

## The Mechanism of Diphenylketene Cycloaddition to a Carbodiimide<sup>1</sup>

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Received November 5, 1969

Diphenylketene undergoes a 1,2-cycloaddition reaction with diisopropylcarbodiimide in high yield to produce the imino- $\beta$ -lactam. Quenching the reaction mixture with water results in the formation of *N*-diphenylacetyl-*N,N'*-diisopropylurea, diphenylacetic acid, and diisopropylurea as well as the normal adduct. When the cycloaddition is run in liquid sulfur dioxide as the solvent, a near-quantitative yield of 1,1-dioxo-2-(*N*-isopropylimino)-3-isopropyl-5,5-diphenylthiazolidine-4-one is produced. These results are interpreted to suggest a two-step process *via* a dipolar intermediate in which the second ring closing step is the slow step.

We have recently reported the 1,2 cycloaddition of various types of ketenes with carbodiimides to produce imino- $\beta$ -lactams.<sup>2</sup> Although the cycloaddition of ketenes across the C=N double bond has been known for many years, the cycloaddition with carbodiimides has only recently appeared, and no reports have been made on the mechanism of this reaction.<sup>3,4</sup> However, several recent communications have indicated that ketene and diphenylketene undergo cycloaddition across the C=N double bond of imines through a two-step process involving a dipolar intermediate.<sup>5-7</sup> These two-step pathways are of course in contrast to ketene cycloadditions to olefins, which are well established to be concerted.<sup>8-13</sup>

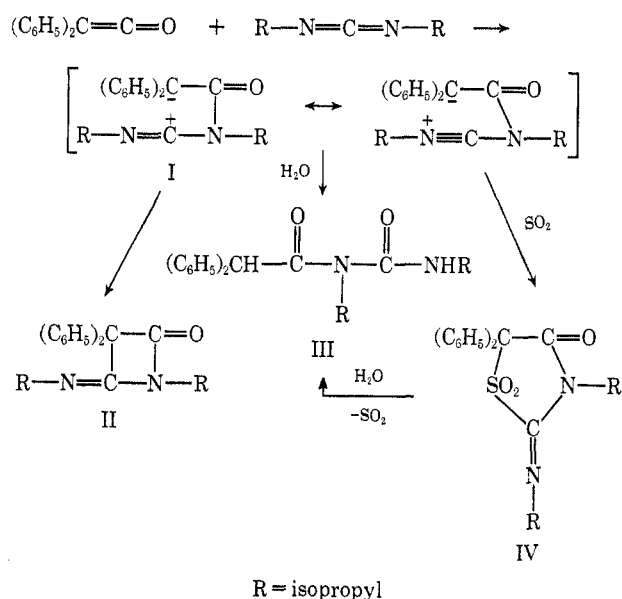
We now wish to report evidence for a polar two-step process involving a dipolar intermediate in the cycloaddition of diphenylketene and diisopropylcarbodiimide. A preliminary report of this work has appeared.<sup>14</sup>

### Results

Diphenylketene reacts smoothly with diisopropylcarbodiimide in benzene at room temperature to produce the imino- $\beta$ -lactam (II) in 90% yield.<sup>2,14</sup> The quenching of the above reaction mixture after 4 min with water results in the formation of a 12% yield of *N*-diphenylacetyl-*N,N'*-diisopropylurea (III), in addition to the normal adduct (II), diphenylacetic acid, and diisopropylurea. A control experiment proved that III could not be produced from II under the reaction conditions. A second control experiment was also necessary to show that III was not the result of a reaction involving the hydrolysis product of diphenylketene (diphenylacetic acid) and diisopropylcarbodiimide. Thus, the reaction of diphenylacetic acid and diisopropylcarbodiimide produced diphenylacetic anhydride

and diisopropylurea as expected and none of the urea III.

The reaction of diphenylketene and diisopropylcarbodiimide was also effected employing liquid sulfur dioxide as the solvent. A near quantitative yield of 1,1-dioxo-2-(*N*-isopropylimino)-3-isopropyl-5,5-diphenylthiazolidine-4-one (IV) was obtained. The hydroly-



sis of IV produced a quantitative yield of III with the loss of sulfur dioxide. A control experiment revealed that IV could not be produced from II under the reaction conditions.

### Discussion

The isolation of III and IV from the respective reaction mixtures as described above is certainly not consistent with a concerted 1,2 cycloaddition. These products are however indicative that this reaction proceeds *via* a dipolar intermediate; *i.e.*, the 1,4-dipolar intermediate is trapped by the addition of water or when formed in liquid sulfur dioxide.

This isolation of such a large amount (12%) of II and a near-quantitative yield of III suggests the dipolar intermediate is relatively long lived. The first step of the cycloaddition must be faster than the second step for such a large amount of the intermediate to build up.

Another interesting possibility for this cycloaddition reaction is that the principle canonical form of the intermediate is V rather than I. Electrostatic considerations would dictate the shape as indicated. Ring clo-

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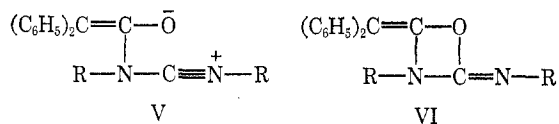
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sure could occur to yield VI which could be the trapped intermediate, and VI could bleed to the  $\beta$ -lactam II. We looked for VI by spectral, thin layer chromatography, and isolation techniques, but found no evidence suggesting this material was formed. Although this alternative pathway is perhaps possible, we prefer a dipolar species such as I.

It was mentioned above that most ketene cycloadditions to olefins are well established to be concerted processes. Since the system being reported is a two-step process, the change in mechanism is probably due to an enhanced stabilization of the intermediate; *i.e.*, the charges can be adequately stabilized by substituents.

### Experimental Section

Benzene was dried by refluxing and distilling from sodium. Isobutyronitrile was dried with 4A molecular sieve. Diphenylketene was prepared by the dehydrochlorination of diphenylacetyl chloride.<sup>15</sup>

**3,3-Diphenyl-1-isopropyl-4-isopropyliminoazetid-2-one (II).**—A solution containing 6.4 g (0.033 mol) of diphenylketene and 4.2 g (0.033 mol) of diisopropylcarbodiimide in 100 ml of benzene was allowed to stand at room temperature for 2 hr. Upon removal of the solvent and recrystallization of the solid residue from ether, II was obtained in 88% yield: mp 108.5–109.5°; ir 1810 (C=O) and 1690  $\text{cm}^{-1}$  (C=N); nmr ( $\text{CCl}_4$ ) 0.80 (d, 6 H), 1.45 (d, 6 H), 3.66 (m, 1 H), 4.03 (m, 1 H), and 7.3 (m, 10 H).

*Anal.* Calcd for  $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}$ : C, 78.7; H, 7.56; N, 8.75. Found: C, 79.0; H, 7.58; N, 8.74.

**N-Diphenylacetyl-N,N'-diisopropylurea (III).**—A solution containing 6.4 g (0.033 mol) of diphenylketene in 50 ml of benzene was added to a solution of 4.2 g (0.033 mol) of diisopropylcarbodiimide in 50 ml of benzene. This reaction mixture was quenched with 25 ml of water after 4 min. The solvent and water were evaporated on a rotatory evaporator; the residue was dissolved in chloroform. This solution was extracted with a dilute sodium hydroxide solution. Acidification of the basic extract resulted in the crystallization of diphenylacetic acid (47%). The chloroform containing the cycloadduct was evaporated and the residue dissolved in ether. The solution was fractionally crystallized to yield the  $\beta$ -lactam II in 40%

yield and the substituted urea III in 12% yield: mp 131–132°; ir 3300  $\text{cm}^{-1}$  (N-H) and 1705  $\text{cm}^{-1}$  and 1760  $\text{cm}^{-1}$  (C=O); nmr ( $\text{CCl}_4$ )  $\delta$  1.13 (doublet 6 H), 1.3 (doublet 6 H), 3.8 (multiplet 1 H), 4.3 (multiplet 1 H), 5.15 (singlet 1 H), and 7.2 (multiplet 11 H).

*Anal.* Calcd for  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_2$ : C, 74.5; H, 7.75; N, 8.28. Found: C, 74.4; H, 7.82; N, 8.23.

**Treatment of Diphenylacetic Acid with Diisopropylcarbodiimide (Control).**—To a solution containing 6.4 g (0.033 mol) of diphenylacetic acid in 100 ml of benzene was added 4.2 g (0.033 mol) of diisopropylcarbodiimide. The solution turned brownish yellow with the slight evolution of heat. The solution was quenched with 20 ml of water after 5 min and the mixture stirred for 30 min. The solvent was evaporated and the residue dissolved in chloroform. Diphenylacetic acid was removed from the chloroform solution by extraction with a dilute sodium hydroxide solution. Evaporation of the chloroform solution yielded only diisopropylurea and a small amount of diphenylacetic anhydride. There was no indication N-diphenylacetyl-N,N'-diisopropylurea had been produced.

**Cycloaddition of Diphenylketene and Diisopropylcarbodiimide in Sulfur Dioxide (IV).**—To a solution of 7.3 g (0.057 mol) of diisopropylcarbodiimide in 125 ml of liquid sulfur dioxide at  $-78^\circ$  was added 11 g (0.057 mol) of diphenylketene. The solution was allowed to warm to a gentle reflux at about  $-10^\circ$ . After 1 hr, the solvent was removed with an aspirator to yield 20 g (90%) of 1,1-dioxo-2-(N-isopropylimino)-3-isopropyl-5,5-diphenylthiazolidin-4-one (IV): mp 119–122° (gas liberated at melting point); attempts to recrystallize IV resulted in the loss of sulfur dioxide; ir ( $\text{CCl}_4$ ) 1710 (C=O), 1695 (C=N), 1305  $\text{cm}^{-1}$  ( $\text{SO}_2$ ); nmr ( $\text{CCl}_4$ )  $\delta$  1.1 (complex set of doublets,  $J_{\text{HH}} = 6$  cps, 12 H), 3.7 (multiplet 1 H), 5.0 (multiplet 1 H), and 7.3 (multiplet 10 H); mass spectrum parent peak 384, p-64 (loss of  $\text{SO}_2$ ).

*Anal.* Calcd for  $\text{C}_{21}\text{H}_{24}\text{N}_2\text{SO}_3$ : C, 65.6; H, 6.3; N, 7.3. Found: C, 65.1; H, 7.0; N, 7.1.

**Hydrolysis of 1,1-Dioxo-2-(N-isopropylimino)-3-isopropyl-5,5-diphenylthiazolidin-4-one (IV).**—A solution of 2 g of IV in 200 ml of ether was treated with 20 ml of water. The mixture became warm with the evolution of sulfur dioxide. The mixture was warmed on a steam bath until the evolution of sulfur dioxide ceased. The ether layer was separated and evaporated yielding 1.7 g (97%) of N-diphenylacetyl-N,N'-diisopropylurea (III). (For characterization see Experimental Section for III above).

**Treatment of 1-Isopropyl-4-isopropylimino-3,3-diphenylazetid-2-one (II) with Sulfur Dioxide.**—A 0.1-g portion of II in 10 ml of liquid sulfur dioxide was allowed to stand at  $-78^\circ$  for 24 hr. The solvent evaporated as the reaction vessel was allowed to warm to room temperature. An ir spectrum of the residue was identical with that of II. Thin layer chromatography revealed only one component which had the same  $R_f$  value as II.

**Registry No.**—Diphenylketene, 525-06-4; II, 20452-64-6; III, 21420-67-7; IV, 24867-12-7.

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