SYNTHESIS AND REACTIONS OF NOVEL TROPONO[4,5-*b*]OXEPINES

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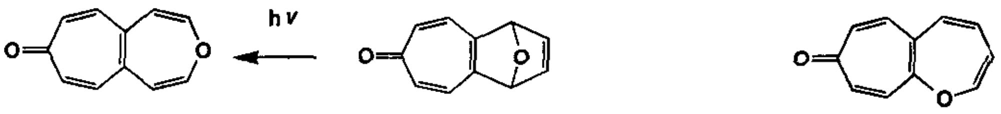
Abstract - Reaction of pyridazine *N*-oxides with 4,5-didehydrotropone resulted in the formation of the novel tropono[*4,5-b*]oxepines and some chemical properties of the new ring system were examined.

The synthesis of new fully unsaturated heteroepines has recently attracted much attention and fused oxepines condensed with aromatic six-membered rings such as benzene[1,2] and pyridine[3] rings have also been prepared. However, oxepines condensed with seven-membered rings have not been reported except for tropono[4,5-*d*]oxepine (1),[4] which was obtained by the photochemical rearrangement of the oxanorbornadiene derivative (2). We report here the first synthesis of the tropono[4,5-*b*]oxepines (3) and the results of several reactions of this new ring system.

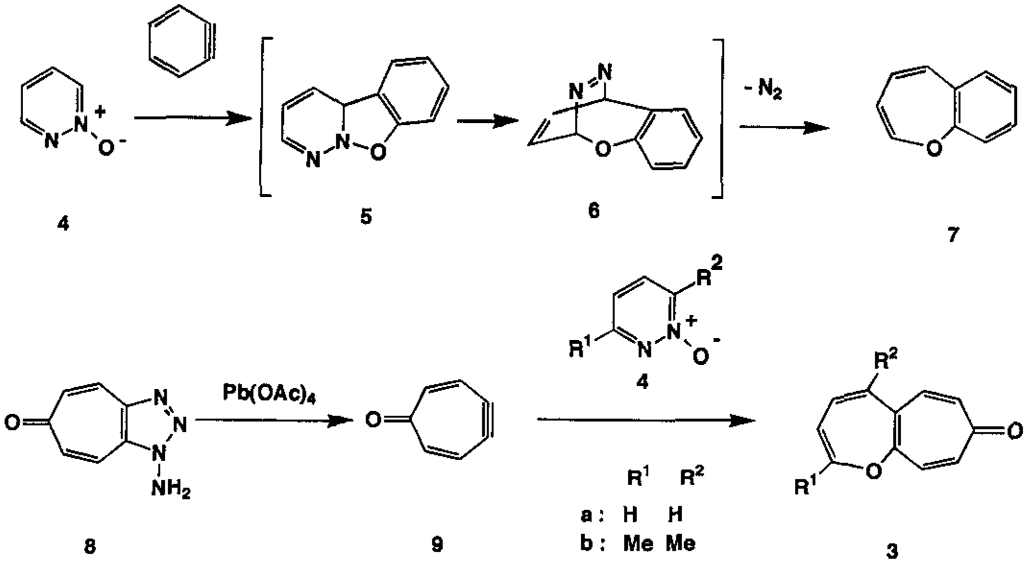


1 2 3

Scheme 1

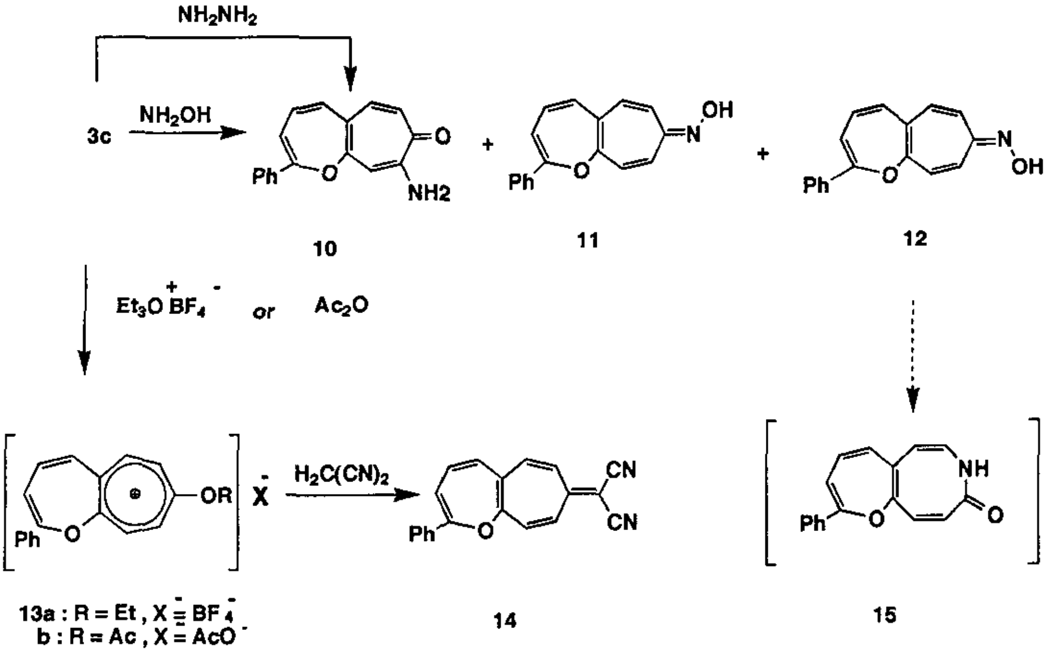
We have already reported that the reaction of pyridazine *N*-oxides (4) with benzyne gave 1-benzoxepines (7) *via* the initially formed unisolable cycloadducts (5) and the rearrangement intermediates (6),[2] and pyridynes and quinolynes were also reacted with **4** to give the corresponding pyridoxepines and quinoxepines.[3] These results prompted us to examine the reaction of 4,5-didehydrotropone with pyridazine *N*-oxides.

1-Aminotropono[4,5-*d*]-1,2,3-triazole (**8**) was oxidized with lead tetraacetate in methylene chloride-dimethyl sulfoxide at 0 °C to generate 4,5-didehydrotropone (**9**),[5] which was trapped in situ with a large excess of pyridazine *N*-oxides (**4a,b**) giving rise to the expected tropono[4,5-*b*]oxepines (**3a,b**)[6] as the sole isolable products in the yields (**3a**, 35%; **3b**, 60%) calculated from the triazole (**8**). These oxepines (**3**) are interesting new fused ring compounds in which an electron-rich oxepine ring is fused with an electron-deficient nonbenzenoid aromatic tropone ring, and were characterized by elemental and spectral analyses and the results of several chemical studies.



Scheme 2

In the ^{1}H-nmr spectrum of **3a**, all four oxepine ring protons, particularly 3- and 4-protons, resonated expectedly at lower fields (δ 2-H, 6.27; 3-H, 5.86; 4-H, 6.48; 5-H, 6.70) than those of 1-benzoxepine (δ 2-H, 6.14; 3-H, 5.35; 4-H, 5.93; 5-H, 6.54).[2] In regard to chemical reactions, the troponoxepines (**3**) did not react with dienophiles such as tetracyanoethylene, 3-phenyl-1,2,4-triazoline-3,5-dione and dimethyl acetylenedicarboxylate, and not undergo intramolecular cycloaddition by irradiation, in contrast to 1-benzoxepines, which are known to readily react with activated dienophiles as dienes[7] and to undergo photo-induced cyclization.[8] These spectral and chemical results indicate that the electron density of the oxepine ring is decreased by the electron-deficient tropon ring and thus the reactivity of the oxepine ring toward such reactions is decreased.



Scheme 3

With regard to the tropone ring of **3**, in the ^{1}H-nmr spectrum of **3a**, the α-protons (δ 7-H, 6.89 and 9-H, 6.98) resonated at lower fields, in contrast, the β-protons (δ 6-H, 7.01 and 10-H, 7.07) appeared at higher fields than those of benzo[*d*]tropone (δ α-H, 6.65 and β-H, 7.27),[9] respectively, and both α- and β-protons of **3a** resonated at lower fields than those of tropono[4,5-*d*]oxepine (**1**) (δ 6.80, br, α- and β-H).[4] However, the chemical behaviors of the tropone ring of **3** are similar to those of monocyclic and benzo-fused tropones. For example, treatment of **3c** with hydrazine gave the 9-amino compound (**10**) and its 7-amino isomer[10] in 55% and 6% yields but no hydrazone of **3c**, whereas the reaction with hydroxylamine afforded two oximes (**11**) (E-form) and (**12**) (Z-form) in 34% and 43% yields as well as **10** (18% yield).[11] The oxepine (**3c**) was successively treated with triethyloxonium fluoroborate and malononitrile gave the dicyanofulvene (**14**)[12] *via* the unisolable tropylium salt (**13a**). The fulvene (**14**) was also obtained by treatment of **3c** with acetic anhydride and malononitrile *via* **13b**. These results are essentially similar to those for tropones.[13] However, all attempts to obtain the oxepinoazocines such as **15** from the oximes (**11**) and (**12**) have been unsuccessful, in contrast to benzotropone oximes, whose benzenesulfonates can be converted to 3-benzazocines by Beckmann rearrangement.[14] Further chemical studies on the new ring system are in progress.

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6. **3a**: mp 90-92 °C; ir (KBr): 1575 (C=O) cm^{-1}; ^{1}H-nmr (CDCl$_3$) δ : 5.86 (1H, dd, 3-H), 6.27 (1H, d, 2-H), 6.48 (1H, dd, 4-H), 6.70 (1H, d, 5-H), 6.89 (1H, dd, 7-H), 6.98 (1H, dd, 9-H), 7.01 (1H, d, 6-H), 7.07 (1H, d, 10-H), $J_{2,3}$= 5.1, $J_{3,4}$=5.6, $J_{4,5}$= 11.0, $J_{6,7}$= 13.0, $J_{7,9}$= 2.6, $J_{9,10}$= 13.2 Hz; **3b**: mp 86-88 °C
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10 **10**: mp 190-192 °C; ^{1}H-nmr (ring protons) (CDCl$_3$) δ : 3- and 4-H (6.30-6.40, m), 5-H (6.75, d), 6-H (7.19, d), 7-H (7.01, d), 10-H (6.77, s), $J_{4,5}$= 11.4, $J_{6,7}$= 12.5 Hz ; the 7-amino isomer of **10**: mp 161-162 °C ; ^{1}H-nmr (ring protons) (CDCl$_3$) δ :3-H (6.38, d), 4-H (6.56, dd), 5-H (6.74, d), 6-H (6.72, s), 9-H (7.03, d), 10-H (7.19, d), $J_{3,4}$= 6.2, $J_{4,5}$= 11.0, $J_{9,10}$= 12.8 Hz.
11. **11**: mp 174-177 °C; **12**: mp 176-179 °C. The oximes(**11**)and(**12**)could be separated by silica gel column chromatography and were characterized by ^{1}H-nmr spectral and X-ray crystallographic analyses. A thermal E-Z interconversion was observed between **11** and **12**, *e.g.*, when they were individually heated at 90 °C in DMSO for 2h, the interconversion was completed existing **11** and **12** in a 4:5 ratio in each solution. Details of these products will be described in a full paper.
12. **14**: mp 169-171 °C; ir (KBr): 2208 (CN) cm^{-1}; ^{1}H-nmr (CDCl$_3$) δ 6.52 (1H, d, 3-H), 6.73 (1H, dd, 4-H), 6.62 (1H, d, 5-H), 6.90 (1H, d, 10-H), 7.20 (1H, dd, 7-H), 7.23 (1H, dd, 9-H), 7.46-7.79 (5H, m, Ph-H), $J_{3,4}$= 6.2, $J_{4,5}$= 11.0, $J_{6,7}$= 12.5, $J_{7,9}$= 2.6, $J_{9,10}$= 12.0 Hz.
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