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THE AMIDE-PHENOL RATIOS AND STRUCTURES IN AMIDE-PICRIC ACID COMPLEXES

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Abstract—Picric acid forms solid, isolable complexes with amides, with the amide-phenol ratio in these complexes being 1:1 for N,N-dialkylsubstituted amides and lactams and 2:1 for N-monoalkylsubstituted amides. With acetamide a 3:1 complex was also obtained, but this was unstable and changed over to the 2:1 complex. It is suggested that these complexes result primarily from H-bonding interactions, and that in solution charge-transfer and proton-transfer structures also contribute.

After a solution of picric acid in N,N-dimethylacetamide was heated 24 hr at 125°, it was possible to isolate two products, dimethylammonium picrate and a 1:1 complex of picric acid and dimethylacetamide, in yields of 42 and 36%, respectively. The complex can be obtained more easily by dissolving the acid and the amide in a minimum amount of acetone and adding ether, and it can be crystallized from acetone-ether to a constant m.p. of 62–64°.

The occurrence of complex formation between amides and phenols, picric acid included, has been demonstrated with fusion diagrams,[1-4] and the intermolecular association of amides with phenols in solution has been studied with IR spectroscopy,[5,6] with UV spectroscopy[7] and with fluorescence quenching techniques.[8] In the above studies the amide-phenol complexes were not isolated and purified. This is true even in the case of the picric acid-dimethylacetamide complex, where the fusion diagram clearly indicates a maximum corresponding to the 1:1 complex, having a m.p. of 60°. However, the preparation and purification of both the picrate[9] and styphnate[10] of 2-piperidone (δ-valerolactam) have been reported.

In the present report the preparation of pure, crystalline amide-picric acid complexes will be described. It will be shown that the amide-phenol ratio in these complexes can vary from 1:1 for N,N-dialkylsubstituted amides to 2:1 for N-monoalkylsubstituted amides, even to 3:1 for unsubstituted amides. The structure of these complexes and the binding forces involved will be considered. In addition some of the chemical reactions will be described.

RESULTS AND DISCUSSION

Table 1 lists the amide-picric acid complexes that have been obtained as solid, crystalline compounds. All can be prepared by dissolving the nitrophenol and an excess of the amide in a minimum quantity of warm acetone, cooling and adding ether, and all of these complexes can be recrystallized from acetone-ether. When the colorless amide is mixed in acetone solution with straw colored picric acid, there is an intensification of the yellow color, suggesting the possibility of some measure of charge-transfer interaction.[11]

The amide-phenol ratios in these complexes follow directly from determinations of the neutralization equivalents. It is of interest that only 1:1 complexes are obtained with N,N-disubstituted amides. These amides can function as acceptors in H-bonding but not as donors. Self-association via H-bonding interactions is not possible, although the high dielectric constants exhibited by these amides are an indication of significant self-association attributable to dipole-dipole interactions.[12]

The cyclic amides (lactams), even those containing N–H bonds, e.g. 2-pyrrolidone and caprolactam, form only 1:1 complexes with picric acid, but with non-cyclic, mono-N-substituted amides we have observed only an amide-phenol ratio of 2:1. This observation, it will be argued subsequently, is of some significance. With acetamide, 2:1 and 3:1 complexes were obtained.

Table 2 lists some solid complexes obtained with amides and a few other phenols. All of these complexes, even those with acetamide and N-methylacetamide, have

Table 1. Amide-picric acid complexes

Amide	Amide-Picric Acid Ratio	MP – °C	Neutralization Equivalent Calcd.	Fd.
N,N-Dimethylformamide	1:1	43-46	302	303
N,N-Dimethylacetamide	1:1	62-64	317	322
N,N-Diethylacetamide	1:1	81-83	344	351
N,N-Di-n-propylacetamide	1:1	43-45	372	373
N,N-Dimethylacetoacetamide	1:1	42-44	358	358
N-Formylpiperidine	1:1	52-53	342	344
N-Acetylpiperidine	1:1	55-57	356	358
N-Methylpyrrolidone	1:1	53-55	328	333
2-Pyrrolidone	1:1	99-101	314	314
Caprolactam	1:1	70-71	342	344
δ-Valerolactam	1:1	91-93	328	331
N-Methylformamide	2:1	35-37	347	356
N-Methylacetamide	2:1	108-109	375	382
N-Methylpropionamide	2:1	48-49	403	408
Acetamide	2:1	71-74	347	349
Acetamide	3:1	42-44	406	406

Table 2. Amide-phenol complexes

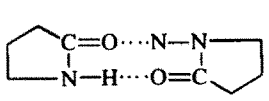
Amide	Phenol	Amide-Phenol Ratio	MP-°C	Neutralization Equivalent Calcd.	Fd.
N-Methylacetamide	p-Nitrophenol	1:1	73-76	212	213
Acetamide	p-Nitrophenol	1:1	96-98	198	199
N,N-Dimethylacetamide	2, 4-Dinitrophenol	1:1	60-62	271	273
N,N-Dimethylacetamide	Pentachlorophenol	1:1	55-58	353	357
N-Methylacetamide	Pentachlorophenol	1:1	127-129	339	341
2-Pyrrolidone	Pentachlorophenol	1:1	136-139	351	353

an amide-phenol ratio of 1:1. The amide-pentachlorophenol complexes were prepared by dissolving the phenol and excess amide in ether and adding hexane.

Amides having N–H bonds available can function as both donors and acceptors in H-bonding. Self-association via H-bonding to form dimers and higher aggregates, both cyclic and linear, is possible. The formation of cyclic dimers and trimers requires a *cis*-conformation of the CO and N–H bonds, but this conformation, present in lactams, is unfavorable in non-cyclic amides except when a bulky substituent is present on nitrogen.[13,14] However, there are indications that the proportion of the *cis*-form in equilibrium is significantly increased when the amide is protonated or H-bonded. The failure to observe other than 1:1 complexes with N,N-disubstituted amides and picric acid and the common occurrence of 2:1 complexes with non-cyclic amides having an available N–H bond and picric acid suggests that the formation of complexes having an amide-phenol ratio greater than 1 may involve a prior or concurrent H-bonded self-association of the amide.

The 2:1 amide-picric acid complexes might then involve some interaction between picric acid and the amide dimer. This interaction can be of the charge-transfer type, which involves orbital overlap and possible electron transfer but no formal bond formation, of the H-bonding type or of both types occurring simultaneously or consecutively. To the extent that H-bonding is involved it is very probably with picric acid as the donor and the amide, either monomeric or self-associated, as the acceptor. There is strong evidence from NMR studies, from IR studies and from basicity studies[14] that the preferred protonation site for amides is the CO oxygen. This is reasonable. Whereas protonation on nitrogen fixes the locus of the positive charge, protonation on oxygen permits delocalization of the charge to oxygen, nitrogen and carbon. Similar considerations make the CO oxygen the preferred H- bond acceptor, and there is IR data to support this conclusion as well.[15]

Based on the foregoing considerations, appropriate structures for the H- bonded complexes can be proposed. With N,N-disubstituted amides H-bonded dimers are not possible, only 1:1 complexes are observed, and these could have the structure shown in **1**. With mono-N-substituted amides, H-bonded dimers, both linear and cyclic, are possible. Formation of a cyclic dimer requires a *cis*-configuration of the CO and N–H bonds about the C–N bond. This is the preferred conformation for the lactam, pyrrolidone, where the dimer would be expected to have structure **2**. For N-methylamides, however, the more probable dimer structure is the linear one, **3**. The pyrrolidone dimer, **2**, has no free CO group available for



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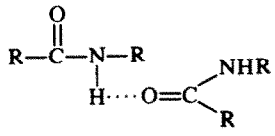

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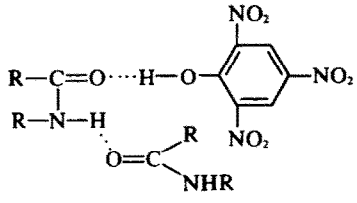
H-bonding and complex formation with picric acid, but the linear dimer, **3**, still has one CO group available to serve as an acceptor in H-bonding. With the lactams, e.g. 2-pyrrolidone, 2-piperidone and caprolactam, the competition is between self-association to form a cyclic, H-bonded dimer and intermolecular association with picric acid to form the 1:1 complex. It is, therefore, reasonable that lactams form only 1:1 complexes and that mono-N-substituted amides preferentially form 2:1 complexes, for which the structure shown in **4** can be proposed.



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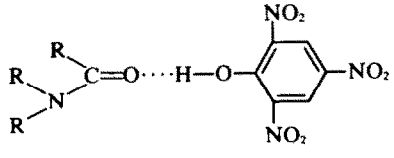
An alternate structural possibility for the 2:1 complex between picric acid and mono-N-substituted amides is that shown in **5**, in which one H-bond is formed with the phenolic hydrogen as donor and the amide CO as acceptor, and the second H-bond results from the nitro group as acceptor and the amide N–H as donor. It should be noted that the *ortho*-nitro group of picric acid can also



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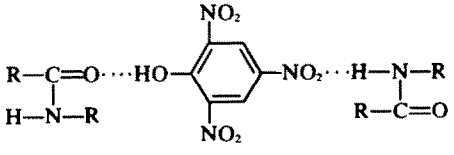

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act as a H-bond acceptor, and that, therefore, isomeric 2:1 complex structures are possible, although none was isolated. It should further be noted that it was not possible to isolate a solid complex from N-methylacetamide and 2,4,6-trinitroanisole, from N-methylacetamide and 1,3,5-trinitrobenzene or from N-methylacetamide and ammonium picrate. It may furthermore be argued that the *cis*-conformation of the CO and N–H bonds in the lactams is not a deterrent to formation of **5**.

All of the foregoing considerations suggest that **4** is a more probable representation of the 2:1 amide-picric acid structures than **5**. However, the isolation of only a 1:1 complex from N-methylacetamide and pentachlorophenol (Table 2) can be offered as contrary evidence, suggesting that a nitro group is necessary for formation of the 2:1 complex and supporting structure **5**. Although we would argue that the available evidence favors structure **4**, we recognize that structure **5** cannot be eliminated as a possibility on the basis of the evidence presently available.

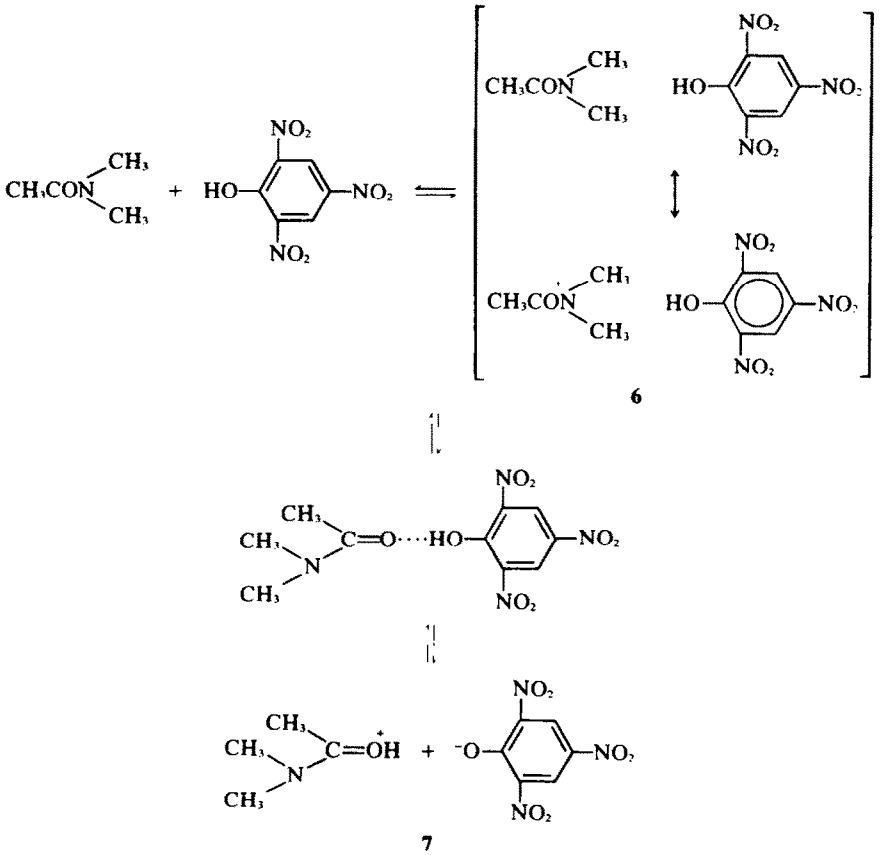
With acetamide and picric acid it was possible to isolate a 3:1 complex (m.p., 42–44°; neutralization equivalent, 406) from at least four separate preparative experiments. However, at least an equivalent number of presumably identical experiments failed to give the 3:1 complex. Moreover, even when obtained, the 3:1 complex was unstable and was transformed on standing or repeated recrystallization from acetone-ether to the 2:1 complex (m.p., 71–74°; neutralization equivalent, 354).

Structures such as **1** and **4** or **5** probably best describe the amide-phenol complexes in the solid state. In solution both charge-transfer structures and structures in which the proton is actually transferred from the phenol to the amide also contribute. Using the dimethylacetamide-picric acid complex as the example, the equilibria shown in Scheme 1 can be proposed to describe the structures to be considered in solution.

Charge transfer interactions, as represented by **6** in Scheme 1, can contribute to conductivity in solution.[16] In the present case, although picric acid is a good electron acceptor, the amides are relatively poor donors, and the contribution of the cation radical and anion radical forms to the total structure is probably minimal. If the amide-phenol complexes exhibit significant conductivity in solution it is best attributed to either ionization of picric acid (proton transfer to solvent) or formation of **7** (proton transfer to amide).

Conductivity measurements on amide-phenol complexes are compiled in Table 3. The measurements are all for 0·05 M solutions in chloroform at 20 ± 1°. The values listed in Table 2 are 10–10,000 times greater than the conductivities of either the amide alone or picric acid alone. The conductivity of 0·05 M picric acid in chloroform at 20 ± 1° is $1{\cdot}1 \times 10^{-9}$ mho-cm^{-1}, while the conductivities of 0·05 M dimethylformamide and 0·05 M dimethylacetamide are $4{\cdot}3 \times 10^{-10}$ and $1{\cdot}5 \times 10^{-10}$ mho-cm^{-1}, respectively. On the other hand, the observed conductivities of the complexes are 20–1000 times smaller than the conductivity ($5{\cdot}9 \times 10^{-5}$ mho-cm^{-1}) found for a true salt, tetra-n-butylammonium fluoroborate. Proton transfer from picric acid to either the solvent or the amide is incomplete in chloroform, and H-bonded structures contribute to the structures of the complexes in solution.

Heating a solution of picric acid in either N,N-



Scheme 1.

Table 3. Conductivities of 0·05 M. Amide-phenol complexes in chloroform at 20 ± 1°C

Amide	Phenol	Amide-Phenol Ratio	Conductivity mho. cm^{-1}
N-Methylacetamide	Picric Acid	2:1	2.4×10^{-6}
Acetamide	Picric Acid	2:1	1.8×10^{-7}
Acetamide	Picric Acid	3:1	4.6×10^{-7}
N,N-Di-n-propylacetamide	Picric Acid	1:1	3.7×10^{-7}
N,N-Dimethylacetamide	Picric Acid	1:1	2.5×10^{-7}
Acetamide	p-Nitrophenol	1:1	1.2×10^{-7}
N,N-Dimethylformamide	Picric Acid	1:1	1.5×10^{-8}

dimethylformamide or N,N-dimethylacetamide at 125° results in the formation of dimethylammonium picrate in good yield. In the N,N-dimethylformamide case, the reaction also results in the liberation of an equivalent amount of carbon monoxide. If the reaction in N,N-dimethylacetamide followed an analogous course, it would be expected to lead to ketene as the accompanying product, and this suggested the possibility that acid-catalyzed decomposition of amides might be a useful procedure for generating ketenes. However, experiments designed to sweep out and trap ketene were unsuccessful.

Other experiments to demonstrate ketene formation were undertaken. When the 1:1 N,N-dimethylacetamide-picric acid complex was refluxed 48 hr. in n-butanol, the products formed were 91·9% dimethylammonium picrate and 63·3% butyl acetate. In a similar experiment with the 2:1 N-methylpropionamide-picric acid complex the products were 68% methylammonium picrate and 33% butyl propionate. The butyl esters could have resulted either from reaction of ketene and methyl ketene, respectively, with butyl alcohol or from alcoholysis of the amides.

A similar experiment with the 1:1 N,N-dimethylformamide-picric acid complex provides some basis for choice between the two possibilities. In this case decomposition to give carbon monoxide would result in the dimethylammonium picrate but no ester, while alcoholysis would result in the formation of both the salt and butyl formate. The products actually found were 64% dimethylammonium picrate and 61% butyl formate. Therefore, in all of the experiments in n-butanol, the esters obtained are best attributed to alcoholysis reactions.

EXPERIMENTAL

Reaction of picric acid with N-N-*dimethylacetamide.* Picric acid (23·0 g; 0·1 mole) in N,N-dimethylacetamide (400 ml) was heated 24 hr at 125°. The soln was stirred with decolorizing charcoal and filtered. The dimethylacetamide was removed by distillation at the water pump. The residue was taken up in acetone, and ether was added. On cooling, 11·6 g (42%) of dimethylammonium picrate precipitated; m.p. 156–159°.

The filtrate was again treated with charcoal. After filtration and removal of the solvents at the water pump, the residue was crystallized from acetone-ether to yield 11·5 g (36%) of the dimethylacetamide-picric acid complex; m.p. 55–60°, after recrystallization from acetone-ether.

Reaction of picric acid with N,N-*dimethylformamide. Detection of carbon monoxide.* A soln of picric acid (11·5 g; 0·05 mole) in N,N-dimethylformamide (25 ml) was connected to a gas burette and maintained at 125°. The gas produced was analyzed periodically by VPC for CO. After 27 hr of heating the soln was poured into ether (400 ml) and left standing overnight. Filtration afforded 4·8 g (35%) of dimethylammonium picrate, m.p. 159–161°. From the gas analyses and rates of gas evolution, it was estimated that over this same time period 335 ml (30%) of CO had been produced.

N,N-*Dimethylacetamide-picric acid, a* 1:1 *complex.* A mixture of picric acid (25 g; 0·11 mole) and N,N-dimethylacetamide (23·6 g; 0·27 mole) was warmed with the minimum amount of acetone required to effect soln. After addition of ether followed by cooling, there was obtained a yield of 32·7 g (93·7%) of yellow crystals; m.p. 60–62°. Recrystallization from acetone-ether raised the m.p. to 62–64°. (Found: N, 17·28. Calcd. for $C_{10}H_{12}N_4O_8$: N, 17·67%).

N-*Methylpropionamide-picric acid, a* 2:1 *complex.* A mixture of picric acid (11·8 g; 0·052 mole), N-methylpropionamide (9·31 g; 0·107 mole) and a small amount of acetone was heated to boiling. The resultant soln was filtered and treated with a large volume of ether. A first crop of 9·2 g, m.p. 47–48°, was obtained. After the filtrate was concentrated, the addition of hexane yielded an additional 5·6 g of the complex; m.p. 47–50°. The total yield was 70·5%. After the two crops were combined and recrystallized from acetone-ether, the m.p. was 48–49°. (Found: N, 17·10. Calcd. for $C_{14}H_{21}N_5O_9$: N, 17·37%).

Acetamide-picric acid complexes. In a typical experiment to form the 3:1 complex, picric acid (11·5 g; 0·05 mole) was dissolved in warm acetone (20 ml) and treated with acetamide (7 g; 0·118 mole). Ether (200 ml) was added, and the filtered soln was stored in the freezer, yielding 12·6 g (79%) of yellow crystals of the 3:1 complex; m.p. 42–44°. Recrystallization from acetone-ether gave m.p. 43–45°. (Found: N, 20·62. Calcd. for $C_{12}H_{18}N_8O_{10}$: N, 20·69%).

On another occasion an attempted repetition of the above procedure gave 15·8 g of the 2:1 complex; m.p. 70–75°. The same reagent quantities in hot chloroform rather than acetone led also to the 2:1 complex.

An attempt to form the 1:1 complex also resulted in the 2:1 complex. Picric acid (2·3 g; 0·01 mole) and acetamide (0·6 g; 0·01 mole) were dissolved in warm acetone (10 ml). After addition of ether (100 ml) the soln was stored in the freezer. After 5 days, 1 g (56%) of the 2:1 complex, m.p. 72–74°, was obtained.

In another experiment the 3:1 complex was first formed, and its transformation to the 2:1 complex was observed. To a soln of picric acid (5·7 g; 0·025 mole) in acetonitrile (10 ml) acetamide (4·4 g; 0·075 mole) was added. The mixture was heated to give a clear soln, treated with ether (100 ml) and cooled overnight in the freezer. The 3:1 complex, m.p. 43–45°, was obtained in 84% yield. (Found: N.E, 406. Calcd. for $C_{12}H_{18}N_8O_{10}$: N.E, 406·3%).

On standing at room temp. the m.p. grew progressively higher. A sample recrystallized from acetonitrile-ether after 1 week at room temp had m.p. 56–70° and neutralization equivalent 385. Another recrystallization from acetonitrile-ether raised the m.p. to 70–73° and lowered the neutralization equivalent to 349. The calculated neutralization equivalent for the 2:1 complex is 347·3.

N-Methylacetamide-pentachlorophenol. Pentachlorophenol (2·7 g; 0·01 mole) and N-methylacetamide (3 ml) were dissolved in the minimum amount of boiling ether. The soln was filtered, hexane was added, and part of the ether was boiled away. On cooling 3·1 g (91%) of product, m.p. 95–105°, crystallized. Recrystallization from ether-hexane raised the m.p. to 127–129°.

(Found: Neut. Equiv. 341·5. Calcd. for 1:1 complex: Neut. Equiv., 339·4).

Reaction of picric acid-amide complexes with n-butanol. The N,N-dimethylformamide-picric acid complex (5 g; 0·0166 mole) in n-butanol (50 ml) was refluxed 70 hr. After cooling, ether was added, and the soln was refrigerated, yielding 4·0 g (64%) of dimethylammonium picrate; m.p. 159–162°. The filtrate was distilled at atmospheric pressure. After the ether was removed, a 34 g fraction of b.p. 90–113° was taken. By VPC analysis this was shown to contain 1·04 g (61%) of butyl formate.

In similar experiments the N,N-dimethylacetamide-picric acid complex yielded 91·9% dimethylammonium picrate and 63·3% butyl acetate after 48 hr of refluxing in n-butanol, and the 2:1 N-methylpropionamide-picric acid complex yielded 68% methylammonium picrate and 33% butyl propionate.

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