Reactions of 3-Aminotropolone with Acyl Halides. Formation of 8*H*-Cyclohept[*d*]oxazol-8-ones

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3-Aminotropolone (**1**) reacted with acetyl chloride and propionyl chloride to give 2-methyl- and 2-ethyl-8*H*-cyclohept[*d*]oxazol-8-ones (**2a** and **2b**), respectively. The reactions with benzoyl chloride and phenylacetyl chloride gave *N*-acylated and *N,O*-diacylated 3-aminotropolones [(**3a** and **3b**) and (**4a** and **4b**)].

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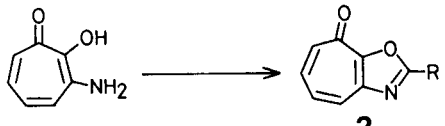
We found that 3-acetyltropolone is very useful as starting material for the synthesis of heterocycle-fused tropone compounds [1]. On the other hand, this compound was readily converted to 3-aminotropolone by Schmidt reaction [2].

It has been reported that 3-aminotropolone (**1**) was heated with acetic anhydride [3], formamide [4], or *p*-nitrobenzaldehyde [4] to give 8*H*-cyclohept[*d*]oxazol-8-one derivatives. We also described the formation of 8*H*-cyclohept[*d*]oxazol-8-ones by the reactions with a variety of orthoesters [2].

In this communiction, we wish to report the reactions of 3-aminotropolone (**1**) with acyl halides.

Results and Discussion.

A mixture of 3-aminotropolone (**3**) and acetyl chloride or propionyl chloride was heated under reflux to afford 2-methyl- and 2-ethyl-8*H*-cyclohept[*d*]oxazol-8-ones [**2a** [4] and **2b** [2]] in 65 and 46% yields, respectively.

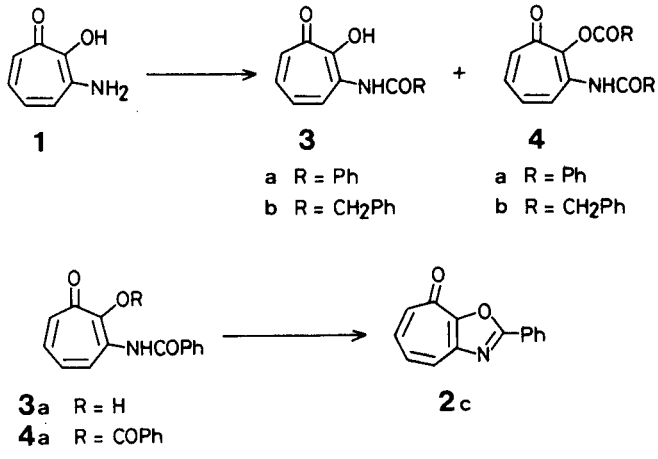


1 **2**

a R = CH_3

b R = CH_2CH_3

However, the reaction of benzoyl chloride gave 3-benzamidotropolone (**3a**) and 3-benzamido-2-benzoyloxytropone (**4a**), as previously reported [4]. The benzoylation of **3a** afforded **4a**, while hydrolysis of **4a** afforded **3a**. Both of **3a** and **4a** were heated in polyphosphoric acid at 170° to cyclize to 2-phenyl-8*H*-cyclohept[*d*]oxazol-8-one (**2c**) [2] in 93 and 58% yields, respectively. The compound (**1**) was heated with phenylacetyl chloride to afford 3-(phenylacetamido)tropolone (**3b**) and 3-(phenylacetamido)-2-(phenylacetoxy)tropone (**4b**). The interconversion between **3b** and **4b** was also observed by phenylacetylation or hydrolysis.



1 **3** **4**

a R = Ph
b R = CH_2Ph

a R = Ph
b R = CH_2Ph

3a R = H
4a R = COPh

2c

However, their cyclization to 8*H*-cyclohept[*d*]oxazol-8-one derivative failed.

EXPERIMENTAL

The melting points were determined with a Yanagimoto MP-S2 apparatus and are uncorrected. The ir spectra were taken on a JASCO IRA-1 spectrophotometer. The ^1H nmr spectra were recorded with a Hitchi-Perkin-Elmer R-24 spectrometer (60 MHz).

Reaction of 3-Aminotropoline (**1**) with Acetyl Chloride.

A mixture of **1** (274 mg, 2.0 mmoles) and acetyl chloride (2 ml) was refluxed for 2 hours. After removal of an excess of the acetyl chloride under reduced pressure, the residue was recrystallized from benzene-hexane to give 2-methyl-8*H*-cyclohept[*d*]oxazol-8-one (**2a**), yield 209 mg (65%), mp 150-151° (lit [3], mp 144-145°).

Reaction of 3-Aminotropolone (**1**) with Propionyl Chloride.

A solution of **1** (137 mg, 1.0 mmole) and propionyl chloride (2 ml) in chloroform (2 ml) was refluxed for 2 hours and worked up, as mentioned above, to give 2-ethyl-8*H*-cyclohept[*d*]oxazol-8-one (**2b**), yield 81 mg (46%), mp 91-93° (lit [2], mp 91-93°).

Reaction of 3-Aminotropolone (**1**) with Benzoyl Chloride.

A solution of **1** (137 mg, 1.0 mmole) and benzoyl chloride (0.5 ml) in chloroform (0.5 ml) was stirred for 1 hour at room temperature. The reaction mixture was diluted with chloroform and washed with water. The chloroform solution was dried over sodium sulfate and evaporated to dry-

ness. The residue was recrystallized from benzene-hexane to afford 3-benzamido-2-(benzoyloxy)tropone (**4a**) as yellow prisms, yield 120 mg (35%), mp 170° (lit [4], mp 174°); ir (chloroform): ν max 3270 (NH), 1730 (C=O), 1670 cm^{-1} (C=O); ^1H nmr (DMSO-d_6): δ 6.8-7.6 (m, 10H), 7.7-8.3 (m, 4H), 9.30 ppm (m, 1H, NH).

The evaporation residue from the mother liquor was recrystallized from benzene-acetone to afford 3-benzamidotropolone (**3a**) as yellow needles, yield 19 mg (8%), mp 147-148° (lit [4], mp 146°); ir (chloroform): ν max 3300 (NH), 1670 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 7.1-7.6 (m, 7H), 7.8-8.1 (m, 2H), 8.0-9.0 (br, 1H, OH), 9.2-9.6 ppm (m, 1H, NH).

Benzoylation of **3a**.

A solution of **3a** (120 mg, 0.5 mmole) and benzoyl chloride (0.5 ml) in chloroform (5 ml) was allowed to stand at room temperature for 2 hours. After removal of the solvent, the residue was chromatographed on two Wakogel B-10 plates (20 × 20 cm^2) with chloroform to give **4a**, yield 127 mg (74%).

Hydrolysis of **4a**.

To a suspended solution of **4a** (173 mg, 0.5 mmole) in methanol (5 ml) was added 1*M* potassium hydroxide solution (5 ml). The mixture was heated on a water bath for 2 hours, neutralized with 3*M* hydrochloric acid, and extracted with chloroform. After removal of the solvent, the residue was recrystallized from methanol to give **3a**, yield 101 mg (84%).

Cyclization of **3a**.

A mixture of **3a** (120 mg, 0.5 mmole) and polyphosphoric acid (1 g) was heated on an oil bath (170°) for 2 hours. The reaction mixture was diluted with water and extracted with chloroform. The chloroform extract was washed with sodium hydrogencarbonate solution and water, and dried over sodium sulfate. After removal of the solvent, the residue was recrystallized from benzene-hexane to give 2-phenyl-8*H*-cyclohept-[*d*]oxazol-8-one (**2c**), yield 103 mg (93%), mp 150-151° (lit [2], mp 149-150°).

Cyclization of **4a**.

A mixture of **4a** (68 mg, 0.2 mmole) and polyphosphoric acid (1 g) was heated on an oil bath (170°) for 2 hours and worked up, as mentioned above, to give **2c**, yield 25 mg (58%).

Reaction of 3-aminotropolone (**1**) with Phenylacetyl Chloride.

A solution of **1** (274 mg, 2.0 mmoles) and phenylacetyl chloride (1 ml) in chloroform (10 ml) was refluxed for 2 hours. The mixture was washed with water and dried over sodium sulfate. After removal of the solvent, the residue was recrystallized from methanol to give 3-(phenylacetamido)-2-(phenylacetoxy)tropone (**4b**) as pale yellow prisms, yield 429 mg (57%), mp 143°; ir (chloroform): ν max 3300 (NH), 1760 (C=O), 1690 cm^{-1} (C=O); ^1H nmr (DMSO-d_6): δ 2.95 (br s, 1H, NH), 3.84 (s, 2H, $OCOCH_2Ph$), 3.90 (s, 2H, $NHCOCH_2Ph$), 6.8-7.5 ppm (m, 14H).

Anal. Calcd. for $C_{23}H_{19}NO_4$: C, 73.98; H, 5.13; N, 3.75. Found: C, 74.12; H, 5.08; N, 3.86.

After evaporation of the solvent from the mother liquor, the residue was recrystallized from methanol to give 3-(phenylacetamido)tropolone (**3b**) as pale yellow needles, yield 82 mg (16%), mp 129-131°; ir (chloroform): ν max 3280 (NH), 1680 cm^{-1} (C=O); ^1H nmr (DMSO-d_6): δ 3.891 (s, 2H, CH_2), 7.1-7.4 (m, 9H), 9.1-9.5 ppm (m, 2H, NH + OH).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.43; H, 5.10; N, 5.65.

Phenylacetylation of **3b**.

A solution of **3b** (128 mg, 0.5 mmole) and phenylacetyl chloride (0.5 ml) in chloroform (5 ml) was refluxed for 2 hours. After removal of the solvent, the residue was chromatographed on two Wakogel B-10 plates (20 × 20 cm^2) with chloroform to give **4b**, yield 37 mg (20%).

Hydrolysis of **4b**.

To a suspended solution of **4b** (187 mg, 0.5 mmole) in methanol (5 ml) was added 1*M* potassium hydroxide solution (5 ml). The mixture was heated on a water bath for 2 hours, neutralized with 3*M* hydrochloric acid, and extracted with chloroform. After removal of the solvent, the residue was recrystallized from methanol to give **3b**, yield 96 mg (75%).

REFERENCES AND NOTES

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