tilled or recrystallized from benzene–ligroin mixtures. These reactions were carried out using 0.02–0.04 mol of the nitrile. The results are summarized in Table III.

**Registry No.**—**1**, 7436-85-3; **2**, 16212-28-5; **3**, 31413-58-8; **4**, 10472-00-1; **5**, 31413-60-2; **15a**, 31413-61-3; **15b**, 31413-62-4; **16a**, 15732-02-2; **16b**, 31413-64-6; **16c**, 31413-65-7; **17b**, 31413-66-8; **17c**, 31413-67-9; **20a**, 31413-68-0; **20b**, 31413-69-1; sodium methoxide, 124-41-4; *O*-(3,3-dichloro-2-methyl-1-methoxyallyl)-3,3-dichloro-2-methylacrolein, 31443-67-1.

**Acknowledgment.**—We are indebted to Mr. E. S. Peterson for the nmr spectra and their interpretation, to Mr. Frank Lang for his assistance in several of the experiments, and to the Robert A. Welch Foundation (Grant AF-169) for their generous financial assistance.

# Carbodiimide–Sulfoxide Reactions. XI.[1a] Reactions of Carboxylic Acids, Hydroxamic Acids, and Amides

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The mild acid-catalyzed reactions of DMSO and DCC with carboxylic acids, hydroxamic acids, and carboxamides have been examined. Reactions with carboxylic acids, or with the corresponding hydroxamic acids, lead to methylthiomethyl esters and to *N*-acylureas. In the case of hydroxamic acids, minor amounts of products arising from rearrangements of the Lossen type are also found. In the case of *N*-methoxy-*p*-nitrobenzamide, the major product is the *N*-(1,3-dicyclohexyl-1-ureidomethyl) derivative and lesser amounts of methylthiomethyl *N*-methoxy-*p*-nitrobenzimidates are also formed. Primary carboxamides in both the aromatic and aliphatic series react readily to form *N*-acylsulfilimines which can be oxidized to the corresponding *N*-acylsulfoximines. Nitriles are also formed in these reactions. Comparable reactions of amides with DMSO and phosphorus pentoxide or acetic anhydride gave only minor amounts of *N*-acylsulfilimines, the major products being *N*,*N*′-methylenebiscarboxamides. Photolysis of *N*-acylsulfilimines is shown to proceed primarily *via* formation of an acylnitrene which can either react with the solvent or rearrange to an isocyanate.

Previous papers in this series have shown that dimethyl sulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC) react in the presence of a mild acidic catalyst to form the oxysulfonium intermediate **1**. This species can then be attacked by various nucleophiles such as alcohols,[2] phenols,[3] enols,[4] and oximes,[5] leading to dimethylsulfonium intermediates which can undergo oxidation, rearrangement, or a variety of other reactions. In the case of the reactions of alcohols, the mechanism of the oxidation reaction has been quite carefully studied using isotopes.[1,2b] In the present paper these studies have been extended to cover the acid-catalyzed reactions of DMSO and DCC with carboxylic acids, hydroxamic acids, and carboxamides. In view of the mechanistic similarities of these reactions to those using DMSO activated by acetic anhydride[6] or phosphorus pentoxide,[7] several comparable reactions have been studied using these reagent mixtures.

Our initial reactions were done using *p*-nitrobenzoic acid, which reacted exothermically with 3 molar equiv of DDC and 0.5 molar equiv of anhydrous orthophosphoric acid in a mixture of DMSO and benzene. Following destruction of excess DCC with oxalic acid,[8] two crystalline products were readily isolated and shown to be methylthiomethyl *p*-nitrobenzoate (**5a**) and 1-*p*-nitrobenzoyl-1,3-dicyclohexylurea (**7a**) in yields of 40 and 42%. The formation of methylthiomethyl esters has also been demonstrated by Onodera, *et al.*,[9] following reactions of carboxylic acids with DMSO and phosphorus pentoxide at 70° and can, in both cases, be considered as the products of Pummerer-type rearrangements[10] of the acyloxysulfonium ylide (**3**) according to Scheme I.

The ylide **3** is written as arising *via* the tetracovalent sulfur intermediate **2**, but, as has been discussed in our work on the oxidation of alcohols,[1] could also be formed by a concerted process without accumulation of **2**. Dissociation of the ylide into the methylene methylsulfonium ion **4** and recombination with the carboxylate anion to give **5** is typical of the Pummerer reaction[10] and is similar to what has been previously proposed for the reactions of oximes[5] and 2,6-disubstituted phenols.[3b] An alternative route involving initial reaction of the carboxylic acid with DCC to form the corresponding acid anhydride followed by a typical Pummerer reaction with DMSO cannot be excluded. Indeed, *p*-nitrobenzoic anhydride[11] has been found to react very rapidly with DMSO to form **5a**.

In our previous papers we have considered the direct product of the reaction of an oxygen nucleophile with the DMSO–DCC adduct **1** to be an oxysulfonium salt which subsequently readily loses a proton to form the sulfonium ylide (*e.g.*, **3**). Based upon our more recent results[1] on the mechanism of the DMSO–DCC oxidation of alcohols, however, direct formation of the ylide

(1) (a) For part X, see J. G. Moffatt, *J. Org. Chem.*, **36**, 1909 (1971); (b) Syntex Postdoctoral Fellow, 1966–1968.

(2) (a) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5661, 5670 (1965); (b) A. H. Fenselau and J. G. Moffatt, *ibid.*, **88**, 1762 (1966); (c) for a review see J. G. Moffatt in "Techniques and Applications in Organic Synthesis: Oxidation," Vol. 2, R. Augustine and D. J. Trecker, Ed., Marcel Dekker, New York, N. Y., in press.

(3) (a) M. G. Burdon and J. G. Moffatt, *J. Amer. Chem. Soc.*, **88**, 5855 (1966); (b) M. G. Burdon and J. G. Moffatt, *ibid.*, **89**, 4725 (1967).

(4) A. F. Cook and J. G. Moffatt, *ibid.*, **90**, 740 (1968).

(5) A. H. Fenselau, E. H. Hamamura, and J. G. Moffatt, *J. Org. Chem.*, **35**, 3546 (1970).

(6) (a) J. D. Albright and L. Goldman, *ibid.*, **30**, 1107 (1965); (b) J. D. Albright and L. Goldman, *J. Amer. Chem. Soc.*, **89**, 2416 (1967); (c) Y. Hayashi and R. Oda, *J. Org. Chem.*, **32**, 457 (1967); (d) A. Hochrainer and F. Wessely, *Monatsh. Chem.*, **97**, 1 (1966).

(7) K. Onodera, S. Hirano, and N. Kashimura, *Carbohyd. Res.*, **6**, 276 (1968).

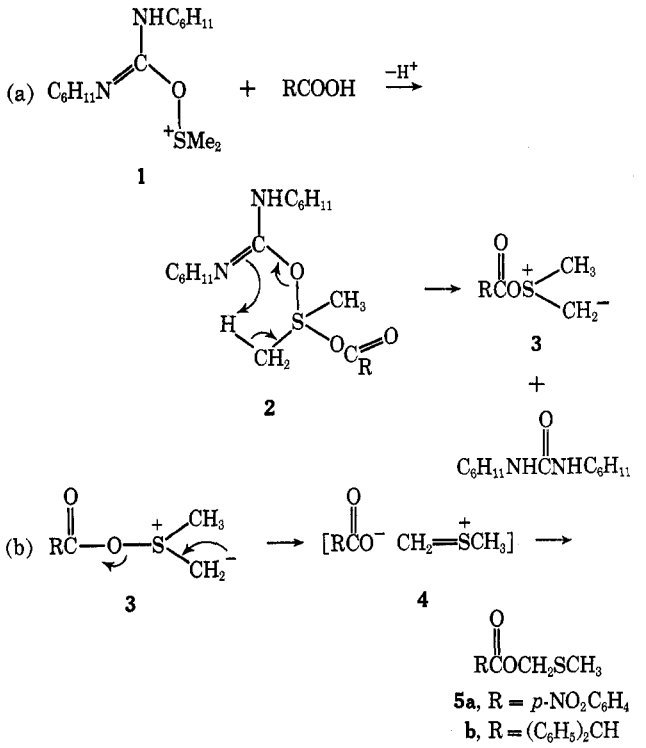
(8) F. Zetzsche and H. Lindler, *Chem., Ber.*, **71B**, 2095 (1938)

(9) K. Onodera, S. Hirano, N. Kashimura, and T. Yajima, *Tetrahedron Lett.*, 4327 (1965).

(10) G. A. Russell and G. J. Mikol in "Mechanism of Molecular Migrations," Vol. 1, B. A. Thyagarajan, Ed., Interscience, New York, N. Y., 1968, p 157.

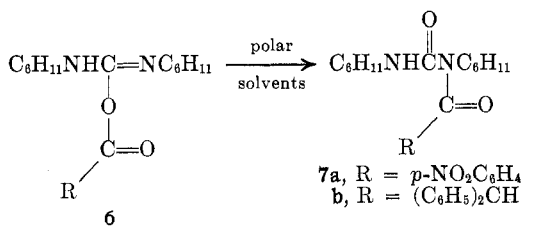
(11) H. Rinderknecht and V. Ma, *Helv. Chim. Acta*, **47**, 163 (1964).

SCHEME I



*via* a cyclic process (*e.g.*, **2** → **3**) is indicated and probably also obtains in reactions involving other nucleophiles such as phenols, oximes, etc.

Formation of the *N*-acylurea **7a** is probably due to direct reaction of the carboxylic acid with DCC, rearrangement of the initial adduct **6** being well known in polar solvents.[12]

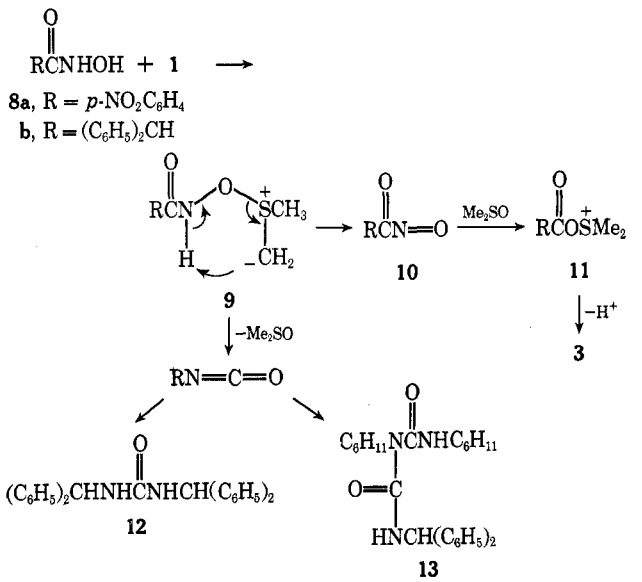


As might be expected, the reaction of *p*-nitrobenzoic acid with DMSO and acetic anhydride at room temperature also gave the methylthiomethyl ester **5a** presumably *via* the ylide **3**. The reaction was, however, slow and after 3 days the isolated yield of **5a** was only 33%. As an example of an aliphatic carboxylic acid, diphenylacetic acid was also allowed to react with DMSO and DCC, giving the methylthiomethyl ester **5b** and the *N*-acylurea **7b** in yields of 69 and 26%, respectively. The formation of these two types of products would thus appear to be quite general from a variety of carboxylic acids.

The hydroxamic acids **8a**[13] and **8b**[14] derived from *p*-nitrobenzoic and diphenylacetic acids were also allowed to react with DMSO and DCC in the presence of anhydrous phosphoric acid. The reaction with **8a** gave the same methylthiomethyl ester **5a** (31%) and acylurea **7a** (42%) as were obtained from the acid, and similarly **8b** gave **5b** and **7b** in yields of 50 and 15%. In addition, the reaction of **8b** gave low yields of two crystalline products identified as 1,3-dibenzhydrylurea (**12**, 10%[15]) and 1,3-dicyclohexyl-1-(benzhydrylaminocarbonyl)urea (**13**, 2%). Both of these minor products would appear to arise *via* a Lossen-type rearrangement[16] of the hydroxamic acid to give benzhydrylisocyanate, which can then react with either benzhydrylamine or dicyclohexylurea. Activation of the hydroxamic acid as a prelude to isocyanate formation could involve either direct reaction with DCC[17] or protonation of the ylide **9**. The related activation of certain oximes as their oxysulfonium derivatives has previously been used to rationalize DMSO–DCC promoted Beckmann rearrangements.[5]

Since the major reaction products starting from either carboxylic acids or the corresponding hydroxamic acids are the same, it is interesting to speculate as to at which point the two reaction pathways become equivalent. A likely probability (Scheme II) is that reaction

SCHEME II



of the hydroxamic acid with the DMSO–DCC adduct **1** leads, as in Scheme I, to an oxysulfonium ylide **9** that collapses intramolecularly to dimethyl sulfide and the nitroso compound **10**. The latter type of compound has been postulated as a reactive intermediate during oxidation of hydroxamic acids with a variety of agents[18] and thermal decomposition of nitrite esters.[19] Reactions of **10** with DMSO would then give the oxysulfonium salt **11** which, by ready loss of a proton, would give the same ylide **3** as arose from the acid itself. By cyclic proton abstractions similar to **9** → **10**, the nitroso compound **10** could be formed regardless of whether the nucleophilic center of **8** was either of the oxygen atoms or the nitrogen of the hydroxamate function.

(12) For review see (a) H. G. Khorana, *Chem. Rev.*, **53**, 145 (1953); (b) F. Kurzer and K. Douraghi-Zadek, *ibid.*, **67**, 107 (1967).

(13) B. E. Hackley, R. Plapinger, M. Stolberg, and T. Wagner-Jauregg, *J. Amer. Chem. Soc.*, **77**, 3631 (1955).

(14) L. W. Jones and C. D. Hurd, *ibid.*, **43**, 2432 (1921).

(15) A. Rahman and M. O. Farooq, *Justus Liebigs Ann. Chem.*, **585**, 200 (1953).

(16) H. L. Yale, *Chem. Rev.*, **33**, 209 (1943).

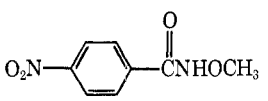
(17) (a) K. Nagarajan, S. Radjappa, and V. S. Iyer, *Tetrahedron*, **23**, 1049 (1967); (b) D. G. Hoare, A. Olson, and D. E. Koshland, *J. Amer. Chem. Soc.*, **90**, 1638 (1968).

(18) (a) B. Szlark and A. F. Al-Sayyab, *J. Chem. Soc.*, 1318 (1964); (b) J. E. Rowe and A. D. Ward, *Aust. J. Chem.*, **21**, 2761 (1968).

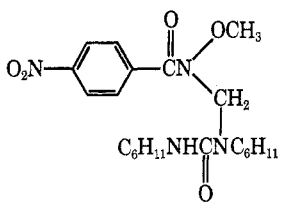
(19) A. L. J. Beckwith and G. W. Evans, *J. Chem. Soc.*, 130 (1962).

In order to avoid the formation of nitroso compounds by the pathway **8** → **10**, *N*-methoxy-*p*-nitrobenzamide (**14**) was prepared and allowed to react in the usual way, giving one major and two minor products in addition to a number of unidentified by-products. The major product, isolated in yields up to 69%, has only been obtained as an extremely viscous, chromatographically homogeneous syrup that decomposes upon attempted short path distillation into **14** and dicyclohexylurea. From its analysis and nmr spectrum this product is clearly a dicyclohexylurea adduct and is assigned the structure *N*-(1,3-dicyclohexyl-1-ureidomethyl)-*N*-methoxy-*p*-nitrobenzamide (**15**). In addition to the expected cyclohexyl, methoxyl, and aromatic protons, the $NCH_2N$ group appears as a two-proton singlet at 5.25 ppm. That this compound has the structure **15** rather than being the isomeric imido ester is confirmed by its ultraviolet spectrum, which is very similar to that of **14** and totally unlike those of **16** and **17**. As expected, treatment of **15** with aqueous acid resulted in its rapid hydrolysis to dicyclohexylurea, **14**, and formaldehyde, the latter being isolated as its dinitrophenylhydrazone.

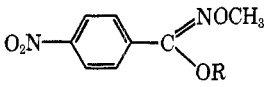
The other major products from reaction of **14** proved to be the syn (5%) and anti (10%) forms of methylthiomethyl *N*-methoxy-*p*-nitrobenzimidate (**16a** and **17a**). That these compounds were indeed imido esters rather than their N-alkylated isomers was shown by the close similarity of their ultraviolet spectra to those of the correspondingly ethyl *N*-methoxy-*p*-nitrobenzimidates (**16b**, **17b**) rather than to **14**. The preparation of **16b** and **17b** was readily achieved by alkylation of **14**



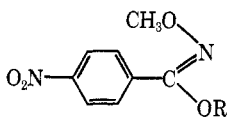
**14**



**15**



**16a**, R = $CH_2SCH_3$
**b**, R = Et



**17a**, R = $CH_2SCH_3$
**b**, R = Et

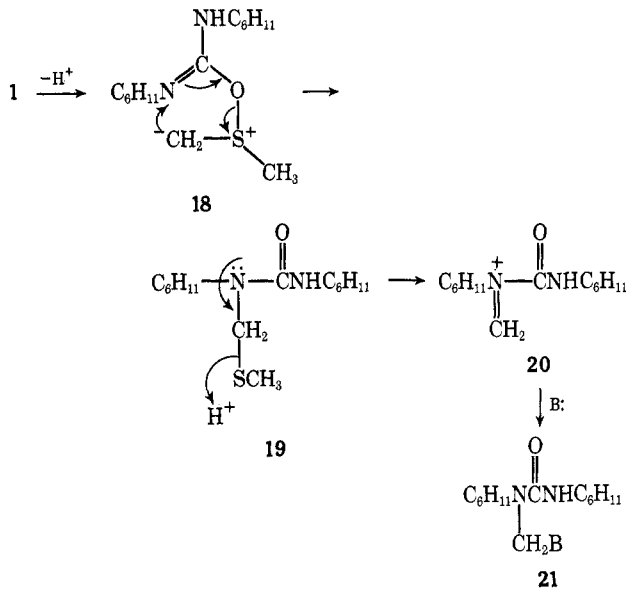
with triethyloxonium fluoroborate, a reagent well known to effect O-alkylation of amides.[20] The assignment of stereochemistry to **16** and **17** is based upon nmr spectroscopy and an extension of the empirical rules developed for oximes.[21] Thus, in the more polar syn isomers (**16a** and **16b**) the $OCH_2S$ and $OCH_2CH_3$ protons are deshielded by the methoxyl group and are shifted downfield 0.24 and 0.25 ppm relative to their anti counterparts. It is interesting to note that in simple oximes of ethyl ketones, the deshielding effect of the hydroxyl group is not noticeable in the β-methyl group.[21b]

(20) H. Meerwein, E. Battenberg, H. Gold, E. Pfeil, and G. Willfang, *J. Prakt. Chem.*, **154**, 83 (1939).

(21) (a) I. Pejković-Tadić, M. Hranisavljević-Jakovljević, S. Nesić, C. Pascual, and W. Simon, *Helv. Chim. Acta*, **48**, 1157 (1965); (b) G. J. Karabatsos and R. A. Taller, *Tetrahedron*, **24**, 3347 (1968).

We have previously observed[3a] the formation of compounds similar to **15** in which a 1,3-dicyclohexyl-1-ureidomethyl group is attached to a nucleophilic center, and many further examples of this type of compound will be found in this paper. These compounds usually appear to arise only during reactions that are rather slow and are, unlike **15**, generally minor products. We tentatively propose the mechanism outlined in Scheme III for the formation of these compounds.

SCHEME III



**18**

**19**

**20**

**21**

From previous studies[1] we know that there is not extensive accumulation of **1** in DMSO–DCC reactions in the absence of a nucleophile. In the presence of relatively poor nucleophiles there is ample opportunity for loss of a proton from **1**, forming a stabilized oxysulfonium ylide **18** which can rearrange *via* a cyclic mechanism forming the *N*-(methylthiomethyl)urea **19** and then lose methyl mercaptan giving the iminium ion **20**. The latter species could then react with a nucleophile forming the observed ureidomethyl derivatives **21**. We have not isolated compound **19** from any DMSO–DCC reaction, but comparable, acid-catalyzed decompositions of compounds containing $NCH_2SCH_3$ functions appear to adequately explain the formation of a variety of products described in this and a forthcoming paper.[22] It is perhaps surprising that **15** proves to be an N-substituted derivative, since it is known that acylation[23] or alkylation with diazomethane[24] or oxonium salts (see above) of *N*-alkoxy arylcarboxamides leads predominantly to O-substituted products.

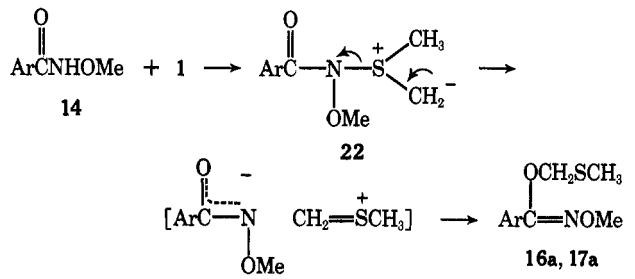
The formation of the imido esters **16a** and **17a** probably occurs by a dissociation–recombination mechanism *via* the sulfonium ylide **22**. A similar mechanism could also involve an initial oxysulfonium ylide rather than **22**, but in view of our results on the reactions of simple amides, we prefer the nitrogen of **14** as the original nucleophile. An alternative cyclic intramolecular

(22) U. Lerch and J. G. Moffatt, *J. Org. Chem.*, in press.

(23) M. T. W. Hearn and A. D. Ward, *Aust. J. Chem.*, **22**, 161 (1969).

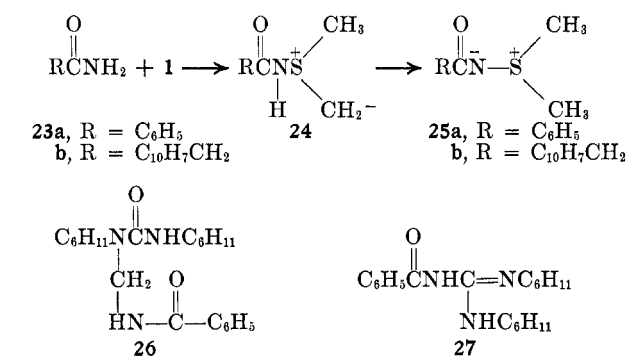
(24) R. Blaser, P. Imfeld, and U. Schindler, *Helv. Chim. Acta*, **52**, 569 (1969).

rearrangement of **22** to **16a** or **17a** is less likely, since it involves nucleophilic attack of the ylide carbanion on oxygen.

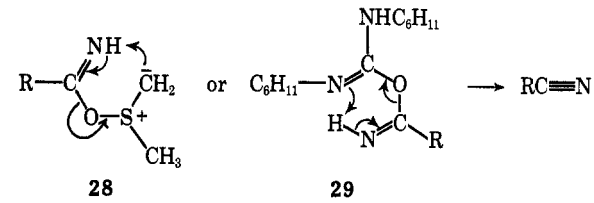


We next turned our attention to the reactions of amides and found that simple primary carboxamides **23** rapidly react with sulfoxides and DCC to form *N*-acyl-*S*,*S*-dialkylsulfilimines (**25**).[25] While *N*-sulfonylsulfilimines have been prepared by many routes,[25] including the reactions of sulfonamides with DMSO and phosphorus pentoxide or acetic anhydride, the latter reactions have been claimed to work only with amides of very strong carboxylic acids (*e.g.*, dichloro- and trichloroacetamide)[26] and *N*-acylsulfilimines have remained relatively poorly studied. The preparation of *N*-benzoyl-*S*,*S*-dimethylsulfilimine (**25a**) has, for example, only very recently been achieved *via* photolysis of 3-phenyl-$\Delta^2$-1,4,2-dioxazolin-5-one in dimethyl sulfide.[27] The reaction of benzamide with DMSO and DCC in the presence of anhydrous orthophosphoric acid, however, rapidly gave **25a** in a yield of 47% together with 12% benzonitrile, and several minor byproducts identified as *N*-(1,3-dicyclohexyl-1-ureidomethyl)benzamide (**26**) and 1-benzoyl-2,3-dicyclohexylguanidine (**27**)[28] by analytical and spectroscopic methods.

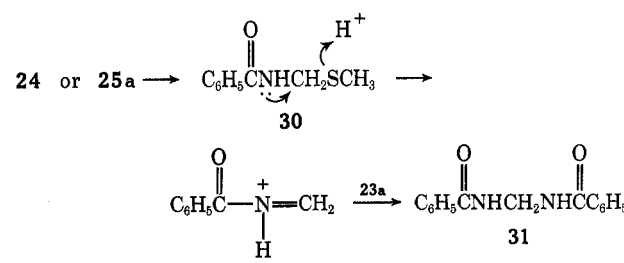
The formation of **25** presumably proceeds *via* initial condensation of the amide with **1** giving the sulfonium ylide **24**, which undergoes a rapid prototropic shift of the labile NH proton to the more stable sulfilimine form.



The formation of benzonitrile in the above reaction may well be the consequence of a competing initial attack of the amide oxygen upon **1** giving the oxysulfonium ylide **28**, which can collapse *via* a cyclic process to the nitrile. An alternative direct dehydration involving only DCC and not DMSO cannot, however, be ruled out, since it was shown that benzonitrile is also formed by reaction of benzamide with DCC and anhydrous phosphoric acid in dimethylformamide, presumably *via* the intermediate **29**. The guanidine **27** can arise *via* the alternative acid-catalyzed addition of the benzamide nitrogen to DCC, while **26** is typical of compounds originating from **20**.



In contrast to the results above, the reactions of benzamide with DMSO and phosphorus pentoxide or acetic anhydride took largely different courses. Thus, the reaction of **23a** with DMSO and phosphorus pentoxide at room temperature gave **25a** in only 13% yield, while the major product (61%) was *N*,*N*′-methylenebisbenzamide (**31**). The latter compound is a well-known product from strong heating of either benzamide[29] or benzonitrile[30] with sulfuric acid in DMSO and has been attributed to condensations with formaldehyde arising from decomposition of DMSO. Similarly, the reaction of benzamide with DMSO and acetic anhydride at 115° gave **31** in 35% yield, although in this case little reaction occurred at room temperature or at 70°. It is not clear whether the formation of **31** in the reactions occurs *via* the ylides **24** or **25a** or directly from the amide **23a** with formaldehyde. Preliminary dehydration of **23a** to the nitrile appears not to be involved, since benzonitrile does not react with DMSO and phosphorus pentoxide under the usual reaction conditions. Treatment of **23a** with paraformaldehyde and anhydrous phosphoric acid in DMSO does slowly give **31**, and this reaction is more rapid using sulfuric acid. On the other hand, the ylide **25a** is converted, in 64% yield, into **31** by heating with 0.1 molar equiv of anhydrous phosphoric acid in dimethylformamide. The conversion of **25a** to **31** can also be achieved, albeit in only 13% yield, by heating with acetic anhydride, the major product in this case being *N*-acetylbenzamide.[31] If indeed the ylides **24** or **25a** are the progenitors of **31**, then a mechanism involving initial rearrangement, probably *via* a dissociation–recombination mechanism, to the amide **30** might be considered.



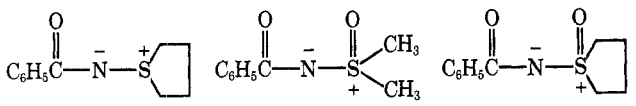
A similar proposal has been made by Sekera and Rumpf[32] to explain the formation of *N*,*N*′-methylenebissulfonamides from sulfonamides and phosphorus pentoxide in DMSO but has been criticized by Martin, *et al.*,[30] for reactions using phenyl cyanate as the activating agent. In the present case, the intermediacy of

(25) For a review on sulfilimines see F. Challenger in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, p 339.
(26) D. S. Tarbell and C. Weaver, *J. Amer. Chem. Soc.*, **63**, 3272 (1954).
(27) J. Sauer and K. K. Mayer, *Tetrahedron Lett.*, 319 (1968).
(28) F. L. Scott, *J. Org. Chem.*, **22**, 1568 (1957).
(29) V. J. Traynelis and W. L. Hergenrother, *ibid.*, **29**, 221 (1964).
(30) D. Martin, H. J. Niclas, and A. Weise, *Chem. Ber.*, **102**, 23 (1969).
(31) C. D. Hurd and A. G. Prapas, *J. Org. Chem.*, **24**, 388 (1959).
(32) A. Sekera and P. Rumpf, *C. R. Acad. Sci.*, **260**, 2252 (1965).

**25a** seems questionable, since treatment of this ylide with DMSO and phosphorus pentoxide at room temperature gives only low yields of **31**. Once again, we have no direct evidence for the formation of an intermediate such as **30**.

The formation of *N*-acylsulfilimines seems to be a fairly general reaction, since the reaction of β-naphthylacetamide (**23b**) with DMSO–DCC gave *S,S*-dimethyl-*N*-(β-naphthylacetyl)sulfilimine (**25b**) in 28% yield together with 31% of β-naphthylacetonitrile.[33] The reaction of benzamide with DCC and anhydrous phosphoric acid in tetramethylene sulfoxide also occurred readily and gave crystalline *N*-benzoyl-*S,S*-tetramethylenesulfilimine (**32**) in 35% yield together with smaller amounts of benzonitrile and **27**. This reaction has not been studied using other activating agents.

Oxidation of both **25a** and **32** was readily achieved using aqueous potassium permanganate and gave the corresponding sulfoximines **33** and **34** in high yield. *N*-Acylsulfoximines are better known than *N*-acylsulfilimines, since they can be prepared by photolysis of acylazides in sulfoxides[34] or by acylation of the parent *S,S*-dialkylsulfoximine.[34a,35] Attempted oxidation of **25b**, however, gave only β-naphthylacetamide in 90% yield.

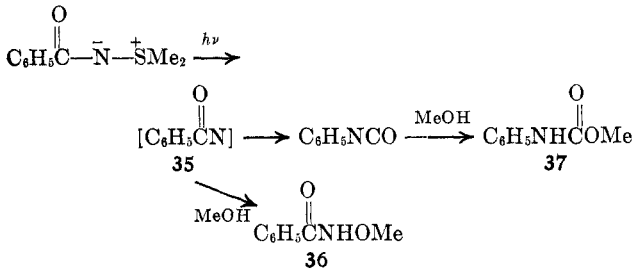


**32** **33** **34**

With the ylide **25a** readily available, a few other simple reactions on this species were undertaken. As would be expected, treatment of **25a** with anhydrous hydrogen chloride in dioxane gave benzamidodimethylsulfonium chloride in high yield. Upon heating at 100° with 2 *N* sodium hydroxide, **25a** was hydrolyzed to a mixture of benzamide and benzoic acid, roughly 20 min being required for disappearance of the starting material. It was completely stable in 2 *N* hydrochloric acid at room temperature for 16 hr but was hydrolyzed to benzoic acid upon heating the solution to 100° for 1.5 hr. There was no decomposition at all upon heating **25a** in DMSO at 115° for 15 hr.

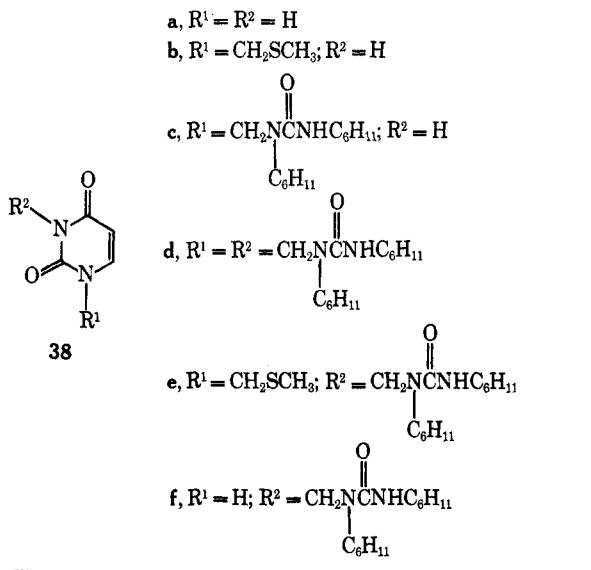
Irradiation of a solution of **25a** in methanol using a low-pressure mercury lamp led quite rapidly to the formation of benzamide (47%), *N*-methoxybenzamide (**36**, 7%),[36] and methyl carbanilate (**37**, 33%),[37] all being identical with authentic samples by tlc, infrared and ultraviolet spectroscopy, and gas–liquid chromatography. The formation of the latter two compounds, both of which are also formed during photolysis of benzoylazide in methanol,[34b] suggests photochemical conversion of **25a** into the acylnitrene **35**,[38] which can then insert into the OH bond of methanol giving **36** or rearrange to phenyl isocyanate, which reacts with methanol giving **37**.

During preparation of authentic **36** through reaction of benzoyl chloride with methoxylamine, the previously undescribed *N*-methoxydibenzamide was isolated in 24% yield.



N-Substituted carboxylic acid amides were found to be much less reactive toward DMSO and DCC. Benzanilide, in fact, was completely inert to even quite prolonged reaction and also failed to react with DMSO and either acetic anhydride or phosphorus pentoxide at room temperature. At 80° with $P_2O_5$ some reaction did occur, giving a considerable number of unidentified minor products.

In recent years there has been a great deal of work done in this laboratory on the oxidation, using the DMSO–DCC method, of isolated sugar hydroxyl groups in nucleosides to the corresponding aldehydo and keto functions.[39] Usually these oxidations are worked up after 3–12 hr depending upon the choice of acid catalyst, and under these conditions only very minor side reactions are observed. If the reactions are allowed to proceed for several days, however, unidentified by-products do appear, and it was of interest to determine what type of reactions could occur on the heterocyclic bases under these conditions. Our initial study involved the reaction of uracil (**38a**) with DMSO, DCC, and anhydrous phosphoric acid. A slow reaction took place and after 7 days five new crystalline products in addition to 24% unreacted **38a** were isolated by preparative tlc. These were all readily shown to be derivatives in which either or both of $N_1$ or $N_3$ of the uracil ring are substituted by methylthiomethyl or 1,3-dicyclohexyl-1-ureidomethyl groups. Based upon elemental analysis and nmr and



**38**

(33) S. C. J. Oliver and J. Wit, *Recl. Trav. Chim. Pays-Bas*, **57**, 90 (1938).

(34) (a) L. Horner and A. Christmann, *Chem. Ber.*, **96**, 388 (1963); (b) L. Horner, G. Bauer, and J. Dourges, *ibid.*, **98**, 2631 (1965).

(35) F. Misani, T. H. Fair, and L. Reiner, *J. Amer. Chem. Soc.*, **73**, 459 (1951).

(36) W. Lossen, *Justus Liebigs Ann. Chem.*, **281**, 186 (1894).

(37) A. W. Hofmann, *ibid.*, **74**, 1 (1850).

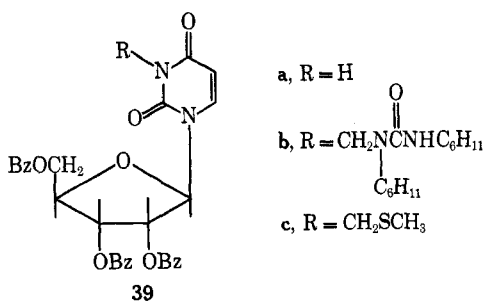
(38) For a review of acylnitrenes see W. Lwowski in "Nitrenes," W. Lwowski, Ed., Interscience, New York, N. Y., 1970, p 185.

(39) (a) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **85**, 3027 (1963); (b) A. F. Cook and J. G. Moffatt, *ibid.*, **89**, 2697 (1967); (c) U. Brodbeck and J. G. Moffatt, *J. Org. Chem.*, **35**, 3552 (1970); (d) unpublished experiments of G. H. Jones, G. B. Howarth, N. P. Damodaran, and J. G. Moffatt.

ultraviolet spectra these compounds have been identified as **38b–f**.

The major products (**38b** and **38c**) were shown to be $N^1$-substituted uracils by their ultraviolet spectra under neutral and alkaline conditions, which closely resemble those of 1-methyluracil [$\lambda_{max}^{pH\,7}$ 267 mμ (ε 9700); $\lambda_{max}^{pH\,12}$ 265 mμ (ε 7000); $\epsilon_{max}^{pH\,7}/\epsilon_{max}^{pH\,12} = 1.37$][40] rather than those of 3-methyluracil [$\lambda_{max}^{pH\,7}$ 259 mμ (ε 7300); $\lambda_{max}^{pH\,12}$ 283 mμ (ε 10,700); $\epsilon_{max}^{pH\,7}/\epsilon_{max}^{pH\,12} = 0.68$].[40] In addition, desulfurization of **38b** gave 1-methyluracil in crystalline form. The 3-substituted uracil derivative **38f** had spectral properties very similar to those of 3-methyluracil and unlike those of the 1-methyl isomer. The orientation of the two substitutents in **38e** could be ascertained by the rather facile decomposition of this compound into **38b**, thus placing the methylthiomethyl group at $N^1$. A similar instability of **38d** with loss of the ureidomethyl group from $N^3$ and formation of **38c** was also noted.

The possible reactions occurring with 2′,3′,5′-tri-*O*-benzoyluridine (**39a**)[41] are obviously fewer in number and closer to our direct interest. Once again, a slow reaction occurred using anhydrous phosphoric acid as the proton source with roughly 10–20% conversion after 24 hr and 50% after 5 days. Since an oxidation reaction using this acid is generally complete within 1–2 hr, no appreciable side reactions involving the uracil ring would be expected to occur within this time. Careful preparative tlc separated the reaction product into two bands, the major one of which (40%) was shown to be $N^3$-(1,3-dicyclohexyl-1-ureidomethyl)-2′,3′,5′-tri-*O*-benzoyluridine (**39b**), which was obtained in an analytically pure form. The ultraviolet spectrum of this compound was consistent with it being an $N^3$-substituted uracil rather than an $O^4$-substituted compound. The minor product proved to be $N^3$-methylthiomethyl-2′,3′,5′-tri-*O*-benzoyluridine (**39c**), the structure of which was immediately obvious from its nmr spectrum. The spectrum of **39c** was somewhat unique in that the $NCH_2S$ protons in the $N^3$ substituent were magnetically nonequivalent, presumably due to restricted rotation, and appeared as an AB quartet ($J_{gem}$ = 13 Hz) centered at 4.95 ppm. Most other compounds containing the $NCH_2SCH_3$ grouping that we have encountered have given nmr spectra in which the $NCH_2S$ protons appear as a singlet.



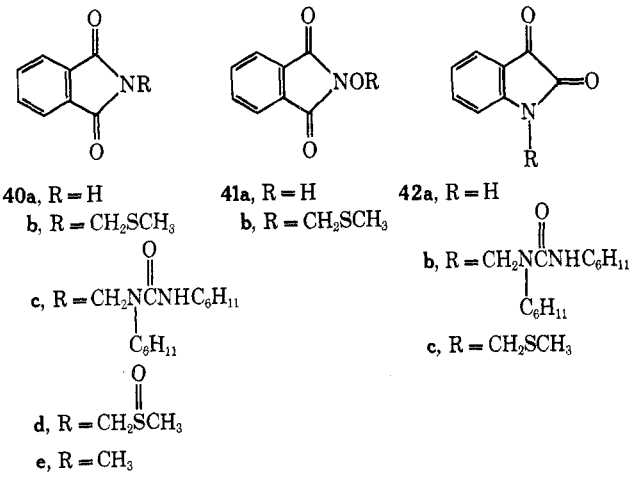

**39**

Very similar types of compounds were obtained from the reaction of phthalimide (**40a**) with DMSO and DCC, the major product in this case being *N*-(methylthiomethyl)phthalimide (**40b**, 38%) while the *N*-(ureidomethyl) compound **40c** was formed in only 2% yield. It is not clear why the ureidomethyl derivative should predominate in the reaction of **39a** and be so suppressed with **40a**. Desulfurization of **40b** gave *N*-methylphthalimide (**40e**) identical with an authentic sample.[42] A similar reaction with *N*-hydroxyphthalimide (**41a**) was quite rapid and gave *N*-(methylthiomethoxy)-phthalimide (**41b**) in 58% yield. In this case, there was no sign of a ureidomethyl derivative.

The nmr spectrum of **41b** was somewhat unusual, since the signals for both the SMe (2.38 ppm) and $OCH_2S$ (5.30 ppm) groups are shifted downfield from the normal positions in methylthiomethyl ethers (about 2.1 and 4.7 ppm, respectively).[2a] The SMe signal is, in fact, closer to that expected for a methyl sulfoxide such as **40d**, but this structure is ruled out both by an independent synthesis of **41b** from the sodium salt of **41a** and chloromethyl methyl sulfide and by the mass spectrum of **41b**, which shows a base peak at *m/e* 61 ($CH_2{=}S^+CH_3$) which would not be expected from **40d**.

Recently it was shown that *N*-hydroxysuccinimide[43] and *N*-hydroxyglutarimide[44] react with DCC in tetrahydrofuran or acetonitrile to form di- and trimeric products. No such products were observed in the present reaction in DMSO.

Finally, the lactam function of isatin (**24a**) was found to react slowly with DMSO–DCC in the presence of anhydrous phosphoric acid. In addition to 55% unreacted **42a**, the major product was found to be *N*-(1,3-dicyclohexyl-1-ureidomethyl)isatin (**42b**, 24%), and *N*-(methylthiomethyl)isatin (**42c**) was formed in only very low yield.




From the work reported in this paper it is clear that the acid-catalyzed reactions of carboxylic acids, hydroxamic acids, and amides with DMSO and DCC lead to a variety of product types. In forthcoming papers,[22] this type of reaction will be extended to yet other nucleophilic functional groups.

## Experimental Section

**General Methods.**—Thin layer chromatography (tlc) was done on 0.25-mm layers of Merck silica gel GF and the products were visualized by their ultraviolet absorption or by spraying with a 5% solution of ammonium molybdate in 10% sulfuric acid followed by brief heating at 150°. Preparative tlc was done on 20 ×

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(41) J. J. Fox, D, Van Praag, I. Wempen, I. L. Doerr, L. Cheong, J. E. Knoll, M. L. Eidinoff, A. Bendich, and G. B. Brown, *J. Amer. Chem. Soc.*, **81**, 178 (1959).

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(43) H. Gross and L. Bilk, *Tetrahedron*, **24**, 6935 (1968).

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100 cm glass plates coated with a 1.3-mm layer of merck silica gel HF. Nuclear magnetic resonance spectra were obtained using Varian A-60 or HA-100 spectrometers and are recorded in parts per million downfield from an internal standard of tetramethylsilane. Mass spectra were obtained using an Atlas CH-4 instrument fitted with a direct inlet system. Elemental analyses were performed by Dr. A. Bernhardt, Mülheim, Germany, and other instrumental analyses were performed by the staff of the Analytical Laboratory of Syntex Research.

**Reactions with *p*-Nitrobenzoic Acid. A. With DMSO–DCC.**—Dicyclohexylcarbodiimide (6.18 g, 30 mmol) was added to a solution of *p*-nitrobenzoic acid (1.67 g, 10 mmol) and anhydrous orthophosphoric acid (1 ml of a 5 *M* solution in anhydrous DMSO) in a mixture of DMSO (10 ml) and benzene (5 ml). After a few minutes the mixture became hot and crystalline dicyclohexylurea separated. After 30 min the mixture was diluted with ethyl acetate and a solution of oxalic acid (2.52 g, 20 mmol) in ethyl acetate was carefully added (gas evolution). After 30 min the dicyclohexylurea was removed by filtration and the filtrate was washed with aqueous bicarbonate and three times with water. The filtrate was dried ($MgSO_4$) and evaporated, leaving a semicrystalline residue that was combined with some solid material that separated during the aqueous extractions and crystallized from hot ethyl acetate, giving 1.50 g (40%) of fine needles, mp 193–195°. This was essentially pure **7a** contaminated with only a trace of dicyclohexylurea. An analytical sample was prepared from acetone: mp 195–196°; $\lambda_{max}^{MeOH}$ 273 mμ (ε 9300); nmr (DMSO-$d_6$) 1.0–2.0 (m, 20, cyclohexyl), 3.1 (m, 1, >CHNHCO), 4.1 [m, 1, >CHN (CO–)$_2$], 7.66 (d, 2, $J$ = 8 Hz, Ar), 7.99 (d, 1, $J$ = 7 Hz, NH), 8.22 ppm (d, 2, $J$ = 8 Hz, Ar).

*Anal.* Calcd for $C_{20}H_{27}N_3O_4$: C, 64.32; H, 7.29; N, 11.25. Found: C, 64.33; H, 7.67; N, 11.18.

The filtrate from crystallization of **7a** was purified by preparative tlc using $CHCl_3$–$CCl_4$ (4:1). Elution of the major band gave 0.96 g (42%) of **5a**: mp 52–53°. [recrystallization from hexane raised the melting point to 53.5–54.5° (lit.[9] mp 54–55°); $\lambda_{max}^{MeOH}$ 259 mμ (ε 13,400); nmr ($CDCl_3$) 2.33 (s, 3, $SCH_3$), 5.46 (s, 2, $SCH_2O$), 8.27 ppm (s, 4, Ar).

*Anal.* Calcd for $C_9H_9NO_4S$: C, 47.57; H, 3.99; H, 6.16; S, 14.11. Found: C, 47.70; H, 4.13; N, 6.01; S, 13.96.

**B. With DMSO–Acetic Anhydride.**—A solution of *p*-nitrobenzoic acid (1.67 g, 10 mmol) in a mixture of DMSO (15 ml) and acetic anhydride (10 ml) was kept at 23° for 3 days. It was then diluted with ethyl acetate and extracted with water and with aqueous sodium bicarbonate, dried, and evaporated *in vacuo*, leaving 0.88 g of a solid residue. Crystallization from hexane gave 0.75 g (33%) of **5a** identical with that above.

**Reaction with Diphenylacetic Acid.**—A mixture of diphenylacetic acid (2.12 g, 10 mmol), DCC (6.18 g, 30 mmol), and anhydrous $H_3PO_4$ (5 mmol) in DMSO (5 ml) and benzene (5 ml) was kept overnight at room temperature. The mixture was diluted with ethyl acetate, filtered, and extracted four times with water. Evaporation of the dried ($MgSO_4$) organic phase left an oil (3.5 g) that was purified by preparative tlc on three plates using benzene–acetone (4:1), giving two main bands. Elution of the slower band gave 1.08 g (26%) of the crystalline *N*-acylurea **7b**, which was recrystallized from ether: mp 161–162°; $\lambda_{max}^{MeOH}$ 253 mμ (ε 500), 260 (510), and 266 (380); $\nu_{max}$ (KBr) 3335, 1665, 1705 $cm^{-1}$; nmr 0.90–2.0 (m, 20, $CH_2$), 3.4–4.3 (m, 2, CHN), 5.29 (s, 1, $Ar_2CHCO$), 6.2 (m, 1, NH), 7.30 ppm (s, 10, Ar); mass spectrum (70 eV) $m/e$ 418 ($M^+$), 293 ($M^+ - C_6H_{11}NCO$), 194 ($Ar_2C{=}C{=}O$).

*Anal.* Calcd for $C_{27}H_{34}N_2O_2$: C, 77.47; H, 8.19; N, 6.69. Found: C, 77.32; H, 7.88; N, 6.78.

Elution of the faster band gave 1.87 g (69%) of a homogeneous oil that was distilled in a Kugelrohr apparatus[45] [bath 150° (0.01 mm)], giving 1.6 g of **5b**: mp 31–31.5°; $\lambda_{max}^{MeOH}$ 252 mμ (ε 500), 258 (600) and 265 (490); nmr ($CDCl_3$) 2.05 (s, 3, $SCH_3$), 5.06 (s, 1, $Ar_2CHCO$), 5.17 (s, 2, $OCH_2S$), 7.30 ppm (s, 10, Ar).

*Anal.* Calcd for $C_{16}H_{16}O_2S$: C, 70.55; H, 5.92; N, 11.75; S, 11.77. Found: C, 70.41; H, 5.86; N, 11.66; S, 11.71.

**Reaction of *p*-Nitrobenzohydroxamic Acid (8a).**—Anhydrous orthophosphoric acid (5 mmol) was added to a soluion of *p*-nitrobenzohydroxamic acid (1.82 g, 10 mmol)[13] and DCC (6.18 g, 30 mmol) in a mixture of DMSO (10 ml) and benzene (5 ml). An exothermic reaction occurred after a few minutes and after 1 hr the mixture was worked up as above giving a mixture almost identical with that from *p*-nitrobenzoic acid. From this, crystalline **5a** and **7a** were isolated in yields of 31 and 42% as above.

**Reaction of Diphenylacetohydroxamic Acid (8b).**—A solution of **8b** (2.27 g, 10 mmol),[14] DCC (6.18 g, 30 mmol), and anhydrous orthophosphoric acid (5 mmol) in DMSO (10 ml) and benzene (5 ml) was kept overnight. After the usual work-up with ethyl acetate, the mixture was purified by preparative tlc using benzene–ethyl acetate (19:1) giving three major bands. Elution of the fastest band gave 1.36 g (50%) of almost pure **5b** (ir and tlc) containing only a trace of another compound. The latter (75 mg, 2%) was isolated by crystallization from benzene–hexane, mp 153–155°, and identified as **13**: $\lambda_{max}^{MeOH}$ 253 mμ (ε 450), 258 (490), 265 (360); $\nu_{max}$ (KBr) 1635, 1695 $cm^{-1}$; nmr ($CDCl_3$) 1.0–2.0 (m, 22, $C_6H_{11}$), 3.06 (d, 1, $Ar_2CHNH$ giving singlet with $D_2O$–$CD_3COOD$), 3.0 and 3.7 (m, 1, NH), 4.24 ppm (br s, 10, Ar); mass spectrum (70 eV) $m/e$ 433 ($M^+$), 308 ($M^+ - C_6H_{11}NCO$), 224 ($C_6H_{11}NHCONHC_6H_{11}$), 209 ($Ar_2CHNCO$).

*Anal.* Calcd for $C_{27}H_{35}N_3O_2$: C, 74.79; H, 8.14; N, 9.69. Found: C, 75.04; H, 7.88; N, 9.79.

Elution of the middle band gave 630 mg (15%) of crystalline **7b**, mp 161–162°, while the slowest band gave, after recrystallization from methanol, 191 mg (10%) of **12**: mp 273° (lit.[15] mp 272–273°); $\lambda_{max}^{MeOH}$ 249 mμ (ε 1600), 255 (1800), 260 (1700); $\nu_{max}$ (KBr) 3325, 1640, 1580 $cm^{-1}$; nmr (DMSO-$d_6$) 5.86 (d, 2, $J$ = 8 Hz, $Ar_2CHNH$ becoming singlet with $CD_3COOD$–$D_2O$), 6.90 (d, 2, $J$ = 8 Hz, $Ar_2CHNH$), 7.25 ppm (s, 20, Ar).

*Anal.* Calcd for $C_{27}H_{24}N_2O$: C, 82.62; H, 6.16; N, 7.14. Found: C, 82.53; H, 6.50; N, 7.14.

***N*-Methoxy-*p*-nitrobenzamide (14).**—A solution of *p*-nitrobenzoyl chloride (3.7 g, 20 mmol) in chloroform (20 ml) was added slowly to a cooled suspension of methoxylamine hydrochloride (1.67 g, 20 mmol) in chloroform (30 ml) and pyridine (5 ml). After 16 hr the solvent was evaporated and the residue was triturated with water. The resulting crystalline product was recrystallized from water and then from ethyl acetate, giving 3.05 g (78%) of **14**: mp 181–183° (lit.[46] mp 180°); $\lambda_{max}^{MeOH}$ 263 (ε 9700); $\lambda_{max}^{1N\ NaOH}$ 241 mμ (ε 8600), 256 (8500), 352 (5000); nmr (DMSO-$d_6$) 3.83 (s, 3, OMe), 8.05 and 8.39 ppm (d, 2, $J$ = 8 Hz, Ar).

**Reaction of *N*-Methoxy-*p*-nitrobenzamide (14).**—Anhydrous orthophosphoric acid (5 mmol) was added to a solution of **14** (1.96 g, 10 mmol) and DCC (6.18 g, 30 mmol) in a mixture of DMSO (10 ml) and benzene (5 ml). After 18 hr the mixture was worked up as usual using ethyl acetate and the organic phase was purified by preparative tlc on three plates using benzene–ethyl acetate (9:1), giving two major ultraviolet absorbing bands and several yellow bands. Elution of the fastest band (567 mg) followed by rechromatography using two passes with benzene–hexane (3:2) gave two bands. Elution of the faster band followed by Kugelrohr distillation[45] gave 256 mg (10%) of the anti imido ester **17a**: mp 33–36°; $\lambda_{max}^{MeOH}$ 221 mμ (ε 8600), 254 (8600), 299 (6300); $\nu_{max}$ (KBr) 1600, 1525, 1350 $cm^{-1}$; nmr ($CDCl_3$) 2.33 (s, 3, $SCH_3$), 3.86 (s, 3, OMe), 5.30 (s, 2, $OCH_2S$), 8.04 and 8.31 ppm (d, 2, $J$ = 8 Hz, Ar).

*Anal.* Calcd for $C_{10}H_{12}N_2O_4S$: C, 46.88; H, 4.72; N, 10.93; S, 12.49. Found: C, 46.96; H, 4.79; N, 10.87; S, 12.44.

The slower band gave 120 mg (5%) of the syn isomer **16a**: nmr ($CDCl_3$) 2.26 (s, 3, SMe), 3.99 (s, 3, OMe), 5.54 (s, 2, $OCH_2S$), 7.99 and 8.20 ppm (d, 2, $J$ = 9 Hz, Ar). Attempted short-path distillation (60° at $10^{-3}$ mm) was accompanied by partial decomposition into **14**.

Elution of the major, slow-moving product gave 1.94 g of a yellow oil that was rechromatographed on three preparative plates using two developments with $CCl_4$–acetone (4:1) giving 1.61 g (38%) of **15** as a very viscous, pale yellow syrup: $\lambda_{max}^{MeOH}$ 263 mμ (ε 10,300); $\nu_{max}$ 1660, 1525, 1350 $cm^{-1}$; nmr ($CDCl_3$) 1.0–2.1 (m, 20, cyclohexyl), 3.50 (s, 3, $OCH_3$), 3.9 (m, 2, >CHN), 5.25 (s, 2, $NCH_2N$), 5.83 (d, 1, $J$ = 7 Hz, NH), 7.90 and 8.31 ppm (d, 2, $J$ = 8 Hz, Ar).

*Anal.* Calcd for $C_{22}H_{32}N_4O_5$: C, 61.09; H, 7.46; N, 12.96. Found: C, 61.40; H, 7.73; N, 12.49.

In another experiment this compound was isolated in 69% yield. Treatment with 1 *N* hydrochloric acid at 100° for 5 min gave dicyclohexylurea, **14**, and formaldehyde, the latter being isolated as its 2,4-dinitrophenylhydrazone.

**Ethyl *N*-Methoxy-*p*-nitrobenzimidate (16b, 17b).**—*N*-Methoxy-*p*-nitrobenzamide (0.98 g, 5 mmol) and triethyloxonium fluoroborate (1.1 g, 5.8 mmol)[20] were stirred overnight in carefully dried methylene chloride (2 ml) and nitromethane (2 ml). After

(45) R. Graeve and G. H. Wahl, *J. Chem. Educ.*, **41**, 279 (1964).

(46) Applied Science Laboratories, State College, Pa.

evaporation of most of the solvent, the mixture was dissolved in ether and extracted with 1 *N* sodium hydroxide to remove some residual **14**. Evaporation of the organic phase left 785 mg of a semicrystalline residue containing roughly equal amounts of **16b** and **17b**. Crystallization from hexane gave the pure, more polar syn isomer **16b**: mp 71–73°; $\lambda_{max}^{MeOH}$ 223 mμ (ε 11,500), 310 (9800); $\nu_{max}$ ($CCl_4$) 1595, 1525, 1355, 1315 $cm^{-1}$; nmr ($CDCl_3$) 1.38 (t, 3, $J$ = 7 Hz, $CH_2CH_3$), 3.95 (s, 3, $OCH_3$), 4.46 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 7.93 and 8.23 ppm (d, 2, $J$ = 9 Hz, Ar).

*Anal.* Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.40; N, 12.50. Found: C, 53.44; H, 5.30; N, 12.60.

Kugelrohr distillation[45] of the mother liquors (100° at $10^{-2}$ mm) gave a partially crystalline mixture of **16b** and **17b**, mp 20–60°. Nmr ($CDCl_3$) included the following resonances for the anti isomer: 1.36 (t, 3, $J$ = 7 Hz, $CH_2CH_3$), 3.78 (s, 3, $OCH_3$), 4.21 (q, 2, $J$ = Hz, $OCH_2CH_3$), 7.91 and 8.21 (d, 2, $J$ = 9 Hz, Ar).

**Reactions with Benzamide (23a). A. With DMSO–DCC.**—Anhydrous phosphoric acid (10 mmol) was added to a solution of benzamide (2.42 g, 20 mmol) and DCC (11.6 g, 56 mmol) in DMSO (5 ml) and benzene (5 ml). The starting material was largely gone after 2 hr and after standing overnight the mixture was worked up with ethyl acetate and oxalic acid. Some products remained in the aqueous extracts and were largely recovered by neutralization to pH 9 followed by repeated extraction with chloroform. The combined organic phases were purified by preparative tlc on four plates using $CCl_4$–acetone (2:3), giving three main bands. Elution of the slowest band and crystaillzation from ether gave 1.71 g (47%) of *N*-benzoyl-*S*,*S*-dimethylsulfilimine (**25a**): mp 108–109.5°; $\lambda_{max}^{MeOH}$ 250 mμ (ε 10,600), 228 (10,300); $\nu_{max}$ (KBr) 1595, 1540, 1330 $cm^{-1}$; nmr ($CDCl_3$) 2.63 (s, 6, $SMe_2$), 7.35 (m, 3, Ar $C_3$, $C_4$, and $C_5$ H), 7.88 ppm (m, 2, Ar $C_2$ H and $C_6$ H); mass spectrum $m/e$ 181 ($M^+$), 166 (M − $CH_3$), 149, 134 [Ar(C=O)NMe$^+$],105 ($ArCO^+$).

*Anal.* Calcd for $C_9H_{11}NO_2$: C, 59.63; H, 6.12; N, 7.73; S, 17.69. Found: C, 59.59; H, 6.21; N, 7.81; S, 17.75.

Elution of the middle band gave 168 mg (7%) of unreacted **23a** while rechromatography of the fast band using two developments with $CCl_4$–acetone (94:6) gave three bands. The fastest of these contained 245 mg (12%) of benzonitrile that was identified by vpc and infrared analysis. The middle band gave 83 mg of an oil that was crystallized from hexane, giving 55 mg (1%) of 1-benzoyl-2,3-dicyclohexylguanidine (**27**): mp 155–156° (lit.[28] mp 155–156°); $\lambda_{max}^{MeOH}$ 267 mμ (ε 17,500), 238 (sh, 11,000); $\nu_{max}$ (KBr) 3300, 1575 $cm^{-1}$; nmr ($CDCl_3$) 1.0–2.0 (m, 20, cyclohexyl), 3.75 (m, 2, >CHNH–), 7.4 (m, 3, Ar), 8.25 (m, 2, Ar); mass spectrum $m/e$ 327 ($M^+$), 245 (M − $C_6H_{10}$).

*Anal.* Calcd for $C_{20}H_{29}N_3O$: C, 73.36; H, 8.93. Found: C, 73.70; H, 8.78.

Elution of the slowest band gave 274 mg (4%) of *N*-(1,3-dicyclohexyl-1-ureidomethyl)benzamide (**26**): mp 146–148° from ether; $\lambda_{max}^{MeOH}$ 227 mμ (ε 12,200); $\nu_{max}$ (KBr) 3260, 1625, 1540 $cm^{-1}$; nmr ($CDCl_3$) 1–2 (m, 20, cyclohexyl), 3.8 (m, 2, CHNH–), 4.85 (d, 2, $J_{H,NH}$ = 6 Hz, –HNC$H_2$–), 6.54 (d, 1, $J$ = 6 Hz, –NHC$H_2$–), 7.5 (m, 3, Ar), 7.8 ppm (m, 2, Ar); mass spectrum (15 eV) $m/e$ 357 ($M^+$), 224 [$C_6H_{11}NH(C{=}O)NHC_6H_{11}$], 143 ($m/e$ 224 − $C_6H_{10}$), 121 ($ArCONH_2^+$).

*Anal.* Calcd for $C_{21}H_{31}N_3O_2$: C, 70.55; H, 8.74; N, 11.75. Found: C, 70.61; H, 8.84; N, 11.93.

Addition of a slight excess of hydrogen chloride in dioxane to a solution of **25a** in acetone led to crystallization of benzamidodimethylsulfonium chloride, which melted with decomposition and gas evolution at 115–130°: $\lambda_{max}^{MeOH}$ 230 mμ (ε 11,400), 235 (10,600), 244 (11,500); nmr ($D_2O$) 3.54 (s, 6, $SMe_2$), 7.84 ppm (m, 5, Ar).

*Anal.* Calcd for $C_9H_{12}NOSCl$: C, 49.65; H, 5.56; N, 6.43; Cl, 16.29. Found: C, 49.90; H, 5.74; N, 6.63; Cl, 16.29.

**B. With Tetramethylene Sulfoxide and DCC.**—Benzamide (2.42 g, 20 mmol), DCC (5.8 g, 56 mmol), and anhydrous phosphoric acid (10 mmol) were allowed to react overnight in tetramethylene sulfoxide (4 ml) and benzene (20 ml). The mixture was diluted with acetone (30 ml) and water (2 ml) and after 5 hr was filtered. The filtrate was neutralized with triethylamine, evaporated *in vacuo*, and chromatographed on six preparative plates using $CCl_4$–acetone (2:3), giving a major, slow-moving band and four faster bands. Elution of the slow band, followed by crystallization from ether, gave 1.45 g (35%) of *N*-benzoyl-*S*,*S*-tetramethylenesulfilimine (**32**): mp 116–117.5°; $\lambda_{max}^{MeOH}$ 253 mμ (ε 10,800), 227 (10,400); $\nu_{max}$ (KBr) 1590, 1535 $cm^{-1}$; nmr ($CDCl_3$) 2.1 (m, 4, $-CH_2-$), 3.19 (t, 4, $-SCH_2$), 7.25 (m, 3, Ar), 8,0 ppm (m, 2, Ar); mass spectrum $m/e$ 207 ($M^+$), 130 (M − $C_6H_5$), 105 ($ArCO^+$), 87 ($C_4H_7S^+$).

*Anal.* Calcd for $C_{11}H_{13}NOS$: C, 63.73; H, 6.32; N, 6.76; S, 15.47. Found: C, 63.95; H, 6.29; N, 6.41; S, 15.86.

Elution of band 2 gave 121 mg (11%) of unreacted benzamide, while bands 3 and 4 gave small amounts of impure materials. Rechromatography of the fastest band using $CCl_4$–acetone (94:6) gave 348 mg (17%) of benzonitrile, identified by vpc, and 285 mg of an oil that was crystallized from hexane giving 132 mg (4%) of **27**, mp 155–156°, that was identical with that from the DMSO reaction.

**C. With DMSO–Phosphorus Pentoxide.**—Phosphorus pentoxide (3.2 g) was slowly added with cooling to DMSO (10 ml) followed, after 20 min, by benzamide (2.42 g, 20 mmol). Colorless needles began to separate after 1 hr and after 6 hr at 23° the mixture was diluted with ethyl acetate and water, cooled, and neutralized with 1 *N* sodium hydroxide. Crystalline **31** (965 mg) was removed and the water-extracted organic phase was evaporated and dissolved in chloroform, giving a further 442 mg of crystalline **31**. The mother liquors were chromatographed on two preparative plates using $CCl_4$–acetone (1:1) giving three major bands. Elution of the faster band and crystallization from ether gave 212 mg (total yield 1.62 g, 61%) of *N*,*N*′-methylenebisbenzamide (**31**): mp 221–223° (lit.[29] mp 219°); $\lambda_{max}^{MeOH}$ 228 mμ (ε 22,500); $\nu_{max}$ (KBr) 3280, 1635, 1525 $cm^{-1}$; nmr (DMSO-$d_6$) 4.93 (t, 2, $J_{H,NH}$ = 5 Hz, $NHCH_2NH$), 7.5 (m, 3, Ar), 8.0 (m, 2, Ar), 9.05 ppm (t, 2, $J$ = 5 Hz, NH); mass spectrum (20 eV) $m/e$ 254 ($M^+$), 149 (M − ArCO), 105 ($ArCO^+$).

Elution of the middle band gave 111 mg (5%) of unreacted **23a**, while elution of the slowest band followed by crystallization from ether gave 460 mg (13%) of **25a**, mp 108–109°, identical with that above.

**D. With DMSO–Acetic Anhydride.**—A solution of benzamide (2.42 g, 20 mmol) in DMSO (5 ml) and acetic anhydride (5 ml) was kept at 115° for 24 hr and then cooled, giving 740 mg of crystalline product. Addition of ether (15 ml) gave a further 140 mg (total yield 880 mg, 35%) of **31**, mp 219–220°. Recrystallization from acetone raised the melting point to 221–223°, identical with that of the material from C.

**E. With DCC in DMF.**—A solution of benzamide (1.21 g, 10 mmol), DCC (5 g), and anhydrous orthophosphoric acid (5 mmol) in DMF (3.5 ml) and benzene (3.5 ml) was kept for 24 hr. After addition of ethyl acetate and water (1 ml) the mixture was kept for 7 hr and filtered. The filtrate was extracted three times with water, dried, and examined by tlc using $CCl_4$, which showed an intense spot of benzonitrile. Quantitative glc indicated the presence of 826 mg (80%) of benzonitrile.

**Photolysis of *N*-Benzoyl-*S*,*S*-dimethylsulfilimine (25a).**—A solution of **25a** (362 mg, 2 mmol) in methanol (85 ml) was irradiated under argon in a quartz tube for 2 hr using a 15-W General Electric G15T8 germicidal lamp. After evaporation of the solvent, the residue was separated into three bands by preparative tlc using $CCl_4$–acetone (7:3). Elution of the fastest band gave 109 mg (33%) of crystalline methyl carbanilate (**37**), mp 46–47° (lit.[37] mp 47°), that was identical with an authentic sample by infrared and ultraviolet spectroscopy and by glc using a 5-ft column of 10% NPGS on Gas-Chrom Q at 155°.[46] Elution of the middle band followed by Kugelrohr distillation[45] at 90° (0.01 mm) gave 20 mg (7%) of *N*-methoxybenzamide[36] that was identical (nmr, ir, uv, and glc) with an authentic sample. The slowest band contained 112 mg (47%) of benzamide.

***N*-Methoxydibenzamide.**—Benzoyl chloride (2.2 g, 15.7 mmol) was added dropwise to a suspension of methoxylamine hydrochloride (1.3 g, 15.6 mmol) in pyridine (5 ml) and chloroform (3 ml) and the mixture was kept for 2 days. The mixture was partitioned between chloroform and 4 *N* hydrochloric acid and the organic phase was washed with water and separated into two bands by preparative tlc using $CCl_4$–acetone (3:2). Elution of the slower band followed by Kugelrohr distillation at 90° (0.01 mm) gave 1.39 g of *N*-methoxybenzamide:[36] $\lambda_{max}^{MeOH}$ 225 mμ (ε 10,100); nmr ($CDCl_3$) 3.75 (s, 3, $OCH_3$), 7.39 (m, 3, Ar), 7.83 (m, 2, Ar), 11.2 ppm (br s, 1, NH). Elution of the fastest band gave 483 mg (24%) of *N*-methoxydibenzamide: mp 82–84° from hexane; $\lambda_{max}^{MeOH}$ 238 mμ (ε 21,400), 252 (sh, 17,300); nmr ($CDCl_3$) 3.92 (s, 3, OMe), 7.5 (m, 8, Ar), 8.21 ppm (m, 2, Ar); mass spectrum (70 eV) $m/e$ 255 ($M^+$), 105 ($ArCO^+$), 77 ($C_6H_5^+$).

*Anal.* Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.62; H, 5.22; N, 5.70.

**Reaction of *N*-Benzoyl-*S*,*S*-dimethylsulfilimine with Acetic Anhydride.**—A solution of **25a** (300 mg, 1.65 mmol) in acetic

anhydride (2 ml) was heated under reflux for 2 hr. After evaporation of the solvent, the residue was purified by preparative tlc using $CCl_4$–acetone (4:1) giving four bands. Elution of the slowest band followed by crystallization from ether–methylene chloride gave 27 mg (13%) of *N,N'*methylenebisbenzamide (**31**), mp 220–222°, identical with the sample from benzamide–DMSO–$P_2O_5$. Elution of the second band gave 18 mg (6%) of benzoic acid while elution of the third band and crystallization from hexane gave 117 mg (44%) of *N*-acetylbenzamide: mp 115° (lit.[31] mp 117–118°); $\lambda_{max}^{MeOH}$ 233 mμ (ε 14,600); $\nu_{max}$ (KBr) 3250, 1740, 1675 $cm^{-1}$; nmr ($CDCl_3$) 2.57 (s, 3, $COCH_3$), 7.6 (m, 3, Ar), 8.0 (m, 2, Ar), 9.67 ppm (br s, 1, NH); mass spectrum (70 eV) *m/e* 163 ($M^+$), 105 ($C_6H_5CO^+$), 77 ($C_6H_5$). Elution of the fastest band followed by Kugelrohr distillation gave 14 mg of a slightly impure oil that was tentatively identified as *N,N*-diacetylbenzamide: nmr ($CDCl_3$) 2.37 (s, 6, $NAc_2$), 7.55 (m, 3, Ar), 7.90 ppm (m, 2, Ar); mass spectrum *m/e* 205 ($M^+$).

**Reaction of 25a with Phosphoric Acid.**—A solution of **25a** (300 mg, 1.65 mmol) in anhydrous DMF (1 ml) containing anhydrous orthophosphoric acid (0.15 mmol) was heated at 140° for 16 hr. Upon cooling, crystalline *N,N'*-methylenebisbenzamide (70 mg) separated. The filtrate was diluted with chloroform, extracted with 0.1 *N* sodium hydroxide, and evaporated. Crystallization from ether gave a further 65 mg (total 64%) of **31**, mp 221–223°. Preparative tlc on the mother liquors using $CHCl_3$–ethyl acetate (85:15) gave 53 mg (26%) of crystalline benzamide, mp 132–133°.

***N*-Benzoyl-*S,S*-dimethylsulfoximine (33).**—A solution of **25a** (1.15 g, 6.4 mmol) and potassium permanganate (1 g, 6.4 mmol) in water (10 ml) was heated at 100° for 10 min. Chloroform was added and after vigorous stirring the precipitated manganese dioxide was removed by filtration and washed with chloroform. Fresh chloroform was added to the aqueous phase and sulfur dioxide was bubbled through. After filtration, the combined chloroform solutions were extracted once with water, dried, and evaporated, leaving 1.18 g (95%) of crystalline material. Traces of impurities were removed by preparative tlc using $CCl_4$–acetone (1:1) and crystallization from water, giving 1.07 g (86%) of **33**: mp 107.5–108° (lit.[34a] mp 107–108°); $\lambda_{max}^{MeOH}$ 238 mμ (ε 18,300); $\nu_{max}$ (KBr) 1612, 1575 $cm^{-1}$; nmr ($CDCl_3$) 3.33 (s, 6, $SMe_2$), 7.35 (m, 3, Ar), 8.1 ppm (m, 2, Ar); mass spectrum (15 eV) *m/e* 197 ($M^+$), 120 ($M - C_6H_5$), 91.

***N*-Benzoyl-*S,S*-tetramethylenesulfoximine (34).**—A solution of **32** (414 mg, 2 mmol) and potassium permanganate (330 mg) in water (5 ml) was heated at 100° for 15 min and excess permanganate was destroyed by addition of acetone followed by sulfur dioxide. After filtration and evaporation of the acetone, colorless crystals (361 mg, 81%) of **34** were obtained and could be recrystallized from water: mp 122–123° (lit.[34b] mp 121–122°); $\lambda_{max}^{MeOH}$ 239 mμ (ε 18,700); $\nu_{max}$ (KBr) 1615, 1575 $cm^{-1}$; nmr ($CDCl_3$) 2.22 (m, 4, $S^+CH_2CH_2$), 3.4 (m, 4, $SCH_2CH_2$), 7.33 (m, 3, Ar), 8.05 ppm (m, 2, Ar); mass spectrum *m/e* 223 ($M^+$), 146 ($M - C_6H_5$), 105 ($ArCO^+$).

*Anal.* Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27; S, 14.36. Found: C, 59.40; H, 5.92; N, 6.43; S, 14.17.

**Photolysis of *N*-Benzoyl-*S,S*-dimethylsulfoximine (33).**—A solution of **33** (394 mg, 2 mmol) in methanol (90 ml) was irradiated under argon as with **25a** above for 18 hr, at which point glc showed the presence of essentially only benzamide and DMSO. No dimethyl sulfone was present. Preparative tlc using $CCl_4$–acetone (1:1) followed by crystallization from benzene gave 156 mg (65%) of benzamide, mp 132–133°, and a trace (5 mg) of an unidentified, less polar compound.

**Reaction of β-Naphthylacetamide (23b).**—A solution of **23b** (1.85 g, 10 mmol), DCC (4.5 g, 22 mmol), and anhydrous orthophosphoric acid (5 mmol) in DMSO (5 ml) and benzene (5 ml) was kept at 23° for 2 days. After addition of ethyl acetate and water (2 ml) the mixture was kept overnight, filtered, and extracted three times with water. The organic phase was purified by preparative tlc on four plates using ethyl acetate–methanol (7:3), giving three bands. Elution of the slowest band followed by crystallization from methylene chloride–ether gave 692 mg (28%) of *S,S*-dimethyl-*N*-(β-naphthylacetyl)sulfilimine (**25b**): mp 93–94°; $\lambda_{max}^{MeOH}$ 225 mμ (ε 33,800), 268 (5700), 276 (5400), 287 (3700); $\nu_{max}$ (KBr) 1550 $cm^{-1}$; nmr ($CDCl_3$) 2.55 (s, 6, $SMe_2$), 3.77 (s, 2, $ArCH_2CO$), 7.2–8.0 ppm (m, 7, Ar); mass spectrum *m/e* 245 ($M^+$), 183 ($ArCH_2CO^+$), 141 ($ArCH_2^+$), 104 ($Me_2SNCO$).

*Anal.* Calcd for $C_{14}H_{15}NOS$: C, 68.53; H, 6.16; N, 5.71; S, 13.07. Found: C, 68.58; H, 6.06; N, 5.88; S, 12.97.

Elution of the middle band gave 353 mg (19%) of unreacted **23b**, while elution of the fastest band gave 524 mg (31%) of β-naphthylacetonitrile: mp 85–86° from hexane (lit.[32] mp 85.5–86°); $\nu_{max}$ (KBr) 2250, 1600, 1510, 1410 $cm^{-1}$; identical with an authentic sample.

**Reaction with Uracil (38a).**—A solution of uracil (2.24 g, 20 mmol), DCC (11.6 g, 56 mmol), and anhydrous phosphoric acid (10 mmol) in a mixture of DMSO (20 ml) and benzene (2 ml) was kept at room temperature for 7 days.

After addition of water and ethyl acetate the solution was filtered and the organic phase was repeatedly extracted with water. Evaporation of the aqueous phase and crystallization from water gave 323 mg of unreacted uracil. Thr organic phase was separated into six bands by preparative tlc on five plates using two developments with $CCl_4$–acetone (3:1). Elution of the fastest band (band 1) gave a solid (270 mg, 2%) that consistently partially decomposed to **38c** during crystallization. Rechromatography using chloroform–ethyl acetate (9:1) gave **38d** as a homogeneous syrup that crystallized upon addition of ether: mp 179–180° with resolidification and decomposition above 240°; $\lambda_{max}^{MeOH}$ 266 mμ (ε 8300); nmr (pyridine-$d_5$) 0.8–2.2 (m, 40, cyclohexyl), 4.0 (m, 4, >CHNH), 5.62 and 5.69 (s, 2, $NCH_2N$), 5.99 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 7.0 and 7.82 (d, 1, *J* = 8 Hz, NH), 8.27 ppm (d, 1, $J_{5,6}$ = 8 Hz, $C_6$ H).

*Anal.* Calcd for $C_{32}H_{52}N_6O_4$: C, 65.72; H, 8.96; N, 14.37. Found: C, 65.84; H, 8.69; N, 14.12.

Rechromatography of band 2 using $CCl_4$–acetone (3:1) removed 378 mg of a more polar decomposition product (**38b**, see below) and gave 362 mg of material which was dissolved in ether leaving some dicyclohexylurea. Crystallization of the soluble portion from ether–methylene chloride gave 157 mg (2%) of 3-(1,3-dicyclohexyl-1-ureidomethyl)-1-(methylthiomethyl)uracil (**38e**): mp 130–132°; $\lambda_{max}^{MeOH}$ 270 mμ (ε 7900); $\nu_{max}$ (KBr) 3250, 1700, 1655, 1540 $cm^{-1}$; nmr (pyridine-$d_5$) 1–2.5 (m, 20, cyclohexyl), 2.20 (s, 3, SMe), 4.9 (m, 2, >CHN), 5.08 (s, 2, $SCH_2N$), 5.57 (s, 2, $NCH_2N$), 5.96 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 7.60 (d, 1, *J* = 6 Hz, NH), 7.85 ppm (d, 1, $J_{5,6}$ = 8 Hz, $C_6$ H); mass spectrum *m/e* 408 ($M^+$), 282 ($M - C_6H_{11}NCO$), 224 (DCU), 172 ($CH_3SCH_2$ – uracil), 125 ($C_6H_{11}NCO$).

*Anal.* Calcd for $C_{20}H_{32}N_4O_3S$: C, 58.79; H, 7.90; N, 13.71; S, 7.85. Found: C, 59.00; H, 7.83; N, 13.87; S, 7.91.

Band 3 contained only a small amount of an unidentified compound, while rechromatography of band 4 using chloroform–ethyl acetate (1:1) gave 207 mg (total recovery 530 mg, 24%) of uracil and a less polar product that was crystallized from methylene chloride–ether, giving 123 mg (2%) of 3-(1,3-dicyclohexyl-1-ureidomethyl)uracil (**38f**) which slowly decomposed above 150°: $\lambda_{max}^{MeOH}$ 262 mμ (ε 6300); $\lambda_{max}^{pH\ 7}$ 262 mμ, $\lambda_{max}^{pH\ 12}$ 292 mμ (ε 8900), $\epsilon_{max}^{pH\ 7}/\epsilon_{max}^{pH\ 12}$ = 0.70; nmr (pyridine-$d_5$) 1–2.7 (m, 20, cyclohexyl), 4.0 (m, 2, >CHN), 5.60 (s, 2, $NCH_2N$), 5.87 (d, 1, $J_{5,6}$ = 7 Hz, $C_5$ H), 7.64 (d, 1, $J_{5,6}$ = 7 Hz, $C_6$ H), 7.91 ppm (d, 1, *J* = 7 Hz, NH).

*Anal.* Calcd for $C_{18}H_{28}N_4O_3$: C, 62.04; H, 8.10; N, 16.08. Found: C, 62.07; H, 8.01; N, 15.50.

Elution of band 5 and crystallization from methanol–ethyl acetate gave 718 mg (10%) of 1-(1,3-dicyclohexyl-1-ureidomethyl)uracil (**38c**) which underwent a change in crystal structure at 185–188° and decomposed without melting above 275°: $\lambda_{max}^{MeOH}$ 262 mμ (ε 10,000), $\lambda_{max}^{pH\ 12}$ 265 mμ (ε 7400), $\epsilon_{max}^{pH\ 7}/\epsilon_{max}^{pH\ 12}$ = 1.35; $\nu_{max}$ (KBr) 3390, 1680, 1640, 1515 $cm^{-1}$; nmr (pyridine-$d_5$) 1–2.3 (m, 20, cyclohexyl), 3.9 (m, 2, >CHN), 5.60 (s, 2, $NCH_2N$) 5.86 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 6.76 (d, 1, *J* = 7 Hz, NH), 8.09 ppm (d, 1, $J_{5,6}$ = 8 Hz, $C_6$ H); mass spectrum *m/e* 348 ($M^+$), 237 ($M$ – uracil), 125 ($C_6H_{11}NCO$), 112 (uracil).

*Anal.* Calcd for $C_{18}H_{28}N_4O_3$: C, 62.04; H, 8.10; N, 16.08. Found: C, 61.92; H, 7.99; N, 16.32.

Elution of band 6 followed by rechromatography using $CCl_4$–acetone (3:2) and rystallization from methylene chloride–ethyl acetate gave 170 mg (total yield 548 mg, 16%) of 1-(methylthiomethyl)uracil (**38b**): mp 170–171°; $\lambda_{max}^{MeOH}$ 267 mμ (ε 9500), $\lambda_{max}^{pH\ 12}$ 265.5 mμ (ε 7000), $\epsilon_{max}^{pH\ 7}/\epsilon_{max}^{pH\ 12}$ = 1.35; $\nu_{max}$ (KBr) 1725, 1670, 1630 $cm^{-1}$; nmr (pyridine-$d_5$) 2.22 (s, 3, SMe), 5.05 (s, 2, $NCH_2S$), 5.89 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 7.65, (d, 1, $J_{5,6}$ = 8 Hz, $C_6$ H), 12.5 ppm (br s, 1, NH).

*Anal.* Calcd for $C_6H_8N_2O_2S$: C, 41.86; H, 4.68; N, 16.28; S, 18.62. Found: C, 41.68; H, 4.60; N, 16.11; S, 18.59.

Desulfurization of a sample of **38b** was effected by stirring in methanol with Davidson sponge nickel catalyst[47] for 60 hr and

(47) Davidson Chemical Division of W. R. Grace & Co., Cincinnati, Ohio.

gave a low yield of 1-methyluracil: mp 225° (lit.[40] mp 231°); $\lambda_{max}^{pH\ 7}$ 266 mμ; $\lambda_{max}^{pH\ 12}$ 264 mμ; $\epsilon_{max}^{pH\ 7}/\epsilon_{max}^{pH\ 12}$ = 1.35.

**Reaction with 2′,3′,5′-Tri-*O*-benzoyluridine (39a).**—A solution of **39a** (1.11 g, 2 mmol), DCC (1.24 g, 6 mmol), and anhydrous phosphoric acid (1 mmol) in DMSO (5 ml) and benzene (3 ml) was kept at room temperature for 5 days. After the usual work-up with ethyl acetate, the mixture was purified by preparative tlc using chloroform–acetone (10:1) which gave 0.51 g (46%) of unreacted uridine and a single faster band containing 0.86 g of a foam. Rechromatography of the latter using two developments with methylene chloride–ether (19:1) separated it into two components. The slower, major product (**39b**, 640 mg, 40%) was obtained as a dry, homogeneous foam: $\lambda_{max}^{MeOH}$ 230 mμ (ε 42,400), 260 (13,000); nmr ($CDCl_3$) 1–2 (m, 20, cyclohexyl), 3.6 (m, 2, >CHN), 4.80 (m, 3, $C_4$′ H and $C_5$′ H), 5.37 (s, 2, $NCH_2N$), 5.74 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 5.85 (m, 2, $C_2$′ H and $C_3$′ H), H), 6.28 (d, 1, $J_{1',2'}$ = 4.5 Hz, $C_1$ H), 7.08 (d, 1, $J$ = 7 Hz, NH), 7.5 (m, 10, Ar and $C_6$ H), 8.1 ppm (m, 6, Ar).

*Anal.* Calcd for $C_{44}H_{48}N_4O_{10}$: C, 66.65; H, 6.10; N. 7.07. Found: C, 66.16; H, 6.07; N, 6.84.

Elution of the faster band gave **39c** (118 mg, 10%) as a homogeneous froth: $\lambda_{max}^{MeOH}$ 229 mμ (ε 38,700), 258 (10,800); $\nu_{max}$ (KBr) 1735, 1675 cm$^{-1}$; nmr ($CDCl_3$) 2.19 (s, 3, SMe), 4.7 (m, 3, $C_4$′ H, $C_5$′ $H_2$), 4.86 and 5.02 (d, 1, $J_{gem}$ = 13 Hz, $NCH_2S$), 5.65 (d, 1, $J_{5,6}$ = 8 Hz, $C_5$ H), 5.8 (m, 2, $C_2$′ H and $C_3$′ H), 6.27 (d, 1, $J_{1',2'}$ = 5 Hz, $C_1$′ H), 7.36 (d, 1, $J_{5,6}$ = 8 Hz, $C_6$ H), 7.3–8.2 ppm (m, 15, Ar).

*Anal.* Calcd for $C_{32}H_{28}N_2O_9S$: C, 62.35; H, 4.58; N, 4.54. Found: C, 62.30; H, 4.62; N, 4.24.

**Reaction with Phthalimide (40a).**—Phthalimide (2.21 g, 15 mmol), DCC (8.7 g), and anhydrous phosphoric acid (7.5 mmol) reacted in DMSO (7.5 ml) and benzene (7.5 ml) for 2 days and worked up in the usual way with ethyl acetate. Direct crystallization of the residue from methanol gave 880 mg (40%) of unreacted **40a**, and chromatography of the mother liquors on three preparative plates using $CCl_4$–acetone (9:1) gave two bands in addition to a further trace (52 mg) of **40a**. Elution of the faster band gave 1.16 g (38%) of *N*-(methylthiomethyl)phthalimide (**40b**): mp 112.5–113.5° from hexane; $\lambda_{max}^{MeOH}$ 218 mμ (ε 20,000), 295 (1700); $\nu_{max}$ (KBr) 1760, 1700, 1615 cm$^{-1}$; nmr ($CDCl_3$) 2.26 (s, 3, SMe) 4.75 (s, 2, $NCH_2S$), 7.80 ppm (m, 4, Ar).

*Anal.* Calcd for $C_{10}H_9NO_2S$: C, 57.95; H, 4.38; N, 6.76; S, 15.36. Found: C, 58.16; H, 4.38; N, 6.85; S, 15.36.

Elution of the slower band gave 512 mg of a crystalline mixture of two compounds, one being nonultraviolet absorbing. Fractional crystallization from hexane gave 121 mg (2%) of pure 2-(1,3-dicyclohexyl-1-ureidomethyl)phthalimide (**40c**): mp 146–148°; $\lambda_{max}^{MeOH}$ 217 mμ (ε 42,500), 296 (2200); $\nu_{max}$ (KBr) 3360, 1780, 1720, 1660 cm$^{-1}$; nmr ($CDCl_3$) 1.0–2.25 (m, 20, cyclohexyl), 3.75 (m, 2, >CHN), 5.10 (s, 2, $NCH_2N$), 6.70 (d, 1, $J$ = 7 Hz, NH), 7.83 ppm (s, 4, Ar); mass spelrum $m/e$ 383 ($M^+$), 301 (M − $C_6H_{10}$), 258 (M − $C_6H_{11}NCO$), 223 [$C_6H_{11}N$-(C=O)$NHC_6H_{11}^+$], 160 (M − 223).

*Anal.* Calcd for $C_{22}H_{29}N_3O_3$: C, 68.90; H, 7.62; N, 10.96. Found: C, 69.30; H, 7.72; N, 11.31.

**Desulfurization of 40b.**—A solution of **40b** (200 mg) in methanol (25 ml) was stirred for 20 hr with about 0.5 g of Davidson sponge nickel.[48] The mixture was filtered and the nickel was washed with hot methanol (300 ml). Evaporation of the combined filtrates left 117 mg of a crystalline residue which was crystallized from ether–hexane, giving 90 mg (58%) of *N*-methylphthalimide (**40e**): mp 132–134° (lit.[42] mp 133.5–134°); $\lambda_{max}^{MeOH}$ 217 mμ (ε 40,700), 231 (16,500), 239 (12,200); nmr ($CDCl_3$) 3.15 (s, 3, NMe), 7.76 ppm (m, 4, Ar).

***N*-(Methylthiomethoxy)phthalimide (41b).**—A solution of *N*-hydroxyphthalimide (1.63 g, 10 mmol), DCC (6.18 g, 30 mmol), and anhydrous phosphoric acid (5 mmol) in DMSO (10 ml) and benzene (10 ml) was kept for 3 hr at 23°. After dilution with ether, the mixture was filtered and the filtrate was extracted theee times with water, dried, and evaporated. The residue was chromatographed on a column of silicic acid using benzene–chloroform (1:3) giving 1.29 g (58%) of crystalline product. Recrystallization from hexane gave 1.17 g (53%) of **41b**: mp 102–103°; $\lambda_{max}^{MeOH}$ 219 mμ (ε 29,000), 237 (sh, 9000), 294 (1500); $\nu_{max}$ (KBr) 1790, 1735 cm$^{-1}$; nmr ($CDCl_3$) 2.38 (s, 3, SMe), 5.20 (s, 2, $OCH_2S$), 7.82 ppm (s, 4, Ar); mass spectrum $m/e$ 223 ($M^+$), 61 ($CH_2$=$SCH_3$).

*Anal.* Calcd for $C_{10}H_9NO_3S$: C, 53.80; H, 4.06; N, 6.28; S, 14.35. Found: C, 53.94; H, 4.20; N, 6.27; S, 14.50.

**Reactions with Isatin (42a).**—A mixture of isatin (2.21 g, 15 mmol), DCC (7 g, 34 mmol), and anhydrous phosphoric acid (7.5 mmol) in DMSO (10 ml) and benzene (5 ml) was kept for 5 days and then worked up as usual with ethyl acetate. Preparative tlc using two developments with $CCl_4$–acetone (9:1) gave unreacted isatin (1.22 g, 55%) and two faster bands. The slower of these (389 mg) contained a mixture of products and was not further investigated. Elution of the faster band and crystallization from ether gave 1.35 g (24%) of red *N*-(1,3-dicyclohexyl-1-ureidomethyl)isatin (**42b**): mp 158–159°; $\lambda_{max}^{MeOH}$ 208 mμ (ε 18,700), 243 (15,700), 250 (13,700), 396 (2400), 425 (370); $\nu_{max}$ (KBr) 3450, 1715, 1645, 1615 cm$^{-1}$; nmr ($CDCl_3$) 1–2.2 (m, 20, cyclohexyl), 3.5 (m, 2, >CHN), 5.21 (d, 1, $J$ = 7 Hz, NH), 5.46 (s, 2, $NCH_2N$), 7.15 (m, 1, Ar), 7.55 ppm (m, 3, Ar); mass spectrum $m/e$ 383 ($M^+$), 258 (M − $C_6H_{11}NCO$), 237 (M − phthalimide), 147 (M − 237), 112 ($C_6H_{11}NH$=$CH_2$).

*Anal.* Calcd for $C_{22}H_{29}N_3O_3$: C, 68.90; H, 7.62; N, 10.96. Found: C, 68.80; H, 7.92; N, 10.84.

Elution of a small, partially resolved band at the front of the fast band gave, after crystallization from ether–methylene chloride, 32 mg (1%) of orange *N*-(methylthiomethyl)isatin (**42c**): mp 128–129°; $\nu_{max}$ (KBr) 1730, 1615 cm$^{-1}$; nmr ($CDCl_3$) 2.16 (s, 3, SMe), 4.84 (s, 2, $NCH_2S$), 7.16 (m, 2, Ar), 7.67 ppm (m, 2, Ar); mass spectrum $m/e$ 207 ($M^+$), 160 (M − $SCH_3$), 146 (M − $CH_3SCH_2$), 132 (M − $CH_3SCH_2N$).

*Anal.* Calcd for $C_{10}H_9NO_2S$: C, 57.97; H, 4.38; N, 6.76. Found: C, 57.63; H, 4.69; N, 6.91.

**Registry No.**—**5a**, 5388-04-5; **5b**, 31280-16-7; **7a**, 14908-53-3; **7b**, 31280-18-9; **12**, 6744-64-5; **13**, 31280-20-3; **14**, 1613-79-2; **15**, 31280-22-5; **16a**, 31280-23-6; **16b**, 31280-24-7; **17a**, 31280-25-8; **17b**, 31280-26-9; **25a**, 19397-91-2; **25b**, 31280-28-1; **26**, 31280-29-2; **27**, 6074-63-1; **31**, 1575-94-6; **32**, 31280-32-7; **33**, 31280-33-8; **34**, 3532-35-2; **38b**, 31280-35-0; **38c**, 31280-36-1; **38d**, 31280-37-2; **38e**, 31280-38-3; **38f**, 31280-39-4; **39b**, 31280-40-7; **39c**, 31280-41-8; **40b**, 20044-28-4; **40c**, 31280-43-0; **40e**, 550-44-7; **41b**, 31280-44-1; **42b**, 31280-45-2; **42c**, 20044-27-3; benzamidodimethylsulfonium chloride, 31280-46-3; *N*-methoxydibenzamide, 31280-47-4; *N*-methoxybenzamide, 2446-51-7; *N*-acetylbenzamide, 1575-95-7.