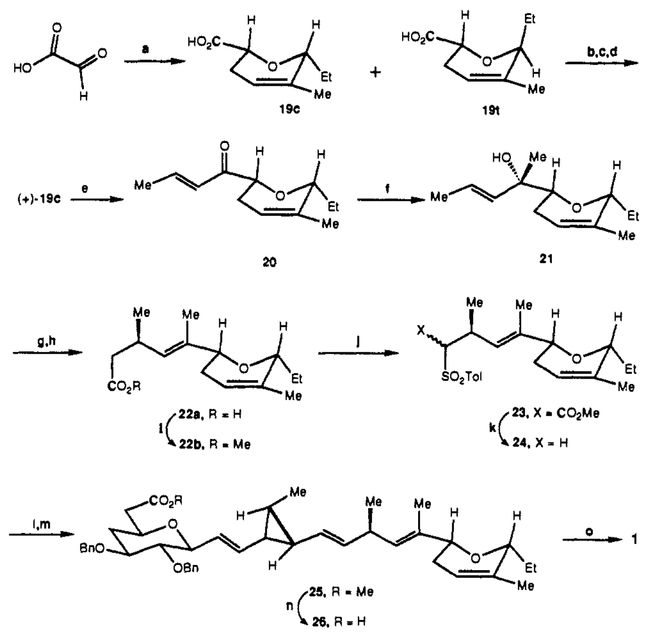
Scheme III[a]



[a] (a) 3-Methyl-1,3-hexadiene, hydroquinone (cat.), $CHCl_3$, sealed tube, 120 °C, 12 h, 81%; (b) 2,4′-dibromoacetophenone, KF, DMF, room temperature, 3 h, then 100 °C, 30 min, 53%; (c) Zn, AcOH (glacial), room temperature, 8 h, 90%; (d) (+)-α-methylbenzylamine, $MeOH/Et_2O$, crystallization, 32%; (e) $(COCl)_2$, DMF (cat.), CH_2Cl_2, 0 °C → room temperature, 2 h, then *trans*-propenyltrimethyltin, $PhCH_2PdCl(PPh_3)_2$ (cat.), HMPA, 70 °C, 3 h, 90%; (f) MeMgBr, THF, 0 °C, 2 h, 92%; (g) Ac_2O, DMAP, Et_3N, CH_2Cl_2, room temperature, 72 h, 72%; (h) LDA, THF, -78 °C, then TBSCl, THF/HMPA, -78 → 60 °C, 1.5 h, then H_3O^+, 61%; (i) CH_2N_2, Et_2O, room temperature, 92%; (j) LDA, THF, -78 °C, then PTSF, THF, -78 °C → room temperature, 24 h, 43%; (k) $(Me)_4N^{+-}OAc$, HMPA, 100 °C, 17 h, 71%; (l) nBuLi, Et_2O/hexane, 0 °C → -42 °C, then **18**, -42 °C, 2 h, 51%; (m) Na(Hg) 6%, MeOH/THF (1:1), -35 °C, 3.5 h, 63%; (n) LiOH, THF/H_2O (3:1), room temperature, 18 h, (o) Li, liquid NH_3/EtOH (5:1), -78 °C, 30 min, 63% from **25**.

apparently complete diastereoselection giving diester **12** (configuration of **12** established by hydrolysis to diacid **3b**, or reduction to diol **3a**). Selective hydrolysis of **12** led ultimately to the acetylene **15**, which on hydroalumination to **16** and condensation with **11** gave 49% of the desired alkenyl β-*C*-glycoside **17**.[13] Detritylation and Dess–Martin oxidation[14] gave **18** in 10 steps and 24% yield from ester **12**.

The C_{14} right half was prepared (Scheme III) by starting with thermal Diels–Alder addition of (*E*)-3-methyl-1,3-hexadiene[15] with glyoxylic acid, producing a 4:1 ratio of **19c**/**19t**.[16] Resolution with (+)-$PhCH(CH_3)NH_2$ gave the requisite (+)-**19c**, $[\alpha]^{21}_D$ = +169.4° (*c* 0.85, EtOH), >98% ee.[17] Its acid chloride gave (*E*)-enone **20**, which underwent chelated Cram MeMgBr addition to yield **21**, converted by Ireland–Claisen rearrangement of its acetate to acids with **22a** predominating by a 12:1 ratio.[7a] Ester **22b** reacted with $p\text{-}MeC_6H_4SO_2F$[18] to yield **23**, which on decarbomethoxylation[19] produced **24** (cf. **4C**) in seven steps (10%) from (+)-**19c**.

Julia condensation of sulfone **24** with aldehyde **18** gave 13-(*E*)-tetraene **25**, accompanied by 8% of the 13(*Z*) isomer. Tetraene **25** was saponified, and careful Birch debenzylation[20] produced the diol acid **1** (63% yield from **25**), identical by 300-MHz ^1H NMR, TLC, and $[\alpha]_D$ with natural **1**. Reaction of synthetic **1** with CH_2N_2 gave ambruticin methyl ester, identical in all respects, including FD-MS, with authentic **1** methyl ester. Thus natural (+)-ambruticin has been prepared for the first time in a convergent synthesis from glyoxylic acid (15 steps in the longest sequence).[21]

Supplementary Material Available: Physical, spectral, and analytical data for compounds **6**, **8**, **9**, **11–15**, **17–21**, **22b**, **24**, **25**, synthetic **1**, natural **1**, and their methyl esters (11 pages). Ordering information is given on any current masthead page.

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(12) Misumi, A.; Iwanaga, K.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 3343. See also: Furuta, K.; Iwanaga, K.; Yamamoto, H. *Org. Synth.* **1989**, *67*, 76. Our diester **12** was homogeneous by ^1H and ^{13}C NMR, indicating a single diastereomer.

(13) Cf.: Posner, G. H.; Haines, S. R. *Tetrahedron Lett.* **1985**, *26*, 1823 and references therein.

(14) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.

(15) This diene was prepared by Wittig methylenation of commercially available (*E*)-2-methylpentenal.

(16) **19c** methyl ester showed ^{13}C NMR signals at δ 78.4 (C-2) and 72.4 (C-6); **19t** methyl ester at δ 76.5 (C-2) and 67.9 (C-6). Cf.: Eliel, E.; Manoharan, M.; Pietruszewicz, K. M.; Hargrave, K. D. *Org. Magn. Reson.* **1983**, *21*, 94. Also: Burke, S. D.; Armistead, D. M.; Schoenen, F. J.; Fevig, J. M. *Tetrahedron* **1986**, *42*, 2787.

(17) The amide from (+)-**19c** and (-)-α-phenylethylamine was homogeneous by GC and ^1H NMR. Acid (-)-**19c** of $[\alpha]^{21}_D$ = -142° (*c* 0.84, EtOH) was reacted with O_3, then H_2O_2/HCO_2H, and then CH_2N_2, to give (L)-dimethyl malate having $[\alpha]^{21}_D$ = -7.31° (*c* 1.92, EtOAc); cf.: Walden, P. *Ber. Dtsch. Chem. Ges.* **1905**, *38*, 386.

(18) Kende, A. S.; Mendoza, J. *J. Org. Chem.* **1990**, *55*, 1125.

(19) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 3435; **1980**, *102*, 4743.

(20) Cf.: Isobe, M.; Ichikawa, Y.; Goto, T. *Tetrahedron Lett.* **1986**, *27*, 963.

(21) We thank Dr. C. J. Wright (Eastman Kodak Research Laboratories) for FD mass spectra and Dr. J. Hodges (Warner Lambert/Parke-Davis Co.) for a sample of natural ambruticin. Partial support of this research by Grant CA-18846, awarded by the National Cancer Institute (NIH), is gratefully acknowledged.

Palladium-Catalyzed Reaction of Methyleneoxazolidinones. Intervention of a Palladium Complex of a Y-Shaped $CH_2C(NTs)CH_2$ Molecule as an Isostructure of Trimethylenemethane

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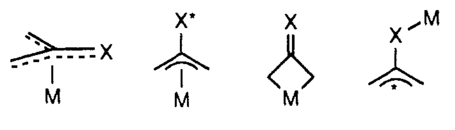
The metal complexes of fully unsaturated Y-shaped molecules, e.g., trimethylenemethane,[1] have been fascinating organic and organometallic chemists. The modes of the metal complexation can be **1a** (η^4), **1b** (η^3), **1c** (η^2), and **1d** (η^1) (see structures) with X representing CH_2 or hetero atoms (an asterisk stands for a radical or ion). The stable complexes of **1a** with X = CH_2[1a,b]



1a (η^4) **1b** (η^3) **1c** (η^2) **1d** (η^1)

and M = Fe, Cr, Mo, Ru, Os, and Ir, with X = O and M = Ru,[2] and with X = S and M = Fe,[3] of **1c** with X = O and M = Ru,[2] Pd,[4] Pt,[5] Os,[6] and Ir,[6] and of **1d** with X = O and M = Fe[7] have

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(1) (a) Deeming, A. J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 4, p 447. (b) Jones, M. D.; Kemmitt, R. D. W. *Adv. Organomet. Chem.* **1987**, *27*, 279. (c) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1. (d) Trost, B. M.; Miller, M. L. *J. Am. Chem. Soc.* **1988**, *110*, 3687 and references therein.

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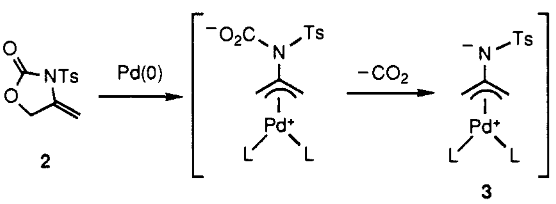
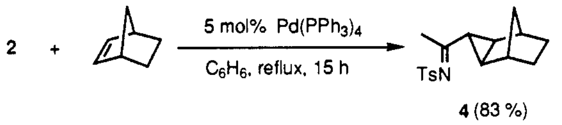
been isolated and structurally characterized, while nothing has been known for the metal complexes of azatrimethylenemethane (**1**; X = nitrogen group). In this paper we describe our approach to the palladium complexes of Y-shaped $CH_2C(NR)CH_2$ molecules. The approach, based on the palladium-mediated decarboxylation[8] of cyclic carbamates **2**[9] (eq 1), has resulted in our finding new catalytic reactions of the $CH_2C(NTs)CH_2$ moiety undergoing unique isomerization–cycloaddition with norbornenes and also [3 + 2 + 1] cyclocoupling with norbornene and CO.



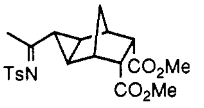
(1)

When 4-methylene-3-(*p*-tolylsulfonyl)oxazolidin-2-one (**2**) (2 mmol) was reacted with norbornene (4 mmol) in the presence of $Pd(PPh_3)_4$ (0.1 mmol) in benzene (5 mL) at reflux temperature for 15 h, *exo*-3-[1-(*N*-tosylimino)ethyl]tricyclo[3.2.1.0^{2,4}]octane (**4**)[10] [tosyl (Ts) = *p*-tolylsulfonyl] was obtained (83% yield), apparently as the result of isomerization at some stages (eq 2).

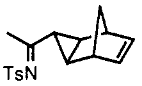


(2)

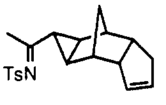
Similarly, the oxazolidinone **2** reacted with other norbornenes to give the corresponding cyclopropanation products in good yields; **5** (69%) from 5-norbornene-2,3-dicarboxylic acid dimethyl ester, **6** (75%) from norbornadiene, and **7** (88%) from dicyclopentadiene.



5 (69 %)



6 (75 %)



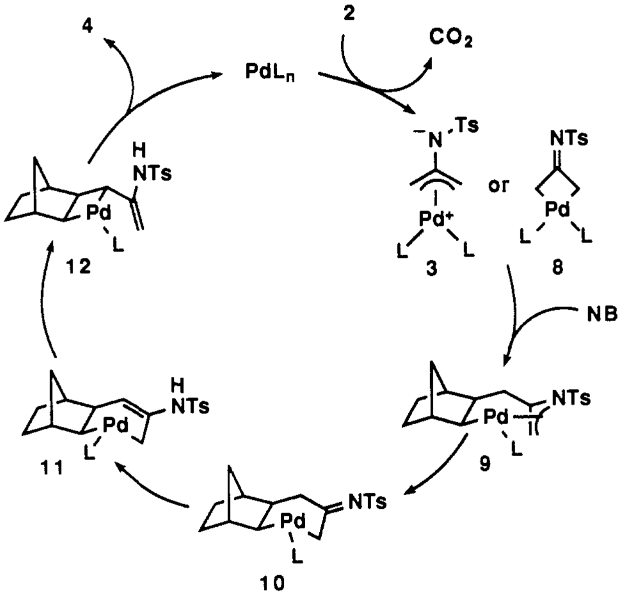
7 (88 %)

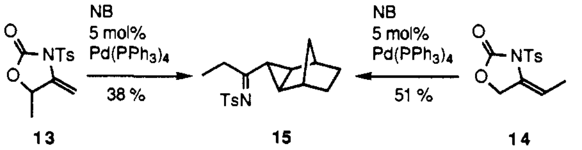
A similar reaction of **2** with styrene and methyl acrylate under the same reaction conditions gave no cycloaddition products. The use of $Pd(CO)(PPh_3)_3$ instead of $Pd(PPh_3)_4$ resulted in the formation of the cyclopropanation product **4** (85%) from **2**. Other transition-metal complexes such as $RhCl(PPh_3)_3$, $RuCl_2(PPh_3)_3$, $Mo(CO)_6$/dppe, and $Pt(PPh_3)_4$ were ineffective in this reaction. The use of a stoichiometric amount of $Ni(cod)_2/PPh_3$ (1:2) promoted the reaction of **2** with norbornene to produce **4** in 35% yield.

A presumed mechanism of the present isomerization–cycloaddition is postulated in Scheme I. Addition of the intermediate **3** (η^3-type) or **8** (η^2-type) to norbornene (NB) would give **9** and then (or directly) **10**. Proton shift giving **11** followed by the 1,3-Pd shift would afford **12**, from which reductive elimination should produce **4**, regenerating Pd(0). A proton shift similar to that from **10** to **12** has been proposed in the reaction of a presumed Pd–[$CH_2C(O)CH_2$] complex with norbornene to afford a cyclopropane derivative.[11]

The intervention of symmetrical intermediate(s) such as **3** and/or **8** is demonstrated by using oxazolidinones **13** and **14** having different substitution patterns (eq 3). The results given in eq 3 imply that a common Pd complex has been produced from both **13** and **14**.

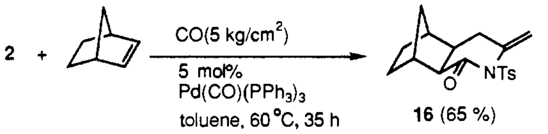
Scheme I





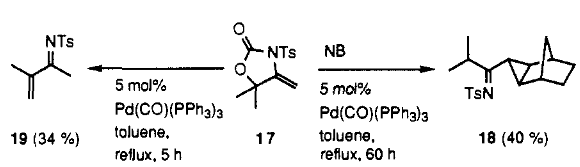
(3)

Intermediate **9** can be intercepted before undergoing isomerization. Namely, when **2** was reacted with norbornene and carbon monoxide (5 kg/cm^2) in the presence of $Pd(CO)(PPh_3)_3$ (5 mol %), [3 + 2 + 1] cyclocoupling took place to give lactam **16** in 65% yield (eq 4).



(4)

Oxazolidinone **17** underwent the isomerization–cycloaddition with norbornene to give **18**, but it afforded an α,β-unsaturated imine **19** catalytically in the absence of norbornene (eq 5). The formation of **19** is accounted for by assuming β-elimination of palladium hydride from a η^2-type palladium complex similar to **8** but with two methyl groups. Further efforts to elucidate the mechanism and to expand the scope of the reactions involving azatrimethylenemethane–metal complexes **1** are in progress.



(5)

Acknowledgment. This work is supported in part by grants from the Ministry of Education, Science, and Culture, Japan. Thanks are also due to the Analytical Center, Faculty of Engineering, Osaka University, for the use of JEOL GSX-400 and Bruker AM600 spectrometers.

Supplementary Material Available: Typical experimental procedures and spectral data for all compounds prepared (3 pages). Ordering information is given on any current masthead page.

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[7] Frey, M.; Jenny, T. A.; Stoeckli-Evans, H. *Organometallics* **1990**, *9*, 1806.

[8] The decarboxylation reaction of allyl carbamate in the presence of Rh, Ni, and Mo catalyst has been reported: Tsuji, J.; Minami, I.; Shimizu, I. *Chem. Lett.* **1984**, 1721.

[9] Preparation of cyclic *N*-tosylcarbamates: Ohe, K.; Ishihara, T.; Chatani, N.; Kawasaki, Y.; Murai, S. *J. Org. Chem.*, in press. See also: Kimura, M.; Kure, S.; Yoshida, Z.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett.* **1990**, *31*, 4887.

[10] The structures of all new compounds were thoroughly established. See supplementary material.

[11] (a) Trost, B. M.; Schneider, S. *J. Am. Chem. Soc.* **1989**, *111*, 4430. (b) Trost, B. M.; Urabe, H. *Tetrahedron Lett.* **1990**, *31*, 615.