

## Accepted Manuscript

Essential structure of orexin 1 receptor antagonist YNT-707, Part II: Drastic effect of the 14-hydroxy group on the orexin 1 receptor antagonistic activity

Sayaka Ohruï, Naoshi Yamamoto, Tsuyoshi Saitoh, Noriki Kutsumura, Yasuyuki Nagumo, Yoko Irukayama-Tomobe, Yasuhiro Ogawa, Yukiko Ishikawa, Yurie Watanabe, Daichi Hayakawa, Hiroaki Gouda, Masashi Yanagisawa, Hiroshi Nagase

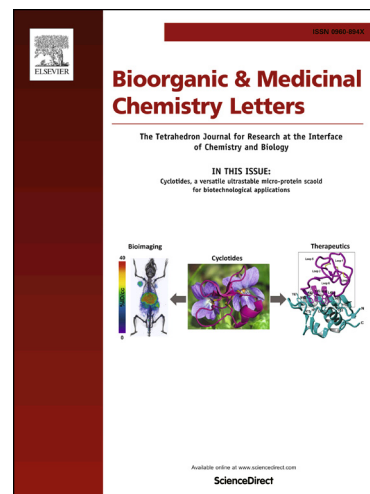
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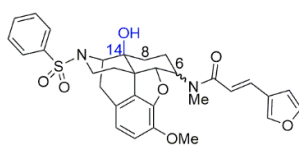
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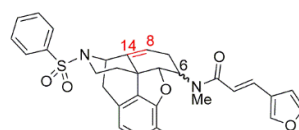
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14-OH derivatives

**2** (6 $\beta$ ) OX<sub>1</sub>R : K<sub>i</sub> = 8.14 nM

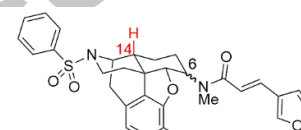
**3** (6 $\alpha$ ) OX<sub>1</sub>R : K<sub>i</sub> = 849 nM



14-dehydration-derivatives

**14** (6 $\beta$ ) OX<sub>1</sub>R : K<sub>i</sub> = 2.06 nM

**13** (6 $\alpha$ ) OX<sub>1</sub>R : K<sub>i</sub> = 17.8 nM



14-H derivatives

**23** (6 $\beta$ ) OX<sub>1</sub>R : K<sub>i</sub> = 1.97 nM

**22** (6 $\alpha$ ) OX<sub>1</sub>R : K<sub>i</sub> = 187 nM

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