October, 1994] © *1994 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, **67**, *2891—2893(1994)* 2891

# Synthesis of 9-Oxa-5-azatricyclo[4.3.0.0$^{3,7}$]nonan-4-ones from 4,4,5-Trihydroxy-2-oxabicyclo[3.2.0]heptane-*exo*-6-carbonitriles by Their Ring Transformation

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**Synopsis.** The hydrolysis of [2+2]cycloadducts **4** or their hydrates **5**, which were obtained from the regioselective photoreactions of 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone (**1**) with cyanoethylenes, afforded the tittle γ-lactams **7** via an interesting ring transformation.

Although photochemical [2+2]cycloaddition reactions of 3(2*H*)-furanones with olefins, which give an oxabicyclo[3.2.0]heptanone ring system, have been reported,[1)] little attention has been paid to the ring-transformation reaction, except for the derivations of dioxabicyclo[3.3.0]octanone[2)] and oxabicyclo[4.3.0]-nonanones.[3)] Since the [2+2]cycloadducts of 4-hydroxy-3(2*H*)-furanone **1** should have a hydroxyl group on the cyclobutane ring, a ring transformation of the strained cyclobutane may be expected.

The present paper describes the synthesis of tricyclic γ-lactams by the ring-transformation reaction of the [2+2]cycloadducts between **1** and cyanoethylenes **2**.

A solution of **1** and acrylonitrile (**2a**), methacrylonitrile (**2b**), or 2-chloroacrylonitrile (**2c**) in acetonitrile was irradiated with a 400 W high-pressure mercury lamp to give [2+2]cycloadducts **3** and/or hydrates **5**; the yields of the products were as follows: **5a** (22%), **3b** (41%) and **5b** (15%), and **3c** (44%) and **5c** (6%), respectively (Scheme 1). Products **3** were assigned as stereoselective [2+2]cycloadducts, 5-hydroxy-4-oxo-2-oxabicyclo[3.2.0]heptane-*endo*-6-carbonitriles, and **5** were assigned as hydrates of the [2+2]cycloadducts **4**, 4,4,5-trihydroxy-2-oxabicyclo[3.2.0]heptane-*exo*-6-carbonitriles on the basis of spectral data. For instance, **3b** showed a strong carbonyl absorption at 1800 cm$^{-1}$ in the IR spectrum (**1**: 1620 cm$^{-1}$). On the other hand, **5b** showed no carbonyl absorption, though hydroxyl absorption appeared at 3380 and 3345 cm$^{-1}$. The regio- and stereochemistry of **3b** and **5b** were confirmed by noting the magnitude of the NOE for two methyl protons (1-Me, 6-Me) with unequivalent methylene protons. The stereochemistry of **5c** (*exo*-CN) was deduced from the mechanism affording tricyclic γ-lactam **7c** by the hydrolysis of **5c**. The properties of [2+2]-cycloadducts **3** and **4** to water were as follows: Compounds **3** were converted into **6** in refluxing water, and were more stable than **4**. Heating of the hydrates **5** at 150 °C gave **4** quantitatively, which were easily converted into **5** by exposing to air.

There is much interest in the reactivity of a strained cyclobutane ring having a hydroxyl group to give a ring-opening product under both basic and acidic conditions.

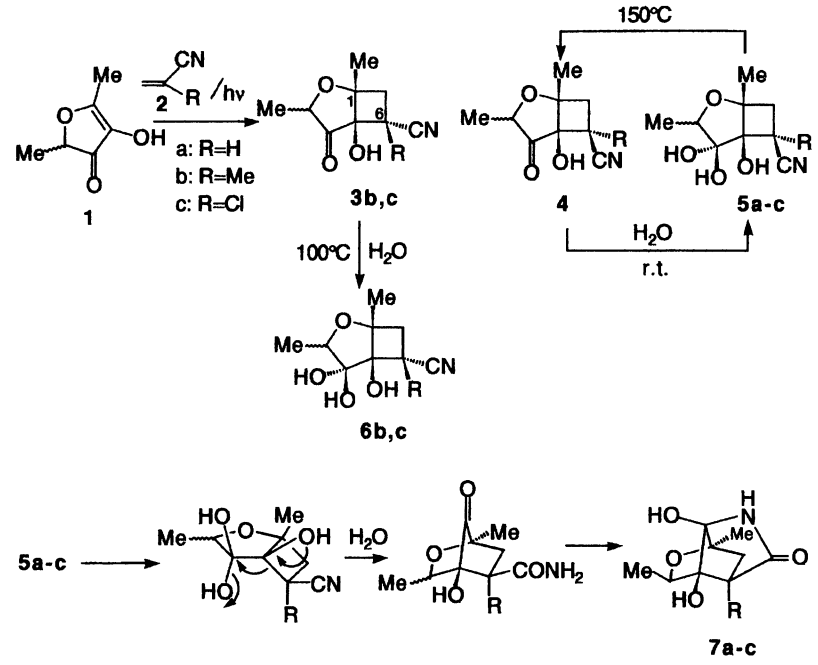
The hydrolysis of the hydrate **5a** with a 1% sodium hydroxide solution at room temperature for 2 h afforded a tricyclic γ-lactam **7a**. Similar treatments of mixtures of **3b** and **4b** (3 : 2 ratio) as well as **3c** and **4c** (7 : 2 ratio) gave **7b** and **7c**, respectively, together with a quantitative recovery of **3b** and **3c** (Table 1). The structure of **7b** was determined by an X-ray crystallographic analysis as being 6,7-dihydroxy-1,3,8-trimethyl-9-oxa-5-azatricyclo[4.3.0.0$^{3,7}$]nonan-4-one (Fig. 1). The structures of **7a** and **7c** were deduced based on a spectral analogy with **7b**. Since compounds **3b** and **3c** (both *endo*-CN) remained unchanged with a base, and **4a**—**c** (*exo*-CN) were easily converted into hydrates **5a**—**c**, the formation of the tricyclic γ-lactams **7** could be explained by a mechanism involving hydrolysis and a ring-transformation reaction from **5** (Scheme 1). In addition, the same γ-lactams were obtained from the hydrolysis of **4** in silica gel (Table 1).

## Experimental

All of the melting points are uncorrected. The $^{1}$H and $^{13}$C NMR spectra were measured with a JEOL JNM-GSX 400 spectrometer in $CDCl_3$ or DMSO-$d_6$. The IR spectra were recorded with a JASCO A-3 spectrometer, and the mass spectra were obtained with a JMS-OISG instrument at 70 eV. Photoirradiation was carried out in a Pyrex tube by using a Riko 400 W high-pressure mercury lamp.

**Photoreactions of 1 with 2a—c.** A solution of **1** (5.00 g, 39.0 mmol) and **2a** (20.6 g, 390 mmol) in acetonitrile (200 cm$^{3}$) under a nitrogen atmosphere was irradiated for 2 h. After removing the solvent and polymer of **2a**, the resulting solid was recrystallized from ethyl acetate to give **5a** (1.73 g, 22%). Similarly, a solution of **1** (2.00 g, 15.6 mmol) and **2b** (13.6 g, 156 mmol) in acetonitrile (200 cm$^{3}$) was irradiated for 2.5 h. After removing the solvent, the residual liquid was submitted to column chromatography (ethyl acetate–hexane (3 : 1)) to give **3b** (1.25 g, 41%) and **5b** (0.48 g, 15%). A similar reaction of **1** (4.00 g, 31.3 mmol) with **2c** (27.3 g, 313 mmol) and the same workup mentioned above afforded **3c** (3.07 g, 44%) and **5c** (0.43 g, 6%).

**5a:** Mp 132—134 °C; IR (KBr) 3550, 3460, 3250, 2250 cm$^{-1}$; $^{1}$H NMR (DMSO-$d_6$) $\delta$=1.03 (3H, s), 1.13 (3H, d, $J$=6.4 Hz), 1.94 (2H, d, $J$=7.6 Hz), 2.92 (1H, t, $J$=7.6 Hz), 3.60 (1H, q, $J$=6.4 Hz), 5.57, 5.81, 6.13 (each 1H, s, OH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=13.89, 16.88, 34.44, 37.87, 78.83,



Scheme 1.

Table 1. Formation of Tricyclic $\gamma$-Lactams **7** from **4** or **5** Using Base and Acid

| Compound | Product (yield/%) Base/Acid |
|---|---|
| **5a** | **7a** (53)/**7a** (0) |
| **3b+4b** | **3b+7b** (71)/**3b+7b** (24)[a)] |
| **3c+4c** | **3b+7c** (29)/**3c+7c** (44)[a)] |

a) Calculated on the basis of **4**.

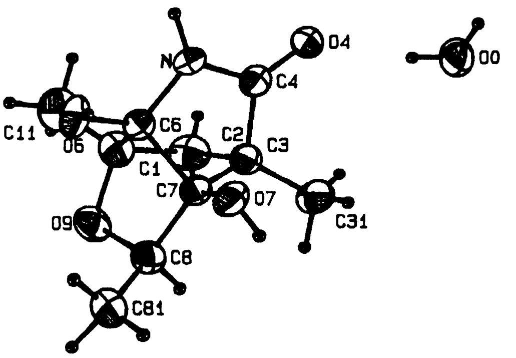


Fig. 1. ORTEP drawing of **7b**.

79.45, 80.53, 98.85, 121.50.

**3b:** Mp 104—105 °C; IR (KBr) 3410, 2260, 1800 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$=1.19 (3H, d, $J$=6.4 Hz), 1.25, 1.35 (each 3H, s), 1.87, 2.78 (each 1H, d, $J$=15.4 Hz), 2.77 (1H, s, OH), 4.70 (1H, q, $J$=6.4 Hz); $^{13}$C NMR (CDCl$_3$) $\delta$= 13.69, 17.37, 22.01, 35.89, 46.06, 71.52, 73.77, 79.50, 121.57, 207.29.

**5b:** Mp 124—126 °C; IR (KBr) 3380, 3345, 2250 cm$^{-1}$; $^{1}$H NMR (DMSO-$d_6$) $\delta$=0.99, 1.49 (each 3H, s), 1.18 (3H, d, $J$=6.4 Hz), 1.57, 2.22 (each 1H, d, $J$=13.2 Hz), 3.96 (1H, q, $J$=6.4 Hz), 5.53, 5.85, 6.17 (each 1H, s); $^{13}$C NMR (DMSO-$d_6$) $\delta$=13.63, 16.52, 21.06, 39.19, 45.85, 70.87, 78.77, 81.69, 91.20, 124.86.

**3c:** Mp 129—130 °C; IR (KBr) 3410, 2260, 1810 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$=1.26 (3H, d, $J$=6.2 Hz), 1.32 (3H, s), 2.63, 3.22 (each 1H, d, $J$=15.4 Hz), 3.34 (1H, s, OH), 4.58 (1H, q, $J$=6.2 Hz); $^{13}$C NMR (CDCl$_3$) $\delta$=13.40, 17.69, 50.92, 56.98, 71.21, 72.83, 80.63, 116.02, 203.10.

**5c:** Mp 152—154 °C; IR (KBr) 3370, 3320, 2260 cm$^{-1}$; $^{1}$H NMR (DMSO-$d_6$) $\delta$=1.04 (3H, s), 1.22 (3H, d, $J$=6.8 Hz), 2.12, 2.75 (each 1H, d, $J$=14.4 Hz), 4.35 (1H, q, $J$=6.8 Hz), 6.29 (2H, s, OH), 6.67 (1H, s, OH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=13.51, 16.58, 50.38, 64.75, 72.52, 79.44, 84.65, 98.84, 119.61. The elemental analyses errors of **3b,c** and **5a—c** for, C, H, and N were within 0.3%.

**Dehydration of 5a—c.** Compounds **5a—c** were heated at 150 °C for 1 h in each sealed tube to give **4a—c**, respectively, which were obtained quantitatively and easily converted into **5a—c** by exposing to the air within a few minutes.

**4a:** $^{1}$H NMR (CDCl$_3$) $\delta$=1.17 (3H, d, $J$=6.4 Hz), 1.30 (3H, s), 2.22 (1H, dd, $J$=14.0, 4.8 Hz), 2.68 (1H, dd, $J$=14.0, 11.2 Hz), 3.28 (1H, dd, $J$=11.2, 4.8 Hz), 3.62 (1H, s, OH), 4.20 (1H, q, $J$=6.4 Hz); $^{13}$C NMR (CDCl$_3$) $\delta$=13.65, 17.61, 31.64, 36.69, 71.85, 76.47, 76.93, 118.04, 206.92.

**4b:** $^{1}$H NMR (CDCl$_3$) $\delta$=1.16 (3H, d, $J$=6.0 Hz), 1.27 (3H, s), 1.58 (1H, s, OH), 1.70 (3H,s), 2.19, 2.43 (each 1H, d, $J$=14.0 H), 4.42 (1H, q, $J$=6.0 Hz).

**4c:** $^{1}$H NMR (CDCl$_3$) $\delta$=1.20 (3H, d, $J$=6.4 Hz), 1.31 (3H, s), 2.83, 2.91 (each 1H, d, $J$=15.2 Hz), 3.32 (1H, s, OH), 4.78 (1H, q, $J$=6.4 Hz).

**Hydration of 3b,c.** A solution of **3b** (0.25 g, 1.3 mmol) in acetone (20 cm$^3$) containing water (0.23 cm$^3$, 130 mmol) was refluxed for 10 d. After removing the solvent, the resulting solid was recrystallized from ethyl acetate to give **6b** (0.15 g, 55%). Similarly, a solution of **3c** (0.12 g, 0.56 mmol) was refluxed for 5 d, and the same workup gave **6c** (0.125 g, 96%).

**6b:** Mp 104—105 °C; IR (KBr) 3680, 3450, 3300, 2347 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$=1.05, 1.56 (each 3H, s), 1.24 (3H, d, $J$=6.6 Hz), 1.91, 2.03 (each 1H, d, $J$=12.8 Hz), 4.23 (1H, q, $J$=6.6 Hz), 5.57, 5.85, 6.06 (each 1H, s, OH).

**6c:** Mp 129—130 °C; IR (KBr) 3410, 2250 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$=1.05 (3H, s), 1.39 (3H, d, $J$=6.4 Hz), 2.53, 2.62 (each 1H, d, $J$=14.4 Hz), 4.14 (1H, q, $J$=6.4 Hz), 6.18 (2H, bs, OH), 6.32 (1H, bs, OH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=12.85, 16.33, 51.04, 61.08, 75.69, 79.14, 81.86, 98.35, 119.31. The elemental analyses errors of **6b,c** for C, H, and N were within 0.2%.

**Hydrolysis of 5a, 4b,c with Base.** A solution of **5a** (0.21 g, 1.1 mmol) in a 1% sodium hydroxide solution (5 cm$^3$) was stirred for 2 h at room temperature; the solution was neutralized with hydrochloric acid. After removing the sodium chloride and the solvent, the resulting solid was recrystallized from 2-propanol to give **7a** (0.11 g, 53%). A similar treatment of a mixture of **3b** and **4b** (2.90 g, 14.9 mmol) (3 : 2 ratio from the $^1$H NMR), which was obtained by a Kugelrohr distillation (120 °C/4 mmHg, 1 mmHg=133.322 Pa) of the irradiation mixture, and the same workup gave **7b** (1.02 g, 71%) with a quantitative recovery of **3b**. A similar treatment of a mixture of **3c** and **4c** (1.27 g, 5.91 mmol) (7 : 2 ratio from the $^1$H NMR), which was obtained by Kugelrohr distillation (120 °C/4 mmHg) of the irradiation mixture, and the same workup afforded **7c** (0.090 g, 29%) with a quantitative recovery of **3c**.

**7a:** Colorless prisms; mp 214—215 °C; IR (KBr) 3450, 3260, 3100, 1690 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$=1.11 (3H, s), 1.13 (3H, d, $J$=6.4 Hz), 1.30 (1H, d, $J$=12.8 Hz), 1.93 (1H, dd, $J$=6.4, 12.8 Hz), 2.14 (1H, dd, $J$=1.2, 6.4 Hz), 3.78 (1H, q, $J$=6.4 Hz), 5.59, 6.21 (each 1H, s, OH), 7.82 (1H, s, NH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=15.44, 17.16, 37.14, 50.00, 71.57, 81.61, 88.29, 91.91, 176.39; MS $m/z$ 199 (M$^+$, 21), 72 (100). Found: C, 54.05; H, 6.63; N, 6.82%. Calcd for $C_9H_{13}NO_4$: C, 54.27; H, 6.53; N, 7.04%.

**7b:** Colorless prisms; mp 234—236 °C; IR (KBr) 3510, 3440, 3300, 1700 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$=0.91, 1.09 (each 3H, s), 1.12 (3H, d, $J$=6.4 Hz), 1.35, 1.57 (each 1H, d, $J$=12.8 Hz), 3.77 (1H, d, $J$=6.4 Hz), 5.32, 6.03 (each 1H, s, OH), 7.84 (1H, s, NH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=8.06, 14.94, 17.02, 44.48, 50.87, 69.67, 81.36, 89.19, 91.29, 177.29; MS $m/z$ 213 (M$^+$, 20), 124 (100). Found: C, 52.01; H, 7.83; N, 6.03%. Calcd for $C_{10}H_{15}NO_4(H_2O)$: C, 51.94; H, 7.40; N, 6.05%.

**7c:** Colorless prisms; mp 222—224 °C; IR (KBr) 3510, 3320, 1698 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$=1.13 (3H, s), 1.17 (3H, d, $J$=6.6 Hz), 1.91, 2.02 (each 1H, d, $J$=12.8 Hz), 3.89 (1H, q), 6.11, 6.60 (each 1H, OH), 8.49 (1H, s, NH); $^{13}$C NMR (DMSO-$d_6$) $\delta$=13.90, 16.24, 46.23, 69.26, 72.48, 81.72, 88.30, 90.05, 169.83; MS $m/z$ 233 (M$^+$, 1), 198 (100). Found: C, 46.18; H, 5.15; N, 5.78%. Calcd for $C_9H_{12}NO_4Cl$: C, 46.26; H, 5.17; N, 5.99%.

**Hydrolysis of 4b,c on Silica gel.** An ethyl acetate solution (3 cm$^3$) or **3b** and **4b** (2.0 g, 10.3 mmol) (3 : 2 ratio) was held in a silica-gel column for 4 d at room temperature; the column (ethyl acetate–hexane (2 : 1)) was then eluted to give **7b** (0.21 g, 24%) and a quantitative recovery of **3b**. A similar treatment of a mixture of **3c** and **4c** (3.11 g, 14 mmol) (7 : 2 ratio) and the same workup afforded **7c** (0.33 g, 44%) and a quantitative recovery of **3c**.

**X-Ray Analysis of 7b. Crystallographic Section.** $C_{10}H_{15}NO_4(H_2O)$, $F_w$=231.25, orthorhombic, space group $P2_12_12_1$, $a$=8.112(1), $b$=18.671(1), $c$=7.526(1) Å, $\alpha$=90.00(1)°, $\beta$=90.00(1)°, $\gamma$=90.00(1)°, $V$=1140.0(1) Å$^3$, $Z$=4, $D_x$=1.347 g cm$^{-3}$.

**Data Collection. Diffractometer:** CAD4 (ENRAF-NOIUS), crystal size: 0.30×0.30×0.37 mm$^3$, radiation: Mo $K\alpha$ (0.71073 Å), monochrometer: graphite, data collection mode: $\omega$–$2\theta$ scan, number of reflections: 1380 (observed), temperature, 297 K.

**Structure Analysis.** Solution: SIR, $R$=0.033, $R_w$= 0.038, software: MOLEN.

**Supplementary Material Available.** The tables for the bond distances, bond angles, structure factors, positional parameter, and their estimated standard deviations, refined displacement parameter expressions, and general displacement parameter expressions of the X-ray crystallography of **7b** are being kept as Document No. 67059 the Office of the Editor of Bull. Chem. Soc. Jpn.

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