Further Studies of Proton Nonequivalence in N-Substituted Amides and Related Compounds[1a]

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Received May 17, 1966

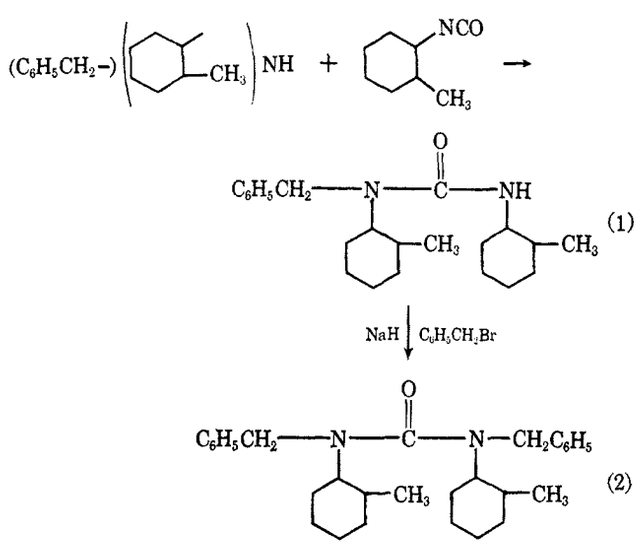
Further studies of proton nonequivalence in N-aryl amides with unsymmetrical *ortho* substitution in the benzene ring are reported. These further studies included the observation of nonequivalence in formamides, other amides with a variety of substituents, carbamylphosphonates $[(RO)_2O{=})P(O{=})CN<^{R''}_{R'}]$, a carbamylmethylenephosphonate, a urea, and a sulfonamide. Possible interaction between slow rotation around the benzene–nitrogen bond and around the carbonyl–nitrogen bond is discussed, and an attempt is made to rationalize the chemical shifts between nonequivalent protons.

In previous papers[2,3] reports were made of the investigations of proton nonequivalence in N-aryl amides with *ortho* substitution in the benzene ring. The purpose of this paper is to report continued studies of proton nonequivalence and related phenomena in a further variety of compounds.

Experimental Section

The general experimental conditions and the methods of preparing and purifying compounds are the same as those employed previously.[2b] Except where otherwise noted, all nmr data are for 25 wt % solutions in $CDCl_3$.

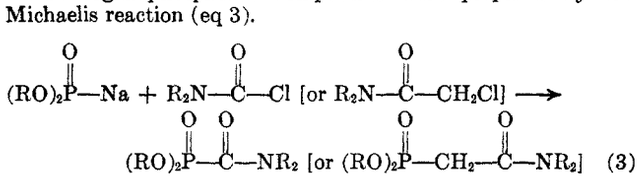
Compound XXVII was prepared stepwise (eq 1 and 2).[4]



(1)

(2)

The organophosphorus compounds were prepared by the Michaelis reaction (eq 3).



(3)

This reaction proceeds in a very straightforward manner except for $(CH_3O)_2P(=O)$ derivatives, with which an extensive side reaction produces a great deal of a soapy, white solid. The carbamyl chloride (or chloroacetamide) intermediates for the reaction were produced by treating the proper amine with phosgene (or chloroacetyl chloride).

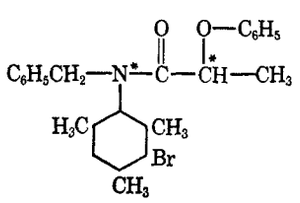
Results and Discussion

Results are reported primarily in Table I. However, the illustrative pmr scans in Figure 1 also contain data.

Degree of Nonequivalence.—The degree of nonequivalence of the methylene protons for the N-ethyl derivatives is evidently very much a function of size of the group R′ and the *ortho* substituent on the benzene ring (See Table I and also data in ref 2.). Increasing the sizes of these groups increases the value of $\langle \nu_1 - \nu_9 \rangle$ almost without exception. Apparently some molecular motion(s) that tend to produce approximate symmetry for the geminal protons are less effective as the sizes of these groups increase. Of course, a number of internal molecular motions each contribute to rotamer preference and/or to the internal field gradient. However, it is especially easy to see that rotamer preference around the ethyl–nitrogen bond might become more pronounced with increasing size of the substituent groups. It is also possible that with larger R′ and *ortho* ring substituents the bonding to nitrogen is forced more out of plane for steric reasons, which could increase the magnetic field gradient at the geminal protons.

The outstanding exception to this trend with size is compound XIII for which the geminal protons are equivalent. The approximate symmetry produced by substitution in both *ortho* positions destroys observably separate identities for the protons. In particular, rotamer preference around the ethyl–nitrogen bond may be drastically reduced, since now it is necessary that an *ortho* substituent be positioned on each side of the approximate plane of the nitrogen atom. This physical arrangement probably improves the approximation to planarity, because the steric crowding is about the same on both sides of the plane.

The necessity for consideration of factors in addition to rotamer preference is apparent from the behavior of the N-benzyl analog XIX, which exhibits nonequivalence. Still further demonstration of the subtle-



A

(1) (a) The information contained in this article was developed during the course of work under Contract AT(07-2)-1 with the U. S. Atomic Energy Commission.

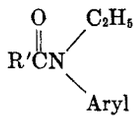
(2) (a) T. H. Siddall, III, and C. A. Prohaska, *Nature*, **208**, 582 (1965); (b) T. H. Siddall, III, and C. A. Prohaska, *J. Am. Chem. Soc.*, **88**, 1172 (1966).

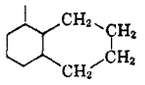
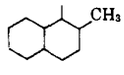
(3) T. H. Siddall, III, *Tetrahedron Letters*, 4515 (1965).

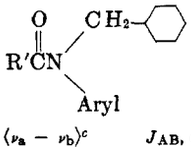
(4) R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1953.

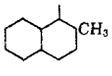
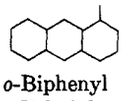
TABLE I

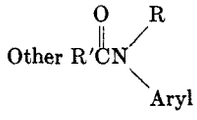
PMR DATA[a]



Compd	R′	Aryl	$\langle \nu_1 - \nu_2 \rangle$[b]	Remarks
I	2-Propyl	*o*-Chlorophenyl	0.67	
II	Methyl	2-Bromo-4-methylphenyl	0.77	
III	Methyl	*o*-Iodophenyl	1.02	
IV	H	*o*-Methylphenyl	Equivalent	Amide isomers
V	H	*o*-Ethylphenyl	Equivalent at 40°	Amide isomers
VI	Methyl		Nonequivalent, broadened at −40° 1.00	
VII	Methyl	2,3-Dimethylphenyl	0.80	
VIII	$C_6H_5OCH_2$	*o*-Methylphenyl	0.9	OCH_2 protons nonequivalent, $\langle \nu_a - \nu_b \rangle \simeq 0.04$ ppm
IX	Cl_3C	*o*-Methylphenyl	Nonequivalent (see discussion)	
X			1.02	
XI			0.90	
XIA	Ethyl		0.87	
XII	Cl		0.62	
XIII	Methyl		Equivalent	
XIV	*t*-Butyl	*o*-Biphenyl	1.08	
XV	$CH_2{=}CHCH_2$	*o*-Methylphenyl	0.72	



Compd	R′	Aryl	$\langle \nu_a - \nu_b \rangle$[c]	J_{AB}, cps	Remarks
XVI	Methyl	*o*-Methylphenyl	0.89	14.0	
XVII	Methyl	*o*-Ethoxyphenyl	0.65	14.9	OCH_2 gives two sets of signals ~0.05 ppm apart
XVIII	$(Ethyl)_3C$	*o*-Methylphenyl	1.75	14	
XIX	Methyl		0.60	13.4	
XX	Methyl		1.43	13.5	
XXI	*t*-Butyl	*o*-Biphenyl	1.88	14.2	
XXII	*t*-Butyl	*o*-Ethylphenyl	1.77	13.8	



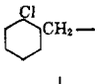
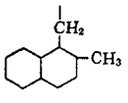
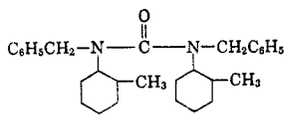
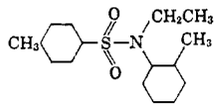
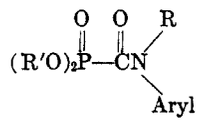
Compd	R′	R	Aryl	Data and remarks
XXIII	Methyl		*o*-Methylphenyl	$\langle \nu_a - \nu_b \rangle = 0.78$, $J_{AB} = 15$ cps
XXIV	Methyl		*o*-Methylphenyl	$\langle \nu_a - \nu_b \rangle = 0.73$, $J_{AB} = 14.4$ cps
XXV	Methyl	$\overset{\gamma}{CH_2}{=}\overset{\beta}{CH}\overset{\alpha}{CH_2}$	*o*-Methylphenyl	$\langle \nu_1 - \nu_5 \rangle^d$ (1st–5th signal of CH_2N octet) = 0.87, J_{AB} = 14.6 cps; J for Hα at low field to Hγ = 2 cps; J for Hα at high field to Hγ = 1.5 cps
XXVI	$(i\text{-Butyl-O})_2\overset{O}{\overset{\|}{P}}CH_2$	Ethyl	*o*-Methylphenyl	(See Figure 1)

TABLE I (*Continued*)

Miscellaneous

Compd		Remarks
XXVII		A substituted urea, Figure 1
XXVIII		A sulfonamide $\langle \nu_1 - \nu_9 \rangle$ = 0.78 ppm at −40°, broad hump at 40°



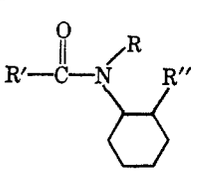
Carbamylphosphonates

Compd	R′	R	Aryl	Data and remarks
XXX	Methyl	Ethyl	*o*-Methylphenyl	See Figure 1a
XXXI	*i*-Butyl	Methyl	*o*-Methylphenyl	Major/minor (~5/1) amide isomers; two equal sets γ-Methyl signals (*i*-butyl) for major, one set for minor; N-methyl in major isomer coupled to phosphorus ~1.3 cps, coupling to P in minor isomer not resolvable. High multiplicity of CH_2OP signals not analyzed
XXXII	*i*-Butyl	Ethyl	*o*-Methylphenyl	Major/minor (~5/1) amide isomers; two equal sets γ-methyl signals for major, one for minor; major and minor β-methyl (N-ethyl) signal sets, major coupled to phosphorus J = 1.2 cps, minor coupling not resolved. Probably two CH_2O sets for major, one for minor; NCH_2 probably nonequivalent for both major and minor
XXXIII	*i*-Butyl	Ethyl		Major/minor (~5/1) amide isomers; two equal sets γ-methyl signals (centers at 0.89 and 0.45 ppm), one set for minor (1.10 ppm); only one β-methyl set observable; only one CH_2O set (3.91 ppm) for major and one for minor (3.22 ppm); NCH_2 probably nonequivalent for both isomers
XXXIV	*i*-Propyl	Methyl		See Figure 1b
XXXV	2-Propyl	$C_6H_5CH_2$		Isomer ratio not certain; four equal β-methyl signals sets for major isomer −1.30, 1.22, 0.82, 0.39 ppm
XXXVI	Ethyl	$C_6H_5CH_2$	*o*-Methylphenyl	Major/minor (5/1) amide isomers. Low-field half of AB pattern of NCH_2 protons apparently coupled to phosphorus (2.0 cps) in major isomer. High-field half mingles with other signals and cannot be distinguished; minor NCH_2 lost in noise. Two β-methyl sets for ethyl of major isomer; one broadened minor set

[a] All data for 25% solution in $CDCl_3$ except where noted. [b] Measured distance between corresponding signals of the halves of the AB spectrum (*i.e.*, first and ninth signals) in parts per million. [c] Chemical shift between methylene protons. [d] Measured distance between first and fifth lines of AB spectrum.

ties that are apparently involved is shown[3] by compound A above which has two separable epimeric isomers. The geminal protons are very nearly, if not entirely, equivalent in one epimer, but nonequivalent in the other.

Interaction with *cis–trans*-Amide Isomerism.—Slow rotation around the amide (carbonyl–nitrogen) bond[5] could add further complications to the pmr spectra of the types of amide discussed in this as well as the previous paper;[2] yet, in general (with exceptions to be noted later) no second sets of pmr signals are observable in the spectra of amides of the type shown



even at low temperature. The absence of observable amide isomerism could depend on either of two explantions:[5] (1) rotation around the amide bond is too rapid; or (2) one amide isomer is thermodynamically so much more stable than the other that the population of the less stable isomer is too low to permit its direct observation.

It seems probable that both factors 1 and 2 come into play depending on the temperature and on the size of the R groups. For acetamides, the maximum temperature at which dual signal sets should be observable is about 30°; with larger R′ groups this temperature should be even lower. This conclusion about acetamides is derived from the following observations: (a) line broadening in the ethyl signals for diethylformamide (DEF) as a 25% solution in *sym*-tetrachloroethylene begins to be observable at 110° (as the temperature is lowered) with our Varian A-60 spectrometer in its normal state of operation; (b) the analogous temperature for diethylacetamide (DEA) is 60°; and

(5) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

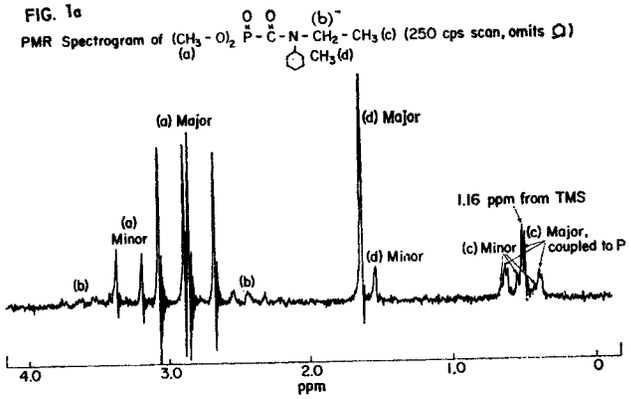


FIG. 1a
PMR Spectrogram of (CH3-O)2 P-C-N-CH2-CH3(c) (250 cps scan, omits Ω)
(a) (b) (d)
(a) Major
(d) Major
1.16 ppm from TMS
(a) Minor
(c) Minor
(c) Major, coupled to P
(d) Minor
(b)
4.0 3.0 2.0 1.0 0
ppm

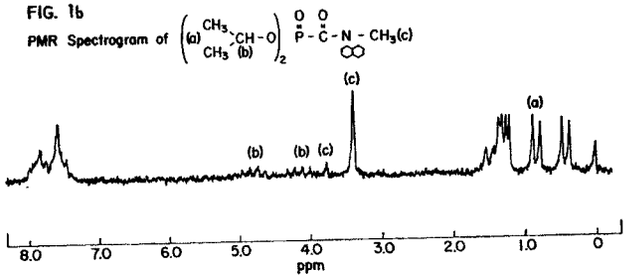


FIG. 1b
PMR Spectrogram of
(a) (b) (c)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
ppm

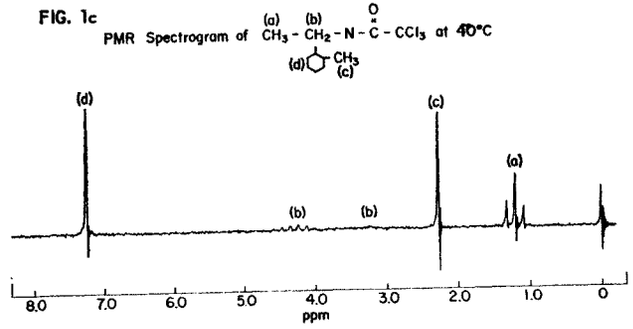


FIG. 1c
PMR Spectrogram of CH3-CH2-N-C-CCl3 at 40°C
(a) (b) (c) (d)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
ppm

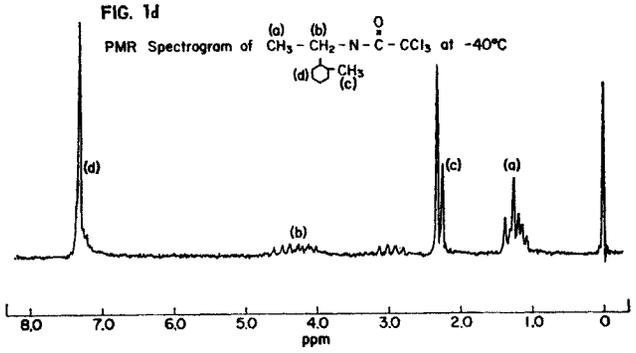


FIG. 1d
PMR Spectrogram of CH3-CH2-N-C-CCl3 at -40°C
(a) (b) (c) (d)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
ppm

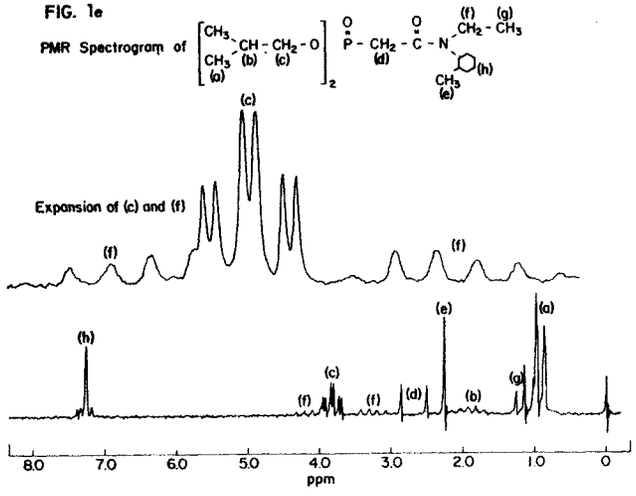


FIG. 1e
PMR Spectrogram of
Expansion of (c) and (f)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
ppm

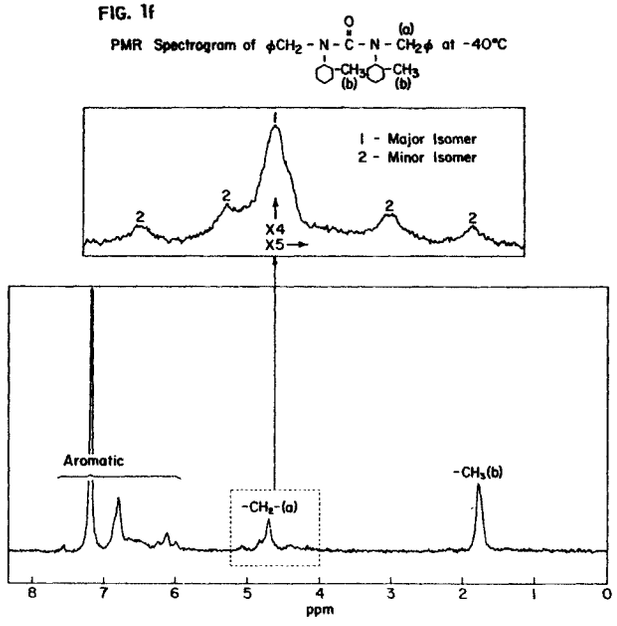
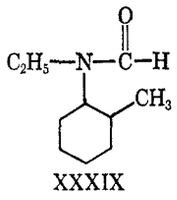


FIG. 1f
PMR Spectrogram of φCH2-N-C-N-CH2φ at -40°C
1 - Major Isomer
2 - Minor Isomer
X4
X5
Aromatic
-CH2-(a)
-CH3(b)
8 7 6 5 4 3 2 1 0
ppm

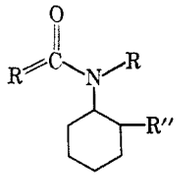
Figure 1.



XXXIX

(c) the analogous temperature for compound XXXIX is 80° (*cis–trans* isomer abundance ratio is ~3:1). If the temperature increment (50°) between DEF and DEA is applied to compound XXXIX then the analogous temperature for the corresponding acetamide (I of ref 2), should be 30°;[6a] yet we have not observed dual sets of signals in compound I of ref 2 or in analogs with larger R′ groups even at −40°. Even if this crude analysis (which does not consider interactions between R′ and R) is in error to some extent, it seems highly unlikely that this temperature should be as low as −40°. Since rotation about the amide bond would not be expected to be rapid for this class of compounds at −40°, factor 2 must also be important.

Slow rotation around the amide bond may have another, more subtle effect on the pmr spectra of these amides. Adams[6b] pointed out some time ago that for some compounds very similar to those examined in our study there is a strong analogy with biphenyls. This becomes more obvious when the amide formula is written



The nitrogen atom and its other substituents are roughly equivalent to the second ring in the biphenyl. In so far as this analogy is valid, then, on the basis of Westheimer's analysis[7] of biphenyl rotation, bending and twisting of other bonds should make important contributions to the energetics of rotation around the nitrogen–benzene bond. As a consequence, rotation around the nitrogen–benzene bond would probably be accompanied by twisting of the amide bond. An amide with less double-bond character (more rapid rotation, easier twisting in the amide bond) should exhibit more rapid rotation around the nitrogen–benzene bond as well.

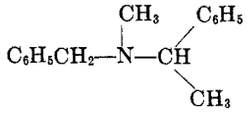
Experimental observation supports such a theory that the amide bond influences slow rotation around the nitrogen–benzene bond. Ureas show no evidence of amide isomerism,[8] which indicates less double-bond character than for simple amides; rotation around the nitrogen–benzene bond should thus be more rapid in ureas than in amides. In accordance, nonequivalence of geminal protons in an appropriately substituted urea (XXVII) does not become observable, as the temperature is lowered, until about −40°. Similar behavior was observed for a substituted sulfonamide (Table I, XXVIII).

(6) (a) This prediction presumes, of course, that there is no marked difference in solvent effects between tetrachloroethane and chloroform. (b) R. Adams, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **10**, 91 (1949).

(7) F. H. Westheimer, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 12.

(8) E. K. Dukes and T. H. Siddall, III, *J. Inorg. Nucl. Chem.*, in press.

The behavior of amines (no double-bond character) supports this view further. Although additional investigation of amines with an *ortho*-substituted benzene ring as a substituent may reveal cases of geminal nonequivalence, we have not observed it in simple cases such as N,N-diethyl *o*-toluidine and N-benzyl *o*-toluidine. On the other hand geminal nonequivalence is clearly observable in the molecule shown below.[9]



In this case, however, since the asymmetry in the molecule is due to the carbon atom, slow rotation around some bond is not required for nonequivalence to be observed.

Formamides.—The formamides IV and V both exhibit *cis–trans*-amide isomerism (isomer ratio ≃3:1) and therefore should provide the opportunity for simultaneous observation of geminal proton nonequivalence and amide isomerism. However, neither shows nonequivalence at 40°, and IV not even at −40°. Nonequivalence of what appears to be several tenths parts per million is shown by V at −40° in the form of a much broadened, but only slightly resolved, hump for the methylene signals.

The biphenyl analogy is helpful in explaining the behavior of the formamides. Presumably with IV the formyl hydrogen (R′) is so small that the H(O=)C group does not seriously impede passage of the *o*-methyl group. As a consequence, rotation around the nitrogen–benzene bond is rapid. However, with V passage of the larger *o*-ethyl group is slightly impeded, and rotation is barely slow enough at −40° for nonequivalence to be observed.

Carbamylphosphonates.—The observations on carbamylphosphonates (structure shown below) listed in

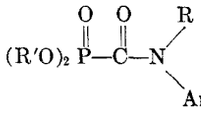


Table I with spectra in Figure 1a and b present additional evidence for the simultaneous operation of complicating factors, for both amides and organophosphorus compounds. Possibly owing to electron delocalization over the entire system, >P(=O)C(=O)N<, the amide bond is stiff enough, in spite of competitive delocalization into the aryl group, to allow the observation of amide *cis–trans* isomerism up to at least 100°. The existence of amide isomers in the ratio of about 5/1 isobservable in the spectra of all compounds of this class listed in Table I. The spectra of the minor isomers are comparatively uncomplicated with only one set of signals for the phosphorus substituents. This observation leads us to postulate that, in the minor isomer, the aryl group is *trans* to the phosphoryl group and its substituents. This arrangement places these substituents a maximum distance from the magnetic field of the aryl group, and would probably prevent observable nonequivalence even though a potential for nonequivalence exists. In the major isomer, the aryl group would be cis to phosphoryl, and therefore in the best position

(9) T. H. Siddall, III, *J. Phys. Chem.*, **70**, 2249 (1966).

to permit observation of nonequivalence of the phosphorus substituents.

In the major isomer the two alkoxy groups themselves are nonequivalent, each as a whole. This follows since the molecule has no symmetry plane. For the 2-propyl compounds there is the additional complication of nonequivalent β-methyl groups within the alkoxy group (because again there is no symmetry plane). This yields five β-methyl signal sets in 2-propoxy compounds (one for the minor and four for the major isomer) and three signal sets for alkoxy groups of the 1-alkoxy compounds (one for the minor and two for the major). Potentially the minor isomer can have as many signals as the major, and is prevented from doing so only by the remoteness of the aryl group. It is always possible, also, that the major isomer will exhibit less than maximum multiplicity because of conincidental degeneracy. One detail that we cannot explain is that methoxy signals for the minor isomer occur at lower field than those for the major isomer in XXX, while the opposite is true of the α-methylene signals of the isobutoxy groups of XXXI–XXXIII.

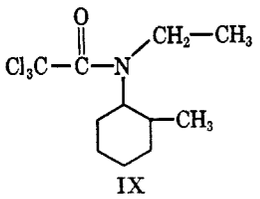
The shift of some of the signal sets for β- and γ-methyl groups of the alkoxy groups to quite high field (see XXXIII–XXXV especially) supports our proposal[2] that *ortho*-substituted aryl groups are not free to rotate around the aryl–nitrogen bond but are trapped in a plane more or less perpendicular to the three atoms directly linked to nitrogen. Such an orientation would place the alkoxy groups in a plane somewhat perpendicular to the plane of the aryl group. This plane contains the diamagnetic component of the anisotropic magnetic field of the aryl group. This effect would lead to high-field shifts.

One small detail adds evidence for our proposal that *cis–trans*-amide isomerism exists in these compounds: the pattern of phosphorus coupling to the N-alkyl substituents. The coupling constant is always greater in the one isomer (the major) than in the other, a fact that is especially clear in the β-methyl signals for XXXI.

It is clear that, in at least the major isomer, the geminal protons in the N-alkyl substituent are nonequivalent. The great multiplicity of signals that is observed and the lack of any observable equivalent pattern (simple quartet) suggest that these protons are nonequivalent in minor isomers as well. However, the low intensity of the signals from these protons and the general complexity and overlap with signals from the α protons in the alkoxy group probably account for the fact that no clear AB pattern can be picked out.

We conclude from the aggregate of our observations that three major mechanisms operate simultaneously to induce geminal proton nonequivalence in the carbamylphosphonates: (1) slow rotation around the amide bond,[5] (2) the preference for the "up" conformation in organophosphorus ester,[10] and (3) slow rotation around the benzene–nitrogen bond.

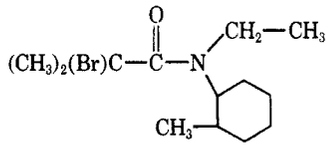
Compound IX seems to provide an exception to the normal rule that *cis–trans*-amide isomerism is not observable in *ortho*-substituted N-aryl amides, except in the case of formamides and carbamyl phosphonates. The spectrum at 40° (Figure 1c) is typical



IX

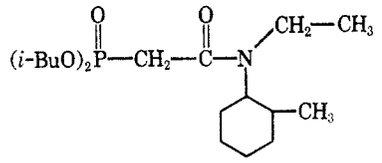
of the existence of one amide isomer or rapid interconversion between *cis* and *trans* forms, except that the high-field half of the methylene spectrum is blurred beyond any obvious resolution. However, at −40° (Figure 1d) there are two sets of *o*-methyl (intensity ratio = 1.9) and β-methyl signals. The high-field part of the methylene signals is now the typical sextet (actually an octet with overlap), but the low-field part is a sextet plus a considerable and not readily analyzable multiplicity of additional signals.

These spectra can be rationalized on the basis of two amide isomers. For the methylene proton signals from the major isomer (1.9 relative intensity) $\langle \nu_1 - \nu_9 \rangle$ = 1.5 ppm, but for the minor isomer $\langle \nu_1 - \nu_9 \rangle$ is so very much smaller that the signals are not resolved into sextets and these methylene signals are intermingled with the lower sextet for the major isomer. At 40° rotation around the amide bond is rapid enough to give single sets of signals *except* for the high-field sextet of the methylene protons. In this case the chemical shift between the signals for the major and minor isomers is so great (1.0 ppm) that even at 40° coalescence is not complete. A similar explanation applies to compound XVII of the previous paper in this series.[2]



XVII

Carbamylmethylenephosphonate XXVI gives a pmr spectrum (Figure 1e) that is typical of a number of



XXVI

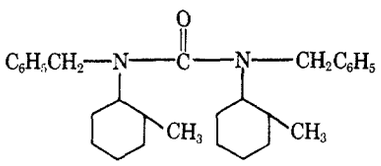
similar compounds that were examined. The spectra of other compounds of this class provided little further information and therefore were not included in this paper. From the fact that only one set of bridge methylene (d), β-methyl (g), and *o*-methyl (e) signals is observed, and by analogy with simple amides, XXVI evidently exhibits no amide isomerism. However, there is extra multiplicity in the signals from all the other aliphatic protons. Even the methine (b) signals comprise two sets.

This extra multiplicity can be explained as arising from the asymmetry in the amide part of the molecule. The expansion in Figure 1 shows that the methylene protons of the isobutyl radicals (c) have six signals. Ordinarily, owing to the fact that $J_{H_cH_b} \cong J_{H_cP}$, these protons give an apparent triplet. The additional splitting (2 cps) is due to the fact that the entire isobutyl

(10) T. H. Siddall, III, and C. A. Prohaska, *J. Am. Chem. Soc.*, **84**, 3467 (1962).

radicals have separate identities. There is a similar though somewhat smaller (~1 cps) splitting for the γ-methyl (a) and the methine (b) signals for the same reason. The isobutyl methylene protons (c) do not appear themselves to be nonequivalent despite their lack of a symmetry element. Still the fact that there is so much multiplicity in the spectrum for the phosphorus substituents suggests that the predominant amide isomer may have the *o*-methylphenyl group *cis* to the phosphoryl group in order to explain the influence of the anisotropic field of the ring over such a distance.

Substituted Urea XXVII.—At a temperature of 40° the spectrum of XXVII shows no multiplicity.



XXVII

However, at −40° (see Figure 1f) the *o*-methyl signal is very broad and the methylene signals apparently are split into two sets. One of these sets is a broad singlet, but the other is an AB pattern ($\langle\nu_a - \nu_b\rangle = 0.62$ ppm, $J_{AB} = 14$ cps). The AB pattern probably arises from slow rotation about the benzene–nitrogen bond, as with the other compounds cited in this report; however the existence of two *sets* of signals could arise either because of (1) *cis–trans*-amide isomerism or (2) the coexistence of epimers. At the moment from experience with other ureas,[8] alternative 2 seems more probable.

Geminal Protons Other Than >NCH₂.—Potentially all pairs of geminal protons in the types of amides described here are nonequivalent. However, in general nonequivalence is not observable for geminal protons α to the carbonyl group. This is true even for carbamylmethylenephosphonates, >POCH₂CON<, and also for the geminal protons of an *o*-ethyl group, although in the latter case the spectrum is skewed enough by the small chemical shift between α and β protons that a small degree of nonequivalence could be masked. For VIII and XVII the introduction of an ether linkage develops a small nonequivalence. Evidently, as a rule, the field gradient is small at these positions in the molecule, and/or internal molecular motions produce a good approximation of symmetry, but the disymmetry supplied by the ether linkage is enough to offset these effects.

Future Work.—Further investigations of molecular asymmetry that arises from slow rotation around the benzene–nitrogen bond are in progress in this laboratory. The pmr spectra are very complex for compounds that have two such centers of slow rotation in close proximity, as in oxalamides for example. This complexity presumably indicates extensive ramifications in the structure of these molecules, ramifications that we have not yet deduced from spectral interpretation. Multiple, unsymmetrical substitution in the benzene ring is also of interest, both for the spectra that are produced and for the effect on the rate of rotation of the benzene ring.

Formation and Alkylation of Di- and Trialkali Salts of 2,2′-Diphenyldiacetamide[1a,b]

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Received July 8, 1966

Mono- and dialkylations of 2,2′-diphenyldiacetamide were effected in liquid ammonia through its dilithio- and tripotassio salts, respectively; these salts were prepared by means of 2 and 3 molecular equiv of lithium amide and potassium amide, respectively. A metallic cation effect in the monoalkylation was observed. Further monoalkylation of one of the products was effected through its tripotassio salt.

Recently, certain imides[2,3] were converted to their dialkali salts by means of 2 molecular equiv of alkali amide in liquid ammonia, and the salts were alkylated with alkyl halides in this medium to form C-alkyl derivatives. For example, N-acetylbenzamide was converted to its dipotassio salt **1** which was benzylated to afford terminal derivative **2**.

$C_6H_5CONCOCH_2K$ (K) — **1**

$C_6H_5CONHCOCH_2CH_2C_6H_5$ — **2**

We have now similarly monoalkylated imide **3** at its benzyl group through its dilithio salt **4** to form **5a–c**, and, more significantly, have dialkylated **3** through its tripotassio salt **6** to give **7a–c**, (Scheme I). The results are summarized in Table I.

Structures **5a–c** were supported by analyses (Table I) and by spectral studies. The infrared spectra had bands at 2.9–3.2 and 5.75–6.1 μ for the N–H and imide carbonyl groups,[4] respectively. The nmr spectra (see Table II) were also consistent with the assigned structures. In each spectrum a singlet (two protons) characteristic of the benzyl methylene hydrogens was present, along with the expected absorption for the methinyl hydrogen attached to the carbon bearing the alkyl substituent.

(1) (a) Supported at Virginia Polytechnic Institute by the Petroleum Research Fund of the American Chemical Society, and at Duke University by the National Science Foundation. (b) Presented at the Southeast-Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec. 3, 1965. (c) To whom inquiries regarding this paper should be addressed at Virginia Polytechnic Institute.

(2) S. D. Work, D. R. Bryant, and C. R. Hauser, *J. Am. Chem. Soc.*, **86**, 872 (1964).

(3) D. R. Bryant and C. R. Hauser, *ibid.*, **83**, 3469 (1961).

(4) See L. J. Bellamy, "The Infrared Spectra of Complex Molecules." 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p 221.