Stereochemistry in Trivalent Nitrogen Compounds. XXVIII. The Conformational Analysis and Torsional Barriers of Imides and Triamides[1]

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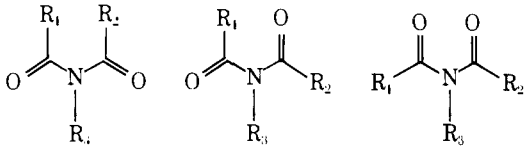
Abstract: The use of low temperature NMR spectroscopy in assignment of configuration and measurement of barriers to torsion about carbonyl–nitrogen bonds in imides and a triamide is described. Configurational assignments were made for six imides (diacylamines), and the barriers to conformational interchange were determined for five of these compounds: diformamide, *E,E* (85%), *E,Z* (15%), 12.9 kcal/mol; *N*-methyldiformamide, *E,E;* diacetamide, *E,Z*, 10.5 kcal/mol; *N*-methyldiacetamide, *E,Z*, 8.0 kcal/mol; dipropionamide, *E,Z*, 10.1 kcal/mol; *N*-methyldipropionamide, *E,Z*, 6.9 kcal/mol. A barrier of 7.5 kcal/mol was obtained for a triamide (triacylamine), *N*-acetyldiformamide. Steric and electronic effects on configurational preferences and rotational barriers are discussed.

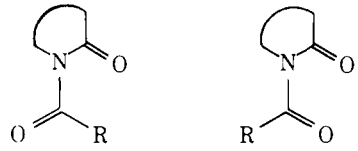
The initial work of Phillips[3a] and Gutowsky[3b] on *N,N*-dimethylformamide demonstrated that overlap between the nitrogen lone pair orbital and the carbonyl π system gives rise to a substantial barrier to rotation about the carbonyl-to-nitrogen bond in amides. Because of this torsional barrier, the amide group constitutes a stereochemically labile configurational unit, and amides which are unsymmetrically substituted at nitrogen exhibit *E–Z* isomerism. Many investigations of the configurational preferences and torsional barriers in a wide range of molecules containing the amide configurational unit have been carried out over the past two decades.[4]

The imide and triamide functional groups also are capable of stereoisomerism, although barriers to configurational change in molecules containing these groups have received considerably less attention. Three configurations (*E,E*, *E,Z*, and *Z,Z*)[5] are possible for acyclic, symmetrical imides (**1**, $R_1 = R_2$). In unsymmetrical imides, where R_1 and R_2 are



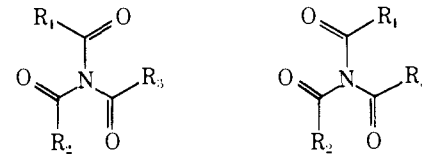
(*E,E*)-**1a** (*E,Z*)-**1b** (*Z,Z*)-**1c**

different, four configurations are possible since **1b** can represent two different stereoisomers. Cyclic imides, in which the two R substitutents are part of the ring, will be constrained to the *E,E* configuration unless the ring is large enough to contain a trans double bond segment. Similarly, *N*-acyl lactams (**2**) are restricted to the *E,Z* and *Z,Z* configurations unless the lactam ring is large.



(*E,Z*)-**2a** (*Z,Z*)-**2b**

Symmetrically substituted triamides can adopt one of two possible configurations (**3a** or **3b**), which can be distinguished by their point groups (C_{3h} and C_s if planarity is assumed). The more symmetrical form, **3a**, has the symmetry of a *triskelion*, the ancient Greek shield device.[6] A triamide can be thought of as being constructed from an acyl radical and an imide radical. There are three possible imide radicals for each triamide and, for the triskelion configuration,



3a (C_{3h}) **3b** (C_s)

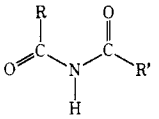
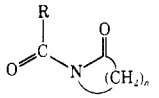
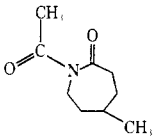
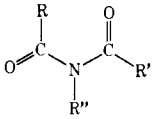
all three fragments have the *E,Z* configuration. By contrast, the pairwise relationships of **3b** are *Z,Z* ($R_1CONCOR_2$), *E,Z* ($R_2CONCOR_3$), and *E,E* ($R_1CONCOR_3$).

As for imides, the number of possible triamide configurations decreases when two of the R groups are incorporated into a sufficiently small ring and increases for unsymmetrically substituted compounds. The two triamides studied in the present work (*N*-acetylsuccinimide and *N*-acetylformimide) provide examples of both situations. The former compound is constrained to a configuration of type **3b**, while the number of possible configurations for compounds of the latter type is increased to four (one triskelion and three non-triskelion configurations).

Although there was no information available when this study was begun concerning the magnitudes of the barriers to stereomutation in imides and triamides, there had been a number of investigations of the configurational preferences in these compounds. A wide variety of experimental tools, including the study of dipole moments,[7–9a] infrared,[8–11] ultraviolet,[9a,11] microwave,[10] and NMR spectroscopy,[9,11] and X-ray diffraction,[12] have been used. The majority of this work is summarized in Table I.

NMR spectroscopy provides a uniquely powerful tool both for determining the configurations of imides and triamides in solution and for studying their barriers to stereomutation. In some cases, symmetry arguments can provide convenient and unambiguous configurational assignments. The acyl groups of the *E,E* and *Z,Z* forms of symmetrical imides are equivalent because of the presence of C_2 axes in these isomers. As a consequence, the chemical shifts of R_1 and R_2 must be equal. The two R groups of the *E,Z* form, however, are diastereotopic and may be expected to exhibit different chemical shifts when torsion about amide bonds is slow on the NMR time scale. While the observation of a single chemical shift might arise from either the *E,E* or *Z,Z* isomer (assuming that stereomutation is slow), the observation of a pair of equally intense resonances for R_1 and R_2 provides evidence for the presence of the *E,Z* configuration.[13] Coalescence of peaks from different conformations and of the resonances from the diastereotopic groups of the *E,Z* form will be observed as stereomutation and topomeri-

Table I. Configurational Studies of Imides

Compd	Phase[a]	Configuration assigned	Method used[b]	Ref
$(HCO)_2NH$	G, L	*E,Z*[c]	Mw, ir	10
$(HCO)_2NCH_3$	Sln	*E,Z*[c]	Dm, NMR	7c
$(CH_3CO)_2NH$	S	*E,Z*[d]	Ir,[e] X-ray	8a,b,g,i, 9a, 12a
	S	*Z,Z*[d]	Ir	8a,b,f,h
	Sln	*E,Z*	Dm, ir	7c, 8e
	S[f]	*Z,Z* and *E,Z*	Ir, X-ray	8d, 12c–e
$(CH_3CO)_2NCH_3$	Sln	*E,Z*[g]	Dm, NMR	7c, 11b
$(C_2H_5CO)_2NH$	S[h]	*Z,Z*	Ir, X-ray	8b,cj,k, 9a, 12b
	Sln	*E,Z*	Ir, dm	8e, 9a
$(CH_3CH_2CH_2CO)_2NH$	S	*Z,Z*	Ir	8b
	Sln	*E,Z*	Ir	8e
$[(CH_3)_2CHCO]_2NH$	S[h]	*Z,Z*	Ir	9a
	Sln	*E,Z*	Ir, dm	9a
$[(CH_3)_3CCO]_2NH$	S[h]	*Z,Z*	Ir	9a
	Sln	*Z,Z*	Ir, dm	9a
$CH_3CO^{15}NHCHO$	Sln	*i*	NMR	9b
$CH_3CH_2CONHCOCH_3$	S	*Z,Z*	Ir	8b,c
	Sln	*E,Z*[j]	Ir	8e
$CH_3CH_2CH_2CONHCOCH_2CH_3$	S	*Z,Z*	Ir	8b
	Sln	*E,Z*[k]	Ir	8e
$C_6H_5CONHCOC_6H_5$	Sln	*E,Z*	Ir, uv, dm	9a
 ($R = C_6H_5$; $R' = CH_3$)	Sln	*E,Z*[l]	Ir, uv, dm	9a
($R = C_6H_5$; $R' = C_2H_5$)	Sln	*E,Z*[l]	Ir, uv, dm	9a
($R = C_6H_5$; $R' = CH(CH_3)_2$)	Sln	*E,Z*[l]	Ir, uv, dm	9a
 ($R = C_6H_5$; $n = 3$)	Sln	*E,Z*	Dm	7b
($R = C_6H_5$; $n = 4$)	Sln	*E,Z*	Dm	7b
($R = C_6H_5$; $n = 5$)	Sln	*E,Z*	Dm	7b
($R = CH_3$; $n = 3$)	Sln	*E,Z*	Dm	7b
($R = CH_3$; $n = 4$)	Sln	*E,Z*	Dm	7b, 11b
($R = CH_3$; $n = 5$)	Sln	*E,Z*	Dm	7b
($R = OC_2H_5$; $n = 4$)	Sln	*E,Z*	Dm	7b
($R = CH_2CH(CH_3)_2$; $n = 4$)	Sln	*E,Z*	Dm	7b
	Sln	*E,Z*	Dm	7b
$(CH_3CO)_2NCH_2CH_3$	Sln	*E,Z*	Dm	11b
$(CH_3CO)_2NCH(CH_3)_2$	Sln	*E,Z*[g]	NMR, dm	11b
$(CH_3CO)_2NCH(CH_3)C_2H_5$	Sln	*E,Z*	Dm, uv	11b
$(CH_3CO)_2NC_6H_5$	Sln	*E,Z*[g]	NMR, dm	11b
$(CH_3CO)_2N(p\text{-}ClC_6H_4)$	Sln	*E,Z*[g]	NMR	11b
$(CH_3CH_2CO)_2NCH(CH_3)C_2H_5$	Sln	*E,Z*	Dm, uv	11b
$[(CH_3)_3CCO]_2NC_6H_5$	Sln	*E,Z*: *E,E*[m]	NMR, dm, ir	11a,b
 ($R = n\text{-}C_4H_9$; $R' = CH_3$; $R'' = CH(CH_3)C_2H_5$)	Sln	*E,Z*[l]	Dm, uv	11b
($R = CH(CH_3)C_2H_5$; $R' = CH_3$; $R'' = CH(CH_3)C_2H_5$)	Sln	*E,Z*[l]	Dm, uv	11b
($R = CH_2CH(CH_3)_2$; $R' = CH_3$; $R'' = CH(CH_3)C_2H_5$)	Sln	*E,Z*[l]	Dm, uv	11b
($R = C_6H_5$; $R' = R'' = CH_3$)	Sln	*E,Z*[l]	Dm, uv, ir	11b
($R = R'' = C_6H_5$; $R' = CH_3$)	Sln	*E,Z*[l]	Dm, uv, ir	11b
($R = R' = CH_3$; $R'' = p\text{-}CH_3OC_6H_4$)	Sln	*E,Z*[g]	NMR	11b
($R = R' = CH_3$; $R'' = CH_2C_6H_5$)	Sln	*E,Z*[g]	NMR, dm	11b
($R = R'' = C_6H_5$; $R' = CH(CH_3)C_2H_5$)	Sln	*E,Z*[l]	Dm, uv, ir	11b
($R = R'' = C_6H_5$; $R' = C(CH_3)_3$)	Sln	*E,Z*[l,n]	Dm, uv, ir	11b
($R = C(CH_3)_3$; $R' = CH_3$; $R'' = C_6H_5$)	Sln	*E,Z*[l]	Dm	11b
$(HCO)_2N\text{–}N(HCO)_2$	S	*Z,Z*: *Z,Z*[o]	X-Ray	12f

[a] G, gas; L, neat liquid; S, solid; Sln, solution. [b] Mw, microwave spectroscopy; ir, infrared spectroscopy; NMR, nuclear magnetic resonance spectroscopy; uv, ultraviolet spectroscopy; dm, dipole moment. [c] A different assignment is made by us for the compound in acetone solution. [d] Two crystal modifications of diacetamide have been found; these correspond to different molecular configurations. [e] A potential barrier of about 27 kcal/mol for rotation about the C–N bonds was estimated[8i] for diacetamide. This value was obtained from an ir study and cannot represent the rotational barrier in solution (see Table II). [f] Complexes with metal halides. [g] The author reports a rotational barrier for this compound. [h] Pellets of the compound in an alkali metal halide were used in one or more of the ir studies of this substance in the solid state. [i] The *Z* configuration was assigned to the partial double bond between the formyl carbon and the nitrogen on the basis of the coupling constant for the formyl and NH protons (+9.8 Hz). [j] The ir spectrum was interpreted in terms of a mixture of both *E,Z* configurations. [k] By analogy to *N*-acetylpropionamide, both *E,Z* isomers are probably appreciably populated. [l] Two *E,Z* isomers are possible for this compound. The authors suggest that the isomer shown predominates. [m] The assignment of the *E,Z* isomer follows clearly from symmetry arguments. The reasoning used in assignment of the *E,E* configuration to the minor form is much less direct, and it could be argued that the singlet observed for this second isomer actually arises from a nonplanar *Z,Z* conformation. [n] The ambient temperature NMR spectrum shows the presence of two isomers in a ratio of 92:8. [o] The *Z,Z* configuration for this compound corresponds to formula 1a, See note 5.

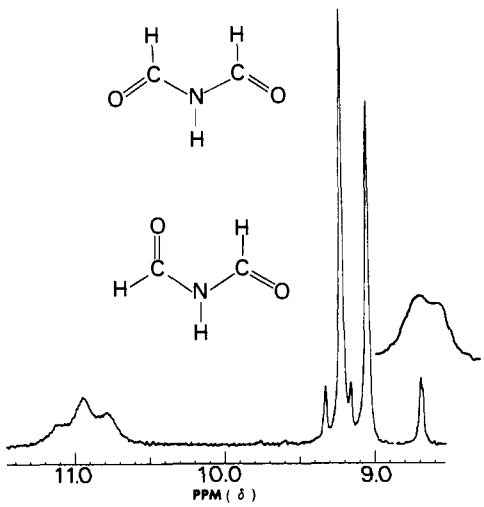


Figure 1. ^{1}H NMR spectrum (60 MHz) of **4a** at −95° in acetone solution. The insert shows the upfield signal at 50 Hz sweep width.

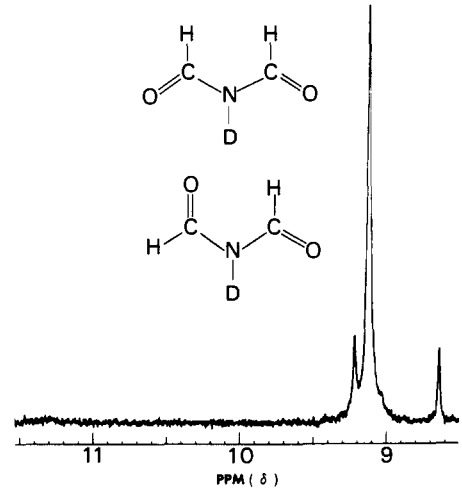


Figure 2. ^{1}H NMR spectrum (60 MHz) of **4c** at −95° in acetone solution.

zation become rapid on the NMR time scale. When rotation about amide bonds is rapid, only a single resonance will be observed for any of the three forms or any mixture of them. The observation of a single resonance therefore does not offer definitive information about configuration unless the low temperature limit has been reached and accidental equivalence of chemical shifts can be excluded. Similarly, the barrier cannot be measured unless more than one configuration is populated, or the single form present has the *E,Z* configuration.

Comparable symmetry arguments can be made for triamides. The triskelion configuration must feature a single resonance if all three R groups are the same. The unsymmetrical (C_s) form has three diastereotopic acyl groups, which should exhibit chemical shift nonequivalence. As a consequence of the symmetry properties of the two configurations, the NMR spectrum for a symmetrical triamide will be dependent on the rate of torsion about amide bonds only if the C_s form is present.

Results and Configurational Assignments

In this study, we have examined the variable temperature proton NMR spectra of six imides: diformamide (**4a**), diacetamide (**5a**), dipropionamide (**6a**), their *N*-methyl derivatives **4b, 5b,** and **6b,** and the deuterated derivative **4c.** In each case, NMR spectral behavior has provided evidence for the assignment of configuration and, for all but two of

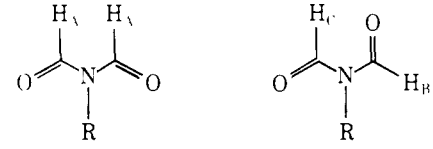
RCONR′COR

4a, R = R′ = H
4b, R = H; R′ = CH_3
4c, R = H; R′ = D
5a, R = CH_3; R′ = H
5b, R = R′ = CH_3
6a, R = CH_2CH_3; R′ = H
6b, R = CH_2CH_3; R′ = CH_3
7, R = H; R′ = $COCH_3$

these compounds, **4a,c** and **4b,** our assignments have been in agreement with those previously obtained using other methods. In all but one case, that of **4b,** variable temperature NMR spectroscopy has permitted measurement of the free energy of activation for stereomutation or topomerization. In order to explore the effect of additional conjugation on amide barriers, we have also examined a triamide, *N*-acetyldiformamide (**7**). The configurational assignments and barriers for these seven compounds are given in Table II and are discussed below.

Diformamide and *N*-Methyldiformamide (4). Previous configurational assignments were available for both diformamide and *N*-methyldiformamide using methods other than NMR spectroscopy (Table I and Discussion below). As indicated above, symmetry arguments can be used to unequivocally identify the *E,Z* configuration, which should give rise to two equally intense resonances for the two diastereotopic protons. In addition, useful information about the configuration of **4a** can be obtained from the HCNH vicinal coupling constants. The cis and trans coupling constants of formamide-^{15}N (1.7 and 13.5 Hz, respectively)[14] provide a model for the HCNH couplings in diformamide, and the difference in magnitude is sufficiently large that reliable configurational assignments can be made.

At −95°, rotation about amide bonds is slow enough that the proton NMR spectra of **4a** and **4c** reflect the presence of two isomers (Figures 1 and 2). The major isomer gives rise to a doublet in **4a** (J_{HNCH} = 10.2 Hz) and a singlet in **4c** (coupling of the formyl protons with the deuterium is not observed at this temperature), while the minor isomer appears as two equally intense singlets in **4c** and two doublets, one of which is barely resolved, in **4a** (J_{HNCH} = 10.0, $J_{HNCH} \simeq 0.7$ Hz). The equally intense doublets of **4a** centered at δ 9.24 and 8.69 must derive from the two formyl

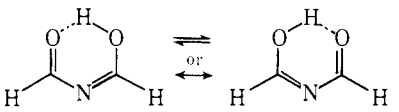


a. R = H
b. R = CH_3
c. R = D

protons, H_B and H_C, in the *E,Z* form. The coupling constants are comparable to, though slightly smaller than, the cis and trans couplings across the amide bond in formamide-^{15}N and permit the assignment of the signals to the two *E,Z* formyl protons; H_C, which has the trans relationship to the N-H proton, must be associated with the low-field doublet having the larger coupling constant, while H_B, which is cis to the N-H proton, gives rise to the upfield doublet with the smaller splitting. The relative chemical shifts of H_B and H_C are in agreement with the expected deshielding of H_C by the anisotropic carbon-oxygen double bond of the other formyl group. The large coupling constant of the major isomer is consistent only with the *E,E* configu-

ration in which the formyl and N-H protons have the trans relationship. This coupling is confirmed by the spectrum of the N-H proton of **4a**, which appears as a broad triplet. Additional peaks are not observed for the N-H proton of the *E,Z* configuration, presumably because these broad peaks of low intensity are obscured by the N-H triplet of the major isomer.

No evidence was obtained for the existence, in measurable amounts, of the enol tautomer **8**. This tautomer would be expected to give rise to a single doublet resonance for the two formyl protons since the shift of the enolic proton from



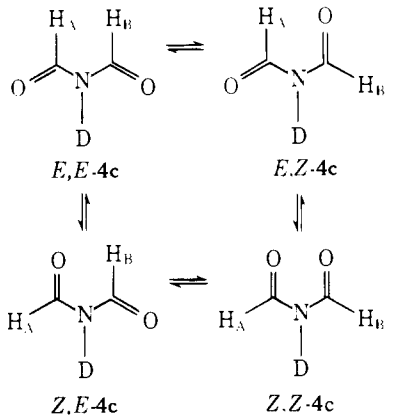
8a **8b**

one oxygen to the other must be very rapid even if the proton were not located equidistant between the two oxygen atoms.[15,16] The close similarity of the chemical shift and the coupling constant in the major isomer of **4a** to those of H_C in the *E,Z* isomer indicates that the major isomer is *E,E*-**4** rather than the cyclic enol tautomer. The absence of the enol tautomer is in accord with the findings of Allenstein and Beyl,[17] who deduced from the infrared spectra of diformamide that the enol form is not present in significant amounts. The decreased tendency of imides to tautomerize, as compared with β-diketones, is not surprising in view of the fact that conjugation is significant even in the keto form of imides.

When the temperature is raised, the three doublets in the NMR spectrum of **4a** begin to broaden and coalesce until finally, at ambient temperature, a single broad resonance is observed for the formyl protons. A combination of two different processes accounts for these changes. The three chemical shifts can be averaged by rotation about the C-N bonds, and rapid intermolecular exchange of the N-H proton results in loss of HCNH couplings. Since intermolecular exchange could have interfered with measurement of the barrier to isomerization, the lineshape analysis was carried out using spectra of the deuterated derivative **4c**.

Possible pathways for topomerization by sequential rotation about C-N bonds are summarized in Scheme I.[18] Ei-

Scheme I



E,E-**4c** *E,Z*-**4c**

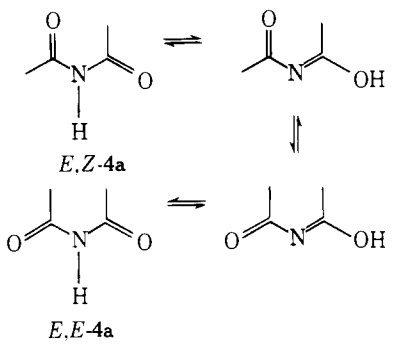
Z,E-**4c** *Z,Z*-**4c**

ther the *E,E* or *Z,Z* isomer could serve as an intermediate in the topomerization of the *E,Z* form (*E,Z*-**4c** ⇌ *Z,E*-**4c**). In principle, the line shapes at intermediate rates of exchange might offer a method for distinguishing between these possibilities. If topomerization of the *E,Z* form were to occur much faster via the *Z,Z* isomer as an intermediate than via the *E,E* isomer, then the two singlets for H_A and H_B in the *E,Z* form of **4c** would be averaged first upon increasing the temperature, while the spectrum of the *E,E* isomer should be essentially unchanged. Only at higher temperatures would the spectrum of the *E,E* form be affected.

However, in practice, the line shapes were not suitable for distinguishing among the various possibilities. Since the singlet which corresponds to the *E,E* form is of much greater intensity than those due to the *E,Z* isomer and lies at an intermediate chemical shift, it does not exhibit much change in line shape. First-order rate constants at the coalescence temperature were obtained by complete lineshape analysis using four mechanistic possibilities: (a) topomerization of *E,Z* via only *E,E* as an intermediate; (b) topomerization of *E,Z* at equal rates via both *E,E* and *Z,Z*; (c) rates of topomerization of *E,Z* via *Z,Z* and *E,E* in a ratio of 20:1; (d) rates of topomerization via *Z,Z* and *E,E* in a ratio of 150:1. The corresponding free energies of activation for topomerization were: (a) 13.0; (b) 12.9; (c) 12.7; (d) 12.6 kcal/mol. Although the spectra do not allow a precise determination of the extent of participation of the *Z,Z* isomer as an intermediate in the topomerization of **4c**, comparison of the experimental spectra taken near the coalescence point with calculated spectra indicates that ratios of 150:1 or greater can be excluded. The reasonably narrow range of values for $\Delta G^{\ddagger}$ obtained (12.6-13.0 kcal/mol) indicates that the results are meaningful even in the absence of detailed mechanistic information. In the discussions which follow, we have arbitrarily selected the barrier which corresponds to topomerization at equal rates via the *E,E* and *Z,Z* forms.

Interconversion of the isomers shown in Scheme I most

Scheme II



E,Z-**4a**

E,E-**4a**

likely proceeds via sequential torsion about carbon-nitrogen partial double bonds. A less probable alternative, outlined in Scheme II for the interconversion of *E,Z*-**4a** and *E,E*-**4a**, involves the intermediate formation of an enol tautomer, which suffers rapid torsion about the carbonyl-to-nitrogen bond. Although available data do not rigorously rule out this type of pathway for the interconversion of isomers, rotation about the C-N bonds of the keto forms appears, at the present time, to be a more probable mechanism. The barriers obtained for **5a** and **5b** (Table II) show that the ability of diacetamide to tautomerize does not result in a faster rate of interconversion of acetyl methyl sites, relative to the *N*-methyl derivative, which cannot tautomerize; the barrier for **5a** is higher by 2.5 kcal/mol.

Comparison of the configurations of diformamide in solution and in the gas phase is made difficult because the relative populations of the *E,E* and *E,Z* forms in the gas phase are not known. Steinmetz[10] presented evidence suggesting that the *E,Z* configuration probably predominates, assuming that the *E,E* isomer would have a larger dipole moment than the *E,Z* form, and therefore would give rise to a much more intense spectrum if it were present. However, the dipole moment of the *E,E* configuration as obtained by

Table II. Configurations and Barriers for Diacyl and Triacylamines

Compd	Solvent	Configuration	$\Delta\nu$, Hz[a]	T_c, °C	k_c,[b] sec^{-1}	k_c,[c] sec^{-1}	$\Delta G^{\ddagger}$,[d] kcal/mol	$\Delta G^{\ddagger}$,[e] kcal/mol
$(HCO)_2ND$ (4c)	Acetone	*E,E* (85%)						
		E,Z (15%)	33.0	−23	19[f]	19[f]	12.9[f]	12.9[f]
$(HCO)_2NCH_3$ (4b)	Acetone	*E,E*						
$(CH_3CO)_2NH$ (5a)	CH_2Cl_2	*E,Z*	17.7	−60	37	74	10.8	10.5
$(CH_3CO)_2NCH_3$ (5b)	Vinyl chloride	*E,Z*	9.2	−113	18	36	8.2	8.0
$(CH_3CH_2CO)_2NH$ (6a)	$CHCl_3$–CH_2Cl_2 2:1	*E,Z*	26.1	−68	36	72	10.4	10.1
$(CH_3CH_2CO)_2NCH_3$ (6b)	$CHClF_2$	*E,Z*	17.6	−133	24	48	7.1	6.9
$(HCO)_2NCOCH_3$ (7)	$CHClF_2$		10.0	−126	20		7.5	*g*

[a] At 60 MHz. [b] Rate constants for topomerization. [c] Except for 4c (see footnote *f*), these are rate constants for rotation to an intermediate conformation which is assumed to be *either* the *E,E or* the *Z,Z* isomer (see also footnote *e*). [d] Free energy of activation for topomerization. [e] Free energy of activation for rotation to an intermediate conformation during topomerization, assuming (except for 4c; see footnote *f*) that only the *E,E* or the *Z,Z* isomer is important as an intermediate. If topomerization proceeded at the same rate via both the *E,E* and *Z,Z* forms, then the rate constants for the *E,Z* ⇌ *E,E* and *E,Z* ⇌ *Z,Z* processes would be equal to the rate constant for topomerization, and the barriers also would be the same. Thus, the rotational barriers in this column are lower limits for 5a, 5b, 6a, and 6b. [f] A range of rate constants and barriers to topomerization ($\Delta G^{\ddagger}$ = 12.6 to 13.0 kcal/mol) were calculated for this compound, depending upon the mechanism assumed for topomerization, as discussed in the text. An arbitrary selection of the values obtained for topomerization at equal rates via both the *E,E* and *Z,Z* forms was made. [g] In the absence of detailed information about the rates of rotation about the three amide C–N bonds, we have used the barrier to topomerization for the rotational barrier of this compound.

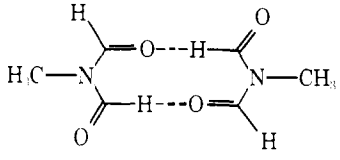
CNDO/2 calculations (vide infra) or estimated from experimental data[7] is lower than that of the *E,Z* configuration.

The infrared spectrum[17] of diformamide in the neat melt has been interpreted[10] in terms of the *E,Z* isomer. This assignment rests largely on the appearance of the two carbonyl (imide I) bands at 1740 and 1679 cm^{-1} for ν_{co}(s) and ν_{co}(as), respectively (the latter being more intense), and on the existence of a peak at 1466 cm^{-1} assigned to the imide II band, which was substantially shifted upon deuteration.

In imides of the *E,Z* configuration, the lower frequency imide I band, ν_{co}(as), is more intense than the higher frequency imide I band, ν_{co}(s), while the ν_{co}(as) peak is weak or absent in *Z,Z* imides. This difference in relative intensities has been used to distinguish between these two configurations. However, the relative intensity of imide I bands is not useful for distinguishing between the *E,Z* and *E,E* configurations. The appearance of the imide I bands in succinimide, which must exist in the *E,E* form, bears a marked resemblance to those of liquid diformamide.[19] The presence of an imide II band may be of some significance because this peak should be absent in the spectrum of an *E,E* imide,[8] as it is in the case of succinimide. The position of the peak in the spectrum of diformamide given the imide II assignment appears to be substantially shifted from the normal position. This absorption in molten **4a** appears at 1466 cm^{-1}, while the corresponding absorptions of diacetamide, dipropionamide, di-*n*-butyramide, *N*-acetypropionamide, and *N*-propionylbutyramide in concentrated solution all fall within the range of 1495–1503 cm^{-1}.[8] It would be somewhat surprising, although possible, for the configuration of diformamide to change from predominantly *E,E* in acetone solution to exclusively *E,Z* in the neat melt. For these reasons, we believe that the configurational assignment for liquid diformamide is not as secure as many of the other assignments of configuration in other imides.

In contrast to the behavior described above for diformamide, no splitting of the formyl and *N*-methyl singlets was observed in the NMR spectra of *N*-methyldiformamide, even at temperatures as low as −100° in deuterated acetone. Similarly, the formyl singlet remains unsplit down to −150° in dimethyl ether (overlap with the solvent resonance prevents observation of the *N*-methyl singlet). Torsion about amide bonds should be slow on the NMR time scale at this temperature, and splitting of the formyl peak would be expected if the *E,Z* configuration were significantly populated. A rough estimate of the barrier for *N*-methyldiformamide (ca. 10 kcal/mol) can be obtained from the barrier in diformamide (12.9 kcal/mol) and the difference (2.5 kcal/mol) between the barriers of diacetamide and *N*-methydiacetamide (Table II). A free energy of activation of 10 kcal/mol corresponds to a coalescence temperature in the neighborhood of −85°, assuming a chemical shift difference of 5 Hz. The behavior observed for **4b** is most consistent with a change from 85% *E,E* for diformamide to exclusively *E,E* for *N*-methyldiformamide within the sensitivity of NMR spectroscopy (~5%).

This conclusion is at variance with the assignment[7c] of a monomeric *E,Z* form in equilibrium with the hydrogen-bonded dimeric structure **9**, based on a dipole moment



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study of **4b** in several solvents. The experimental values for the dipole moment in *p*-dioxane, benzene, and heptane were 1.76, 1.63, and 2.16 D, respectively. These data clearly rule out the possibility of a significant concentration of the *Z,Z* isomer and are, we believe, best accommodated by assuming that the *E,E* isomer predominates. The dipole moment of **4b** in dioxane is intermediate between the values of *N*-methylsuccinimide (1.61 D)[7a] and *N*-methylglutarimide (2.70 D),[7a] both of which must adopt the *E,E* configuration, and is smaller than the value of 3.22 D[7c] for *N*-methyldiacetamide, which has the *E,Z* configuration (vide infra).

In order to obtain further information about the conformational possibilities in these imides, we have carried out CNDO/2 calculations[20] on the three configurations of **4a** and **4b** as well as formamide. In reasonable agreement with the results of microwave studies,[10,21] all three configurations of the imides were calculated to be most stable when the molecules are planar, while a pyramidal structure with a small barrier to nitrogen inversion (4 kcal/mol) was found for formamide. The relative energies and dipole moments for the three configurations of **4a** and **4b** are given in Table III. The dipole moments for the two compounds are in the same order (*Z,Z* > *E,Z* > *E,E*) and are of similar magnitudes. The calculated values are within the ranges of values found experimentally.[7] The relative energies of the three configurations are not very different, and we would not be justified in placing undue reliance on the individual

Table III. Relative Energies and Dipole Moments from CNDO/2 Calculations

	Configuration	Dipole moment, D	Relative energy, kcal/mol
Diformamide (4a)	*E,E*	1.80	0.8
	E,Z	3.53	0
	Z,Z	6.46	1.3
N-Methyldiformamide (4b)	*E,E*	1.75	0
	E,Z	3.49	0.4
	Z,Z	6.28	3.0

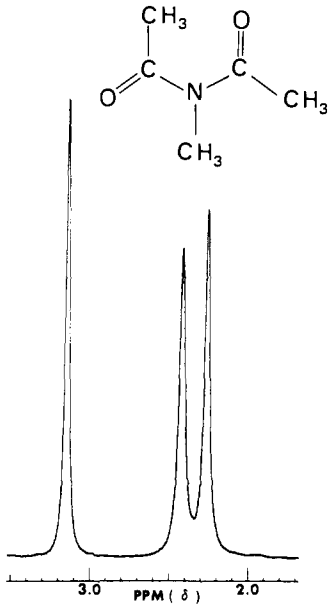
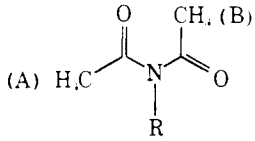


Figure 3. ^{1}H NMR spectrum (60 MHz) of **5b** at −139° in vinyl chloride solution.

values. However, we believe that the trends can be instructive. The reversal of the calculated stabilities of the *E,Z* and *E,E* forms upon introduction of the *N*-methyl group supports our conclusion above that the NMR spectral behavior of **4b** is best accounted for by assuming that the isomer ratio has shifted decisively in favor of the *E,E* configuration.

Diacetamide and *N*-Methyldiacetamide (5). Both diacetamide and *N*-methyldiacetamide had been studied previously and assigned the *E,Z* configuration in solution. Separate crystalline modifications of diacetamide corresponding to the *E,Z* and *Z,Z* configurations have been described (Table I).

The variable temperature proton NMR spectra of **5a** and **5b** confirm the assignments of configuration in solution. At room temperature, the signals from the acetyl methyl groups of both compounds are sharp singlets, which is consistent with fast exchange. As the temperature is lowered (to below −60° for **5a** and below −113° for **5b**), these resonances broaden and split into two singlets of equal intensity. The chemical shift differences are large (17.7 and 9.2 Hz), suggesting a significant effect on the chemical shift of methyl group B by the anisotropy of the carbonyl group of



E,Z-5a, R = H
b, R = CH_3

the other acetyl group. The spectrum of the *N*-methyl group of **5b** (Figure 3) remains unsplit even at low temperatures, as expected for the presence of a single isomer. The free energies of activation for topomerization in **5a** and **5b** were determined at the coalescence point and are given in Table II.

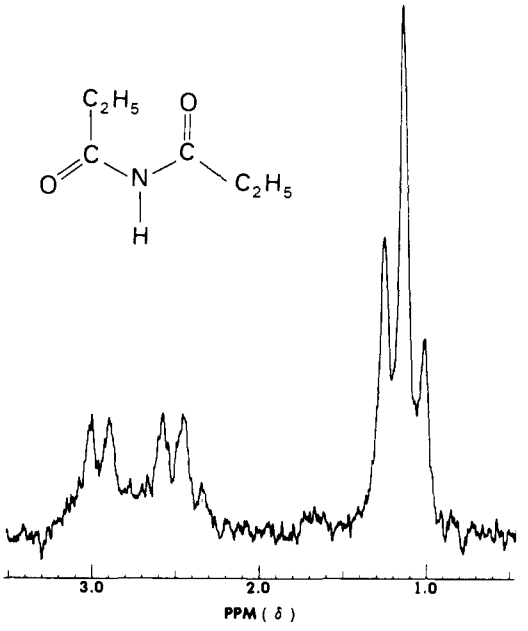


Figure 4. ^{1}H NMR spectrum (60 MHz) of **6a** at −84° in $CHCl_3$-CH_2Cl_2, 2:1.

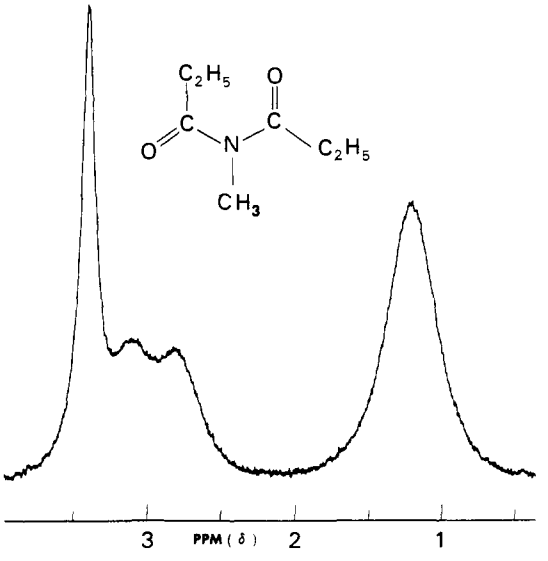


Figure 5. ^{1}H NMR spectrum (60 MHz) of **6b** at −156° in chlorodifluoromethane.

Dipropionamide and *N*-Methyldipropionamide (6). IR spectra, dipole moment data, and X-ray diffraction had been used previously to assign the *Z,Z* configuration to **6a** in the solid state and the *E,Z* configuration in dioxane solution (Table I). The configuration of **6b** had not previously been assigned.

The temperature dependence of the NMR spectra of **6a** and **6b** shows that the *E,Z* configuration predominates in both cases. Two quartets, corresponding to the A portions of the two A_2X_3 spin systems, are found for the two diastereotopic methylene groups in the slow exchange spectrum of **6a** (J_{AX} = 7 Hz, Figure 4), while the chemical shift difference for the methyl triplets is too small to be resolved. The smaller chemical shift difference for the methyl groups is not surprising since they are farther from the anisotropic carbonyl groups. The slow exchange spectrum of **6b** (Figure 5) is similar to that of **6a**, but the signals are considerably

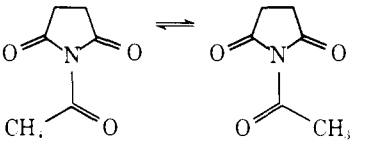
broader because of the lower temperature required, and the individual lines of the two methylene quartets can no longer be resolved; two broad peaks are observed. As for **5b**, the *N*-methyl singlet of **6b** remains unsplit at low temperature, indicating the presence of a single isomer.

The rates at the coalescence temperature were estimated using complete line-shape analysis.

***N*-Acetyldiformamide (7).** With a few exceptions, as noted above, acyclic imides including **5a, 5b, 6a,** and **6b** tend to adopt the *E,Z* configuration in solution. This is fortunate since a barrier to topomerization can be measured only for this configuration. Symmetrically substituted triamides, on the other hand, appear to adopt a configuration (**3a**) in which the acyl groups must exhibit chemical shift equivalence even when rotation about amide bonds is slow. As a consequence, the torsional barrier cannot be determined by DNMR spectroscopy unless the C_s form is appreciably populated.

Most of the evidence for the preferred configurations of triamides derives from infrared and Raman studies of triformamide and *N*-acetyldiformamide.[22] For both compounds, the results were interpreted in terms of the triskelion configuration. These assignments appear quite reasonable as the three imide radicals comprising this form are all of the *E,Z* configuration. The C_s form contains an imide fragment with the *Z,Z* configuration, as noted above. This configuration seems to be significantly destabilized in imides by dipole-dipole interactions, and the existence of the *Z,Z* relationship in **3b** is expected to contribute toward making this form of higher energy.[23] For triamides with groups larger than hydrogen, the C_s forms in which the larger groups are components of imide segments having the *E,E* configuration are likely to be further destabilized by steric interactions.

Two approaches to avoiding the problem of symmetry in the triskelion configuration were tried. In one approach, the triamide was locked into the unsymmetrical configuration by joining two alkyl groups to form a five-membered ring. The methylene groups of *N*-acetylsuccinimide are diastereotopic, and rotation about the acetyl C-N bond results in topomerization, **10a** ⇌ **10b.** The chemical shifts of the two ring methylene groups should be different at tem-



10a 10b

peratures where topomerization is slow. However, no splitting was observed at the lowest temperature attained (−150°). *N*-Acetylsuccinimide suffers from several disadvantages, including the large distance between the ring hydrogens and the acetyl carbonyl group, which probably results in a small chemical shift difference, and the complexity of an AA′BB′ pattern which would be obtained if rotation were slow on the NMR time scale. In addition, it is possible that ground-state destabilization resulting from the unfavorable dipole-dipole interaction in the *Z,Z*-imide fragment significantly lowers the barrier.

A second, more successful, approach was to reduce the symmetry of the triskelion form by replacing one of the formyl groups in triformamide by an acetyl group. The resultant molecule, *N*-acetyldiformamide (**7**) has four possible configurations: one triskelion form and three possible unsymmetrical forms, corresponding to placement of the CH_3 group at the positions occupied by R_1, R_2, or R_3 in **3b.** The triskelion configuration of **7** features two diastereotopic formyl protons whose positions can be interchanged by rotation about all three C-N bonds. This is expected to be the only configuration which is appreciably populated.[22]

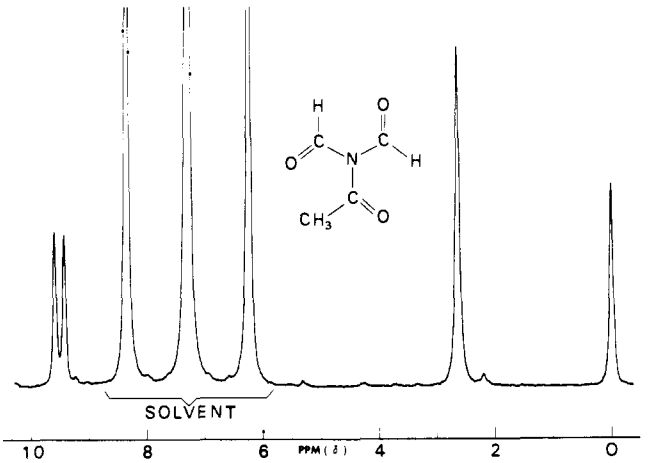


Figure 6. ^{1}H NMR spectrum (60 HMz) of **7** at −142° in chlorodifluoromethane. A small peak at δ 2.2 is due to acetic anhydride, which is present as an impurity.

The proton NMR spectrum of **7** in chlorodifluoromethane at −84° consists of singlets for the formyl and methyl protons, reflecting rapid topomerization. Upon cooling, rotation about amide bonds becomes slow on the NMR time scale, and the formyl resonance broadens and splits into two equally intense singlets centered at δ 9.47 and separated by 10.0 Hz at 60 MHz (Figure 6). The rate constant for topomerization was determined by complete line-shape analysis at −126° and is given in Table II, together with the associated free energy of activation.

The slow exchange spectrum, which features a single peak for the acetyl methyl group, is consistent with the sole presence of the triskelion form suggested by infrared and Raman spectra but does not rigorously rule out the sole presence of a single nontriskelion form.

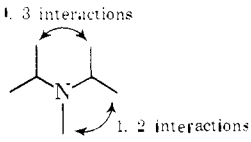
Topomerization of conformation **3a** of *N*-acetylformimide requires rotation about each of the three C-N bonds. It is likely that the transition state involves rotation about a formyl amide bond since acetamides and diacetamides generally exhibit lower barriers than the corresponding formyl compounds.[4]

Discussion

Two factors, dipole-dipole interactions and steric interactions, seem to be of primary importance in determining configurational preferences of imides.

N-Alkyl amides generally adopt the *Z* configuration[4] and, by extension, the *Z,Z* configuration might have been expected to be favored in imides. However, dipole-dipole interactions strongly destabilize this configuration, in which the two carbonyl dipoles are parallel. Significantly, this isomer is only rarely encountered, except in the solid state. In the absence of serious steric interactions, the two forms with lower dipole moments seem to be of comparable stability. Steric interactions should be relatively unimportant for diformamide, and a mixture of the two less polar isomers was observed in acetone solution, with the configuration having the lower dipole moment in excess. This balance can be easily perturbed by steric interactions, which are introduced upon substitution.

Two types of nonbonded interactions which can affect configurational preference may be distinguished: (a) 1,3 interactions; and (b) 1,2 interactions. The displacement of the equilibrium of diformamide by *N*-methyl substitution implies that the 1,2-methyl oxygen cis orientation is more favorable than the 1,2-methyl hydrogen cis orientation. It



may be noted that *N*-methylformamide prefers a conformation in which the *N*-methyl group and the carbonyl oxygen atom are cis. As in the present case, the reasons for this conformational preference are not completely understood.[4]

Substitution of methyl or ethyl groups for the formyl protons of **4a** and **4b** produces severe 1,3-steric interactions in the *E,E* configuration, and **5a, 5b, 6a,** and **6b** are all found experimentally to exist in the *E,Z* configuration. The 1,3 interaction in the *E,Z* configuration between a carbonyl oxygen and an *n*-alkyl group is apparently less destabilizing than the dipole-dipole interaction of the *Z,Z* configuration. When the alkyl group is tertiary, however, the 1,3 interaction of the *E,Z* form is more severe, and the *Z,Z* configuration is preferred for dipivalamide in solution as well as in the solid state.[9a]

The trends in the barriers to stereomutation given in Table II indicate the importance of both electronic and steric factors. Increased conjugation of the amide nitrogen lone pair lowers the barriers to torsion about amide bonds. In amides, rotation about the carbonyl-nitrogen bond involves a transition state in which the nitrogen lone pair is deconjugated from the carbonyl π system. In the transition state for stereomutation or topomerization of imides, the nitrogen lone pair is deconjugated from one carbonyl group but remains conjugated with a second carbonyl. If the free energy of activation for torsion in amides is qualitatively related to the delocalization energy of the amide group, that for imides corresponds to the difference between the delocalization energies of amides and imides. For triamides, the corresponding comparison is between the delocalization in a triamide and an imide.

The experimental evidence demonstrates conclusively that increased conjugation of the nitrogen lone pair lowers torsional barriers. However, a quantitative assessment of whether the substitution of a second and a third acyl group has the same effect depends on the precise series of compounds examined. If one takes formamide as a model compound and examines the successive replacement of hydrogen atoms by acyl groups, the decrease is nearly linear, ca. 5 kcal/mol per acyl group: formamide,[24] 17.8 kcal/mol; **4a,** 12.9 kcal/mol; **7,** 7.5 kcal/mol. If, on the other hand, dimethylformamide is taken as a model, a different result is obtained; the effect of replacement of the first acyl group has a much greater effect than the second. In order to make this comparison, a barrier of ca. 10 kcal/mol is estimated for *N*-methyldiformamide, as discussed above. Using this estimated value, the effect of the second acyl group lowers the barrier by more than twice as much as the third: *N,N*-dimethylformamide,[4] 21 kcal/mol; *N*-methyldiformamide, 10 kcal/mol; **7,** 7.5 kcal/mol. The difference in barriers is greater than any error expected in the estimation of the barrier for **4b.** The reasons for the remarkable difference in the two comparisons are connected with the effects of steric factors and N-methylation on barriers in amides and imides.

The effect of steric factors on amide torsional barriers can be predicted by consideration of steric hindrance in the ground and transition states for torsion. If the amide group were planar, large substituents on the carbonyl carbon and on the amide nitrogen would lie in close proximity, and van der Waals repulsion would lead to ground-state destabilization, possibly via deformations of the ground state which decrease steric repulsion at the expense of amide conjugation. This destabilization should not affect the transition state, in which the substituents at the carbonyl carbon and at nitrogen are staggered. Thus, increasing the steric bulk of substituents at either the carbonyl carbon or nitrogen should lead to lowered amide torsional barriers.

The data supporting this naive expectation are, in some cases, ambiguous.[4] Increasing the size of the substituent at the carbonyl group from hydrogen to methyl or ethyl to isopropyl leads to decreased torsional barriers for *N,N*-dimethyl amides:[4] dimethylformamide, 21 kcal/mol; dimethylacetamide, 18.1 kcal/mol; *N,N*-dimethylpropionamide, 17.6 kcal/mol; *N,N*-dimethyl-2-methylpropionamide, 16.2 kcal/mol. However, the possibility of a superimposed electronic (inductive) effect cannot be excluded. Interestingly, when the substituent becomes very large (e.g., 2,4,6-trimethylphenyl), the barrier again increases: *N,N*-dimethyl-2,4,6-trimethylbenzamide,[25] 22.5 kcal/mol.

The effect of substitutents at amide nitrogen is even more ambiguous. Replacement of the hydrogen atoms of formamide by methyl groups actually raises the barrier: formamide, 17.8 kcal/mol; dimethylformamide, 21 kcal/mol. An increase, although a smaller one, is also observed in the acetyl series: acetamide,[26] 16.9 kcal/mol; *N,N*-dimethylacetamide,[4] 18.1 kcal/mol. It would appear that an inductive effect overwhelms a smaller steric effect. A series of *N,N*-dialkylacetamides[27] does seem to have barriers in the direction expected: *N,N*-dimethylacetamide, 18.1 kcal/mol; *N,N*-diethyl acetamide, 16.9 kcal/mol; *N,N*-di-*n*-propyl acetamide, 17.0 kcal/mol; *N,N*-diisopropylacetamide, 15.7 kcal/mol.

The trends in the imide series are more in accord with those expected on the basis of naive steric arguments. The barrier decreases by 2.4 kcal/mol as the substituent at the carbonyl carbon is changed from H to methyl and suffers a smaller decrease, 0.4 kcal/mol, when the substituent is changed from methyl to ethyl. The corresponding difference in the amide series, between *N,N*-dimethylformamide and *N,N*-dimethylacetamide is about 3 kcal/mol, while *N,N*-dimethylpropionamide appears to have about a barrier of approximately the same magnitude as that in the dimethylacetamide.[4]

Although the effect of substituent changes at the carbonyl group in the imides is comparable to that in the amides, the effect of N-methylation is quite different in the two series. Comparison of the barriers of **5a** and **6a** with those of **5b** and **6b** indicates that replacement of an imide proton by an *N*-methyl group lowers the barrier. The effect is slightly greater for the dipropionamides than for the diacetamides. This is not surprising, given that steric congestion is probably greater in the dipropionamides. It is this reversal in the effect of N-methylation which is responsible for the different assessments of the effects of adding a second and a third acyl group, as discussed above. The reversal may indicate that steric effects are magnified in the imide series, perhaps because of greater planarity, or that inductive effects are less important.

Experimental Section

NMR spectra were obtained using a Varian A-60A spectrometer equipped with a variable temperature accessory. The spectra were calibrated by the side-band technique, using a Hewlett-Packard 523B counter. Chemical shifts are reported in δ units, relative to internal tetramethylsilane. Temperatures were measured by replacement of the sample tube with an open tube containing a suitable solvent and a copper-constantan thermocouple. The melting point of *n*-pentane was used to assure the calibration of the thermocouple-potentiometer system in the low temperature range. Temperatures measured in this way are estimated to be accurate to ±2°. We regard the uncertainty in free energies of activation to be ca. ±0.2 kcal/mol, except for compounds **4c, 6a,** and **6b.** For the

latter two compounds, insensitivity of the line shape to the rate constant near the coalescence point leads to a larger uncertainty, on the order of ±0.4 kcal/mol. There is a comparable uncertainty in the barrier of **4c** (ca. ±0.4 kcal/mol) which arises from the ambiguity in the mechanism for topomerization discussed above.

First-order rate constants at the coalescence point were determined by comparison of experimental spectra with theoretical line shapes obtained by calculation using three computer programs. Program CLASET, used for compounds **6a** and **6b**, was written by Dr. D. Kost. It calculates theoretical spectra of exchanging ethyl methylene protons based upon the quantum mechanical equations for the AB system and using subspectral analysis to simulate coupling to the methyl group. A multisite classical mechanical program for exchanging singlets obtained from Professor M. Saunders was used for compound **4c**. Theoretical spectra for the remaining compounds, **5a**, **5b**, and **7**, were obtained with program CLAS, a classical mechanical two site program for exchanging singlets.

The CNDO/2 calculations were carried out using a slightly modified version of the program given in ref 20. Bond lengths (in Å) and angles were estimated from experimental values (est) or obtained by iteration (it) [formamide: C–N 1.36 (it); C–O 1.25 (it); C–H, 1.09 (est); N–H 1.07 (it); ∠HCO 120° (est); ∠NCO, 120° (est); ∠CNC 120° (est); *N*-methyldiformamide: C–N 1.36 (est); C–O 1.27 (it); C–H 1.09 (est); N–CH_3 1.47 (est); ∠HCO 120° (est); ∠NCO 120° (est); ∠CNC 120° (est); ∠HCH (109.5° (est)].

Diacetamide and *N*-methyldiacetamide were obtained commercially from Aldrich and Eastman Organic Chemicals, respectively. The *N*-methyldiacetamide was purified by column chromatography on Florisil, followed by distillation.

Diformamide, (4a) and Diformamide-*d*[17] (4c). Dry acetic acid (25.3 g) was added dropwise to a cooled (0°) suspension of 40 g of the sodium salt of diformamide[17] in 900 ml of anhydrous ether. The cooling bath was removed, and the mixture was stirred at room temperature for 24 hr and then filtered. Most of the ether was removed in vacuo, and 125 ml of petroleum ether was added. The solid was filtered, washed with petroleum ether, dried in vacuo over anhydrous calcium sulfate, and recrystallized from ether, yield 23.0 g, mp 39–40° (lit.[17] mp 41.5°).

The N-deuterated imide was prepared from diformamide by exchange with D_2O and removal of the D_2O at room temperature under high vacuum, followed by crystallization from ether. Finally, most of the small amount of **4a** remaining (ca. 10%) was converted to **4c** by treatment of an acetone solution of the imide with D_2O and removal of the deuterated water by drying over molecular sieves.

***N*-Methyldiformamide[17] (4b).** The sodium salt of diformamide (40 g) was combined with dimethyl sulfate (53.1 g) and the mixture warmed in a flask equipped with reflux condenser and drying tube until a *vigorous* reaction began *suddenly*. The flask was immediately cooled in an ice bath and, after the reaction had subsided, the mixture was heated at 200° for 30 min. After being allowed to cool to room temperature, the reaction mixture was extracted with ether. Removal of the ether at the rotary evaporator and distillation of the residue under reduced pressure afforded the product as a clear, colorless liquid. The room temperature NMR spectrum (neat liquid) exhibited singlets at δ 3.03 (methyl protons) and 9.11 (formyl protons) in a ratio of 3:2 (lit.[7c] δ 3.05 and 9.10, neat liquid).

Dipropionamide (6a). Propionamide (85.7 g), propionic anhydride (634 ml), and a catalytic amount of dry HCl were heated together (bath temperature, 163°) for 45 min in a flask equipped with reflux condenser and drying tube. The product solidified upon distillation of propionic acid and excess anhydride under reduced pressure and was recrystallized twice from dichloromethane, yield 24.5 g, mp 152.5–153.5° (lit.[28] mp 154°).

***N*-Methyldiproplonamide[29] (6b).** A mixture of methylamine hydrochloride (51 g) and propionic anhydride was allowed to react for 4 hr at reflux temperature, while a stream of nitrogen was passed through the solution. Distillation of the reaction mixture afforded 31 g of crude product, which was purified by chromatography on Florisil, followed by distillation, yield 16.5 g. A gas chromatogram (10-ft 10% FFAP on Chromosorb W, 135°) indicated a purity of >99%.

***N*-Acetyldiformamide (7).** The sodium salt of **4a** was added with stirring to ice-cold[30] distilled water (1.8 l.), and a cold aqueous solution of $AgNO_3$ (30.3 g in 120 ml) was added *immediately*. The silver salt precipitated as a voluminous white solid which was collected by filtration and washed with ice water (200 ml) and methanol (400 ml). The solid was stirred with 400 ml of a mixture of methanol and ether (1:1), filtered, washed three times with 100-ml portions of ether and dried overnight in a vacuum desiccator, yield 31.2 g of $(HCO)_2NAg$.

A suspension of the finely powdered silver salt (31.2 g) in 30 ml of dry ether was cooled to 0°, and an ethereal solution of acetyl chloride (45.1 g in 40 ml) was added dropwise with stirring. The mixture was allowed to stir at 0° for 48 hr and filtered. The solid was washed with 100 ml of dry ether, and the combined ethereal solutions were concentrated under vacuum. Distillation of the residue under reduced pressure afforded the triamide (10.5 g). In addition to peaks for the formyl and methyl protons of *N*-acetylformimide, the NMR spectra of each of the fractions exhibited small absorptions near δ 2.2 due to trace amounts of acetic anhydride (Figure 6).

***N*-Acetylsuccinimide.[31–33]** A mixture of succinimide (50 g) and acetic anhydride (386 ml) was refluxed for 225 min and cooled to room temperature. The excess acetic anhydride was removed under vacuum and the residue distilled (55.9 g of distilled product). A small amount of the compound (15 g) was recrystallized from ether, yield 10.3 g, mp 41–42° (lit.[32] mp 40–41°).

References and Notes

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(5) (a) Before the introduction of the *E–Z* nomenclature,[5b] the descriptive designations W for the π system in **1a**, S (or sickle) for that in **1b**, and U for that in **1c** were used. These can be ambiguous; the π system has the W shape in *E,E*-diacetamide, while the carbon–nitrogen skeleton has the U form. The configurational designations for amides and imides are derived from examination of priority sequences in the canonical structures which have double bonds between the carbonyl carbon and amide nitrogen. Those given for **1a**, **1b**, and **1c** imply the priority sequences: R < O and R′ < COR and correspond to the correct configurational designations in the majority of instances, including all of the compounds examined in this study. In a few situations, the priority sequences are different and the configurational designations will also be different. The stereoformula for *E,E*-1,1-diacetylhydrazine, for example, corresponds to **1c** rather than **1a** since NH_2 > $COCH_3$. Discussions below, except as indicated, assume the relationships given between configurations and configurational designations. (b) J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Am. Chem. Soc.*, **90**, 509 (1968).

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Kinetic Differentiation Between I_d and D Mechanisms for Axial Base–Ligand Exchange in Alkyl(base)cobaloximes

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Abstract: Axial base–ligand exchange in alkyl(base)cobaloximes has been shown to occur by a purely dissociative (D) mechanism in chloroform. A method for distinguishing between closely related mechanisms solely on the basis of kinetics was demonstrated. Pyridine was found to react approximately ten times faster than tri-*n*-butylphosphine with the five-coordinate "base-off" complex produced during the ligand exchange process, even though tri-*n*-butylphosphine coordination is thermodynamically favored. A linear correlation between log K and $\bar{\sigma}$ for substitution of piperidine by various 4-substituted pyridines was found. Factors controlling thermodynamic and kinetic coordination of bases are discussed.

It has been proposed that exchange of the 5,6-dimethylbenzimidazole axial base in coenzyme B_{12} affects the reactivity of the carbon-cobalt σ-bond.[2] Considerable evidence has been presented that during enzymatic reactions which involve coenzyme B_{12} the carbon-cobalt bond is broken.[3] It is reasonable to assume that the carbon-cobalt bond may become activated for rupture by prior axial base ligand dissociation. It is significant therefore to initially study the mechanism of ligand exchange in coenzyme B_{12} or a suitable model system. The alkylcobaloximes have been shown to serve as good models for coenzyme B_{12}, the pyridine-based cobaloxime being especially appropriate due to the similarity of the pyridine and imidazole structures. For this reason, methyl(pyridine)cobaloxime was chosen as the substrate for initial study.

Considerable current interest exists in the mechanisms of ligand exchange in organometallic compounds. It has only been possible in a few cases, however, to establish the detailed nature of the mechanism. The study of a mechanism can be divided into two segments:[4] the dissection of the mechanism into elementary steps which is referred to as the stoichiometric mechanism, and the analysis of the detailed nature of the individual steps which is the study of the intimate mechanism. As was pointed out by Langford and Gray,[4] obtaining information on the intimate mechanism (e.g., determining whether the exchange is associative or dissociative in nature) is generally a relatively simple process, while establishing the stoichiometric mechanism is difficult. In most instances, a large amount of data from several different types of kinetic and stereochemical studies must be analyzed before a firm conclusion can be made concerning the stoichiometric mechanism. This situation results from the inability of kinetics to distinguish between two or more mechanisms when the exchanges are studied in coordinating solvents. For instance, for dissociative mechanisms when exchanges are performed in water, it is only possible to observe replacement of the leaving ligand by water (hydrolysis) and the subsequent replacement of water by entering ligand (anation).

In contrast, in noncoordinating solvents, two distinct dissociative mechanisms can be distinguished for reactions which proceed to completion.[4] The dissociative interchange (I_d) process involves the formation of an outer-sphere complex, $M(L)_nX\cdot Y$ (eq 1), followed by the replacement of X by Y in the outer coordination sphere (eq 2a). Then X dissociates from the outer coordination sphere (eq 2b). In most cases eq 2b is much faster than eq 2a, and, for kinetic purposes, they can be considered as a single step.

$$M(L)_nX + Y \overset{K}{\rightleftharpoons} M(L)_nX\cdot Y \quad (1)$$

$$M(L)_nX\cdot Y \xrightarrow{k_{2a}} M(L)_nY\cdot X \quad (2a)$$

$$M(L)_nY\cdot X \xrightarrow[\text{fast}]{k_{2b}} M(L)_nY + X \quad (2b)$$

The purely dissociative (D) mechanism (eq 3 and 4) involves dissociation of the leaving group to give an intermediate, $M(L)_n$, of reduced coordination number.