

Base Catalyzed Isomerization of 1,3-Diallyl-2-imidazolidinone
to 1,3-Bis(1-propenyl)-2-imidazolidinone

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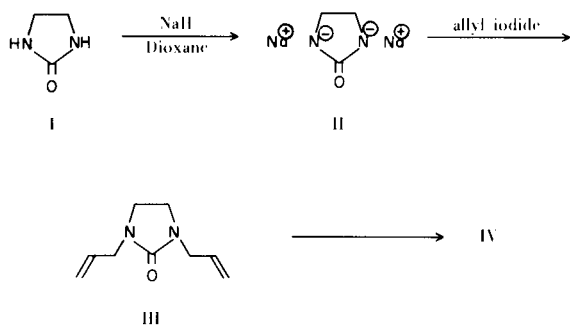
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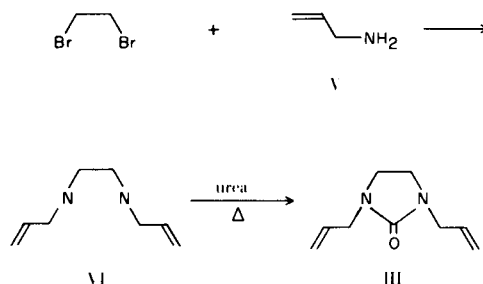
In the course of the synthesis of a series of *N,N'*-di-substituted cyclic ureas and thioureas for pharmacological study we obtained an unexpected product from the *N*-allylation of 2-imidazolidinone using sodium hydride (3). In order to prove unequivocally the structure of the product obtained we used both spectroscopic methods and an alternate synthetic route. This paper reports the isomerization reaction which occurred in the attempted synthesis of 1,3-diallyl-2-imidazolidinone III.

2-Imidazolidinones and 2-imidazolidinethiones have exhibited central nervous system (CNS) stimulant and/or depressant activities (3,4). *N*-Alkylation of these parent molecules results in enhanced CNS activity (3).

Fones (5) has used sodium hydride in the *N*-alkylation of amides. Using sodium hydride and allyl bromide, he also prepared *N*-allyl acetanilide in 73% yield. However, when we attempted to synthesize 1,3-diallyl-2-imidazolidinone III using the alkylation procedure described earlier in the literature (4,5), the unexpected product IV was obtained. The ir and nmr spectra indicated that the product IV did not have the structure of III.



In order to show that the product IV was different from the expected product, we synthesized 1,3-diallyl-2-imidazolidinone III *via* a different route, using the method described by Mistry and Guha (6). The physical properties and the ir and nmr spectra of III and IV are quite distinctly different (see Tables I and II).



The product obtained from the *N*-alkylation IV is a crystalline solid melting at 82.5-83.5°, and III is a pale yellow liquid boiling at 178-180° (0.3 mm Hg).

Results and Discussion.

The characteristic out-of-plane deformation bands near 990 cm^{-1} and 920 cm^{-1} of the $-\text{CH}=\text{CH}_2$ group (7), which can be clearly seen in the ir spectra of allylamine and *N,N'*-diallylethylenediamine, were apparently missing in the ir spectrum of IV. The characteristic out-of-plane deformation absorption bands of the $-\text{CH}=\text{CH}_2$ group were also indicated by the ir spectrum of 1,3-diallyl-2-imidazolidinethione VII, which we synthesized by reacting *N,N'*-diallylethylenediamine with carbon disulfide (3). The most characteristic absorption bands are summarized in Table I. The nmr spectra of the compounds with terminal double bonds, *eg.* allylamine, 1,3-diallyl-2-imidazolidinone and 1,3-diallyl-2-imidazolidinethione all show very similar absorption and splitting patterns. The coupling constants assigned to the $-\text{CH}_2-\text{CH}=\text{CH}_2$ function are in very good agreement with those reported in the literature (8,9). Careful analysis of the nmr spectrum of IV revealed that it contains four types of protons and the spectrum agrees with the proposed structure with the chemical shifts and the coupling constants given in Table II. Thus, the product IV was an isomerized product, in which migration of the terminal double bond had occurred. This type of double bond migration, catalyzed either by an acid or a base, is known in olefinic hydrocarbons and in steroids (10). Usually the double bond migration occurs to give the thermodynamically more stable product, that is, the more

TABLE I

IR Absorption Frequencies (cm^{-1})

Compound	ν C=C	ν C-N	ν C=O	ν C-H	δ C-H
V. Allylamine	1642 (m)	1416 (m)		3003 (m) 3096 (m)	999 (s) 918 (s)
VI. <i>N,N'</i> -Diallyl- ethylenediamine	1639 (m)	1412 (m)		3077 (m) 3096 (m)	994 (s) 917 (s)
III. 1,3-Diallyl- 2-imidazolidinone	1645 (m)	1412 (s)	1669 (s)	3115 (m) 3003 (m)	992 (s) 929 (s)
IV. 1,3-Bis(1-propenyl)- 2-imidazolidinone	1656 (s)	1414 (s)	1692 (s)	3049 (w)	962 (s)
			ν C=S		
VII. 1,3-Diallyl- 2-imidazolidine- thione	1637 (m)	1409 (s)	1325 (s)	3077 (m) 2976 (m)	990 (s) 931 (s)

m = medium, s = strong, w = weak.

TABLE II

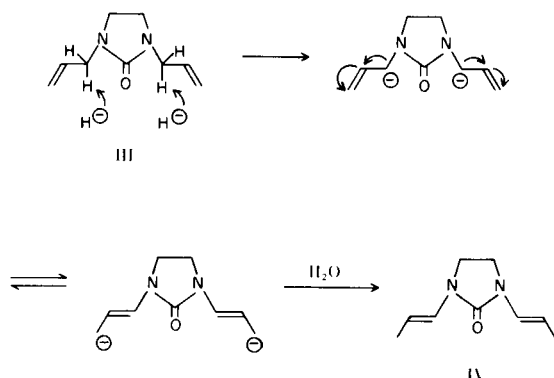
NMR Data

Compound	Chemical Shift (δ) (ppm)	Coupling Constant (cps)
V.	(a) 1.53 Singlet (1) (b) 3.30 Two doublets (c) 5.03 Multiplet (d) 5.13 Multiplet (e) 5.92 Multiplet	
VII.	(a') 3.52 Singlet (b) 4.25 Two triplets (c) 5.10 Multiplet (d) 5.13 Multiplet (e) 5.87 Multiplet	$J_{bc} = 1.5$ $J_{bd} = 0.7$ $J_{be} = 5.5$
III.	(a') 3.30 Singlet (b) 3.85 Two triplets (c) 5.15 Multiplet (d) 5.37 Multiplet (e) 5.85 Multiplet	$J_{bc} = 1.5$ $J_{bd} = 0.5$ $J_{be} = 5.5$
IV.	(a') 3.58 Singlet (b) 1.72 Two doublets (d) 4.68 Two quartets (e) 6.78 Two quartets	$J_{bd} = 7.0$ $J_{be} = 1.7$ $J_{de} = 15.0$

(1) From ref. 12.

highly substituted olefin.

The double bond migration must have occurred after the product III was formed, due to the presence of hydride ion which was used in 25% excess. The basic strength of hydride ion is sufficient to pull off the allylic hydrogens which had been rendered more acidic by the dipolar urea grouping. The carbanion thus generated can rearrange to produce the thermodynamically controlled product IV. The mechanism of the double bond migration is depicted as follows.



When III was treated with sodium hydride in dry dioxane, its conversion to IV occurred in quantitative yield. This confirmed the proposed mechanism of isomerization.

EXPERIMENTAL

The melting point was determined on a Fisher melting point block and the value was corrected. The elemental analyses were performed by C. F. Geoger, Ontario, California. The ir and the nmr spectra were taken on a Perkin-Elmer Infracord Spectrophotometer and a Varian A-60 Spectrometer, respectively. The nmr spectra were run in deuterated chloroform using tetramethyl silane as the internal reference.

1,3-Bis(1-propenyl)-2-imidazolidinone (IV).

To 8.6 g. (0.1 mole) of 2-imidazolidinone in 250 ml. of dry dioxane under nitrogen, 6.0 g. (0.25 mole) of a sodium hydride-mineral oil dispersion was added portionwise with stirring. The reaction temperature was raised and maintained at 60-65° for 2 hours, cooled to room temperature, and 32.0 g. (0.25 mole) of allyl iodide in 100 ml. of dry dioxane was added dropwise with stirring. After 2 hours stirring at room temperature the mixture was refluxed for 2 hours. The reaction mixture was filtered hot to remove the sodium iodide precipitate. The solvent was evaporated and the syrupy residue crystallized upon trituration with water. The product IV was recrystallized twice from ethanol-water, yield, 11.28 g. (68%).

Anal. Calcd. for $C_9H_{14}N_2O$: C, 65.03; H, 8.49; N, 16.85. Found: C, 64.72; H, 8.33; N, 17.15.

N,N'-Diallylethylenediamine (VI) (11).

To 114.0 g. (2.0 moles) of allylamine at 0°, 94.0 g. (0.5 mole)

of ethylene bromide was added dropwise with stirring. The mixture was allowed to react for 2 hours at 0°, 4 hours at room temperature and an additional 2 hours at gentle reflux. At the end of this period the reaction mixture was cooled and made strongly alkaline by addition of ice-cold 50% sodium hydroxide solution. The basic mixture was extracted three times with ether. The combined ether extract was washed with water, dried over anhydrous sodium sulfate, and the ether evaporated. The diamine VI was fractionally distilled and the constant boiling fraction at 194-198° was collected (yield, 69.3 g., 49.5%).

1,3-Diallyl-2-imidazolidinone (III).

A mixture of 14.0 g. (0.1 mole) of *N,N'*-diallylethylenediamine (VI) and 6.0 g. (0.1 mole) of urea was heated at a gentle reflux with stirring for six hours. The reaction mixture was cooled, dissolved in ether, and washed with ice-cold water, cold 1*N* hydrochloric acid, and finally with cold water. The ether solution was dried and the solvent was evaporated. The residue was fractionally distilled and the fraction boiling at 178-180° (0.3 mm Hg) was collected and further purified by redistillation, (yield, 10 g. 40%).

Anal. Calcd. for $C_9H_{14}N_2O$: C, 65.03; H, 8.42; N, 16.87. Found: C, 65.11; H, 8.49; N, 16.89.

Isomerization of III to IV.

A mixture of 500 mg. of III and 500 mg. of 50% sodium hydride emulsion in mineral oil in 15 ml. of dry dioxane, under anhydrous conditions, was refluxed for two hours with stirring. The reaction mixture was cooled and the excess sodium hydride destroyed by the addition of 95% ethanol. The mineral oil was removed by treatment with charcoal and hot filtration. The volume was reduced to 2 ml. and 2 ml. of water was added. The product crystallized in almost quantitative yield (430 mg.) from ethanol-water. Its melting point and the nmr spectrum were in complete agreement with that of IV.

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