The Beckmann Rearrangement of α-Santonin Oxime

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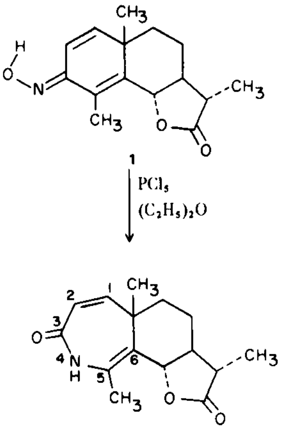
A recent note describing the Beckmann rearrangements of tetrahydro-α-santonin oximes (1) prompts us to report on the same rearrangement of the oxime of α-santonin. Although the chemistry of α-santonin oxime (**1**) has been investigated in some detail (2), the Beckmann rearrangement, which may provide an insight into the configuration of the oxime, has not been studied. In fact, little attention has been given to the Beckmann rearrangements of oximes of cross-conjugated dienones (3).



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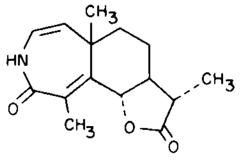
Treatment of **1** with phosphorus pentachloride in anhydrous ether gave, on work-up, the lactam **2**, identified on the basis of analytical and spectral data, and by hydrogenation. The nuclear magnetic resonance (nmr) spectrum of **2** displayed doublets at δ 6.85 (H-1, $J_{1,2}$ = 9.5 Hz) and at δ 6.42 (H-2), and a singlet at δ 3.75 (NH), the latter disappearing upon addition of deuterium oxide.

Comparison with lactams (4) of similar structure to **3** indicates that H-1 and H-2 should appear at much higher field than that observed for **2**. Furthermore, the amino proton of **3** would likely be coupled to H-2 (not observed in the nmr spectrum of **2**). The infrared (ir) spectrum (potassium bromide) of **2** exhibited an N-H stretching band at 2.84 μ, lactone carbonyl stretching at 4.70 μ, and unsaturated lactam carbonyl stretching at 6.00 μ and 6.41 μ. Hydrogenation of an acetone solution of **2**, using 5% palladium on charcoal as the catalyst, gave a mixture of the known 4-aza-A-homo-*cis*-tetrahydro-α-santonin and its *trans* isomer (1).



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In conclusion, α-santonin oxime undergoes a normal Beckmann rearrangement with phosphorus pentachloride. Assuming that 1 does not isomerize prior to rearrangement, the configuration of the oxime is as indicated.

EXPERIMENTAL

α-Santonin Oxime (**1**).

The following procedure was found to be the most convenient for preparing pure **1** in good yields. A mixture of α-santonin (25.0 g., 0.102 mole), hydroxylamine hydrochloride (26.0 g., 0.375 mole), pyridine (25 ml.), and ethanol (100 ml.) were refluxed with stirring for 3 hours. The solution was cooled and concentrated *in vacuo* to a small volume. Addition of water precipitated the oxime which was filtered and washed well with pentane. Recrystallization from 70% ethanol, followed by drying overnight in an oven at 100°, gave 21.0 g. (80%) of pure dry oxime, m.p. 219-221° (lit. (5) m.p. 230° dec.). The melting point of hydrated oxime (prior to oven drying) was 228-230° dec. The nmr spectrum of **1** was identical to that reported by Pinhey and Sternhell (6).

Beckmann Rearrangement of α-Santonin Oxime.

To an ice-cold solution of α-santonin oxime (11.0 g., 42.1 mmoles) in anhydrous ether (900 ml.) was added phosphorus pentachloride (11.4 g.). The reaction mixture was stirred for 27 hours and then poured over crushed ice. Filtration gave crude lactam **2**. Two recrystallizations from 58% ethanol gave 2.89 g. (26%) of analytically pure **2**, m.p. 168-170° dec.; ir (potassium bromide): 2.84 μ (NH), 5.70 μ (C=O, lactone), 6.00 μ and 6.41 μ (C=O and C=C, lactam ring); nmr (DMSO-d_6): δ 1.06 (d, *CH*$_3$-CH, J = 6.0 Hz), δ 1.16 (s, *CH*$_3$-C$\leqslant$), δ 2.03 (s, CH_3C=), δ 3.75 (s, NH), δ 4.94 (d, *CH*-O), δ 6.42 (d, H-2), and δ 6.85 (d, H-1, $J_{1,2}$ = 9.5 Hz); mass m/e 261 (M^+).

Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.95; H, 7.33; N, 5.36. Found: C, 68.97; H, 7.08; N, 5.41.

Hydrogenation of **2**.

Lactam **2** (0.39 g.) and 5% palladized charcoal (0.050 g.) in acetone (40 ml.) were shaken for 18 hours in a hydrogen atmosphere. Standard work-up gave a mixture of 4-aza-A-homo-*cis*-tetrahydro-α-santonin and its *trans* isomer, identified by comparison with the properties reported in the literature (1).

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