtually zero in the five-membered ring. The absence

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[5] J. E. Kilpatrick, E. J. Prosen, K. S. Pitzer, and F. D. Rossini, *J. Res. Nat. Bur. Stand.*, **36**, 559 (1946).

[6] A. Schriesheim and C. A. Rowe, Jr., *J. Amer. Chem. Soc.*, **84**, 3160 (1962).

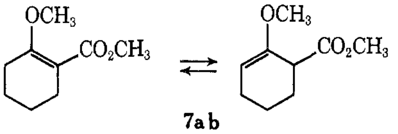
[7] L. Bateman and J. I. Cunneen, *J. Chem. Soc.*, 2283 (1951).

[8] R. Damico, *J. Org. Chem.*, **33**, 1550 (1968), has presented evidence that $CH_2CO_2CH_3$ and CH_2OCH_3 groups are somewhat less stabilizing than alkyl groups, presumably because the inductive effect of the oxygenated function is transmitted through the methylene group. The magnitude of the free energy correction for this effect would be small, however, and less than the uncertainty involved in the value assumed here for the alkyl group stabilization.

[9] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 215.

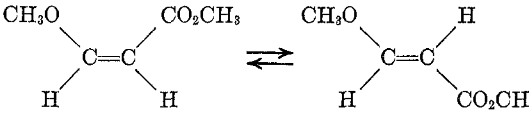
of a *cis* steric interaction in the cyclopentene derivative may reasonably be accommodated by the concept of increased external bond angles (>120°) about the double bond in the cyclopentene ring resulting from the enhanced "s" character of these bonds.[10]

The destabilizing *cis* interaction of the two polar functions, methoxy and methoxycarbonyl, in the six-membered ring is quite large as demonstrated by the strong displacement of the tautomeric equilibrium in **7ab** in favor of the β,γ isomer, in which the interaction is relieved.[11] A value of +3.4 kcal/mol for this interaction may be assessed directly from the observed free energy change by means of the free energy contributions already derived for the alkyl and ester groups. Since both **7a** and **7b** have two alkyl and one methoxy substituent on the olefinic bond, the effects of these substituents cancel one another. The observed free energy change (−1.2 kcal/mol), then, simply reflects the balance of the stabilization afforded by the ester function (−2.6 kcal/mol) and the destabilization due to the *cis* interaction in **7a**, corrected by 0.4 kcal/mol for the mixing contribution to the formation of **7b**. The magnitude of this value of the *cis* interaction of methoxy and methoxycarbonyl is confirmed by the geometric equilibrium value measured for the methyl 3-methoxypropenoates, **14ab**.



7ab

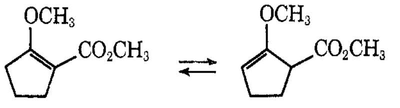
$\Delta G^\circ_{25°} = -1.2$ kcal/mol



14ab

$\Delta G^\circ_{100} = -3.6$ kcal/mol

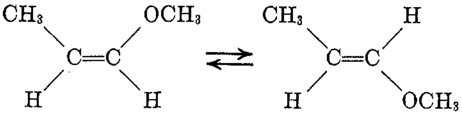
Not unexpectedly, the magnitude of the destabilizing *cis* interaction of methoxy and methoxycarbonyl groups in the cyclopentene system is smaller than that found for the cyclohexene and open chain cases.[12] In the system, **3ab**, the α,β isomer is still dominant, but a marked shift toward the β,γ isomer is apparent when the system is compared with its parent, **1ab**, and its methyl analog, **2ab**. A destabilizing *cis* effect of 1.8 kcal/mol for the two oxygenated functions in the cyclopentene system may be derived in the manner described above for the cyclohexene system.



3ab

$\Delta G^\circ_{25°} = +0.4$ kcal/mol

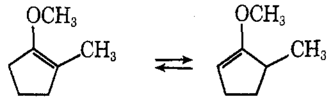
A measure of the *cis* effect of methyl and methoxy groups in the cyclohexene system is provided by the acyclic methyl propenyl ether equilibrium. From this value, and other literature data,[13] it is evident that the *cis* effect of methyl *vs.* methoxy is quite small, even about normal olefinic bonds of ~120°. It may safely be assumed that the *cis* interaction of these same groups in the cyclopentene system is zero.



12ab

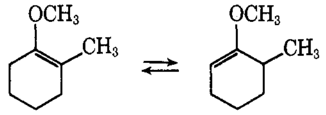
$\Delta G^\circ_{25} = -0.1$ kcal/mol

Examination of the enol ether systems, **4ab** and **8ab**, reveals that the favored isomer in both ring systems is the one with the *less* heavily substituted double bond, a result which can only mean that some effect is more than offsetting the 2.3 kcal/mol stabilization anticipated from the methyl group in **4a** and **8a**. While a part of this effect can be attributed to the diminution of the alkyl stabilizing effect by the extra opposed hyperconjugative effect in the "a" isomer (netting 0.5 kcal/mol in favor of "b"), and an additional 0.4 kcal/mol can be attributed to the mixing contribution in favor of the "b" isomer, there remains a residual of 1.8 kcal/mol in the system **4ab** to be accounted for. In the six-membered cycle, correction for a minor *cis* interaction of 0.1 kcal/mol still leaves an energy term of 1.6 kcal/mol destabilizing **8a** relative to **8b**. We assign this destabilizing contribution of 1.6–1.8 kcal/mol[14] to an opposed conjugative interaction between alkyl and



4ab

$\Delta G^\circ_{25} = -0.4$ kcal/mol



8ab

$\Delta G^\circ_{25} = -0.3$ kcal/mol

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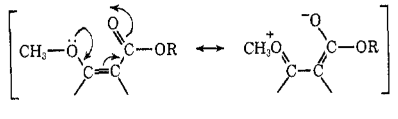
[10] (a) S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spangler, and M. J. Urbigkit, *Tetrahedron*, **19**, 1625 (1963); (b) S. J. Rhoads and A. W. Decora, *ibid.*, **19**, 1645 (1963); (c) S. J. Rhoads, *J. Org. Chem.*, **31**, 171 (1966).

[11] While it might have been expected that extended conjugation between the ether and ester functions would stabilize the α,β isomer relative to the β,γ, this clearly is not the case. Nor is there any infrared spectral evidence for such an interaction; both esters, **3a** and **7a**, exhibit carbonyl stretching bands of a frequency considered normal for simple α,β-unsaturated esters (ref 4). If extended conjugation with the ether function were important in these systems, a detectable decrease in the carbonyl frequency might be anticipated.



[12] The "*cis*" interaction is considered to be a composite of steric and dipole–dipole interactions of the methoxy and methoxycarbonyl groups in the six-membered ring and open chain systems but to reflect only a polar interaction in the cyclopentene system. This view follows from the absence of a *cis* effect between methyl and methoxycarbonyl in **2ab** and the relative sizes of methyl and methoxy as judged by conformational free energy differences. See ref 9, p 236.

[13] T. Okuyama, T. Fueno, and J. Furukawa, *Tetrahedron*, **25**, 5409 (1969).

[14] The difference in the residuals in **4ab** and **8ab** may have its origin in conformational effects as discussed by F. Johnson, *Chem. Rev.*, **68**, 375 (1968). We believe these effects to be minor ones, however, and for the present have chosen to neglect them.

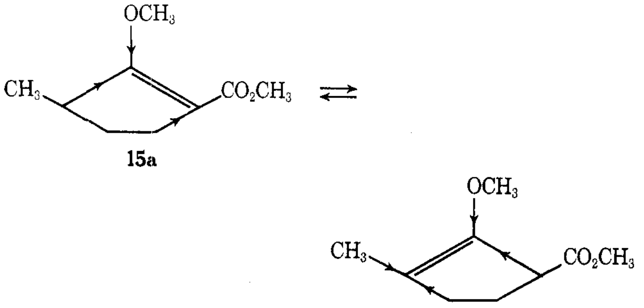
alkoxy groups, similar in nature to that which diminishes the stabilizing power of alkyl groups when opposed on double bonds.[15] Since the "a" isomer in the enol ether systems, **4ab** and **8ab**, has two such oppositions and the "b" isomer has only one, the net effect will be to shift the equilibrium to the less heavily substituted isomer.

The very powerful conjugative interaction of the methoxy group with the double bond has been remarked by others[8,16] and is illustrated by the equilibrium value for the methyl 4-methoxybutenoate system, **10ab**, in which the conjugative power of methoxy is pitted against that of methoxycarbonyl. Application of the values for the free energy contributions of methoxycarbonyl (−2.6 kcal/mol), alkyl (−2.3 kcal/mol), and the opposed alkyl methoxy effect (+1.7 kcal/mol) to the observed free energy change (−2.5 kcal/mol) permits the evaluation of the free energy of stabilization of the methoxy group as −6.8 kcal/mol,[17] the value given in Table I.

$$\underset{\textbf{10ab}}{CH_3OCH_2CH{=}CHCO_2CH_3} \longrightarrow CH_3OCH{=}CHCH_2CO_2CH_3$$

$$\Delta G^\circ_{92} = -2.5 \text{ kcal/mol}$$

As a system suitable for testing the validity of the approach used in this study and the reliability of the values of the free energy contributions deduced, we have examined the system **15ab**, which brings together the three variable groups as substituents on the three carbon allylic system of a cyclopentene ring.


15a **15b**

The free energy change for this system, calculated by considering the free energy contributions of the stabilizing groups and destabilizing effects to each of the isomers, is +0.7 kcal/mol corresponding to an equilibrium composition, 76% **15a** and 24% **15b**. Equilibrated by the iodine–cyclohexane method[4] at 25°, the system showed an actual composition of 67% **15a** and 33% **15b** for $\Delta G^\circ = +0.4$ kcal/mol. We consider the agreement between the calculated and experimental values sufficiently good to warrant further investigation of substituted cyclic systems.

Experimental Section

Infrared spectra were recorded as thin films with a Perkin-Elmer Model 621 spectrophotometer. Nmr spectra were run in carbon tetrachloride solution with TMS internal standard with a Varian HA-100 instrument. A Varian-Mat CH-5 mass spectrometer was used to obtain the mass spectra. Glpc analyses employed 2-m columns of 10% SE-30 on Gas-Chrom P at 120°.

Methyl 3-Methyl-2-methoxy-1-cyclopentenecarboxylate (15a).—Prepared by a Dieckmann cyclization of dimethyl α-methyladipate,[18] 5-methyl-2-methoxycarbonylcyclopentanone (bp 106–108° at 14 mm, ir 1752 s, 1725 s, 1655 w, 1614 w cm^{-1})[19] was treated with diazomethane in the manner described earlier[4] for the preparation of its unmethylated parent. Purified by preparative glpc, **15a** showed ir 1706, 1687, 1624 cm^{-1}; nmr δ 3.81 (s, 3, OCH_3), 3.52 (s, 3, CO_2CH_3) 2.7 (m, 1, allylic tertiary), 2.44 (m, 2, allylic CH_2), 1.97 and 1.35 (m, 2, CH_2), 1.04 (d, 3, CH_3, J = 6.7 Hz); mass spectrum (70 eV) m/e 170 (M^+), 155, 138, 123, 111.

Methyl 3-Methyl-2-methoxy-2-cyclopentenecarboxylate (15b).—Isolated by glpc trapping from isomerization mixtures, **15b** showed the spectral properties: ir 1735, 1690 cm^{-1}; nmr δ 3.58 (s, 3, OCH_3), 3.49 (s, 3, OCH_3), 3.6–3.3 (br m, tertiary allylic H α to ester), 2.5–1.9 (br complex, 4, CH_2CH_2), 1.57 (m, 3, CH_3); mass spectrum (70 eV) m/e 170 (M^+), 155, 139, 123, 111.

Equilibration of 15a and 15b.—Equilibrium was established using the iodine–cyclohexane system described earlier[4] (0.7 M in ester, 0.003 M in iodine). Approached from both sides, the equilibrium composition was found to be 67 ± 1% **15a** and 33 ± 1% **15b** by glpc analysis.

Calculations.—The free-energy calculations follow from the relationships

$$\underset{a\rightarrow b}{\Delta G^\circ} = -RT \ln K$$

$$\underset{a\rightarrow b}{\Delta G^\circ} = \Sigma\Delta G^\circ\text{x(isomer b)} - \Sigma\Delta G^\circ\text{x(isomer a)}$$

Registry No.—**15a**, 25662-45-7; **15b**, 25662-46-8.

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[15] H. O. House and V. Kramer, *J. Org. Chem.*, **28**, 3362 (1963), have proposed the same explanation for the greater stability of the less heavily substituted isomer in tautomeric equilibria involving enolate anions and enol ethers. It is noteworthy that corresponding enol acetates exhibit the opposite relative stabilities; *i.e.*, the more heavily substituted isomer is the more stable. Presumably, these contrasting results reflect the diminished conjugative power of the acetoxy group in opposing the alkyl contribution.

[16] (a) J. Hine, L. G. Mahone, and C. L. Liotta, *ibid.*, **32**, 2600 (1967); (b) C. D. Broaddus, *J. Amer. Chem. Soc.*, **87**, 3706 (1965).

[17] This value may be compared with a value of 5.8 kcal/mol estimated in unpublished work of Doering and Vollrath, quoted in ref 16b. The difference in this value and ours stems mainly from our method of evaluation which takes into account the effect of opposed alkyl and alkoxy conjugation.

[18] J. P. Schaefer and J. J. Bloomfield, *Org. React.*, **15**, 43 (1967).

[19] See ref 10a for characteristics of the infrared spectra of enolizable β-keto esters.