Figure 2.

in order to allow time for the coordinative interactions between the aldehyde and TiCl$_4$ to be completely established at this low temperature. After adding allylsilane over the course of 30 min and stirring for 20 min, the reaction was then quenched with water.[9]

From the above experiments, it was shown that the quantitiy of TiCl$_4$ added is clearly an important factor in controlling the reaction course. The reaction selectivity versus the quantity of TiCl$_4$ added produced a unique curve, as shown in Figure 1A. Undoubtedly, maximum anti selectivity was observed with values near 1.0 equiv. of TiCl$_4$, but the range of effective concentrations of TiCl$_4$ over which the anti isomer dominated was very limited. The anti selectivity decreased as the quantity of TiCl$_4$ was decreased from 1.0 molar equiv, and the syn isomer was, surprisingly, ultimately favored over the anti by a ratio of 8:1 with 0.5 equiv of TiCl$_4$. On the other hand, the anti selectivity rapidly decreased as the quantity of TiCl$_4$ was increased over 1.0 equiv.

We interpret this trend in terms of *two differently derived species* (aldehyde–TiCl$_4$, 1:1 and 2:1 complexes), which could proceed to the respective transition states. The existence of substrate–Lewis acid 2:1 complexes has been previously reported[10] in solid and/or solution states. Thus, the selectivity found with 0.5 equiv of TiCl$_4$ could be described as arising from reaction via the 2:1 complex. On the other hand, the anti selectivity observed with 1.0 equiv is consistent with β-chelation, a characteristic of aldehydes with β-alkoxy groups; in such cases, β-chelation

is more effective than α-chelation (Figure 2A). The disturbance of β-chelation, with excess TiCl$_4$ over 1.0 equiv, resulted in lower anti selectivity.

In the case of *N*-Cbz-prolinal **3**, it is extremely interesting to note that high syn selectivity[11] (28:1) was obtained in the reaction with 0.5 equiv of TiCl$_4$, but not with 1.0 equiv, as shown in Figure 1B. This selectivity apparently arises from a transition state via the aldehyde–TiCl$_4$ 2:1 complex and is consistent with the result with serinal **1**. The complete lack of selectivity with 1.0 equiv is undoubtedly attributable to the difficulty in achieving α-chelation, which must intervene between the aldehyde carbonyl and *N*-Cbz groups.

In contrast, the reaction of *acyclic N*-Cbz-valinal **5** using 1.0 equiv of TiCl$_4$ resulted in high syn selectivity, which tends to substantiate the validity of an ordinary α-chelation mechanism, via a 1:1 complex, as shown in Figure 2B. The α-chelation in such an acyclic system is stable enough to withstand the presence of excess TiCl$_4$, as shown in Figure 1C. From this point of view, the absence of α-chelation in serinal and prolinal systems may be traceable to a common structure which contains the α-cyclic moiety. A similar syn selectivity, in a 5:1 ratio, was observed in the case of *N*-Cbz-phenylalaninal, as expected.

The diastereofacial selectivity is obviously achieved via conformations demanding entirely different steric factors, in the case where α-chelation is hindered by the inherent structural characteristics of the aldehydes (**1** and **3**) in the Lewis acid mediated reactions. We accordingly invoke the role of an aldehyde–TiCl$_4$ 2:1 complex, in order to explain the high syn stereoselectivity unexpectedly observed at 0.5 molar equiv of TiCl$_4$. It could be envisioned that the diastereoface may be *amphiphilically*[12] distinguished by the second aldehyde coordinated to the TiCl$_4$, as shown in Figure 2C. Further studies on diastereoselectivity as it pertains to the quantity of Lewis acid used, on representative acyclic aldehydes, are in progress and will be reported in due course.

(9) After acidic workup, the crude allylated materials consisted of deprotected product and five- and six-membered acetonides; treatment with 10% HCl–THF gave a mixture of *syn*-**2** and *anti*-**2**.

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(12) Amphiphilic effect: The second coordinated aldehyde in the 2:1 complex may fulfill the role of a bulky aluminum reagent such as "MAD" to achieve the moderate anti-Cram selectivity: Maruoka, K.; Itoh, T.; Sukurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588. LePage, T. J.; Wiberg, K. B. *Ibid.* **1988**, *110*, 6642.

Construction of Fused-Ring Skeletons Based on Photochemical Rearrangements of Bicyclo[3.2.1]oct-6-en-2-ones and Application to a Total Synthesis of (±)-Δ$^{9(12)}$-Capnellene

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Summary: A method for preparation of bicyclo[3.3.0]-oct-7-en-2-ones has been developed on the basis of the photochemical [1,3]-acyl migration of 8,8-disubstituted bicyclo[3.2.1]oct-6-en-2-ones and applied to a total synthesis of (±)-Δ$^{9(12)}$-capnellene, a linear triquinane.

Sir: Photochemical behavior of β,γ-unsaturated ketones has been investigated extensively.[1] From a synthetic point

Table I. Photochemical Transformation of Bicyclo[3.2.1]oct-6-en-2-ones

entry	ketone	W	X	Y	Z	conditions[a]	products (yield, %)	recov, %
1	8a	H	Bn	H	Me	A	10 (99)	
2	8a	H	Bn	H	Me	B	7a (32), 9a (18), 10 (+)[b]	
3	8a	H	Bn	H	Me	C	7a (38), 9a (21)	
4	8a	H	Bn	H	Me	D		99
5	8b	H	Ph	H	Me	B	9b (60)	16
6	8c	H	Ph	Me	H	B	9c (48)	18
7	8d	Me	Bu	H	Me	E	7d (60)	9
8	8d	Me	Bu	H	Me	C	7d (53)	20
9	8e	Me	Bu	H	H	E	7e (50), 12 (5)	20
10	8e	Me	Bu	H	H	B	7e (65), 12 (+)[b]	20

[a] Reactions were carried out under following conditions: A, irradiation of an ether solution ($<5 \times 10^{-3}$ M) through a Pyrex filter by a high-pressure Hg lamp (100 W); B, irradiation of an acetone solution under similar conditions with A; C, a sensitized reaction with 1-indanone (3 equiv) using a Xenon short arc lamp (500 W) and a UV-35 filter; D, a sensitized reaction with benzophenone (10 equiv) using the same equipment as C; E, irradiation of a benzene solution under similar conditions with A. [b] Less than 2% (by NMR).

Scheme I[a]
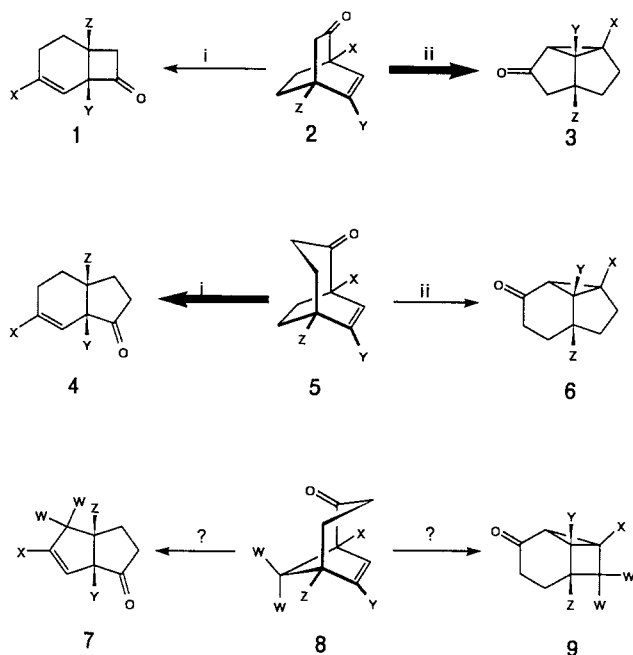
[a](i) Direct irradiation through Pyrex; (ii) triplet sensitization.

of view, the [1,3]-acyl shift and the oxadi-π-methane rearrangement ([1,2]-acyl shift) of the unsaturated system are useful methods for skeletal transformation. Scheme I shows such photochemical conversion of typical bridged bicyclic β,γ-unsaturated carbonyl systems into fused polycyclic ketones. Among them, the [1,2]-acyl shift of bicyclo[2.2.2]oct-5-en-2-ones (2) to give tricyclo[3.3.0.0^{2,8}]-octan-3-ones (3)[2] and the [1,3]-acyl shift of bicyclo-[3.2.2]non-6-en-2-ones (5) into bicyclo[4.3.0]non-4-en-7-ones (4)[3] are known as practical methods. We report herein skeletal transformations of bicyclo[3.2.1]oct-6-en-

2-ones (8)[4] that can be controlled by selection of their substituents (vide infra).

Quantitative conversion of the ketone 8a into the cyclopentadiene (10) has been observed under the conditions of direct excitation (run 1 in Table I). This outcome indicates that the hydrogen transfer of the diradical intermediate 11 proceeds quite effectively.
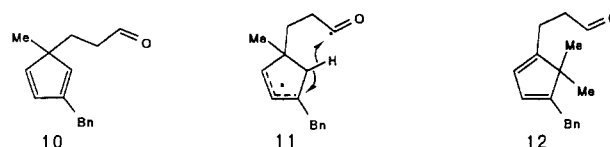
Reactions of 8a under sensitization conditions (runs 2 and 3) gave both the [1,3]- and [1,2]-acyl migration products 7a and 9a. When benzophenone was used as the sensitizer (run 4), the bridged bicyclic ketone 8a was recovered completely. Since the difference between the energy of triplet state of 1-indanone (75 kcal/mol)[6] and that of benzophenone (69.2 kcal/mol)[6] is small, variation of the sensitizer seemed to be an ineffective method for the product control. Therefore, we attempted to select the reaction course by changing the substituents of 8.

The [1,2]-acyl migration products 9b and 9c were derived effectively from the bridgehead phenyl derivatives (8b and 8c, respectively) by irradiation in acetone (runs 5 and 6). Thus, introduction of an aromatic substituent is the way to prepare the [6-4] fused ring system selectively.

To avoid formation of the cyclopentadiene, we prepared the ketone 8d having no hydrogens at the C-5 and -8 positions. In fact, only the [1,3]-acyl shift product 7d was obtained from 8d by irradiation through Pyrex (run 7). To our surprise, the sensitized reaction of 8d gave again only 7d (run 8). Direct irradiation of the substrate 8e, having a hydrogen at the C-5 position, gave the [5-5] fused ring ketone 7e and a small amount of the cyclopentadiene 12, which should be formed via the hydrogen shift of the intermediate diradical 13 (run 9). Formation of 12 was diminished by using acetone as the solvent (run 10). Thus, the necessity is the C-8 substituents for the photochemical preparation of the [5-5] fused ring system 7 from the

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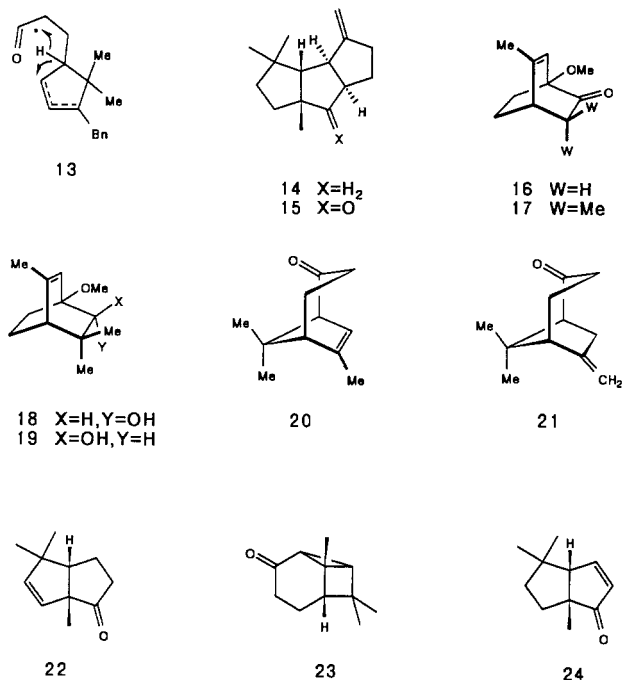
bicyclo[3.2.1]oct-6-en-2-ones (8).

The latter transformation has been applied to a total synthesis of (±)-$\Delta^{9(12)}$-capnellene (14).[7,8] Treatment of 16 with t-BuOK, MeI in THF followed by reduction with

LiAlH$_4$ gave a ca. 1:1 mixture of the *exo*- and *endo*-alcohols (18 and 19, respectively) in 80% overall yield. Pinacol-type rearrangement[9] of 18 proceeded by heating under reflux with TsOH (1 equiv) in benzene for 2 h to give a 5:1 mixture of the desired ketone 20 and the exocyclic olefin 21 in 95% yield. The isomeric alcohol 19 was recycled to 17 by Collins oxidation in 97% yield, because of inertness to the conditions for the rearrangement.

A photochemical reaction of 20 by irradiation in acetone gave the [5–5] fused ring ketone 22 and the [1,2]-acyl migration product 23 in 51% and 13% yields, respectively, when the reaction was stopped at 81% of conversion. This outcome indicates that, in the case of runs 8 and 10, steric crowding within the substrates due to the substituents is a factor that diminishes formation of the [1,2]-acyl migration products.

Catalytic hydrogenation of 22 followed by treatment with t-BuOK and ClCOOCH$_2$CH=CH$_2$, and then with Pd(OCOMe)$_2$ in MeCN[10] gave the ketone 24, in 52% overall yield, from which (±)-14 had already been derived.[8h]   An alternative route to 14 is the sequential treatment of 24 with (1) the copper reagent, LiCu(C(= CH$_2$)CH$_2$CH$_2$OSiMe$_2$-t-Bu)$_2$,[11] (2) acetic acid in aqueous THF, (3) TsCl and NEt$_3$ in CH$_2$Cl$_2$, (4) LiN(SiMe$_3$)$_2$ in THF (to give the triquinane 15 in 86% overall yield from 24), (5) LiAlH$_4$ in ether, (6) NaH, imidazole, CS$_2$, and then MeI, and (7) (n-Bu)$_3$SnH and AIBN in toluene (to give the hydrocarbon 14 in 26% overall yield from 15). The spectral data of 14, thus obtained, was identical with those of (±)-$\Delta^{9(12)}$-capnellene.[8e]

Supplementary Material Available: Experimental procedure for the preparation of 8a and spectral properties for 7a,d,e, 8a–e, 9a–c, 10, 12, 15, 17–20, 22, and 23 (7 pages). Ordering information is given on any current masthead page.

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Enantioselective Construction of a Quaternary Asymmetric Carbon Center: A Versatile Synthesis of α-Alkyl α-Amino Acids

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Summary: The enantioselective construction of a quaternary asymmetric carbon center was developed through reaction of the dianions derived from the chiral half esters of monosubstituted malonic acids with 2 molar equiv of LDA and alkyl halides. Alkylation in the reverse sequence preferentially gave the same diastereoisomer. The alkylated half esters were transformed into α-alkyl α-amino acids.

Sir: The enantioselective transformation of prochiral malonic acids into unsymmetrical molecules would be one of the preferred methods for providing versatile chiral

building blocks[1] for the synthesis of optically and biologically active compounds. While this type of asymmetric synthesis is common in enzymatic conversions,[2] examples of its use in chemical transformation are rare.[3]   Previously

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