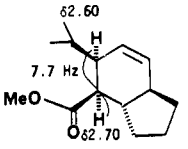
and that the benzylic methylene at C-1′, which upon irradiation caused sharpening of H-3 and H-4, was coupled to an olefinic proton at δ 5.72 (H-2′). This olefinic proton also is coupled to H-3′ (δ 5.36, $J$ = 15 Hz), thus defining trans geometry. The $^1$H NMR decoupling data readily extend the structure to C-8′, which forms a *cis*-olefin with C-7′ ($J$ = 9.8 Hz). H-8′ shows no further coupling.

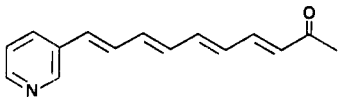
Change of solvent from $C_6D_6$ to $CD_2Cl_2$, while obscuring the lowfield region, clarified the remaining upfield $^1$H NMR signals. The multiplet at δ 2.65 (H-6′) is coupled by 6.2 Hz to a doublet of doublets at δ 2.75 (H-14′). This chemical shift suggests that C-14′ bears the acetyl group. H-14′ is further coupled to a multiplet at δ 1.54 (H-13′) by 11.0 Hz. This proton (H-13′) is further coupled to $^1$H signals at δ 1.15 ($J$ = 6 Hz) and 0.93 ($J$ = 9 Hz) assigned to $CH_2$-12′ and also to a signal at δ 2.0 ($J$ = 10 Hz) assigned to H-9′. Chemical shifts and coupling constants define the six-membered ring of the hydrindene system and the relative stereochemistry of the four chiral carbons: the three protons at C-14′, C-13′, and C-9′ must be axial, while the 6.2-Hz coupling between H-6′ and H-14′ indicates a cis relationship and hence an equatorial H-6′.[8] Synthetic analogue **2** supports this assignment.[9] Absence of coupling




**2**

between H-9′ and H-8′ is necessitated by a dihedral angle of 90° as seen in a Dreiding model of **1**. Three remaining methylene groups at C-10′, C-11′, and C-12′ give rise to complex and overlapping multiplets (Table I) but uniquely encompass the five-membered ring.

Pulo'upone has no close analogue among natural or synthetic products. Aside from nicotine and related alkaloids, simple substituted pyridines other than the common coal tar substituents are rare in nature. The closest structural relative of pulo'upone (**1**) is navenone A (**3**), the




**3**

major constituent of the alarm pheromone of *Navanax inermis*, a related cephalaspidean mollusk.[10,11] Because of the small quantity of pulo'upone available to us, we could not evaluate its biological activity in an ecological or anthropocentric context. Interestingly, 2-alkylpyridines of various chain lengths have been evaluated as antibacterials.[12]

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(8) We thank one of the referees for this suggestion.
(9) Roush, W. R.; Gillis, H. G.; Ko. A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269–2283.
(10) Sleeper, H. L.; Fenical, W. *J. Am. Chem. Soc.* **1977**, *99*, 2367–2368.
(11) Sleeper, H. L.; Paul, V. J.; Fenical, W. *J. Chem. Ecol.* **1980**, *6*, 57–70.
(12) Birchenough, M. J. *J. Chem. Soc.* **1951**, 1263–1266.

## Application of Kinetic, Asymmetric Selection to the Breaking of Molecular Symmetry

*Summary:* Reaction of the chiral glyoxylate **1** with 1 equiv of diene **2** in dichloromethane at −78 °C in the presence of a stoichiometric amount of stannic chloride afforded the ene adduct **3** in 74% chemical yield after chromatographic purification. The combination of the face selectivity of the glyoxylate with that of the bicyclo[3.3.0]octadiene provided for selection between the enantiotopically related rings of **2** and effected a selective breaking of molecular symmetry.

*Sir:* In recent articles[1,2] Bertz has drawn attention to disadvantages attending the presence of symmetrically related but remote functionality within a synthetic intermediate. While his conclusions are valid in general, such molecular properties in fact can be turned to advantage when the symmetry element present is a mirror plane. In this case, the symmetrically disposed portions of the molecule are actually enantiotopic rather than identical and thus, in theory, can be differentiated by reagents capable of chiral recognition. The application of such selectivity not only has the advantage that the reaction is controlled to only one site but also, and as a direct consequence, that it results in the creation of new elements of chirality with induction of asymmetry. While the utility of enzymes for the differentiation of enantiotopically related functionality has already been realized,[3] we know of no example of the application of the recently developed and powerful methods for asymmetric induction such as the Sharpless oxidation[4] to such selection.

In 1982 we reported[5] on the reactions of 8-phenylmenthol glyoxylate (**1**) for the induction of asymmetry through both Grignard addition to and ene reactions of the aldehyde functionality. Subsequently, we discovered that this same reagent is capable of effecting kinetic resolution of selected alkenes and wish to illustrate this feature here as it applies to the selective breaking of molecular symmetry in diene **2**. Note that the two double bonds are enantiotopically related by reflection through the mirror plane of symmetry present in **2** and that the bridgehead atoms are thus prochiral (Figure 1). Reaction of the glyoxylate **1** with 1 equiv of diene **2** in dichloromethane at −78 °C in the presence of a stoichiometric amount of stannic chloride afforded the ene adduct **3** in 74% chemical yield after chromatographic purification. The $^{13}$C NMR

(1) Bertz, S. H. *Tetrahedron Lett.* **1983**, *24*, 5577.
(2) Bertz, S. H. *J. Chem. Soc., Chem. Commun.* **1984**, 218.
(3) For a recent example using pig liver esterase and a compilation of other enzymatic applications, see: Francis, C. J.; Jones, J. B. *J. Chem. Soc., Chem. Commun.* **1984**, 579.
(4) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.
(5) Whitesell, J. K.; Bhattacharya, A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 988. Whitesell, J. K.; Bhattacharya, A.; Aguilar, D. A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 989.

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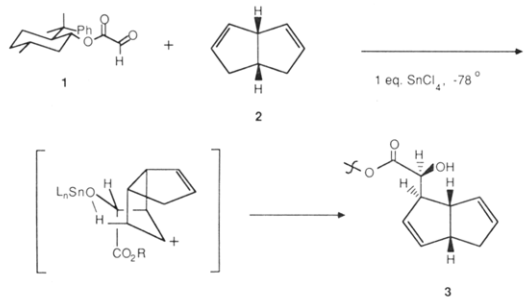


Figure 1.

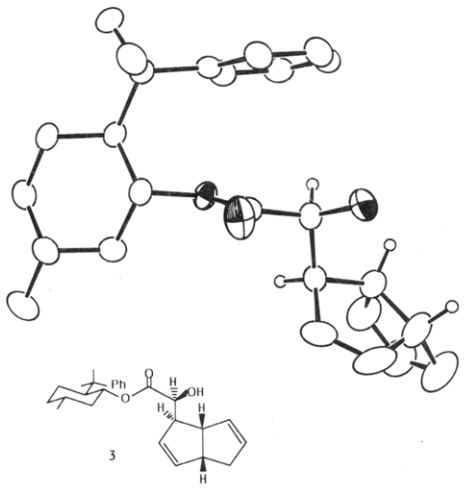


Figure 2.

spectra of the product both before and after purification were consistent with the presence of only one diastereomer.[6] The relative and absolute stereochemical relationships were determined by a single-crystal, X-ray analysis (Figure 2).[7] In accord with our previous observations of high levels of asymmetric induction with **1**, the reaction occurred on only one face of the aldehyde and, in addition, had been limited to the exo face of the bicyclo[3.3.0]octadiene. In addition, only one of the two enantiotopically related rings of diene **2** underwent reaction, the result of the combination of the two face selectivities operating in concert on the transition state.[8]

To our knowledge this is the first practical example of a nonenzymatic reaction that shows selective breaking of molecular symmetry. We anticipate that this concept will find application in the synthesis of a range of natural products and ourselves are pursuing its use in the synthesis of iridoid terpenes.

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(6) The $^{13}C$ spectrum of the crude reaction product showed the largest impurity peaks to be less than 5% of those for **3**.

(7) We have accumulated a large body of experimental observations for the ene reactions of glyoxylate **1** which is consistent with a two-step mechanism where the stereochemical outcome is controlled in the second or a proton-transfer step leading from an intermediate carbocation to product.

(8) We are grateful to Dr. Steven Larsen of the University of Texas at Austin for this analysis. Full details will appear in the near future in a complete accounting of our research involving asymmetric induction in the ene reactions of **1**.

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## Synthesis of Dichlorocyclobuta[*b*]benzofuran-2a-carboxylic Derivatives and 3-(Trichlorovinyl)coumarin through the Cross Photocycloadduct of Coumarin and Tetrachloroethylene

*Summary:* Treatment of the cross photocycloadduct of coumarin and tetrachloroethylene with nucleophiles gives dichlorocyclobuta[*b*]benzofuran-2a-carboxylic derivatives in excellent yields via lactone-opening, cyclobutene formation and intramolecular $S_N2'$ displacement or affords 3-(trichlorovinyl)coumarin in a high yield via cyclobutene formation followed by [2 + 2] cycloreversion.

*Sir:* Photochemical cyclobutanation of a heterocyclic ring system often brings about highly enhanced reactivity in the heterocyclic ring as observed in the reaction of coumarin dimers and their derivatives.[1] Our continuing studies on this subject have led us to examine a cross photocycloaddition of coumarin and tetrachloroethylene to prepare 1,1,2,2-tetrachloro-1$\alpha$,2$\alpha$,2a$\alpha$,8b$\alpha$-tetrahydro-3*H*-cyclobuta[*c*]chromen-3-one (**1**), with an expectation that cyclobutane-fused pyrone compounds would undergo some attractive reactions such as ring-expansion or rearrangement.[2]

In this communication we wish to report the reaction of **1** with nucleophiles, resulting in a ring contraction to 1,2-dichloro-2a$\alpha$,7b$\alpha$-dihydrocyclobuta[*b*]benzofuran-2a-carboxylic derivatives (**4**) or in a cycloreversion via cyclobutene formation to give 3-(trichlorovinyl)coumarin (**7**).

The typical procedure for the preparation of the cross photocycloadduct is as follows: 14.54 g (0.10 mol) of coumarin and 3.14 g (0.017 mol) of benzophenone were dissolved in a mixture of tetrachloroethylene (633.6 g, 3.82 mol) and benzene (36.0 g). The solution was irradiated with 500-W high-pressure mercury lamp through Pyrex filter for 28.5 h. After concentration of the reaction mixture under reduced pressure, silica gel column chromatographic separation gave 9.52 g (30.5%) of **1**.[3]

Treatment of **1** with butylamine or alkali smoothly gave two compounds in a ratio depending on the basicity and/or the amount of the nucleophile used, but neither of them was the simple lactone-opened derivative (**2a,b**). By spectroscopic analysis the compounds were revealed to be **3**[4] and 4.[5] The result means that dehydrochlorination causing cyclobutene formation took place immediately after lactone-opening reaction of **1**. The formation of **4** proceeds through the ring closure of **3** via intramolecular $S_N2'$ displacement by the attack of the phenoxy anion on the $sp^2$ carbon in the cyclobutene ring. This ring-closure step was more influenced by the basicity of the nucleophile than the cyclobutene formation step (runs 2–8, Table I).

(1) (a) Yonezawa, N.; Hasegawa, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 367. (b) Hasegawa, M.; Saigo, K.; Katsuki, H.; Yonezawa, N.; Kanoe, T. *J. Polym. Sci., Polym. Chem. Ed.* **1983**, *21*, 2345. (c) Saigo, K.; Yonezawa, N.; Sekimoto, K.; Hasegawa, M.; Ueno, K.; Nakanishi, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1000. (d) Yonezawa, N.; Yoshida, T.; Hasegawa, M. *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1083.

(2) (a) Hanifin, J. W.; Cohen, E. *J. Org. Chem.* **1968**, *33*, 2811. (b) Hanifin, J. W.; Cohen, E. *J. Org. Chem.* **1971**, *36*, 910. (c) Haywood, D. J.; Hunt, R. G.; Potter, C. J.; Reid, S. T. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2458. (d) Shimo, T.; Somekawa, K.; Kuwakino, S.; Tsuge, O.; Kanemasa, S. *Chem. Lett.* **1984**, 1503.

(3) **1**: mp 144–145 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 4.22 (d, 1 H, $J$ = 10 Hz), 4.59 (d, 1 H, $J$ = 10 Hz), 7.07–7.43 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 50.7 (d), 50.8 (d), 89.8 (s), 93.9 (s), 114.3 (s), 117.5 (d), 125.2 (d), 129.5 (s), 131.0 (d), 151.6 (s), 158.9 (s); IR (KBr) $\nu$ 1770, 930, 820, 805, 775, 745, 700 $cm^{-1}$. Anal. Calcd for $C_{11}H_6Cl_4O_2$: C, 42.35; H, 1.93; Cl, 45.46. Found: C, 42.23; H, 2.06; Cl, 45.04. On the basis of $^1H$ NMR spectrum of the reaction mixture, it was confirmed that 42% of coumarin converted to **1**, 13% to anti head-to-head coumarin dimer, and trace amount (less than 0.5%) to syn head-to-head and anti head-to-tail coumarin dimers. No other products could be detected.

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