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THE CLEAVAGE OF TWO CARBON-CARBON BONDS IN A WOLFF-KISHNER REDUCTION

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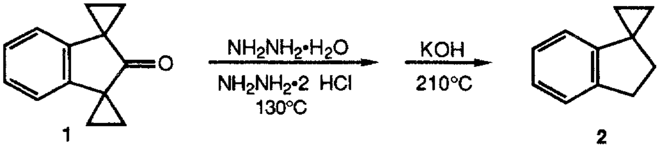
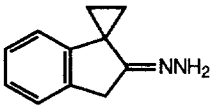
Abstract. The reaction of dispiro[cyclopropane-1,1'-indan-3',1"-cyclopropane]-2'-one (**1**) under Wolff-Kishner conditions gives spiro[cyclopropane-1,1'-indan] (**2**) in which the ketone has been reduced and two bonds of one cyclopropane ring have been cleaved.

The Wolff-Kishner reaction is a classic method for the complete reduction of aldehyde and ketone carbonyl functions to methyl and methylene groups.[1] Although cases in which a Wolff-Kishner reduction is accompanied by loss or migration of heteroatoms or double bonds α to the carbonyl group are well documented,[1] only a few instances in which a single α carbon-carbon bond is cleaved during the reaction have been reported.[1a,2] In this communication we wish to report the Wolff-Kishner reduction of a ketone which is accompanied by the cleavage of two carbon-carbon bonds of a cyclopropane ring α to the carbonyl group. To the best of our knowledge, this type of cleavage has not been previously reported under these conditions.

Treatment of **1** with an excess of hydrazine hydrate and hydrazine dihydrochloride at 130°C followed by addition of potassium hydroxide afforded the product **2** in 36% yield. The identity of **2**, in which the carbonyl group is reduced and a cyclopropane ring lost, was established by comparison with an authentic sample.[4]. Workup of the reaction prior to treatment with base gave the hydrazone **3**. Both the structurally similar **4**, according to the report of Conia,[5] and **5** under the same conditions give the hydrocarbons expected with intact cyclopropane rings.



1 **2**



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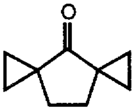

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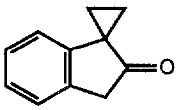

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In our investigation of this novel "ethylene extrusion" we have followed the course of this reaction by GC/MS[6] as illustrated in Figure 1. We find that **1** is converted to an intermediate with a mass of 198 ($C_{13}H_{14}N_2$) which is then rapidly transformed to a second isomeric intermediate before conversion to **3**. The intermediates have been assigned as **6** and **7**, as shown in Scheme 2, based on low- and high-resolution GC/MS data (EI and CI).[7]

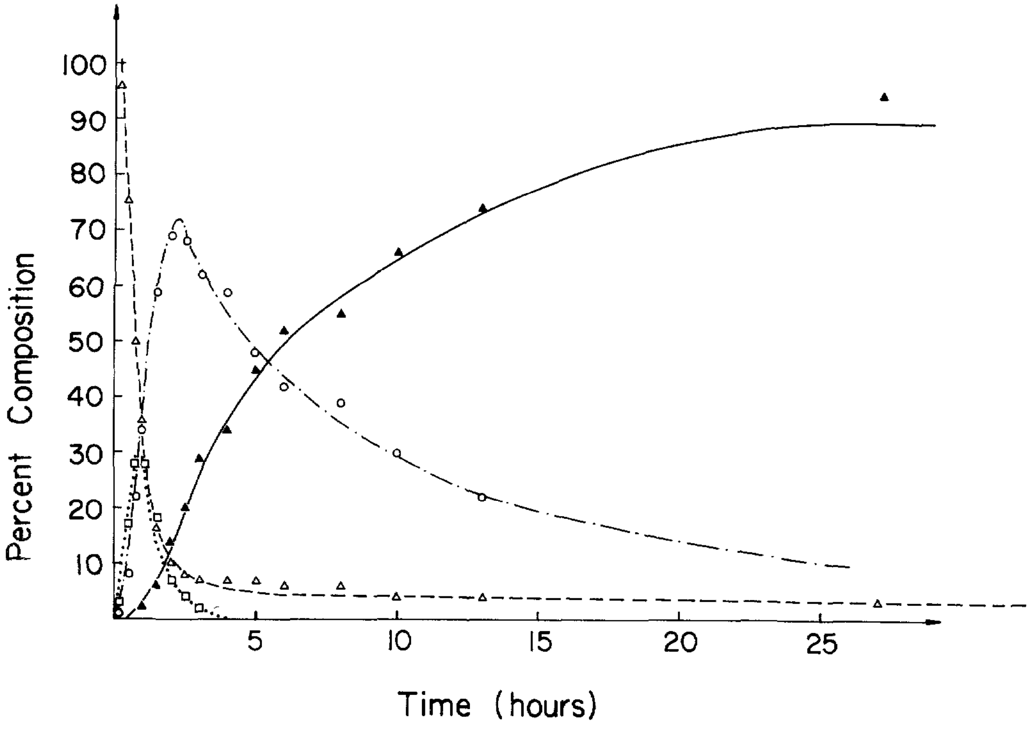
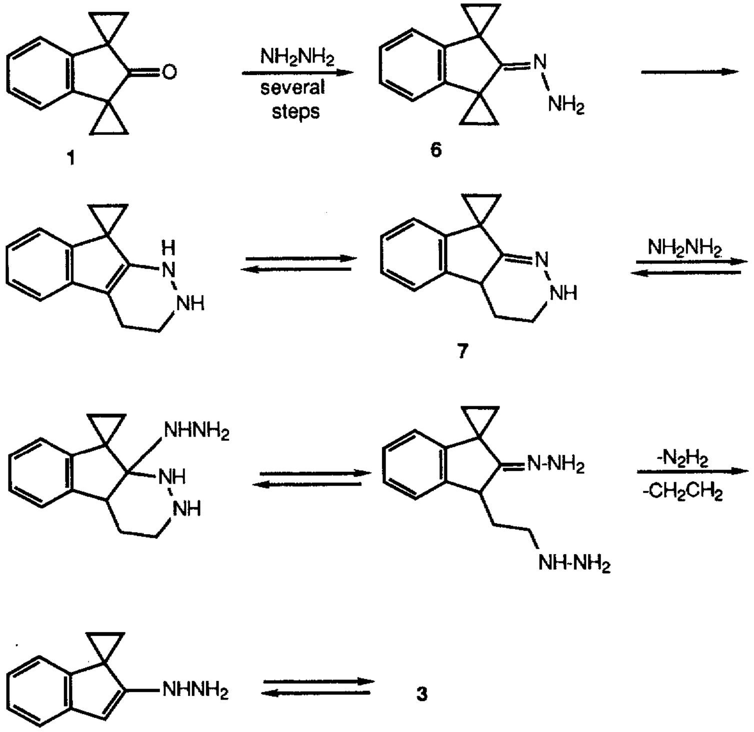


Figure 1. Composition of the reaction mixture *vs* time; **1** (Δ), **3** (▲), **6** (□) and **7** (○).

We suggest that this reaction proceeds as shown in Scheme 2. The first formed intermediate **6** is converted to **7** and the "ethylene extrusion" reaction occurs when **7** reacts with a second hydrazine molecule followed by the elimination of diimide and ethylene. Further work will be needed to delineate the scope of this reaction and to evaluate the proposed mechanism.

Scheme 2



Acknowledgment. We are grateful to the National Science Foundation and the National Institute of Health for support of this work, to Professor D. Y. Curtin for valuable discussions and to Dr. Richard Milberg for performing the GC-CI/EI and GC-High Resolution MS experiments.

References and Notes

1. For a review of the Wolff-Kishner reaction, see: (a) Reusch, W. in Reduction; Augustine, R. L. Ed.; Marcel Dekker Inc., New York, NY, 1968, p. 171-185. (b) Szmant, H. H. *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 120. (c) Todd, D. *Org. React.* **1948**, *4*, 378.
2. (a) Kupchan, S. M.; Abushanab, E. *Tetrahedron Lett.* **1965**, 3075. (b) Bumgardner, C. L.; Freeman, J. P. *Tetrahedron Lett.* **1964**, 737. (c) Gustafson, D. H.; Erman, W. F. *J. Org. Chem.* **1965**, *30*, 1665.
3. A mixture of **1** (552 mg, 3.0 mmol), hydrazine hydrate (12.0 g, 205 mmol) and hydrazine dihydrochloride (2.5 g, 24 mmol) in 60 mL of triethylene glycol was stirred for 24 h at 130°C. The mixture was then treated with 4.0 g of KOH and the temperature raised to 210°C by distillation of the low boiling materials. After the mixture was allowed to cool, it was combined with the distillate, poured into cold water and extracted twice with pentane. Purification by MPLC using hexane as the eluant afforded 154 mg (36%) of **2**: ^{1}H NMR ($CDCl_3$) δ 0.86-0.94 (m, 4H), 2.11 (t, 2H), 3.04 (t, 2H), 6.64-6.68 (m, 1H), 7.08-7.22 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 16.3, 26.8, 30.7, 118.2, 124.0, 125.5, 126.4, 143.6, 148.0; MS (70 eV) m/e 144 (M^+, 65), 129 (100), 115 (37). Workup of the reaction mixture prior to treatment with KOH afforded 185 mg (36%) of **3**: ^{1}H NMR ($CDCl_3$) δ 1.19-1.23 (m, 2H), 1.46-1.50 (m, 2H), 3.63 (s, 2H), 4.88 (br s, NH_2), 6.75-6.78 (m, 1H), 7.16-7.31 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 20.9, 30.0, 32.3, 118.4, 124.6, 136.0, 127.3, 137.2, 146.3, 159.3; MS (70 eV) m/e 172 (M^+, 99), 156 (100), 154 (28), 144 (15), 141 (20), 128 (76), 115 (51), 102 (10), 77 (17), 63 (19), 51 (15); High-resolution MS calcd. for $C_{11}H_{12}N_2$ m/e 172.1000, found 172.1004.
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6. Aliquots were drawn from the reaction mixture, worked up in H_2O and analyzed on a 30 m X 0.25 mm SE-52/54 bonded phase FSOT capillary column.
7. **6**: MS (70 eV) m/e 198 (M^+, 80), 182 (83), 169 (91), 167 (100), 154 (45), 153 (44), 140 (23), 139 (23), 127 (34), 115 (46), 63 (19), 51 (14); High-resolution MS calcd. for $C_{13}H_{14}N_2$ m/e 198.1157, found 198.1153. **7**: MS (70 eV) m/e 198 (M^+, 100), 182 (5), 169 (33), 154 (34), 141 (43), 128 (17), 115 (37), 63 (11), 51 (6); High-resolution MS calcd. for $C_{13}H_{14}N_2$ m/e 198.1157, found 198.1145.

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