A Convenient Synthesis of 3-Aminotropolone and Its Reactions with Orthoesters. Formation of 8*H*-Cyclohept[*d*]oxazol-8-ones

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Synopsis. Schmidt reaction of 3-acetyltropolone gave 3-acetamidotropolone, which was hydrolyzed to afford 3-aminotropolone (**3**). The compound **3** reacted with orthoformate, orthoacetate, orthopropionate, and orthobenzoate to give the corresponding 2-substituted 8*H*-cyclohept[*d*]oxazole-8-one derivatives.

Recently, we found and reviewed that 3-acetyltropolone is very useful as starting material for the synthesis of heterocycle-condensed troponoid compounds.[1] In this series, we reported that 3-acetyltropolone and its methyl ethers reacted with hydroxylamine to afford 8*H*-cyclohept[*d*]isoxazol-8-one and 8*H*-cyclohept[*c*]isoxazol-8-one as a major and minor product, respectively.[2] It is also known that 3-aminotropolone reacted with formamide, acetic anhydride, or *p*-nitrobenzaldehyde to give 8*H*-cyclohept[*d*]oxazol-8-ones,[3,4] while 2-amino-3-hydroxytropone reacted with acetic anhydride to give 4*H*-cyclohept[*d*]oxazol-4-one.[5,6] The 1,3-dipolar addition of arenecarbonitrile oxide to tropone gave 4*H*-cyclohept[*d*]isoxazol-4-one derivatives.[7]

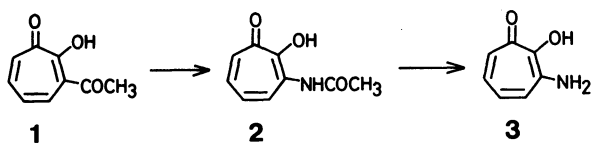
Previously, 3-aminotropolone was prepared from 3-nitrotropolone[8] or 3-bromotropolone.[9] On the other hand, it was reported that Schmidt reaction of 4-acetyltropolone afforded 4-aminotropolone.[10]

In a series of 3-acetyltropolone chemistry, we wish to report the convenient synthesis of 3-aminotropolone by Schmidt reaction of 3-acetyltropolone and its conversion to 8*H*-cyclohept[*d*]oxazole-8-ones by reactions with orthoesters.

Results and Discussion

When we applied the Schmidt reaction to 3-acetyltropolone (**1**),[11] 3-acetamidotropolone (**2**)[3] was isolated. The compound **2** was readily hydrolyzed to give 3-aminotropolone(**3**), whose averall yield based on **1** was 56%.

A mixture of 3-aminotropolone (**3**) and triethyl orthoformate or triethyl orthoacetate was heated under reflux to afford respectively 8*H*-cyclohept[*d*]oxazole-8-one (**4a**)[4] (44%) and its 2-methyl derivative (**4b**)[3] (73%). In the NMR spectrum of the compound **4a**, the H-2 proton in the oxazole ring is observed at lower magnetic field (δ=8.21) than the H-2 proton in oxazole ring (δ=7.95).[12] In a similar manner, the reaction with triethyl orthopropionate and trimethy orthobenzoate gave 2-ethyl- and 2-phenyl-8*H*-cyclohept[*d*]oxazol-8-ones (**4c** and **4d**) in 80 and 10% yields, respectively.



1 **2** **3**

Scheme 1.

Experimental

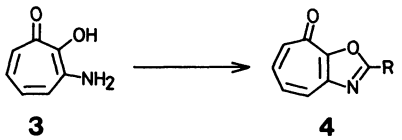
Measurements. The melting points were determined with a Yanagimoto MP-S2 melting point-measuring apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer, and the UV spectra on a Hitachi EPS-3T spectrophotometer. The NMR spectra were recorded with a Hitachi R-24 spectrometer (60 MHz).

3-Acetamidotropolone (2). Sodium azide (2.60 g, 40 mmol) was added to a solution of 3-acetyltropolone (**1**) (3.28 g, 20 mmol) in chloroform (40 ml). Concentrated sulfuric acid (10 ml) was carefully dropped into the mixture in an ice-cooled bath under stirring. After stirring for 2 h at room temperature, the chloroform was removed by decantation. After cold water (80 ml) was added to the residue, a precipitate was collected and recrystallized from methanol to give 2.3 g (66%) of 3-acetamidotropolone (**2**) as colorless needles: mp 119—120 °C (lit,[3] 107—108 °C); IR ($CHCl_3$) 3315 (NH), 1702 cm^{-1} (C=O); NMR ($CDCl_3$) δ=2.30 (3H, s, CH_3), 7.0—7.6 (3H, m), 9.1—9.4 (1H, m, NH).

3-Aminotropolone (3). 3-Acetamidotropolone (**2**) (2.0 g) in 50% sulfuric acid (22 ml) was heated on a water bath for 1 h. The mixture was neutralized with sodium hydrogencarbonate solution, acidified slightly with 30% acetic acid, and extracted with chloroform. The evaporation residue from the extract was recrystallized from benzene–petroleum ether to give 1.3 g (85%) of 3-aminotropolone (**3**) as yellow needles: mp 86 °C (lit,[8] 86 °C); NMR ($CDCl_3$) δ=5.6—6.7 (2H, br, NH_2), 6.6—7.5 (m, 4H).

Reaction of 3-Aminotropolone (3) with Triethyl Orthoformate. A mixture of 3-aminotropolone (**3**) (137 mg, 1.0 mmol) and triethyl orthoformate (2 ml) was refluxed for 2 h. After cooling, the precipitate was collected and recrystallized from benzene–hexane to give 65 mg (44%) of 8*H*-cyclohept[*d*]oxazol-8-one (**4a**) as pale yellow needles: mp 149—150 °C (lit,[4] 150—151 °C); IR ($CHCl_3$) 1625 cm^{-1} (C=O); UV (CH_3OH) 237 (log ε 4.56), 310 nm (3.94); NMR ($CDCl_3$) δ=6.8—8.0 (4H, m), 8.21 (1H, s, H-2).

Reaction of 3 with Triethyl Orthoacetate. A mixture of **3** (274 mg, 2.0 mmol) and triethyl orthoacetate (2 ml) was refluxed for 2 h. The reaction mixture was dissolved in chloroform and twice washed with water. After removal of the solvent, the residue was recrystallized from benzene–hex-



3 **4**

a R = H
b R = CH_3
c R = CH_2CH_3
d R = Ph

Scheme 2.

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ane to give 234 mg (73%) of 2-methyl-8*H*-cyclohept[*d*]oxazol-8-one (**4b**) as pale yellow needles: mp 150—151 °C (lit,[3] 144—145 °C); IR ($CHCl_3$) 1640 cm^{-1} (C=O); UV (CH_3OH) 243 (log ε 4.44), 312 nm (3.68); NMR ($CDCl_3$) δ=2.67 (3H, s, CH_3), 6.9—7.8 (4H, m).

Reaction of 3 with Triethyl Orthopropionate. A mixture of **3** (274 mg, 2.0 mmol) and triethyl orthopropionate (2 ml) was refluxed for 2 h and worked up, as mentioned above, to afford 280 mg (80%) of 2-ethyl-8*H*-cyclohept[*d*]oxazol-8-one (**4c**) as pale yellow needles: mp 92—93 °C (from benzene–hexane); IR ($CHCl_3$) 1640 cm^{-1} (C=O); UV (CH_3OH) 245 (log ε 4.49), 312 nm (3.83); NMR ($CDCl_3$) δ=1.50 (3H, t, J=7 Hz, CH_3), 3.03 (2H, q, J=7 Hz, CH_2), 6.9—7.8 (4H, m). Found: C, 68.51; H, 5.21; N, 7.92%. Calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00%.

Reaction of 3 with Trimethyl Orthobenzoate. A solution of **3** (137 mg, 1.0 mmol) and trimethyl orthobenzoate (182 mg, 1.0 mmol) in chloroform (2 ml) was refluxed for 2 h. After removal of the solvent, the residue was chromatographed on a Wakogel B-10 plate (30×30 cm^2) with ethyl acetate to give 23 mg (10%) of 2-phenyl-8*H*-cyclohept-[*d*]oxazol-8-one (**4d**) as pale yellow needles: mp 149—150 °C (from benzene–hexane); IR ($CHCl_3$) 1640 cm^{-1} (C=O); UV (CH_3OH) 275 (log ε 4.42), 349 (sh, 3.84), 365 nm (sh, 3.63); NMR ($CDCl_3$) δ=7.0—7.8 (7H, m,), 8.1—8.5 (2H, m, H-2′,6′). Found: C, 75.32; H, 4.06; N, 6.28%. Calcd for $C_{14}H_9NO_2$: C, 75.50; H, 3.96; N, 6.26%.

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