Asymmetric Photocatalyzed Addition of Cyclic Amines to the Chiral 5-(*l*)-Menthyloxy-2(5H)-furanone

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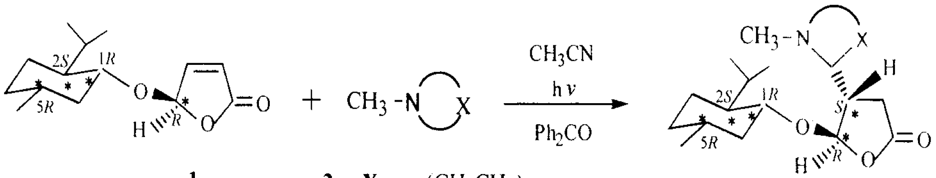
Abstract: The benzophenone-initiated photoaddition of N-methyl amines **2** to the chiral synthon **1** proceeds in a regiospecific and highly stereocontrolled fashion to give the C-C photoadducts containing a newly stereogenic center **3a-3c**. The enantiomerically pure N-C photoadducts, amino butenolides **5a-5c** have been obtained from the enantioselective photoaddition of secondary cyclic amines **4** with the chiral synthon **1** under the same conditions.

Keywords: Asymmetric photocatalysed conjugate addition, enantiomerically pure C-C photoadducts, secondary cyclic amine, enantiomerically pure N-C photoaducts.

In recent years, considerable attention has been focused on the synthesis and properties of chiral butenolides because of their multifunctional nature and versatility on enantioselective transformation reactions[1,2]. Despite extensive studies of this research work on asymmetric reactions but little effort has been devoted towards photochemical synthesis of some chiral γ-substituted 2-(5H)-furanones[3]. Among the previous work, the tertiary amines used in the photocatalysed conjugate additions to 5-substituted 2(5H)-furanones were the first examples[3d], and the secondary cyclic amines have been not used yet in the photocatalysed additions. For this reason, it spurred us to study on the asymmetric photoadditions of N-methyl cyclic amines **2** and secondary cyclic amines **4** to 5-(*l*)-menthyloxy-2(5H)-furanone **1**. As an extension of our research program on the synthesis and asymmetric reaction of chiral γ-butenolides[1b], we have now investigated photocatalyzed conjugate additions of cyclic amines and alcohols to chiral 5-alkoxy-2(5H)-furanones. In this paper, we would like to report the regiospecific and stereoselective additions of various N-methyl cyclic amines **2** to 5-(*l*)-menthyloxy-2(5H)-furanone **1** under irradiation with a 450 W medium pressure lamp (Pyrex, 350nm) in acetonitrile in the presence of benzophenone as a photocatalyzer to afford the photoadducts **3a-3c** in 24-50% yields with d.e.≥98% (**Scheme 1**), and the photocatalyzed conjugate additions of various secondary cyclic amines **4a-4c** to chiral butenolide **1** under the same conditions to give N-C adducts **5a-5c** in 34-58% yields with d.e.≥98% (**Scheme 2**) which can be transformed to several chiral amino alcohols or amino esters.

Scheme 1



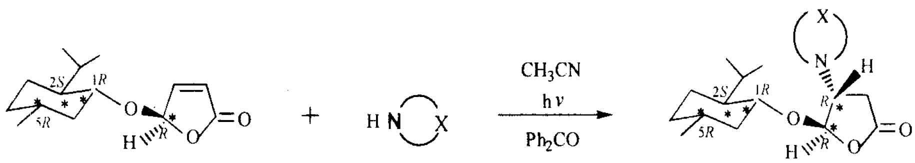
1

2a X = $-(CH_2CH_2)_2-$
b X = $-CH_2(CH_2)_3CH_2-$
c X = $-(CH_2)_2O(CH_2)_2-$

3a X = $-CH_2CH_2CH_2-$
b X = $-CH_2(CH_2)_2CH_2-$
c X = $-(CH_2)_2OCH_2-$

The mechanism of this photocatalysed reaction would appear to be analogous to that proposed by Fraser-Reid[4], and involves excitation of benzophennone to the triplet (*n*, π*) state with subsequent abstraction of a hydrogen atom from the various cyclic amines and Michael addition of the resultant radical **6** and **7** to the chiral synthon **1**. The photolysis time was 1-4 h, upon which **1** had been consumed as monitored by TLC. Most of the benzophenone could be recovered unchanged, but variable amounts of benzopinocol **8** were also obtained, together with some unexpected compounds.

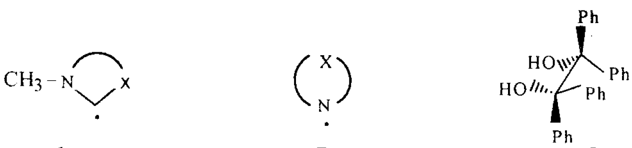
Scheme 2



1

4a X = $-(CH_2CH_2)_2-$
b X = $-CH_2(CH_2)_3CH_2-$
c X = $-(CH_2)_2O(CH_2)_2-$

5a X = $-(CH_2CH_2)_2-$
b X = $-CH_2(CH_2)_3CH_2-$
c X = $-(CH_2)_2O(CH_2)_2-$



6 **7** **8**

The structures of all photo-products were identified on the basis of satisfactory elemental analytical data and spectroscopic data ([α]20589, IR, 1H NMR, ^{13}C NMR and MS)[6].

As an extension of the above work, other N-methyl cyclic amines *e.g.* nicotine and N-trimethylsilyl cyclic amines, alcohols, aldehydes, acetals can be used in the asymmetric photocatalyzed conjugate additions to 5-(l)-menthyloxy-2(5H)-furanone 1 to concisely synthesize more new optically active compounds, which are currently in progress.

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5. **3a**, 1. 22g, (24%), m. p. 110~112℃; $[\alpha]^{20}_{589}$ =-104. 5($CHCl_3$); IR (KBr): ν=2960, 2925, 2800, 1782, 1170, 962cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$)δ: 0. 70-1. 60 (16H, m, menthyl's H), 1. 60-2. 00 (5H, m, H_{17}、H_{18}、H_{3b}), 2. 10 (2H, m, H_7), 2. 25 (1H, m, H_{16}), 2. 31 (3H, s, H_{20}), 2. 55 (2H, m. H_{19}), 2.82 (1H, dd, J=9.9 Hz, H_4), 3.08 (1H, m, H_{3a}), 3.49 (1H, ddd, J=7.2, 7.2, 3.6 Hz, H_6), 5.60 (1H, s, H_5); ^{13}C NMR (75MHz, $CDCl_3$)δ: 15.6, 20.9, 22.2, 23.0, 25.4, 27.0, 31.2, 31.3, 34.3, 39.9, 40.8, 42.7, 47.7, 57.1, 66.5, 77.1, 102.3, 176.4; MS(*m/z*): 323(M^+,2), 184(M^+-menthyl, 100), 84($C_5H_{10}N^+$, 100); Anal. Cacl. for $C_{19}H_{33}NO_3$: C 70.55, H 10.28, N 4.33; Found: C 70.70, H 10.43, N 4.09.
   5c. 2.58g (50%), m.p. 116~117℃; $[\alpha]^{20}_{589}$=-166.9($CHCl_3$); IR (KBr): ν=2960, 2923, 2857, 1781, 1122, 942cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$)δ: 0.77 (3H, d, J=6.9 Hz, H_{15}), 0.87 (3H, d. J=6.6 Hz, H_{14}), 0.94 (3H, d, J=6.6 Hz, H_{12}), 1.05 (3H, m, H_{11}, H_9), 1.22 (1H, m, H_8), 1.39 (1H,

m, H_{13}). 1.64 (2H, m, H_{10}), 2.05 (2H, m, H_7), 2.53 (5H, m, H_{17}, H_{21}, H_{3b}). 2.77 (1H, dd, J=18.8 Hz. H_4), 3.13 (1H, m, H_{3a}), 3.55 (1H, ddd, J=10.2, 10.2, 4.2 Hz, H_6), 5.63 (1H, s, H_5): ^{13}C NMR (75MHz, $CDCl_3$)δ: 15.6, 20.8, 22.2, 23.0, 25.4, 31.3, 34.2, 39.5, 47.7, 50.2, 66.3, 77.1, 101.4, 174.3; MS(*m/z*): 325(M^+,15), 113($C_6H_{11}NO^+$,100); Anal. Cacl. for $C_{18}H_{31}NO_4$: C 66.43, H 9.60, N 4.31; Found: C 66.77, H 9.85, N 4.48.

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