product **6b**: mp 151–152 °C dec (lit.[2] mp 165–168 °C); ^{1}H NMR (DMSO-d_6) δ 8.04 (bs, 1 H), 6.49 (bs, 2 H), 4.30 (bs, 2 H), 2.38–2.52 (m, 4 H), 1.58–1.65 (m, 4 H); ^{13}C NMR (DMSO-d_6) δ 166.2, 157.0, 130.1, 116.4, 102.4, 25.6, 23.9, 22.7, 22.4; MS *m/z* 211 (9), 180 (100). Anal. Calcd for $C_9H_{13}N_3OS$: C, 51.2; H, 6.2. Found: C, 51.0; H, 6.1.

3-Hydroxy-4,5-cyclohexanopyrazolo[3,4-*c*]pyridazine (10b) and Its Hydrazinium Salt (9b). A. From Ethyl 2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (5b). A mixture of 1.43 g of **5b**,[26] 2 mL of 97% hydrazine, and 4 mL of abs ethanol was heated under reflux ($CaSO_4$ drying tube) for 12 days during which aliquots were removed for NMR analysis. The only peaks observed in the aromatic region of the ^{13}C spectrum were due to either the reactant or the product. A solid in the condenser was identified by MS as sublimed **5b** containing a small amount of sulfur. Removal of the solvent on a rotary evaporator left the hydrazonium salt **9b** (87% taking into account the removed aliquots): mp 227–231 °C dec; ^{1}H and ^{13}C NMR cf. Table I.

The salt **9b** was acidified with glacial acetic acid to give the pyrazolo[3,4-*c*]pyridazine **10b** (total yield 57% taking into account the removed aliquots): mp slowly decomposes above 200 °C; ^{1}H and ^{13}C NMR cf. Table I; MS *m/z* 190 (100), 189 (16), 175 (5), 134 (5), 119 (14), 118 (9). It was not possible to get a satisfactory analysis on this compound: HRMS *m/z* 190.0863, theory for $C_9H_{10}N_4O$ is 190.0856.

B. From Methyl 2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (5c). A mixture of 1.0 g of **5c**, 1.5 mL of 97% hydrazine, and 3 mL of methanol was heated under reflux ($CaSO_4$ drying tube), and aliquots were removed for ^{13}C NMR analysis over a period of 8 days. The presence of hydrazide **6b** was clearly evident in the aromatic region. Isolation as described above gave the pyridazine **10b** in 46% yield, taking into account the removed aliquots.

C. From 2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carbohydrazide (6b). A solution of 500 mg of the hydrazide **6b**, 1.5 mL of 97% hydrazine, and 3 mL of abs ethanol was heated under reflux ($CaSO_4$ drying tube) for 2 days. The solvents were removed on a rotary evaporator to give 500 mg (94%) of the pyrazolo[3,4-*c*]pyridazine hydrazonium salt **9b** with ^{1}H and ^{13}C spectra identical to the product of the reaction of the ethyl ester **5b** and hydrazine.

Acknowledgment. This research was supported by Grant P-152 from the Robert A. Welch Foundation and by the TCU Research Fund.

Registry No. **2a**, 22288-78-4; **2b**, 35212-85-2; **3a**, 137844-98-5; **3b**, 99027-29-9; **4a**, 137844-99-6; **4b**, 137845-00-2; **5a**, 4651-81-4; **5b**, 4506-71-2; **5c**, 108354-78-5; **6b**, 22721-28-4; **7a**, 137845-01-3; **7b**, 137845-02-4; **8**, 4974-47-4; **9a**, 137845-03-5; **9b**, 137845-05-7; **10a**, 2125-85-1; **10b**, 137845-04-6; acetophenone, 98-86-2; hydrazine, 302-01-2.

Construction of the Bicyclo[6.3.0]undecane Skeleton via Ring Opening of Tricyclo[6.3.0.0^{1,4}]undecan-5-ones

Kiyomi Kakiuchi,* Keisuke Fukunaga, Mamoru Jimbo, Bunji Yamaguchi, and Yoshito Tobe

Department of Applied Fine Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

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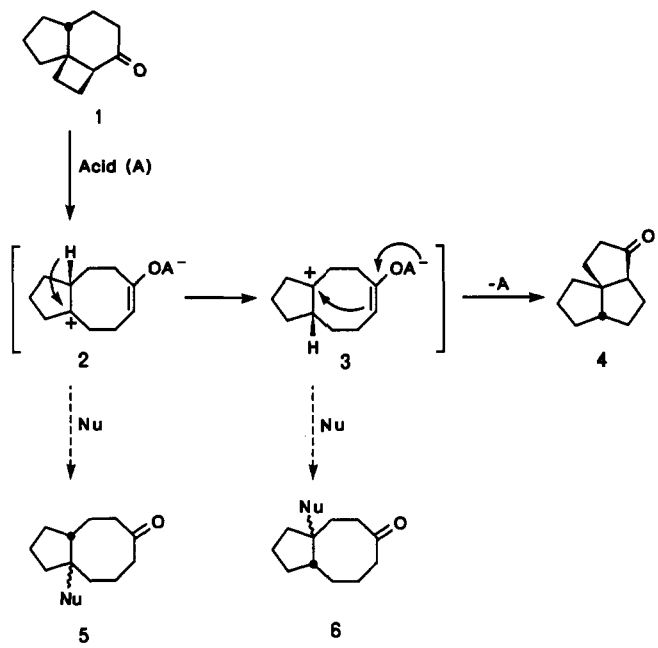
Considerable attention has been paid to the development of methodologies for the construction of 5-8 and 5-8-5 fused ring compounds because of the recent isolation and identification of many biologically active natural products containing these carbocyclic skeletons.[1] Recently we reported that tricyclo[6.3.0.0^{1,4}]undecan-2-one (**1**) rearranged under the action of acid catalysts through a new pathway to give the 5-5-5 angularly fused ketone, tricyclo[6.3.0.0^{1,5}]undecan-4-one (**4**).[2] This novel rearrangement has been applied to the total syntheses of some triquinane natural products[2,3] and to the construction of tetra- and spiroquinane skeletons.[4,5] We also proposed the mechanism shown in Scheme I in which the fission of the central cyclobutane bond takes place in the initial step to generate eight-membered-ring cation **2**. Subsequent 1,2-hydride shift and transannular cyclization of the cation **3** give **4**.[2] On the basis of this mechanism, we envisaged that if the cation intermediates **2** and **3** could be intercepted efficiently by a nucleophile (Nu) leading to bicyclo[6.3.0]undecane derivatives such as **5** and **6**, a new method for construction of the 5-8 fused ring system would be provided. From this viewpoint, we have investigated the reactions of **1** and its methyl derivatives **11** and **15** with a variety of acid (electrophile)–nucleophile combinations and found that the 5-8 fused compounds **7a,b**, **8a,b**, **12**, and **16** are obtained as dienol esters instead of the expected products like **5** and **6** arising from nucleophilic capture.

Scheme I



We first carried out reactions of **1** under the conditions which had been employed in the acid-catalyzed rearrangement of bicyclo[4.2.0]octanones[6] to intercept the respective cation intermediates. Starting ketone **1** was, however, recovered unchanged in reactions with 35% HCl in ether at 35 °C for 100 h and TsOH in acetic acid at 55 °C for 120 h. Treatment with 50% H_2SO_4 in THF at 55 °C gave a complex mixture of products after prolonged reaction time (120 h). Furthermore, with TMSOTf[7] in $CHCl_3$ at rt for 60 h, ketone **1** was recovered unchanged.

(1) For example, see: Feldman, K. S.; Come, J. H.; Kosmider, B. J.; Smith, P. M.; Rotella, D. P.; Wu, M.-J. *J. Org. Chem.* **1989**, *54*, 592 and references cited therein.

(2) Kakiuchi, K.; Ue, M.; Tsukahara, H.; Simizu, T.; Miyao, T.; Tobe, Y.; Odaira, Y.; Yasuda, M.; Shima, K. *J. Am. Chem. Soc.* **1989**, *111*, 3707.

(3) Ue, M.; Ohnishi, Y.; Kobiro, K.; Kakiuchi, K.; Tobe, Y.; Odaira Y. *Chem. Lett.* **1990**, 149.

(4) Kakiuchi, K.; Hirano, N.; Shimizu, T.; Suwa, M.; Kobiro, K.; Tobe, Y.; Odaira, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3039.

(5) Kakiuchi, K.; Ohnishi, Y.; Kobiro, K.; Tobe, Y.; Odaira, Y. *J. Org. Chem.* **1991**, *56*, 463.

(6) Kakiuchi, K.; Kumanoya, S.; Kobiro, K.; Tobe, Y.; Odaira, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3358 and references cited therein.

(7) It has been reported that this reagent was useful for the ring opening of cyclopropyl ketones, see: Demuth, M.; Mikhail, G. *Tetrahedron* **1983**, *39*, 991.

0022-3263/92/1957-1021$03.00/0

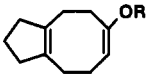
Table I. Ring-Opening Reactions of Ketone 1

entry	reagent (equiv)	solv	temp, °C	time, h	products, % yield[a] 4	7a,b	8a,b
1	TMSI (2)	CCl_4	0 to rt	18	26[b]		
2	BBr_3 (1.2)	CH_2Cl_2	-93	1	71[c]		
3	BF_3·OEt_2 (0.55) $Zn(OAc)_2$ (1.1)	Ac_2O	0	6	14	65	8[d]
4	BF_3·OEt_2 (0.55)	Ac_2O	0	0.5	9	11[b]	
5	BF_3·OEt_2 (0.1)	Ac_2O	-40	3	4	73	5[d]
6	$AlCl_3$ (0.55) $Zn(OAc)_2$ (1.1)	Ac_2O	0	6	16	60	9[d]
7	$SnCl_4$ (0.05)	Ac_2O	-50	5	9	76	1
8	CF_3SO_3H (0.05)	Ac_2O	-50	6	7	72	3[d]
9	BF_3·OEt_2 (0.1)	$(EtCO)_2O$	0	3	22	43	8[d]

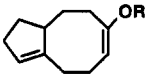
[a] All reactions were carried out using 100 mg of 1. Yields were based on consumed 1 after separation of products by flash chromatography (SiO_2). [b] Many peaks observed by GLC. [c] Some unidentified products were obtained. [d] Very small amount (~3%) of enol esters of 1 and 4 were also obtained.

The desired 5-8 fused products were not isolated in the reactions with TMSI[8] and BBr_3[9] which have been shown to be useful for the ring opening of nopinone derivatives (entries 1 and 2, Table I). It seems reasonable to consider from these results that under the conditions described above the cation intermediate **2** is not formed or elimination of acid (A) from an enol or enolate of **2** or **3** predominates over attack of nucleophiles, probably because the bond between the carbonyl oxygen and acid is relatively weak. Consequently we used the acetyl cation generated from acetic anhydride (Ac_2O) and acid as an electrophile according to the method reported recently by Yoshikoshi[10] and Rigby.[11] Reaction of **1** with BF_3·OEt_2 and $Zn(OAc)_2$ in Ac_2O gave the 5-8 fused dienol ester **7a** along with a small amount of its regioisomer **8a** and ketone **4** (entry 3).[12] In the absence of $Zn(OAc)_2$, similar treatment of **1** yielded a complex mixture of products containing **4** and **7a** in a ca. 1:1 ratio (entry 4). However, when the reaction was undertaken with a small amount of BF_3·OEt_2 at low temperature (-40 °C), the yield and selectivity of **7a** increased dramatically (entry 5), although it has been reported that $Zn(OAc)_2$ was essential to the ring opening of the nopinone derivatives.[10,13] At higher reaction temperature, the rearrangement to **4** competes with deprotonation from the cation intermediates **2** and/or **3**. Other acids such as $AlCl_3$, $SnCl_4$, and CF_3SO_3H were also effective in this case (entries 6–8). Reaction of **1** in propionic anhydride ($(EtCO)_2O$) instead of Ac_2O required a higher reaction temperature and gave the dienol esters **7b** and **8b** along with a considerable amount of **4** (entry 9). The difference in the product distributions between $(EtCO)_2O$ and Ac_2O is due to the larger steric hindrance and to less electrophilicity of the propanoyl cation derived from $(EtCO)_2O$ than those of the acetyl cation.

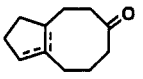
The bicyclo[6.3.0]undec-1(8)-ene structure of the dienol esters **7a,b** was established unambiguously by the identity of enone **9**, derived from **7a,b** by alkaline hydrolyses, with an authentic sample prepared independently according to the literature.[14] The position of the enolate double bond of **7a,b** was assigned as formulated since 12 allylic protons were observed in the ^1H NMR spectra. The structure of the minor product **8a** was tentatively assigned by 2D ^1H–^1H COSY spectroscopy. Since hydrolysis of **8b** gave the same enone **10** as that from **8a**, **8b** should have the angular double bond as the same position as that of **8a**. These enol esters were probably produced from cation intermediates **2** and/or **3** (A = $^+C(O)R$) by deprotonation. Thus, despite evidence that cations **2** and **3** could not be intercepted by a nucleophile as we assumed at the outset, the reaction afforded the desired 5-8 fused ring system with reasonable efficiency.



7a R=COMe
7b R=COEt

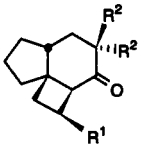


8a R=COMe
8b R=COEt

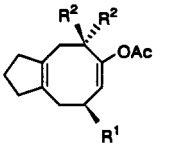


9 $\Delta^{1,8}$
10 $\Delta^{8,9}$

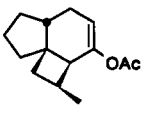
In order to explore the applicability of this reaction, we next examined the reactions of the ketones **11** and **15** having methyl groups under the similar conditions. Reaction of monomethyl-substituted ketone **11** with BF_3·OEt_2 and $Zn(OAc)_2$ in Ac_2O gave the 5-8 fused product **12** in only 18% yield; the enol ester **13** was obtained as the major product (63%) along with the angularly fused ketone **14** (6%). Reaction of α,α-dimethyl ketone **15**, in which the enolization of the substrate is less likely, with BF_3·OEt_2 in Ac_2O furnished dienol ester **16** and the angularly fused ketone **17** in 90% yield in a 1:1 ratio.



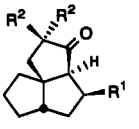
11 R^1=Me, R^2=H
15 R^1=H, R^2=Me



12 R^1=Me, R^2=H
16 R^1=H, R^2=Me



13



14 R^1=Me, R^2=H
17 R^1=H, R^2=Me

Experimental Section

Instruments for the measurement of spectra and the technique of chromatography were the same as were used in the previous work.[2] Reactions of **1** with 35% HCl–Et_2O,[6] TsOH–AcOH,[6] 50%

(8) Dieter, R. K.; Pounds, S. *J. Org. Chem.* **1982**, *47*, 3714.
(9) Boger, D. L.; Mullican, M. D.; Hellberg, M. R.; Patel, M. *J. Org. Chem.* **1985**, *50*, 1904.
(10) Kato, M.; Kamat, V. P.; Tooyama, Y.; Yoshikoshi, A. *J. Org. Chem.* **1989**, *54*, 1536.
(11) Rigby, J. H.; Senanayake, C. *J. Org. Chem.* **1988**, *53*, 440.
(12) Very small amount of a mixture of enol esters of **1** and **4** was also obtained. However enol esters of **5** and **6** (Nu = OAc) were not detected.
(13) Other additives such as NaOAc, KOAc, $Hg(OAc)_2$, LiCl, and AcOH were tried, but most of **1** was recovered.
(14) Fitjer, L.; Kanschik, A.; Majewski, M. *Tetrahedron Lett.* **1985**, *26*, 5277.

H_2SO_4–THF,[6] TMSOTf–$CHCl_3$,[7] TMSI–CCl_4,[8] and BBr_3–CH_2Cl_2[9] were carried out according to the literature.

Bicyclo[6.3.0]undeca-1(8),4- and -4,8-dien-4-yl Acetates (7a and 8a). To a stirred suspension of 1 (100 mg, 0.61 mmol) and $Zn(OAc)_2$ (123 mg, 0.67 mmol) in Ac_2O (2 mL) was added dropwise freshly distilled BF_3·OEt_2 (41 μL, 0.33 mmol) at 0 °C under N_2. The resulting mixture was stirred at 0 °C for 6 h, and ice–water was added. Stirring was continued for an additional 30 min at rt, and the mixture was extracted with ether. The combined extracts were washed with water, aqueous $NaHCO_3$ solution, and brine, successively, and dried ($MgSO_4$). Evaporation of the solvent followed by flash chromatography (elution with ether–petroleum ether, 7:93) of the crude product gave **7a** (78 mg, 65%), **8a** (10 mg, 8%), 4[2] (13 mg, 14%), and 1 (5 mg) along with a small amount (4 mg, 3%) of an inseparable mixture of enol acetates of 1 and 4, whose structures were established by alkaline hydrolyses to the parent ketones. Results using other acid–Ac_2O pairs are listed in Table I.

7a: IR (neat) 3000, 1750, 1680, 1365, 1225, 1180, 1075, 1050, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.30 (t, J = 7.3 Hz, 1 H), 2.51–2.29 (m, 12 H), 2.09 (s, 3 H), 1.80–1.70 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 169.98 (s), 149.78 (s), 133.64 (s), 133.31 (s), 116.56 (d), 39.64 (t, 2 C), 30.13 (t), 28.76 (t), 26.47 (t), 23.11 (t), 21.75 (t), 21.06 (q); MS m/e (rel intensity) 206 (M^+, 16), 164 (64), 146 (67), 94 (100), 93 (78), 79 (77), 43 (93); HRMS calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1304.

8a: IR (neat) 3030, 1750, 1680, 1365, 1225, 1200, 1110, 1075, 1055, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45 (br s, 1 H), 5.28 (dd, J = 8.3, 7.8 Hz, 1 H), 2.64–2.52 (m, 2 H), 2.42–2.24 (m, 5 H), 2.15–2.01 (m, 6 H, containing s at 2.10), 1.90 (ddd, J = 18.6, 9.3, 4.4 Hz, 1 H), 1.66–1.49 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 169.82 (s), 150.59 (s), 147.85 (s), 128.44 (d), 116.28 (d), 45.56 (d), 34.68 (t), 32.84 (t), 32.07 (t), 29.87 (t), 28.68 (t), 24.55 (t), 21.06 (q); MS m/e (rel intensity) 206 (M^+, 8), 163 (56), 106 (58), 94 (92), 93 (49), 79 (57), 43 (100); HRMS calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1301.

Bicyclo[6.3.0]undeca-1(8),4- and 4,8-dien-4-yl Propionates (7b and 8b). Reaction of 1 (100 mg, 0.61 mmol) with BF_3·OEt_2 (7.5 μL, 0.06 mmol) in $(EtCO)_2O$ (2 mL) at 0 °C for 3 h as described above gave **7b** (57 mg, 43%), **8b** (11 mg, 8%), and 4 (22 mg, 22%) along with a small amount (4 mg, 3%) of an inseparable mixture of enol propionates of 1 and 4, whose structures were established by alkaline hydrolyses to the parent ketones.

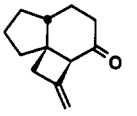
7b: IR (neat) 3000, 1750, 1680, 1350, 1260, 1220, 1185, 1075, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.28 (t, J = 7.3 Hz, 1 H), 2.51–2.28 (m, 14 H, containing q at 2.37, J = 7.8 Hz), 1.81–1.72 (m, 2 H), 1.16 (t, J = 7.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 173.87 (s), 149.77 (s), 133.63 (s), 133.34 (s), 117.91 (d), 39.67 (t), 39.64 (t), 30.16 (t), 28.82 (t), 27.67 (t), 26.47 (t), 23.11 (t), 21.76 (t), 9.10 (q); MS m/e (rel intensity) 220 (M^+, 11), 94 (45), 93 (47), 57 (100); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1458.

8b: IR (neat) 3020, 1750, 1680, 1340, 1250, 1210, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.47–5.44 (m, 1 H), 5.28 (t, J = 7.8 Hz, 1 H), 2.65–2.52 (m, 1 H), 2.43–2.25 (m, 7 H, containing q at 2.38, J = 7.3 Hz), 2.16–2.02 (m, 3 H), 1.95–1.85 (m, 1 H), 1.63–1.48 (m, 3 H), 1.16 (t, J = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 173.39 (s), 150.58 (s), 147.91 (s), 128.39 (d), 116.35 (d), 45.55 (d), 34.68 (t), 32.13 (t), 32.10 (t), 29.88 (t), 28.74 (t), 27.62 (t), 24.60 (t), 9.10 (q); MS m/e (rel intensity) 220 (M^+, 6), 163 (48), 94 (45), 57 (100); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1458.

Bicyclo[6.3.0]undec-1(8)-en-4-one (9).[14] A mixture of **7a** (120 mg, 0.58 mmol) and K_2CO_3 (120 mg, 0.87 mmol) in methanol (2 mL) was stirred at 0 °C for 2 h. Water was added, and the mixture was extracted with ether. The combined extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent followed by flash chromatography (elution with ether–petroleum ether, 10:90) of the crude product gave **9** (76 mg, 72%) whose IR and ^{13}C NMR spectra are identical with a sample prepared according to Fitjer's method.[14] Reaction of **7b** (9 mg, 0.04 mmol) with K_2CO_3 as described above gave **9** (7 mg, quant).

Bicyclo[6.3.0]undec-8-en-4-one (10). Reactions of **8a** (55 mg, 0.27 mmol) and **8b** (6 mg, 0.04 mmol) with K_2CO_3 as described above gave **10** (37 mg, 84% and 4 mg, 89%, respectively): IR (neat) 3020, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.41 (br s, 1 H), 2.81 (br s, 1 H), 2.62 (td, J = 11.5, 3.3 Hz, 1 H), 2.25–2.17 (m, 7 H), 2.08–1.75 (m, 5 H), 1.71–1.61 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 216.10 (s), 144.70 (s), 130.51 (d), 47.17 (d), 40.98 (t), 39.67 (t), 31.70 (t), 30.56 (t), 28.32 (t), 27.92 (t), 26.79 (t); MS m/e (rel intensity) 164 (M^+, 53), 106 (100), 64 (70), 91 (80), 79 (76); HRMS calcd for $C_{11}H_{16}O$ 164.1201, found 164.1212.

(1*S,3*S**,4*S**,8*R**)-3-Methyltricyclo[6.3.0.0^{1,4}]undecan-5-one (11).** A mixture of 3-methylenetricyclo[6.3.0.0^{1,4}]undecan-5-one (18)[2] (600 mg, 3.37 mmol) and 10% palladized carbon (100 mg) in AcOEt (40 mL) was stirred overnight at rt under 1 atm of H_2. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography (elution with ether–petroleum ether, 5:95) of the crude product gave **11** (393 mg) and a mixture of **11** and its epimer **19** (150 mg, 72:28). Analytical sample of **19** was obtained as a mixture of 9:1 by preparative GLC. The stereochemistry of the methyl group was assigned by ^1H NMR spectra in the presence of the shift reagent Eu(DPM)$_3$; the methyl protons of **11** exhibit greater shifts than those of **19**.



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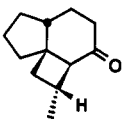


19

11: IR (neat) 1700, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.77–2.67 (m, 2 H), 2.43–2.34 (m, 1 H), 2.26–2.10 (m, 2 H), 2.01–1.83 (m, 3 H), 1.78–1.73 (m, 2 H), 1.64–1.47 (m, 4 H), 1.39–1.28 (m, 1 H), 1.02 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.68 (s), 52.50 (d), 45.92 (s), 44.07 (d), 41.68 (t), 40.89 (t), 39.78 (t), 30.81 (t), 28.14 (d), 27.07 (t), 23.62 (t), 18.45 (q); MS m/e (rel intensity) 178 (M^+, 6), 137 (71), 108 (100), 94 (48), 79 (26), 69 (32); HRMS calcd for $C_{12}H_{18}O$ 178.1357, found 178.1337.

19: IR (neat) 1700, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.52–2.38 (m, 3 H), 2.28 (dddd, J = 6.6, 5.4, 5.4, 1.5 Hz, 1 H), 2.14–2.01 (m, 2 H), 1.98–1.86 (m, 2 H), 1.72–1.46 (m, 6 H), 1.41–1.31 (m, 1 H), 1.13 (d, J = 5.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 213.6 (s), 57.30 (d), 47.94 (s), 42.96 (d), 41.34 (t), 39.15 (t), 37.37 (t), 29.86 (t), 28.24 (t), 22.99 (t), 21.30 (d), 18.45 (q); MS m/e (rel intensity) 178 (M^+, 30), 136 (46), 108 (100), 94 (49); HRMS calcd for $C_{12}H_{18}O$ 178.1357, found 178.1350.

6-Methylbicyclo[6.3.0]undeca-1(8),4-dien-4-yl Acetate (12), (1*S,3*S**,4*S**,8*R**)-3-Methyltricyclo[6.3.0.0^{1,4}]undec-5-en-5-yl Acetate (13), and (1*R**,5*S**,6*S**,8*S**)-6-Methyltricyclo[6.3.0.0^{1,5}]undecan-4-one (14).** Reaction of 11 (100 mg, 0.56 mmol) with BF_3·OEt_2 (35 μL, 0.31 mmol) and $Zn(OAc)_2$ (113 mg, 0.62 mmol) in Ac_2O (2 mL) at 0 °C to rt for 24 h as described above gave **12** (15 mg, 18%), **13** (52 mg, 63%), **14** (4 mg, 6%), the enol acetate of **14** (7 mg, 6%), and **11** (33 mg). The structures of **13** and the enol acetate of **14** were established by alkaline hydrolysis to **11** and **14**, respectively. Reaction of **11** (55 mg, 0.31 mmol) with $AlCl_3$ (82 mg, 0.62 mmol) in CH_2Cl_2 (3 mL) was done according to the procedure described previously[2] to give **14** (37 mg, 67%).

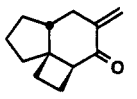
12: IR (neat) 3000, 1750, 1680, 1365, 1220, 1150, 1105, 1075, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.04 (dd, J = 7.3, 1.1 Hz, 1 H), 3.11–2.98 (m, 1 H), 2.79–2.68 (m, 1 H), 2.61 (dt, J = 16.9, 4.4 Hz, 1 H), 2.49–2.20 (m, 6 H), 2.14–2.04 (m, 5 H, containing s at 2.08), 1.80–1.70 (m, 2 H), 1.04 (d, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.91 (s), 148.22 (s), 133.71 (s), 133.39 (s), 123.09 (d), 40.20 (t), 39.60 (t), 37.71 (t), 30.10 (t), 29.08 (d), 26.72 (t), 22.79 (q), 21.87 (t), 21.10 (q); MS m/e (rel intensity) 220 (M^+, 6), 160 (77), 94 (60), 93 (65), 84 (61), 69 (100), 43 (59); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1435.

13: IR (neat) 3000, 1750, 1680, 1360, 1220, 1160, 1110, 1085, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.46 (dd, J = 5.5, 2.6 Hz, 1 H), 2.67–2.57 (m, 1 H), 2.51 (m, 1 H), 2.35 (m, 1 H), 2.18–2.11 (m, 2 H), 2.08 (s, 3 H), 1.97–1.87 (m, 2 H), 1.71–1.34 (m, 6 H), 0.96 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.29 (s), 148.47 (s), 112.78 (d), 45.37 (s), 42.26 (d), 39.09 (d), 39.00 (t), 35.01 (t), 29.11 (d), 28.98 (t), 25.42 (t), 21.32 (q), 20.68 (t), 17.52 (q); MS m/e (rel intensity) 220 (M^+, 2), 136 (100); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1486.

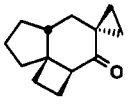
14: IR (neat) 1730, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46–2.33 (m, 1 H), 2.29 (ddt, J = 17.6, 7.8, 2.0 Hz, 1 H), 2.25–2.13 (m, 2 H), 2.07–1.96 (m, 3 H), 1.86 (td, J = 12.2, 8.3 Hz, 1 H), 1.79–1.52 (m, 5 H), 1.39 (td, J = 12.2, 8.3 Hz, 1 H), 1.34–1.22 (m, 1 H), 1.07

(d, J = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 221.65 (s), 62.82 (d), 59.40 (s), 51.46 (d), 43.00 (t), 41.39 (t), 41.27 (t), 38.62 (d), 35.80 (t), 35.36 (t), 27.06 (t), 15.45 (q); MS m/e (rel intensity) 178 (M^+, 47), 109 (77), 96 (100); HRMS calcd for $C_{12}H_{18}O$ 178.1357, found 178.1375.

(1*S,4*S**,8*R**)-5,5-Dimethyltricyclo[6.3.0.0^{1,4}]undecan-5-one (15).** Cyclopropanation of 6-methylenetricyclo[6.3.0.0^{1,4}]-undecan-5-one (**20**)[15] (1.62 g, 9.20 mmol) using Me_3SOI and NaH–DMSO was carried out according to the procedure of Corey[16] to give cyclopropyl ketone **21** (1.18 g, 68%) after flash chromatography (elution with ether–petroleum ether, 5:95): IR (neat) 3050, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.81 (dd, J = 8.5, 7.0 Hz, 1 H), 2.6–1.1 (m, 15 H), 0.9–0.5 (m, 2 H).



20



21

A mixture of **21** (188 mg, 0.99 mmol) and platinum(IV) oxide (150 mg, 0.66 mmol) in acetic acid (7 mL) was stirred at rt for 3 h under 1 atm of H_2. The mixture was filtered through a pad of Celite, and the filtrate was concentrated to give the crude product containing **15** and overreduced alcohols. To a stirred solution of pyridine (1.39 mL, 17.3 mmol) in CH_2Cl_2 (10 mL) was added chromium(VI) oxide (866 mg, 8.66 mmol) at rt. The mixture was stirred for 20 min, and then a solution of the above product in CH_2Cl_2 (5 mL) was added in one portion at rt. The mixture was stirred for additional 1 h, and the solution was decanted from the residue, which was washed with ether. The combined organic solutions were washed twice with 10% NaOH, 10% HCl, aqueous $NaHCO_3$, and brine, successively, and dried ($MgSO_4$). Evaporation of the solvent followed by flash chromatography (elution with ether–petroleum ether, 5:95) of the crude product gave **15** (152 mg, 80% from **21**).

15: IR (neat) 1700, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.77 (dd, J = 9.3, 4.9 Hz, 1 H), 2.32–2.14 (m, 2 H), 2.07–1.91 (m, 2 H), 1.89–1.65 (m, 5 H), 1.58–1.43 (m, 4 H), 1.21 (s, 3 H), 1.06 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 220.58 (s), 51.68 (s), 47.80 (d), 44.80 (t), 43.42 (s), 40.04 (d), 39.20 (t), 35.30 (t), 31.55 (t), 27.41 (q), 25.40 (q), 24.01 (t), 21.82 (t); MS m/e (rel intensity) 192 (M^+, 12), 108 (100); HRMS calcd for $C_{13}H_{20}O$ 192.1514, found 192.1511.

3,3-Dimethylbicyclo[6.3.0]undeca-1(8),4-dien-4-yl Acetate (16) and (1*R,5*S**,8*S**)-3,3-Dimethyltricyclo[6.3.0.0^{1,5}]undecan-4-one (17).** Reaction of **15** (45 mg, 0.23 mmol) with BF_3·OEt_2 (5.8 μL, 0.046 mmol) in Ac_2O (1 mL) at 0 °C for 19 h as described above gave **16** (20 mg, 45%), **17** (16 mg, 45%), and **15** (8 mg). Reaction of **15** (50 mg, 0.26 mmol) with $AlCl_3$ (69 mg, 0.52 mmol) in CH_2Cl_2 (2.5 mL) was done according to the procedure described previously[2] to give **17** (43 mg, 86%).

16: IR (neat) 3000, 1750, 1660, 1355, 1210, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.22 (t, J = 9.5 Hz, 1 H), 2.55–2.47 (m, 4 H), 2.44–2.37 (m, 2 H), 2.29–2.19 (m, 4 H), 2.12 (s, 3 H), 1.79–1.69 (m, 2 H), 1.08 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 169.91 (s), 154.79 (s), 134.79 (s), 131.50 (s), 116.67 (d), 42.45 (t), 41.75 (s), 39.52 (t), 39.15 (t), 31.07 (t), 28.09 (q, 2 C), 22.16 (t), 21.92 (t), 21.12 (q); MS m/e (rel intensity) 234 (M^+, 6), 98 (100); HRMS calcd for $C_{15}H_{22}O_2$ 234.1619, found 234.1642.

17: IR (neat) 1730, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (t, J = 6.4 Hz, 1 H), 2.22–2.12 (m, 1 H), 1.98–1.78 (m, 6 H), 1.76–1.52 (m, 4 H), 1.48–1.40 (m, 1 H), 1.34–1.25 (m, 1 H), 1.10 (s, 3 H), 1.05 (s, 3 H): ^{13}C NMR ($CDCl_3$) δ 225.80 (s), 60.18 (d), 55.49 (s), 53.25 (d), 50.95 (t), 47.50 (s), 43.12 (t), 33.36 (t), 33.30 (t), 29.56 (t), 26.96 (t), 26.54 (q), 24.63 (q); MS m/e (rel intensity) 192 (M^+, 47), 135 (100), 80 (53); HRMS calcd for $C_{13}H_{20}O$ 192.1514, found 192.1532.

Acknowledgment. Thanks are due to the Instrumental Analysis Center, Faculty of Engineering, Osaka University, for assistance in obtaining NMR and mass spectra on JEOL JNM-GTX-400 and Bruker AM-600, and JEOL JMS-DX303 spectrometers, respectively.

Registry No. **1**, 136780-97-7; **4**, 92590-09-5; **7a**, 137946-48-6; **7b**, 137946-49-7; **8a**, 137946-50-0; **8b**, 137946-51-1; **9**, 102794-91-2; **10**, 137946-52-2; **11**, 137946-53-3; **12**, 137946-54-4; **13**, 137946-55-5; **14**, 137946-56-6; **14** enol acetate, 137946-61-3; **15**, 137946-57-7; **16**, 137946-58-8; **17**, 91854-72-7; **18**, 138124-75-1; **19**, 138124-76-2; **20**, 138124-77-3; **21**, 137946-59-9; $Zn(OAc)_2$, 557-34-6; Bf_3·OEt_2, 109-63-7; $(EtCO)_2O$, 123-62-6; BBr_3, 10294-33-4; $AlCl_3$, 7446-70-0; $SnCl_4$, 7646-78-8; CF_3SO_3H, 1493-13-6.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **7a,b**, **8a,b**, and **10–17** and 2D ^1H–^1H COSY spectrum of **8a** (25 pages). Ordering information is given on any current masthead page.

(15) Ue, M.; Tsukahara, H.; Kobiro, K.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Tetrahedron Lett.* **1987**, *28*, 3979.
(16) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1313.

Higher Order Zinc Cuprate Reagents. Very High 1,3-Chirality Transfer Reaction of γ-(Mesyloxy)-α,β-unsaturated Carbonyl Derivatives

Yoshinori Yamamoto,*,† Yukiyasu Chounan,† Miwa Tanaka,† and Toshiro Ibuka‡

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan, and Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan

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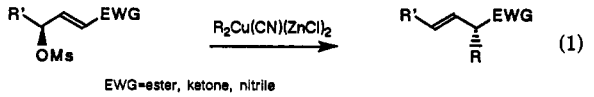
We previously reported that chiral γ-(mesyloxy)-α,β-unsaturated esters undergo, 1,3-chirality transfer to form chiral α-alkyl-β,γ-unsaturated esters with high optical purity using organocopper–BF_3 reagents.[1] The use of BF_3 was essential in this highly efficient chirality transfer reaction. However, in some cases, this strong Lewis acid caused undesired side reactions and prevented the use of acid-labile functional groups. Development of milder reagents with wide applicability is highly desirable.

We wish to report that higher order zinc cuprates $R_2Cu(CN)(ZnCl)_2$, prepared from CuCN and 2 equiv of RZnCl, react with γ-(mesyloxy)-α,β-unsaturated esters, ketones, and nitriles in an anti-S_N2' manner without the assistance of BF_3·OEt_2 to give the corresponding 1,3-chirality transfer product with very high de in essentially quantitative yield (eq 1). The method for the preparation



EWG=ester, ketone, nitrile (1)

of higher order zinc cuprates is shown in eq 2. A THF

$$RLi + ZnCl_2 \xrightarrow[-78 \rightarrow 0\ °C]{THF} RZnCl + LiCl \qquad (2)$$

$$2(RZnCl + LiCl) + CuCN \xrightarrow[-78 \rightarrow 0\ °C]{THF} R_2Cu(CN)(ZnCl)_2 + 2LiCl$$

solution of alkylzinc chloride and LiCl, prepared from RLi and $ZnCl_2$, was added to a THF slurry of 0.5 equiv of CuCN. Needless to say, "higher order" does not mean that the copper species possesses the structure $R_2Cu(CN)(ZnCl)_2$, but indicates that the stoichiometry of R, Cu, CN, and ZnCl is 2:1:1:2.[2] Previously, "lower order" zinc cuprates have been prepared by the reaction of CuCN·2LiX

† Tohoku University.
‡ Kyoto University.

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