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CYCLIZATION OF N-CINNAMOYL PHTHALHYDRAZIDE

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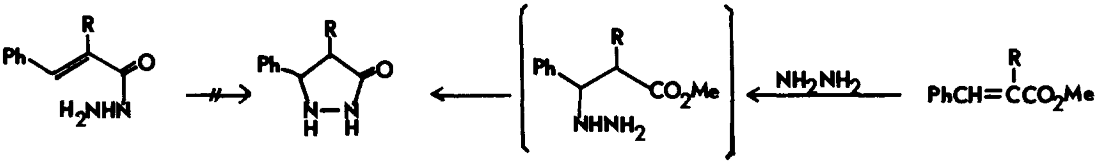
Recently Baldwin and his students proposed an interesting set of rules for predicting whether or not intramolecular cyclization will readily occur.[1] As one of the examples chosen to illustrate these rules, the facile cyclization of methyl β-hydrazino hydrocinnamate (Ia) to 5-phenyl-3-pyrazolidinone (IIIa) was contrasted with the failure of cinnamoyl hydrazine (IIa) to give IIIa under forcing conditions.[2] Some time ago, we also experienced a similar failure in an attempt to obtain 4,5-diphenyl-3-pyrazolidinone (IIIb) from the corresponding hydrazide IIb.[3]

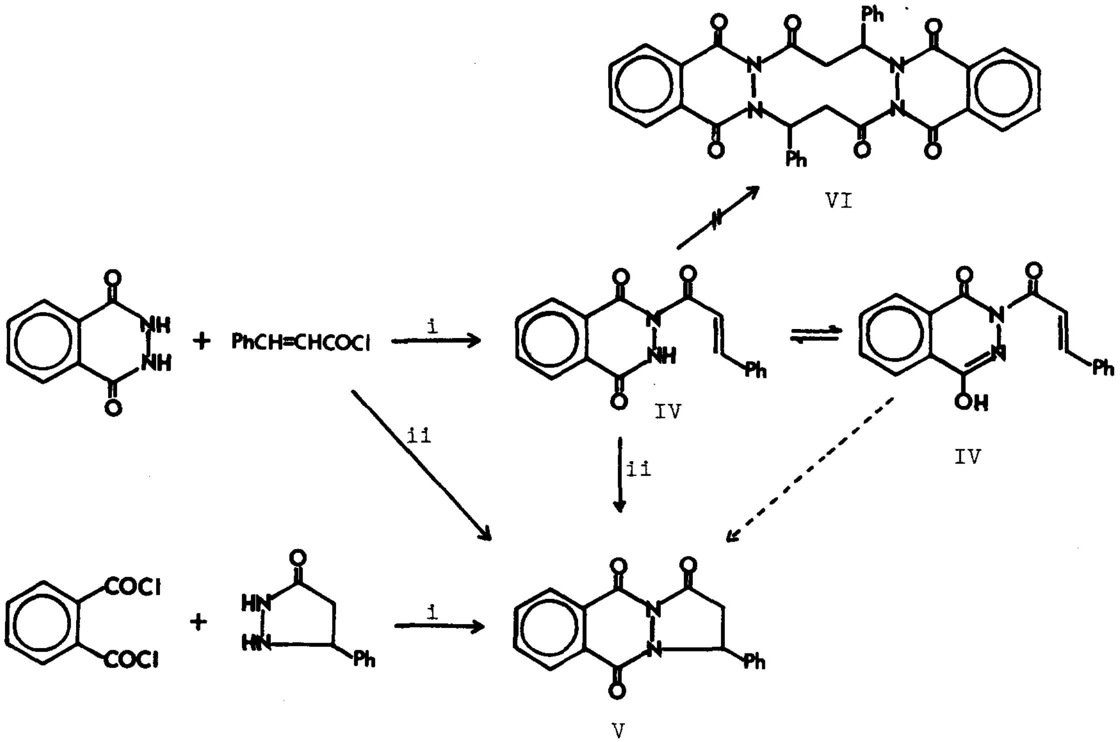


II III I

a) R = H b) R = Ph

Although the nucleophilicity of the terminal NH_2 group of hydrazides is known to be drastically reduced by the carbonyl group,[4] we were nonetheless puzzled by the failure of IIa[2] and IIb to undergo an intramolecular Michael addition even under forcing conditions. It was felt that perhaps the unsubstituted hydrazides would not survive the conditions necessary for cyclization.[5] We now report results which seem to suggest that factors other than geometric and stereochemical considerations[1] may also play a role in determining whether cyclization will occur readily especially when heteroatoms are involved.[6]

The reaction of cinnamoyl chloride with phthalhydrazide in toluene at reflux for 15 hrs in the presence of pyridine gave N-cinnamoyl phthalhydrazide (IV) as colorless needles, mp. 208-209°. Its infrared spectrum exhibited three C=O absorptions at 1720, 1670 and 1650 cm^{-1}. One of the olefinic hydrogens of the cinnamoyl group appeared as a doublet centered at δ 7.0 while the other olefinic hydrogen was buried in the complex aromatic absorption centered at δ 7.92 (10 H).[7] In addition, a fairly sharp singlet at δ 12.4 seems to suggest that IV actually exists in the enolic form IV'.[8] Upon being heated in o-dichlorobenzene at reflux for 15 hrs, N-cinnamoyl phthalhydrazide was converted to a new compound V, mp. 197-198°, isomeric with IV whose infrared spectrum was totally different from that of IV. In addition to the aromatic absorptions, the nmr spectrum of V displayed a doublet of doublets at δ 5.9 assigned to the hydrogen β to the C=O group and another pair of doublets of doublets at δ 3.60 and 2.84 assigned to the two hydro-



i) Reflux in toluene with pyridine ii) Reflux in o-dichlorobenzene overnight gens α to the carbonyl group. The same compound was obtained from the reaction of phthaloyl chloride with 5-phenyl-3-pyrazolidinone (IIIa), a reaction which serves to establish its structure while at the same time removing the possibility that two molecules of IV reacted via a double Michael addition to give VI. A perusal of the literature with the benefit of our results as a guide revealed that similar cyclizations were reported to occur under forcing conditions. Stetter and Findeisen[9] had earlier described the cyclization of 3-pyrazolidinones bearing acryloyl substituents at N^1; similarly Zinner and Böse[10] were able to obtain the bicyclic 3-pyrazolidinone from the treatment of 1-crotonyl-4-substituted-1,2,4-triazolidine-3,5-diones with sodium hydride.

The author thanks Prof. J. E. Baldwin for valuable discussions.

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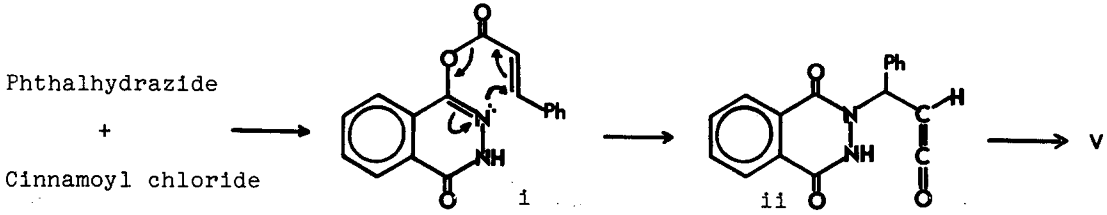
2. W. O. Gotfredsen and S. Vangedal, Acta Chem. Scand., 9, 1498 (1955).
3. Of course, IIIb is easily obtained from the reaction of α-phenylcinnamic acid and its derivatives with hydrazine; L. A. Carpino, J. Am. Chem. Soc., 80, 599, 601 (1958); J.-P. Anselme, Unpublished results.
4. P. J. Drueger in "The Chemistry of the Hydrazo, Azo and Azoxy Groups," S. Patai, Ed., John Wiley and Sons, New York, 1975, p. 161.
5. P. A. S. Smith, "Open-chain Nitrogen Compounds," W. A. Benjamin, Inc., New York, N. Y., 1966, p. 177.
6. Prof. Baldwin has indeed pointed this out in reference 1, p. 738.

7. The stability and spectral data of IV militates against the possibility that acylation occurred at the oxygen atom to yield (i) followed by rearrangement to (ii) which could then cyclize to V.



8. A. R. Katritzky and J. Lagowski, Adv. Heterocyclic Chem. 1, 339 (1963). If indeed IV exists as IV', the sp^2 hybridization of the nitrogen atom would provide a favorable geometry for cyclization. These results have been discussed with Prof. Baldwin who agrees with these views.

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