The Photochemistry of Benzophenone Azine[1]

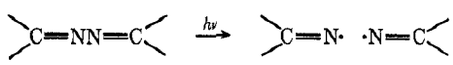
JOSEPH GORSE, III, AND ROGER W. BINKLEY*[2]

Department of Chemistry, Cleveland State University, Cleveland, Ohio 44115

Received July 22, 1971

Benzophenone azine (1) has been found to be the beginning point for two different types of photochemical reaction. The first of these is a molecular rearrangement leading to 1,3,3-triphenylisoindole (5) while the second is a photoreduction resulting in the formation of 1,1,1′,1′-tetraphenylazomethane (7). 1,1,1′,1′-Tetraphenylazomethane (7) has also been found to be photochemically unstable yielding 1,1,2,2-tetraphenylethane (2) and diphenylmethane (3). 1,1,2,2-Tetraphenylethane (2) has been previously shown to decompose upon photolysis to give *cis*-stilbene (4), 1-(2-biphenylyl)-1,2-diphenylethane (6), and biphenyl (8). All of these compounds (2–8) are isolated from the photolysis of benzophenone azine (1).

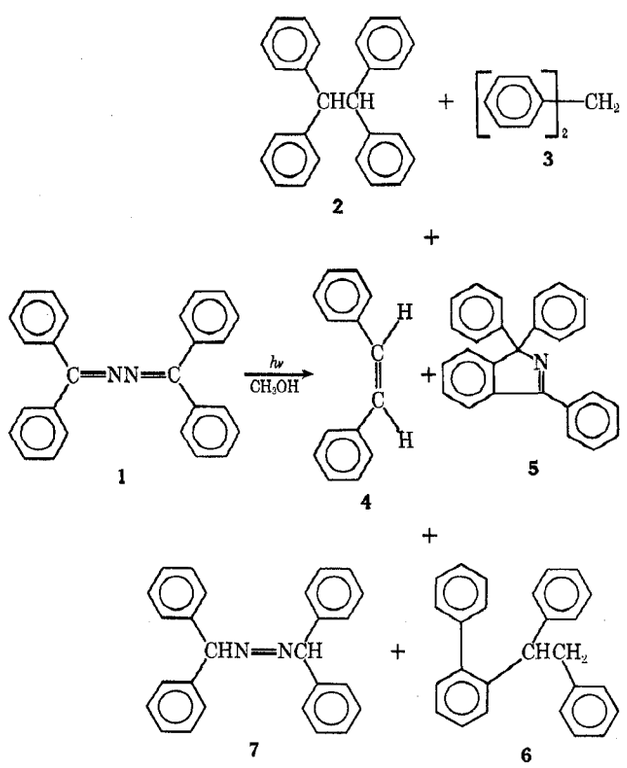
Benzophenone azine (1) has been found to be photochemically unique among azine systems. It does not participate in nitrogen–nitrogen bond homolysis, the major light-initiated reaction experienced by other acyclic azines.[3] It does, however, undergo two reac-

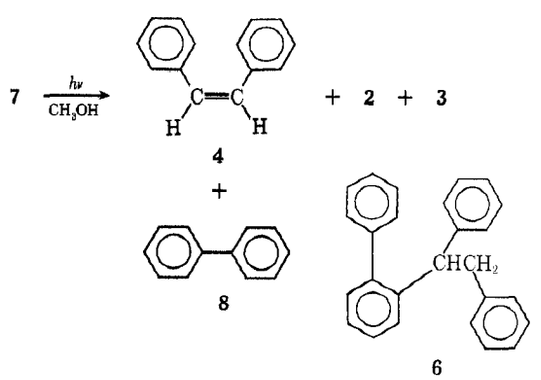


tions, a photoreduction and a molecular rearrangement. At this time we would like to describe our findings related to these two photochemical reactions of benzophenone azine (1).

Results

Vycor-filtered irradiation of 3.00 mmol of benzophenone azine (1) in 1200 ml of methanol under nitrogen for 24 hr with a 450-W Hanovia mercury-vapor lamp produced, after solvent removal, a dark yellow oil containing some solid material. Chromatography on Florisil separated the reaction mixture into seven fractions, one of which was unreacted starting material. Three of the remaining six photoproducts were easily identified as 1,1,2,2-tetraphenylethane (2, 10%), diphenylmethane (3, 8%), and *cis*-stilbene (4, 2%) by comparison of their ir and nmr spectral data (and melting point for 2) with those of commercial materials. Spectral data (nmr, ir, and uv) indicated the 1,3,3-triphenylisoindole (5), 1-(2-biphenylyl)-1,2-diphenylethane (6), and the 1,1,1′,1′-tetraphenylazomethane (7) structures for the remaining three photoproducts. Independent syntheses of these compounds and their comparison with the isolated photoproducts confirmed the assignment of structures 5, 6, and 7 to these three products (isolated in 43, 4, and 2% yields, respectively).





Benzophenone azine (1) was not photochemically reactive under all conditions. Replacing the Vycor filter (transparent above 210 nm) by a Pyrex filter (transparent above 280 nm) completely stopped its photochemical reaction. Also, conducting the reaction in benzene caused reaction to cease.[4] Photolysis in cyclohexane or 2-propanol, however, gave the same reaction observed in methanol.

The photolysis of 1,1,1′,1′-tetraphenylazomethane (7) under the same conditions as benzophenone azine (1) led to a much more rapid and less complex reaction (3 mmol completely reacted in 45 min). The following five photoproducts were formed: 1,1,2,2-tetraphenylethane (2, 58%), 1-(2-biphenylyl)-1,2-diphenylethane (6, 18%), diphenylmethane (3, 10%), *cis*-stilbene (4, 5%), and biphenyl (8, 2%).[5]

(1) Paper VIII in a series on the photochemistry of unsaturated nitrogen-containing compounds. For paper VII see R. W. Binkley, *J. Org. Chem.*, **35**, 2796 (1970).

(2) Author to whom inquires should be addressed.

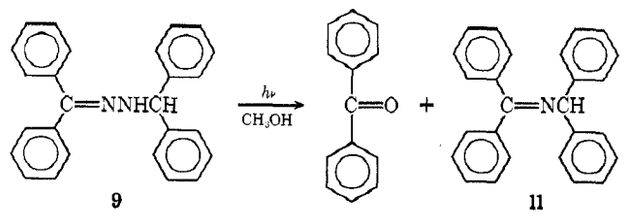
(3) (a) J. F. Ogilvie, *Chem. Commun.*, 359 (1965); (b) R. K. Brinton, *J. Amer. Chem. Soc.*, **77**, 842 (1955); (c) R. W. Binkley, *J. Org. Chem.*, **33**, 2311 (1968).

(4) The lack of reactivity of benzene may be because it is a poor hydrogen donor or because it absorbs higher energy light or for both of these reasons.

(5) It is likely that biphenyl was present in the reaction mixture from benzophenone azine (1) photolysis; however, its amount was too small to be detected.

It has been previously shown[6] that 1-(2-biphenylyl)-1,2-diphenylethane (6), *cis*-stilbene (4), and biphenyl (8) arise from the photolysis of 1,1,2,2-tetraphenylethane (2).

Vycor-filtered irradiation of benzophenone benzhydrylhydrazone (9) under the same conditions as the benzophenone azine (1) irradiation resulted in the formation of the following five photoproducts: benzophenone[7] (10, 58%), diphenylmethane (3, 11%), 1,1,2,2-tetraphenylethane (2, 11%), 1-(2-biphenylyl)-1,2-diphenylethane (6, 4%), and benzhydrylidenebenzhydrylamine (11, 7%). Of these five photoproducts,



9 10 11

+

2 + 3 + 6

three (2, 3, and 6) had been obtained and identified in the irradiation of benzophenone azine (1). The remaining two (10 and 11) were assigned structures after comparison with independently obtained samples.

Discussion

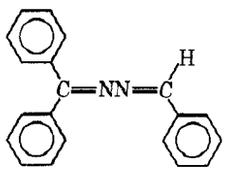
The photochemical reaction of benzophenone azine (1) has several unique aspects which merit discussion. Benzophenone azine (1) occupies a place by itself in azine photochemistry because it (a) gives no evidence of participation in the nitrogen–nitrogen bond cleavage process, the major reaction process in other azine systems; (b) undergoes a photoreduction to produce an azo system [1,1,1′,1′-tetraphenylazomethane (7)]; (c) experiences a complex molecular rearrangement leading to an isoindole [1,3,3-triphenylisoindole (5)].

The lack of formation during photolysis of 1 of any products such as benzophenone imine or benzophenone which would have arisen from a simple N–N fragmentation is one of the initially surprising aspects of its photochemistry. There appear to be two possible explanations for this lack of reactivity. First, the π system of benzophenone azine (1) is a considerably extended one when compared to other azines studied.[3] This factor may result in the formation of an excited state which is quite different in reactivity from those encountered in other azine systems. This type of change in reactivity is known in ketone photochemistry, where extending the π system changes the lowest excited state from an $n \rightarrow \pi^*$ to a $\pi \rightarrow \pi^*$ state. A second possible explanation for the lack of formation of simple nitrogen–nitrogen bond cleavage products is that N–N bond homolysis and hydrogen migration may be a concerted process. In this case the absence of a hydrogen atom directly attached to the azine system would prevent reaction.

(6) J. A. Ross, W. A. Schumann, D. B. Vashi, and R. W. Binkley, *J. Org. Chem.*, in press. The mechanism for formation of various products from photolysis of 1,1,2,2-tetraphenylethane (2) is discussed in this paper.

(7) Benzophenone imine hydrolyses to benzophenone under the conditions of this experiment (see ref 1).

The former of these two possibilities is in best agreement with experimental observation. The first fact relating to this question is that in the photolysis of benzhydrylidene benzylidene azine (12), where a



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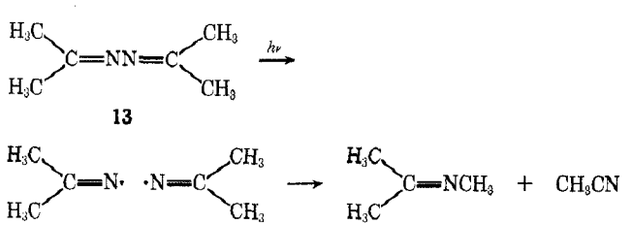
hydrogen bound to the azine system does exist, no products from an N–N bond cleavage are formed. Such a result argues against azine homolysis being dependent upon the presence of a transferable hydrogen atom. A second piece of information, arising from the recently reported photolysis of acetone azine[8] (13), also speaks against the presence of an azine bound hydrogen being necessary for N–N bond homolysis. Acetone azine (13) cleaves photochemically to produce imino radicals (experimentally observed) which react further to form the methylimine of acetone and acetonitrile. Clearly, 13 undergoes a cleavage of the nitrogen–



13

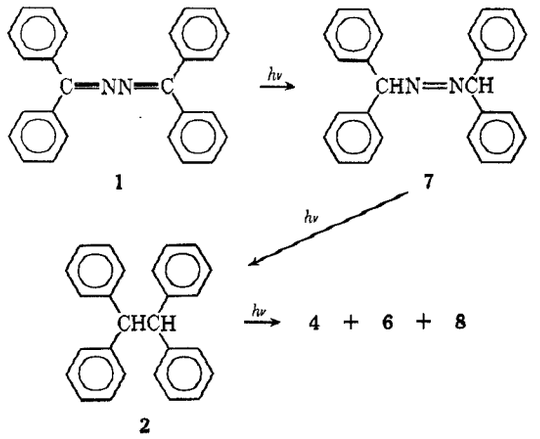
nitrogen bond independent of a hydrogen atom transfer process.

As mentioned above, the photoreduction of benzophenone azine (1) to 1,1,1′,1′-tetraphenylazomethane (7) is one of the unique aspects of its photochemistry. In this reaction, as in most photoreduction processes, the usual source of hydrogen atoms is the reaction solvent. Also in the case of benzophenone azine (1) assigning this role to the reaction solvent is supported by the fact that no reaction of 1 takes place in the poor hydrogen donor benzene.[4] Perhaps the most interesting facet of this reduction process is that it makes possible the series of photochemical transformations leading from benzophenone azine (1) to the various hydrocarbon rearrangement and fragmentation products (2, 3, 4, 6, and 8) (Scheme I). The products from individual photolyses of 1,1,1′,1′-tetraphenylazomethane (7) and 1,1,2,2-tetraphenylethane[6] (2) provide convincing evidence that these two are intermediates in this reaction series.

In contrast to the series of reactions just described where intermediates have been isolated and themselves irradiated, the intermediate stages of the conversion of benzophenone azine (1) into 1,3,3-triphenylisoindole (5) are not well understood. The studies which have been made relating to the mechanism of this reaction serve primarily to eliminate a variety of possible intermediates; however, they are able to provide an indirect indication of the course which this reaction is following.

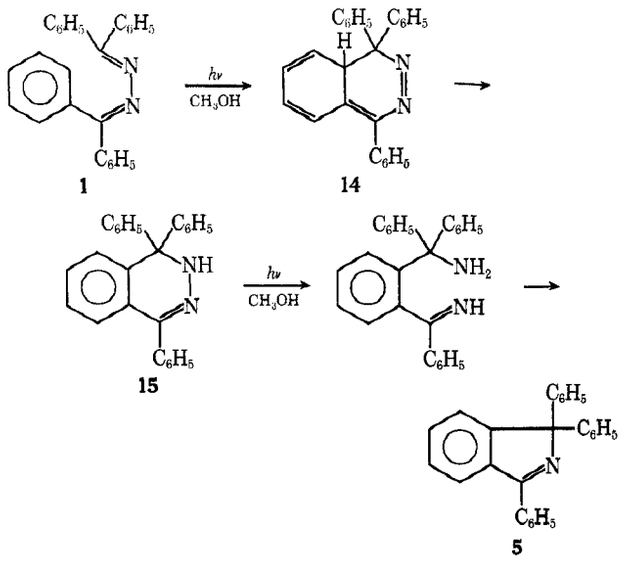
(8) (a) D. G. Horne and R. G. W. Norrish, *Proc. Roy. Soc., Ser. A.*, **315**, 301 (1970); (b) R. K. Brinton and S. Chang, *Ber. Bunsenges. Phys. Chem.*, **72**, 217 (1968).

SCHEME I

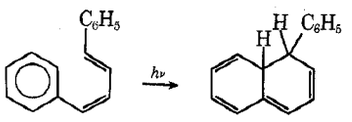


We would like to propose the mechanism shown in Scheme II as being, at present, the best explanation for

SCHEME II

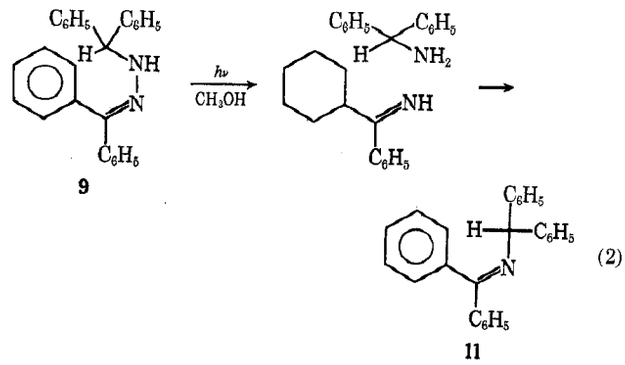


the formation of 1,3,3-triphenylisoindole (**5**) from the photolysis of benzophenone azine (**1**). This mechanism proposes the photochemical cyclization of **1** to produce the dihydrophthalazine intermediate **14**. This reaction is analogous to the known photochemical closure of 1,4-diphenylbutadienes to phenyl-substituted dihydronaphthalenes[9] (eq 1). The dihydronaphthalene system



(1)

is, of course, easily aromatized by oxidation to a substituted naphthalene. The dihydrophthalazine **14**, which cannot undergo a similar oxidation, is proposed to rearomatize *via* a hydrogen migration to an aromatic dihydrophthalazine (**15**). This mechanism further suggests that upon photolysis, **15** rearranges to give 1,3,3-triphenylisoindole (**5**) in a manner analogous to the observed rearrangement of benzophenone benzhydrylhydrazone (**9**) to give benzhydrylidenebenzhydrylamine (**11**)[10] (eq 2).



(2)

The results from the photolysis of benzophenone azine (**1**) may be summarized by saying that it participates in two photochemical processes. The first of these is a photoreduction to give 1,1,1′,1′-tetraphenylazomethane (**7**), a compound which reacts photochemically to give 1,1,2,2-tetraphenylethane (**2**) and diphenylmethane (**3**). The second is a rearrangement, probably passing through dihydrophthalazine intermediates, to give 1,3,3-triphenylisoindole (**5**).

Experimental Section

Vycor-Filtered Irradiation of Benzophenone Azine (1) in Methanol.—Benzophenone azine[11] (1.08 g, 3.00 mmol) in 1200 ml of methanol was irradiated for 24 hr with a 450-W Hanovia high-pressure quartz mercury-vapor lamp which had been lowered into a water-cooled quartz immersion well. Prepurified nitrogen was passed through the solution for 1 hr prior to irradiation and a slow stream of nitrogen was continued during photolysis. A Vycor filter was placed between the reaction mixture and the light source.

After 24 hr, the solvent was removed by distillation *in vacuo* below 30°, leaving a dark yellow mixture of solid and liquid. The residual solid was chromatographed on an 85 × 2.5 cm Florisil column slurry packed in 1:9 ether–hexane; 60-ml fractions were collected. The column was eluted as follows: 0.5 l. of hexane, 0.5 l. of 1:49 ether–hexane, 0.5 l. of 1:24 ether–hexane, 0.5 l. of 1:12 ether–hexane, 0.5 l. of 1:6 ether–hexane, 0.5 l. of 1:3 ether–hexane, 0.5 l. of 1:1 ether–hexane, and 0.5 l. of ether.

Fractions 7 and 8 afforded 13.5 mg (0.08 mmol) of diphenylmethane, identified by ir and nmr spectral comparison with a known sample.[12] Fraction 9 gave 4 mg (0.02 mmol) of *cis*-stilbene, also identified by comparison with a known sample.[12] Fractions 14–19 produced 21 mg of a clear oil which crystallized on standing and was recrystallized from hexane to give 13.5 mg (0.04 mmol) of 1-(2-biphenylyl)-1,2-diphenylethane, mp 80° (lit.[6] mp 79–81°), identified by nmr and mixture melting point comparison with an authentic sample.[6] Fractions 20–25 yielded 33 mg of 1,1,2,2-tetraphenylethane, mp 205–210° (lit.[13] mp 209–211°), also identified by nmr and mixture melting point comparison with an authentic sample.[12] Fractions 27–31 gave 24 mg of a crystalline solid which was recrystallized from ethanol to give 7 mg (0.02 mmol) of 1,1,1′,1′-tetraphenylazomethane, mp 110–114° (lit.[14] mp 115°), identified by nmr and mixture melting point comparison with an authentic sample.[14] Fractions 34–40 afforded 726 mg (2.00 mmol) of unreacted benzophenone azine. Fractions 43–48 produced 173 mg of a yellow oil which crystallized on standing and was recrystallized from ethanol to

(9) (a) G. J. Fonken, *Chem. Ind.* (London), 1327 (1962); (b) C. C. Leznoff and R. J. Haywark, *Can. J. Chem.*, **48**, 1842 (1970).

(10) E. S. Huyser, R. H. S. Wang, and W. T. Short, *J. Org. Chem.*, **33**, 4323 (1968).

(11) D. H. R. Barton, R. E. O Brien, and S. Sternhell, *J. Chem. Soc.*, 470 (1962).

(12) Aldrich Chemical Co., Inc., 940 W. St. Paul Ave., Milwaukee, Wis. 53233.

(13) H. Blitz, *Justus Liebigs Ann. Chem.*, **296**, 220 (1897).

(14) S. G. Cohen and C. H. Wang, *J. Amer. Chem. Soc.*, **77**, 2457 (1955).

give 148 mg (0.43 mmol) of 1,3,3-triphenylisoindole, mp 145° (lit.[15] mp 145.5°), identified by comparison with a known sample.[15]

Pyrex-Filtered Irradiation of Benzophenone Azine (1) in Methanol.—The reaction procedure was the same as that described for the Vycor-filtered irradiation of 1 except that a Pyrex filter was used and the reaction time was extended to 72 hr. At the end of this time no reaction had taken place.

Vycor-Filtered Irradiation of Benzophenone Azine (1) in Benzene.—The procedure was again the same as the irradiation procedure for 1 in methanol except that the solvent was changed to benzene. The irradiation time was 72 hr. No reaction was observed.

Vycor-Filtered Irradiation of 1,1,1′,1′,-Tetraphenylazomethane (7) in Methanol.—The irradiation and isolation procedures were the same as those used in the Vycor-filtered irradiation of 1 except that 1.09 g (3.00 mmol) of 1,1,1′,1′-tetraphenylazomethane was irradiated and the irradiation time was 45 min.

Fractions 7 and 8 afforded 61 mg of a mixture of biphenyl and diphenylmethane. Rechromatography separated this pair into 9 mg (0.06 mmol) of biphenyl and 51 mg (0.30 mmol) of diphenylmethane, both identified by ir and nmr spectroscopy. Fraction 9 yielded 27 mg (0.15 mmol) of *cis*-stilbene, also identified by ir and nmr spectroscopy. Fractions 14–19 gave 180 mg of 1-(2-biphenylyl)-1,2-diphenylethane, mp 75–78°. Fractions 20–25 produced 511 mg (0.54 mmol) of 1,1,2,2-tetraphenylethane, mp 206°. Fractions 27–31 gave 22 mg of unreacted 1,1,1′,1′-tetraphenylazomethane.

(15) W. Theilacker, H.-J. Bluhm, W. Heitmann, H. Kalenda, and H. J. Meyer, *Justus Liebigs Ann. Chem.*, **673**, 96 (1964).

Vycor-Filtered Irradiation of Benzophenone Benzhydrylhydrazone (9) in Methanol.—The isolation and irradiation procedures were the same as those used in the Vycor-filtered irradiation of 1 except that the material irradiated was benzophenone benzhydrylhydrazone (9) and the irradiation time was 4.5 hr.

Fractions 7 and 8 gave 33 mg (0.20 mmol) of diphenylmethane, identified by ir spectroscopy. Fractions 14–19 gave 24 mg (0.07 mmol) of 1-(2-biphenylyl)-1,2-diphenylethane, mp 65–69°. Fractions 20–24 afforded 66 mg of 1,1,2,2-tetraphenylethane, mp 205–207°. Fractions 25–27 yielded 53 mg of a white solid, recrystallized from ethanol to give 38 mg (0.13 mmol) of benzhydrylidenebenzhydrylamine, mp 150° (lit.[10] mp 152°), identified by comparison with an authentic sample. Fractions 34–39 produced 189 mg (1.04 mmol) of benzophenone, identified by ir spectroscopy. Fractions 50–55 afforded 448 mg (1.21 mmol) of unreacted starting material.

Vycor-Filtered Photolysis of Benzhydrylidene Benzylidene Azine (12) in Methanol.—The photolysis and isolation procedures were the same as those described for the Vycor-filtered irradiation of 1 except that 3.00 mmol of benzhydrylidene benzylidene azine[16] (**14**) were irradiated. No single product could be isolated in sufficient quantity for identification; in particular, no benzonitrile, benzophenone, or benzaldehyde were isolated.

Registry No.—**1**, 983-79-9.

Acknowledgment.—The authors gratefully acknowledge the support of the National Science Foundation (GP 16664) for this research.

(16) S. S. Hirsch, *J. Org. Chem.*, **32**, 2433 (1967).

Studies on the Acylation of Some 6-Aminouracil Derivatives

JAEWON L. SHIM, ROLF NIESS, AND ARTHUR D. BROOM*[1]

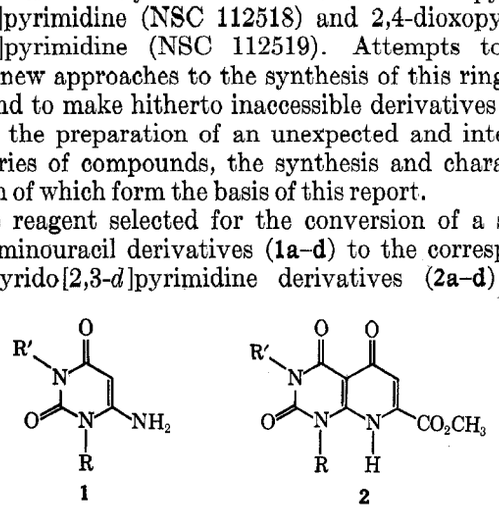
Department of Biopharmaceutical Sciences, College of Pharmacy, University of Utah, Salt Lake City, Utah 84112

Received July 26, 1971

Attempts to prepare pyrido[2,3-*d*]pyrimidine derivatives by the reaction of various alkyl 6-aminouracils with dimethyl acetylenedicarboxylate have led instead to the synthesis of 6-amino-5-(3-carbomethoxy-2-propynoyl)-uracils (**3**). It was found, using acetylation as a model reaction, that acylation occurs at C-5 if an alkyl group is present on N-1 of 6-aminouracil; in the absence of such a substituent the 6-acetamido derivative is formed. Reduction of **3** leads to cis olefin formation. The pmr spectra and some mechanistic considerations are discussed.

Antitumor activity against Walker muscular tumor in rats has recently been demonstrated for 4-oxopyrido-[2,3-*d*]pyrimidine (NSC 112518) and 2,4-dioxopyrido-[2,3-*d*]pyrimidine (NSC 112519). Attempts to develop new approaches to the synthesis of this ring system and to make hitherto inaccessible derivatives have led to the preparation of an unexpected and interesting series of compounds, the synthesis and characterization of which form the basis of this report.

The reagent selected for the conversion of a series of 6-aminouracil derivatives (**1a–d**) to the corresponding pyrido[2,3-*d*]pyrimidine derivatives (**2a–d**) was dimethyl acetylenedicarboxylate. This compound has been widely used in the synthesis of a variety of heterocyclic compounds.[2] Attack usually occurs at the triple bond in a Michael-type reaction followed by cyclization either through the other carbon of the acetylene or through the β-carbomethoxy group, depending on whether nucleophilic or electrophilic attack is appropriate. The only reported use of an acetylenic compound in the synthesis of pyrido[2,3-*d*]pyrimidines appeared in a 1958 German patent[3] and involved the use of 3-phenylprop-1-yn-3-one with 6-aminouracil to give 2,4-dioxo-7-phenylpyrido[2,3-*d*]-pyrimidine. This product would require attack upon the triple bond by carbon 5 of the pyrimidine. Such attack is reasonable based upon the elegant studies of Taylor and coworkers on the total synthesis of the antibiotic fervenulin and its derivatives,[4] in which a 6-aminouracil reacted with diethyl azodicarboxylate yielding the product of attack by the pyrimidine carbon 5 on the nitrogen of the reagent.



1 **2**

a, R = R′ = CH_3
b, R = CH_3; R′ = H
c, R = R′ = $CH_2C_6H_5$
d, R = R′ = H

(1) (a) This research was supported by Research Grant T491 from the American Cancer Society; (b) to whom correspondence should be addressed.

(2) J. B. Hendrickson, R. Rees, and J. F. Templeton, *J. Amer. Chem. Soc.*, **86**, 107 (1964).

(3) H. Pasedach and M. Seefelder, German Patent 1,040,040 (1958); *Chem. Abstr.*, **55**, 6507e (1961).

(4) E. C. Taylor and F. Sowinski, *J. Amer. Chem. Soc.*, **90**, 1374 (1968); **91**, 2143 (1969).