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ASYMMETRIC [2+2] PHOTOCYCLOADDITION REACTION OF A CHIRAL DIOXOPYRROLINE TO 2-(TRIMETHYLSILYLOXY)BUTADIENE: CHIRAL SYNTHESIS OF *ERYTHRINA* ALKALOIDS[1)]

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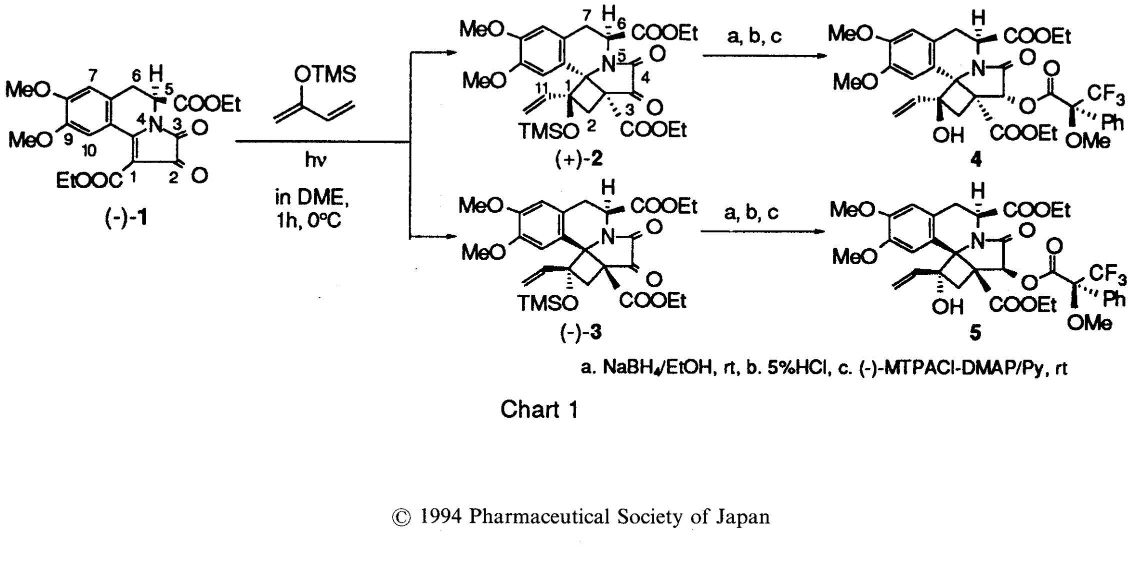
The detailed stereochemical pathway of [2+2] photocycloaddition reaction of isoquinolinodioxopyrroline to 2-(trimethylsilyloxy)butadiene was clarified by using an enantiomerically pure substrate. The photoadducts were converted into the synthetic intermediates of *Erythrina* alkaloids, providing an efficient synthetic method in optically active forms.

KEYWORDS [2+2] photocycloaddition; face selectivity; chiral dioxopyrroline; photo-epimerization; cycloreversion; *Erythrina* alkaloid

[2+2] Photocycloaddition of dioxopyrroline to olefins has been intensively investigated to clarify factors controlling the stereochemical pathway of the reaction.[2)] In this communication, we describe an asymmetric [2+2] photocycloaddition reaction of a chiral isoquinolinodioxopyrroline to 2-trimethylsilyloxybutadiene, which not only revealed the detailed stereochemical outcome of the above photocycloaddition reaction but also provided a new synthetic method of chiral *Erythrina* alkaloids.

The chiral dioxopyrroline (-)-**1** of (5*S*)-configuration (mp 147-149°C, $[\alpha]_D^{22}$ -73.0°) was prepared from L-DOPA in a similar way as described in the synthesis of the corresponding methyl ester.[3)]

A solution of (-)-**1** and 2-trimethylsilyloxybutadiene (2 mol eq) in dimethoxyethane (DME) was irradiated for 1 h at 0°C under a high-pressure mercury lamp with a Pyrex filter (≥ 300 nm) to give the two adducts **2**[4)] (56%) and **3**[4)] (11%). The adducts showed opposite Cotton effects ([θ] +1100° at 378 nm for **2** and [θ] -3600° at 375 nm for **3**), suggesting that they are enantiomeric concerning the stereochemistry of the cyclobutane ring juncture (C2a and C11b). The stereochemistry of the vinyl and OTMS groups at C-1 was elucidated by the fact that adducts **2** and **3** showed similar chemical reactivities with that of the corresponding photoadduct[5)] which lacks 6-ethoxycarbonyl group; thus the vinyl and OTMS group are in *exo*- and *endo*-configuration, respectively. The enantiomer excess (ee) of the adducts was determined as 20% for the major adduct (+)-**2**[6)] and >99% for the minor adduct (-)-**3**[6)] from the respective diastereomer excess (de) observed in the ^{1}H-NMR spectra of the derived (-)-(*R*)-α-methoxy-α-trifluoromethylphenylacetate **4** and **5** (Mosher's ester)[7)] which were prepared by the route shown in Chart 1. Their absolute stereo-



a. $NaBH_4$/EtOH, rt, b. 5%HCl, c. (-)-MTPACl-DMAP/Py, rt

Chart 1

chemistries were established by conversion into the known erythrinan derivatives[8] described below (Chart 4).

The low ee of (+)-**2** suggested that this cycloaddition accompanied epimerization of C_6-COOEt group in one of the product (-)-**3**, which resulted in the enantiomer of (-)-**2**. In fact, the ee of **2** was found to largely depend on the reaction time. Short irradiation (30 min) of (-)-**1** and the diene (2 mol eq) at 0°C gave (+)-**2** of 78% ee[9a] and (-)-**3** of >99% ee in 57% and 16% yields, respectively.

The more detailed pathway was evidenced from the following experiments. The dioxopyrroline (-)-**1** was recovered without any loss of its optical activity by irradiation in DME for 1 h. Irradiation of (-)-**3** of >99% ee in DME at 0°C for 3 h gave (±)-**2** [9b] in 18% yield. The formation of the racemate indicated that (-)-**3** underwent not only the epimerization of the C_6-COOEt group but also cycloreversion of the cyclobutane ring and recombination of the formed (-)-**1** with 2-trimethylsilyloxybutadiene. A similar irradiation of (-)-**3** in the presence of the diene (10 mol excess) gave (+)-**2** of 88% ee,[9c] though the chemical yield was low (25%), indicating that the cycloreversion-recombination process was accelerated in the presence of the excess diene.[10] Irradiation of (+)-**2** of 70% ee under a similar condition slowly produced (-)-**3** of 31% ee[11a] in 10% yield with recovery of (+)-**2** in 78% yield without change of its ee. Similar irradiation of (+)-**2** of 70% ee in the presence of the diene (10 mol excess) gave (-)-**3** of 56% ee[11b] in 10% yield with recovery of (+)-**2** in 69% yield without loss of its ee. The partial racemization of (-)-**3** in these reactions must be due to the direct epimerization of (+)-**2** to (+)-**3**, since, if (+)-**3** were produced from (-)-**2** through cycloreversion-recombination, the ee of the recovered (+)-**2** should decrease.

From the above results, the whole reaction process is depicted as shown in Chart 2, where steps shown by bold arrows were observed in the photocycloaddition reaction of (-)-**1** to the diene. Reaction rates of each step can be evaluated as $k_1 > k_2 > k_3 > k_4 > k_5 > k_6$: in these, cycloaddition is greatly accelerated by the presence of the excess diene, since the reaction is bimolecular.

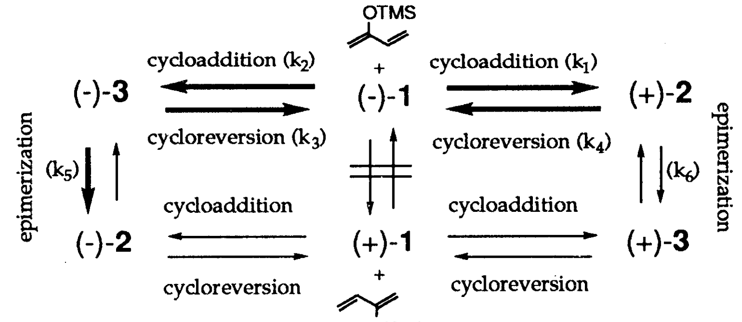


Chart 2

Accepting the above scheme, the face selectivity (k_1/k_2) of the diene to (-)-**1** in the photocycloaddition was estimated approximately as 2.5 (which is suggested by the early stage ratio of (+)-**2** *vs.* (-)-**3**), indicating that the β-face addition is more favorable than the α-face addition, the result being in distinct contrast to Diels-Alder cycloaddition[3] of the diene to the same substrate, where the α-face addition was exclusively observed under high pressure conditions. Thus, the major path of the photochemical step may be explained by assuming that (-)-**1** reacts to the diene by taking the COOEt equatorial conformation (A), where the aromatic ring is appreciably twisted from the average plane toward the α-face (dihedral angle of C1-C10b-C10a-C10 is *ca.* -31°), giving steric hindrance for approaching the diene from α-face (Chart 3). Although (-)-**1** takes the COOEt axial conformation (B) (in which the corresponding dihedral angle is *ca.* +23°) at the ground state (X-ray analysis),[3] the calculated steric energy differ-

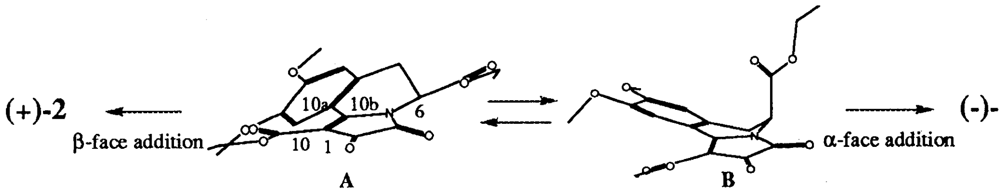
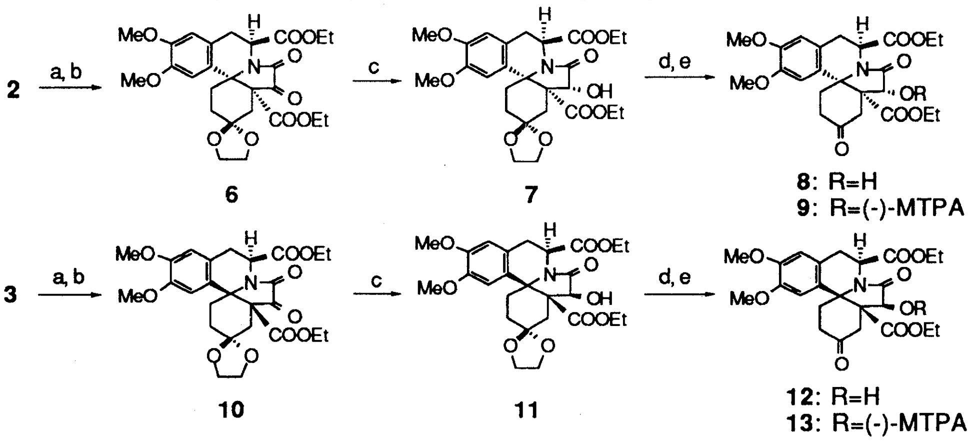


Chart 3

ence between A and B is small (0.6 kcal/mol).[12] Preferentially the reaction from A gives (+)-**2** and that from B gives (-)-**3** with a ratio of 2.5:1.

Photoadducts (+)-**2** and (-)-**3** were converted into synthetic intermediates of *Erythrina* alkaloids without loss of their ee. A solution of (+)-**2** of 20% ee in toluene was heated under reflux at 120°C for 2 h and the crude pyrolysate was treated with ethylene glycol in CH_2Cl_2 catalyzed by BF_3•Et_2O at room temperature to give the ketal **6**[13] (71% from **2**). Reduction of **6** with $NaBH_4$ in ethanol gave the alcohol **7**[13] (100%), which afforded the ketone **8**[13] (70%) by deacetalization. Similarly, (-)-**3** of >99% ee was converted into the acetal **10**[13] (86% from **3**), the alcohol **11**[13] (84%), and then the ketone **12**[13] (95%). Erythrinans **8** and **12** were identical with the authentic samples obtained by an intramolecular cyclization method[8] in the spectral data and TLC behavior except for optical rotations. The derived Mosher's esters (**9** and **13**) were of 20% and >99% de, respectively. Thus the present synthesis provides a new method to synthesize *Erythrina* alkaloids in optically active forms.



a. toluene, 120°C, 2h, b. $(CH_2OH)_2$-BF_3•Et_2O/CH_2Cl_2, rt, 20h, c. $NaBH_4$/EtOH, rt, d. 5%HCl, e. (-)-MTPACl-DMAP/Py, rt

Chart 4

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4) **2**: mp 107-108°C, $[\alpha]_D^{22}$ -2.2° (c=0.45, $CHCl_3$), IR (KBr): 1769, 1727. ^{1}H-NMR: δ 0.04 (9H, s, $SiMe_3$), 0.71, 1.27 (each 3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.29, 3.40 (each 1H, d, J=13 Hz, H-2), 3.0-3.2 (2H, m, H-7), 3.78, 3.84 (each 3H, s, OMe), 3.77, 4.14 (each 2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.1-5.5 (3H, m, H-6, $C=CH_2$), 5.87 (1H, dd, J=9, 18 Hz, -CH=C), 6.60 (2H, s, ArH). **3**: mp 116-118°C, $[\alpha]_D^{22}$ -27.4° (c=0.44, $CHCl_3$), IR (KBr): 1773, 1754, 1725. ^{1}H-NMR: δ 0.07 (9H, s, $SiMe_3$), 1.08, 1.14 (each 3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.25, 3.32 (each 1H, d, J=13 Hz, H-2), 2.86 (1H, dd, J=7, 15 Hz, H-7), 3.22 (1H, dd, J=2, 15 Hz, H-7), 3.79, 3.86 (each 3H, s, OMe), 4.10 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 4.13 (2H, dq, J=2, 7 Hz, $COOC\underline{H}_2CH_3$), 4.84 (1H, dd, J=2, 7 Hz, H-6), 4.9-5.6 (3H, m, $CH=CH_2$), 6.67, 6.70 (each 1H, s, ArH).

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6) Signs of (-) and (+) represent those at 375 nm, since their $[\alpha]_D$ values are very small.

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9) a) mp 111-112 °C, $[\alpha]_D$ -6.3° (c=1.1, $CHCl_3$), CD (c=0.04, MeOH) $[\theta]^{25}$ (nm): +4300 (378) (positive maximum), -1200 (320) (negative maximum); b) No Cotton effect; c) CD (c=0.05, MeOH) $[\theta]^{25}$ (nm): +4800 (378), -1400 (320).

10) In these cases, **3** was not recovered from the reaction mixture, though its presence was suggested by an HPLC analysis.

11) a) CD (c=0.1, MeOH) $[\theta]^{25}$ (nm): -1000 (375) (negative maximum), -1100 (365) (negative maximum); b) CD (c=0.1, MeOH) $[\theta]^{25}$ (nm): -2000 (375), -2100 (365).

12) The least steric energies for A and B calculated by Chem 3D program (Quality =1) were 50.6 and 50.0 kcal/mol, respectively.

13) **6**: gum, $[\alpha]_D^{22}$ +1.6° (c=0.6, $CHCl_3$). **7**: gum, $[\alpha]_D^{22}$ +0.7° (c=1.0, $CHCl_3$). **8**: mp 211-213°C, $[\alpha]_D^{22}$ -0.7° (c=1.0, $CHCl_3$). **10**: mp 238-240°C, $[\alpha]_D^{22}$ -72.5° (c=1.0, $CHCl_3$). **11**: gum, $[\alpha]_D^{22}$ -69.4° (c=1.0, $CHCl_3$). **12**: gum, $[\alpha]_D^{22}$ -31.7° (c=1.0, $CHCl_3$).

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