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The Syntheses of Phencyclone and Dihydrophencyclone

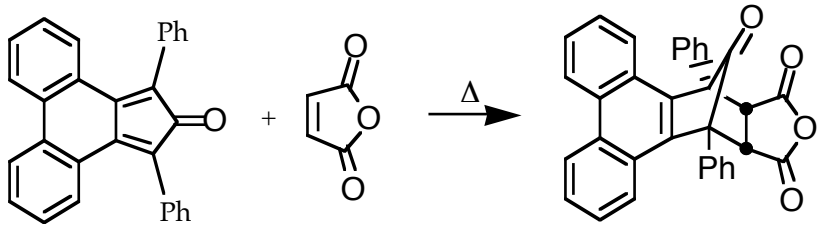
William R. Forsyth, Gerald A. Weisenburger, and Kurt W. Field*
Department of Chemistry, Bradley University
Peoria, IL 61625
*Author to whom correspondence should be addressed.

ABSTRACT

The base promoted condensation of 1,3-diphenylacetone and phenanthrenequinone can be used to synthesize either phencyclone or dihydrophencyclone. When the condensation is performed at room temperature using solid potassium hydroxide and approximately equimolar quantities of the ketone and quinone in ethanol solvent, high purity phencyclone is produced in moderate yield. However, in refluxing ethanol and a 2:1 molar ratio of the quinone:ketone, the dropwise addition of ethanolic potassium hydroxide affords high purity dihydrophencyclone in moderate yield.

INTRODUCTION

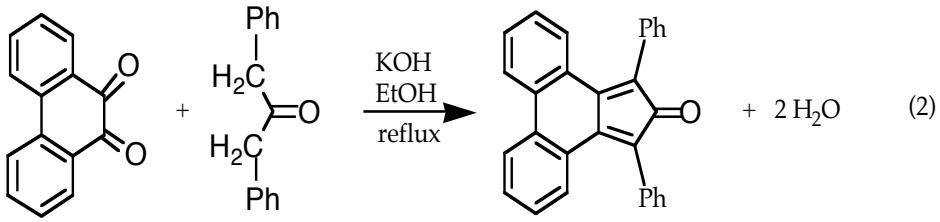
The formation of Diels-Alder adducts from substituted cyclopentadienones (cyclones) and alkenes is well documented (Allen et al. 1964; Dilthey et al. 1937; Harrison 1991; Mackenzie 1960; Sasaki et al. 1976; Yasuda et al. 1980; Yasuda et al. 1981). Phencyclone, **1**, has been shown to form endo [4 + 2] π-cycloadducts with various dienophiles including styrenes and a number of cyclic alkenes, e.g. eq 1. The high reactivity and high regio- and periselectivity make phencyclone an ideal diene for Diels-Alder reactions (Sasaki et al. 1976; Yasuda et al. 1980; Yasuda et al. 1981).



(1)

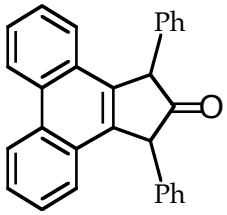
Phencyclone **1** Maleic Anhydride

Phencyclone is usually synthesized via a base promoted aldol condensation, eq 2 (Dilthey et al. 1935). Experimental difficulties and yield inconsistencies encountered



1

during these syntheses are also well documented. For example, Harrison (1992) reports that the preparation of **1** as suggested by Vaughn-Williams (1971) does not lead to the formation of **1** but instead yields dihydrophencyclone, **2** . Perhaps Allen's



Dihydrophencyclone

2

(1964) statement, "phencyclone is not easy to prepare", accurately summarizes the utility of the published synthetic sequences leading to **1**.

Previous preparations of **1** require scrupulous temperature control coupled with the lengthy addition of the alcoholic base solution (Allen et al. 1964; Dilthey et al. 1935; Harrison 1992). We report, herein, a preparation of **1** that is very reproducible, affords reasonable yields, and avoids the necessity of temperature control and the dropwise addition of base.

RESULTS AND DISCUSSION

A systematic investigation of the experimental parameters associated with the preparation of phencyclone confirmed that reaction temperature is the critical variable. By running the reaction at room temperature, we have found that the preparation of **1** is easy to execute and very reproducible. Above ca. 60 °C dihydrophencyclone becomes the predominant product (Harrison 1991). A second experimental modification involved the introduction of the potassium hydroxide. The need for dropwise addition of the alcoholic

base was eliminated by combining the phencyclone precursors and solvent before adding solid potassium hydroxide. Note, literature methods used potassium hydroxide-alcohol solutions; however, these solutions degrade upon standing and must be prepared just prior to use. Finally, using the conditions described above, we optimized two additional experimental parameters, base concentration and reaction time, which ultimately led to the procedure described below.

EXPERIMENTAL SECTION

General.
Infrared absorption (IR) spectra were recorded on a Nicolet Model 205 instrument. Steady-state ultraviolet-visible (UV-vis) absorption spectra were recorded on a Perkin-Elmer Model 552 spectrometer and are expressed as λ_{max} in nm (log ε). The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Instruments Inc. ARX 400. Analytical high-performance liquid chromatography (HPLC) was performed with a Gilson Medical Electronics instrument equipped with a Model 112 UV/vis detector and an Alltech 5 μm 4.6 x 250 mm Econosphere C_{18} column with 25% water in acetonitrile as eluant at 1.0 mL/min. Melting points, determined on a Thomas-Hoover capillary apparatus, were not corrected. 1,3-Diphenylacetone and phenanthrene-quinone (99%) were used as received (Aldrich).

Phencyclone, 1, (1,3-Diphenyl-2-cyclopenta[l]-phenanthrene-2-one) [5660-91-3].
1,3-Diphenylacetone (0.584 g, 2.78 mmol), phenanthrenequinone (0.532 g, 2.58 mmol), and 25 mL of 95% ethanol were combined. Upon the addition of solid potassium hydroxide pellets (1.0 g, 17.8 mmol) the initially orange heterogeneous mixture darkened. After stirring at room temperature for 30 min., the black precipitate was isolated by vacuum filtration and washed with 2 x 5 mL of cold ethanol. The solid was dried in vacuo to give 0.720 g (1.88 mmol, 73%) of the title compound: mp 206.8-208.4 °C; IR (KBr) 1700 cm^{-1} (C=O); UV (cyclohexane) 300.5 (4.4); ^{13}C NMR ($CDCl_3$) δ 200.16 (<u>C</u>=O). HPLC analysis revealed that **1** did not contain dihydrophencyclone and was of greater purity than **1** prepared by other methods. Multiple preparations of **1**, via this procedure, performed by several individuals averaged 73% (high 81%, low 68%).

Dihydrophencyclone, 2.
1,3-Diphenylacetone (0.262 g, 1.25 mmol), phenanthrenequinone (0.503 g, 2.42 mmol), and 25 mL of 95% ethanol were heated to reflux with stirring. A freshly prepared solution of 10% ethanolic KOH (1 mL) was then added dropwise over a five minute period, after which the heterogeneous mixture was stirred for an additional 60 min. After cooling the solution, the desired material was isolated by vacuum filtration, washed with 3 x 10 mL of cold ethanol, and dried in vacuo yielding a dull ivory solid (0.368 g, 0.957 mmol, 77%): IR (KBr) 1746 cm^{-1} (C=O); UV (cyclohexane) 258.2 (4.3); ^{1}H NMR ($CDCl_3$) δ 5.19 (sp^3 C<u>H</u>); ^{13}C NMR ($CDCl_3$) δ 58.92 (sp^3 <u>C</u>H), 123.37, 126.51, 126.94, 127.11, 127.27, 128.16, 128.55, 128.75, 131.20, 135.53, 137.37, 210.55 (<u>C</u>=O). HPLC analysis of **2** confirmed its high purity and the absence of **1**.

CONCLUSION

A systematic investigation of the experimental variables associated with the base promoted condensation of 1,3-diphenylacetone and phenanthrenequinone afforded a much improved preparation of phencyclone. Similar studies revealed that dihydrophencyclone was best prepared by a procedure similar to that described by Dilthey (1935).

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