Reaction of Diphenylcyclopropenone with N-Acylamidine Derivatives.
Synthetic and Mechanistic Implications

Silvio Cunha* and Albert Kascheres

Instituto de Química, Universidade Estadual de Campinas, CP 6154, 13083-970, Campinas - SP, Brazil

A reatividade de ciclopropenonas frente a derivados de N-acilamidinas foi investigada. Difenilciclopropenona reagiu com N-benzoilacetamidina e com N-(metoxicarbonil)benzamidina formando 1,2-diidro-3H-pirrol-3-onas em rendimentos moderados, porém alquilfenilciclopropenonas não reagiram com os mesmos nucleófilos investigados. A teoria dos orbitais moleculares de fronteira foi empregada para racionalizar a formação dos produtos.

In this work, the reactivity of cyclopropenones toward N-acylamidine derivatives was investigated. Diphenylcyclopropenone reacted with N-benzyolacetamidine and N-(methoxycarbonyl)benzamidine affording 1,2-dihydro-3H-pyrrol-3-ones in moderate yields. However, alkylphenylcyclopropenone did not react. The formation of the compounds is examined mechanistically within frontier molecular orbital considerations.

Keywords: diphenylcyclopropenone, N-acylamidines, 1,2-dihydro-3H-pyrrol-3-ones

Introduction

Over the past four decades, the fascinating chemistry of cyclopropenones has attracted considerable attention both in utilization as a synthetic building block1 and as rare naturally occurring compounds2. Our systematic interest in the use of cyclopropenone chemistry in the construction of a wide variety of heterocycles3 prompted us to study the behavior of cyclopropenones towards N-acylamidine derivatives. Additionally, N-acylamidines can be envisioned as enaminone aza analogs (an “aza-enaminone”). Enaminones are versatile nucleophiles toward diphenylcyclopropenone (1) in the synthesis of nitrogen-containing compounds, Scheme 13a,d,h. Because of the ambiphilic and ambident proprieties of cyclopropenones, the reactions of this class of compound with nucleophiles is a complex matter1b-c. Herein we present our results of the reactions of cyclopropenones with N-acylamidine derivatives with emphasis on synthetic and mechanistic implications.

Results and Discussion

Diphenylcyclopropenone (1) reacted smoothly with N-benzyolacetamidine (5) in benzene under reflux. An insoluble, crystalline solid was isolated, and this material was a 1:1 adduct as indicated by mass spectrum and NMR integration. The NMR spectrum contained two low field N-H protons which suggests their participation in intramolecular hydrogen bonding. Moreover, the IR spectrum which showed an intense carbonyl absorption at 1640 cm⁻¹, ruled out the formation of a 1,5-dihydro-2H-pyrrol-2-one nucleus analogous to 23h, for which this absorption appears at 1695-1700 cm⁻¹. To accommodate these spectral features
structure 6 (Scheme 2) was proposed in agreement with the carbonyl absorption (1638-1650 cm⁻¹) of some model 1,2-dihydro-3H-pyrrol-3-ones⁴.

The structure 6 was corroborated by analysis of a long-range heterocorrelation (COLOC) spectrum of derivative 7. This showed a correlation (3J) of the carbonyl C-4 with the methyl group at C-5 as well as the other correlations indicated in structure 7 (Scheme 2) in agreement with the regiochemistry assigned to 6. No such correlations would be observed if a 1,5-dihydro-2H-pyrrol-2-one analogous to 2 had formed.

This reaction proved to be very sensitive to substitution both in the cyclopropenone and in the “aza-enaminone”. While diphenylcyclopropenone reacted with N-(methoxycarbonyl)benzamidine (8) to afford 9 in good yield, it failed to react with derivatives 10 and 11 under the conditions employed (Scheme 2). In addition, compounds 5 and 8 did not react with methylphenyl-cyclopropenone and isopropylphenylcyclopropenone, showing that formation of the 1,2-dihydro-3H-pyrrol-3-one nucleus is effective only with 1 (1 is more reactive towards nucleophiles than are alkylphenylcyclopropenones because it has the lower-lying LUMO⁵).

Recently, we demonstrated that reactivity of cyclopropenones can be rationalized by a frontier orbital approach in combination with the hardness-softness concept⁵. The results of AM1⁶ calculations, as implemented in the SPARTAN 4.0 package⁷, are shown in Scheme 3. Thus, it would appear that reaction of 1 is kinetically favored for the tautomeric forms of 5 and 8,

![Scheme 2](image_url)

![Scheme 3](image_url)
wherein the terminal imine nitrogen has the largest HOMO coefficient. A slow and irreversible attack at the phenyl-C of 1 followed by an electrocyclic five-membered ring formation results in the regiochemistry observed for compounds 6 and 9.

The present study complements the reported 1H formation of the dihydropyrrolone nucleus from diphenylcyclopropenone and enamiones, furnishing a convenient route to 1,2-dihydro-3H-pyrrol-3-one derivatives and expands the frontier of utilization of cyclopropenones as synthetic building blocks for densely substituted heterocyclic compounds.

Experimental

Melting points were determined on a Hoover-Unimelt apparatus and are uncorrected. Infrared spectra were recorded as KBr discs on a Perkin Elmer FT-IR 1600 instrument. NMR spectra were obtained for 1H at 300 MHz and for 13C at 75 MHz using a Varian Gemini 300 or a Bruker AC300P spectrometer. Chemical shifts are reported in ppm downfield from reference. HRMS were obtained on a Fisons VG Autospec. N-Benzoylacetamidine, N-(methoxycarbonyl)benzamidine and diphenylcyclopropenone were prepared according to known procedures.

Reaction of N-Benzoylacetamidine (5) with 1: A solution of 206.5mg (1mmol) of diphenylcyclopropenone (1) and 173.8mg (1mmol) of N-benzoylacetamidine (5) in 10cm3 of benzene was heated at reflux with stirring for 1 day (the solution turned yellow and a precipitate began to form after 30 min.), after which time the reaction mixture was cooled at room temperature, petroleum ether was added and allowed to cool in the freezer (25°C). The solution was decanted from the solid that formed was separated from the solvent and was recrystallized from CH2Cl2/hexane affording 115.1mg, 41% yield, mp 240-242°C. The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for a fellowship to SC.

Acknowledgments

The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for a fellowship to SC.

References


Received: November 17, 2000
Published on the web: April 23, 2001
FAPESP helped in meeting the publication costs of this article.