methanol under reflux afforded the desired olefinic acid **8** in high yield.

In summary, we developed an efficient and enantioselective method for the synthesis of *N*-cbz-5*S*-amino-6-phenyl-hex-3*Z*-enoic acid in high yields. This method could be applied to a large scale preparation of the olefinic acid **8** up to a kg scale without any problem.

Experimental Section

General Procedures. Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR Spectra were recorded on a Jeol GSX500 spectrometer with chemical shifts expressed in δ units (ppm) relative to tetramethylsilane. FAB Mass spectra were recorded on a Jeol JMS-DX300 Mass Spectrometer. Thin-layer chromatography was conducted with E. Merck silica gel 60 F_{254} plates. Column chromatography was performed using E. Merck silica gel 60 (230-400 mesh). Unless otherwise noted, reactions were conducted under a nitrogen atmosphere.

1-(2-triphenylphosphoniumethyl)-4-methyl-2,6,7-trioxa-bicyclo-[2,2,2]-octane bromide (6). A mixture of bromo orthoester **5** (11.7 g, 50 mmol), triphenylphosphine (19.6 g, 75 mmol) and sodium bicarbonate (5.0 g, 60 mmol) was refluxed in acetonitrile for 48 hrs and concentrated to 30 mL. After addition of 50 mL of dichloromethane the resulting mixture was filtered through celite. Removal of the solvent under reduced pressure afforded a white gummy solid. Trituration in ether gave pure orthoester salt **6** as a white powder which was dried over P_2O_5 under vacuum (21.7 g, 87%): mp 196-197 ℃; ^{1}H NMR (DMSO-d_6) δ 0.85 (s, 3H), 1.83 (m, 2H), 3.59 (m, 2H), 3.84 (s, 6H), 7.75-7.92 (m, 15H); ^{13}C NMR (DMSO-d_6) δ 13.09, 16.24 (d, J=55.2), 29.96, 30.01, 72.23, 107.30 (d, J=15.5), 117.39 (d, J=82.2), 130.02, 134.20, 134.98; FAB MS, 419 (M-Br).

***N*-Cbz-5*S*-amino-6-phenyl-hex-3*Z*-enoic acid (8).** To a stirred solution of orthoester salt **6** (6.08 g, 12 mmol) in 60 mL of dry THF was added 2.19 g (11 mmol) potassium bis(trimethylsilyl)amide at −30 ℃ and the resulting mixture was stirred for 1 hr. The mixture was treated slowly with a solution of 3.0 g (10.6 mmol) of cbz-L-phenylalanal in 20 mL of THF (over 10 min.). The mixture was stirred for 1 hr at −30 ℃, for additional 1 hr at room temperature, then queched with water (10 mL). Concentration followed by flash column chromatography (using hexane : ethyl acetate : triethylamine, 80 : 18 : 2) afforded pure 5-L-(*N*-benzyloxycarbonyl) amino-6-phenyl-hex-3-*Z*-enyl-4'-methyl-2',6'-7'-trioxabicyclo-[2',2',2']-octane **7** as an oil.

A solution of **7** (2.5 g, 6 mmol) in *t*-butanol (60 mL), water (12 mL) and conc. HCl (7 mL) was refluxed for 10 hr. After removal of the solvent under reduced pressure the residue was dissolved in 5% aqueous K_2CO_3 solution and then washed three times with dichloromethane (30 mL×3). The aqueous layer was adjusted to pH 2, extracted with ethyl acetate (50 mL×2), and dried over anhydrous $MgSO_4$. Concentration of the organic layer afforded the target compound **8** in 91% yield (3.27 g) from cbz-L-phenylalanal: mp 90-91 ℃; $[\alpha]_D$=+30.6 (c=0.10, methanol); ^{1}H NMR (DMSO-d_6) δ 2.64 (m, 1H), 2.80 (m, 2H), 2.99 (m, 1H), 4.41 (m, 1H), 4.98 (s, 2H), 5.45 (dd, 1H), 5.52 (m, 1H), 7.14-7.39 (m, 10H), 7.49 (d, 1H), 12.20 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.09, 41.64, 50.15, 65.19, 122.72, 126.89, 127.97, 128.33, 128.89, 128.93, 129.81, 132.63, 137.42, 138.52, 155.34, 172.24; Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.76, H, 6.24, N, 4.13. Found: C, 70.65, H, 6.25, N, 4.15.

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Efficient Syntheses of 2-Acetyl-7-formylbenzofuran and 2-Acetyl-7-(formylmethyl)benzofuran through the Oxidative Cleavage of Allylbenzofuran with Osmium Tetraoxide/Sodium Periodate

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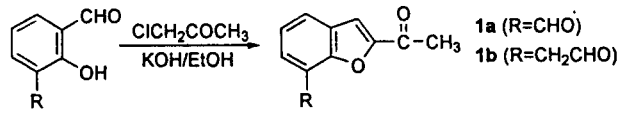
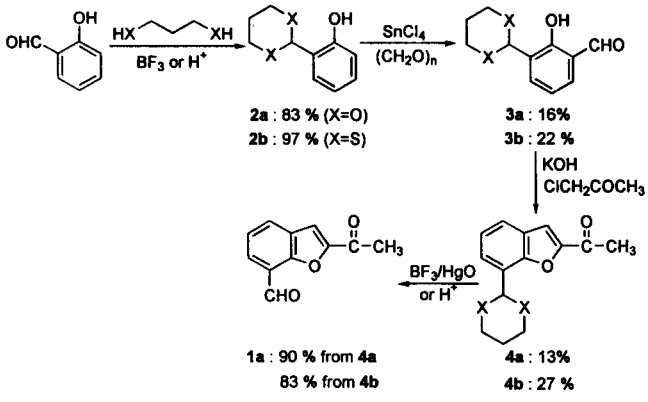
In connection with a program directed toward the synthesis of soft analogs of bufuralol,[1] we needed to synthesize 2-acetyl-7-formylbenzofuran (**1a**) as well as 2-acetyl-7-(formylmethyl)benzofuran (**1b**) as key intermediates. Since literature survey showed that there were no reports on the preparations of the desired intermediates, it is therefore important to develop efficient routes to two intermediates. In the several synthetic methods for benzofurans, cyclization reaction of substituted 2-hydroxybenzaldehydes with chloroacetone is used in the most common approach for the synthesis of the substituted 2-acetylbenzofurans as shown below.[2]

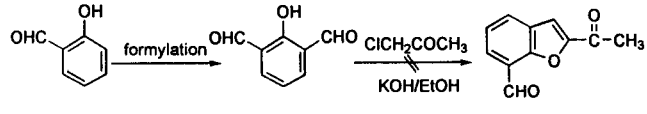




Scheme 1.

Nevertheless, it is well known that the introduction of formyl group at C-6 position of salicylaldehyde by electrophilic formylation reaction is quite difficult because the resulting di-aldehyde is very prone to polymerize under either acidic or basic conditions *via* inter or intramolecular polymerization.[3] In addition, the furan ring in benzofuran with the weak aromatic character is readily cleaved by oxidizing agents,[4,5] which precludes the usage of oxidative cleavage of alkenes with ozone for introduction the formyl group into benzofuran ring.[6] Therefore, the oxidative cleavage of alkenes[7] should be carefully applied for introduction of the formyl groups into benzofuran system. Fortunately, we have found that a combination of catalytic amount of osmium tetraoxide and sodium periodate can convert alkenylbenzofuran to alkanoylbenzofuran without opening the furan ring. Herein, we report efficient synthetic methods of 2-acetyl-7-formylbenzofuran as well as 2-acetyl-7-(formylmethyl)benzofuran using a mild oxidative cleavage reaction with osmium tetraoxide/sodium periodate system.

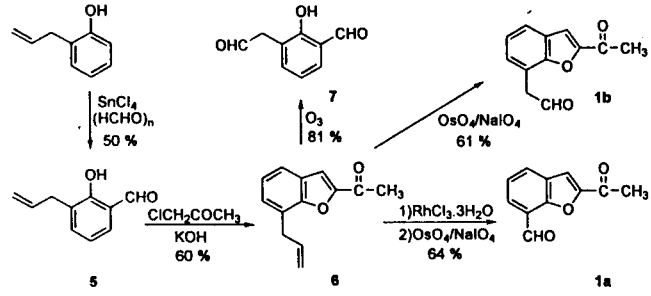
Initially, as of preliminary studies, we attempted to introduce formyl group directly to the C-7 position in benzofuran.



Formylations of salicylaldehyde under various conditions such as Reimer-Tiemann reaction,[8] Duff reaction[9] and tin(IV) chloride/formaldehyde[10] were attempted. Unfortunately, all of the formylations gave the phenol resin as a major product with invariably low yield of 6-formylsalicylaldehyde. The cyclization of 6-formylsalicylaldehyde with chloroacetone[2b] also resulted in tarry polymer with trace amount of product because the formyl group was polymerized under the reaction condition.

In an effort to prevent the formyl group from polymerization, we first converted the electron-withdrawing formyl group into electron-releasing acetal group by protecting with 1,3-propanediol (Scheme 1).

The acetalization of salicylaldehyde with 1,3-propanediol[11] gave **2a** in 83% yield. Unfortunately, the formylation of **2a** with $SnCl_4$/formaldehyde under the optimized condition[10] afforded **3a** in only 16% yield with an unidentified polymer. The resulting **3a** was then cyclized with chloroacetone in KOH ethanolic solution[2b] to give **4a** in 13% yield. Finally,



Scheme 2.

the deprotection of acetal group in acidic condition[11] gave the desired 2-acetyl-7-formylbenzofuran (**1a**) in 90% yield. In spite of successful synthesis of **1a**, above synthesis was not applicable for the large scale reaction because not only the total yield from the starting material was very low (1.5% yield from salicylaldehyde), but also the deprotection of acetal group was observed during the formylation step due to evolution of HCl gas. As an alternative protecting group of formyl group, we then used 1,3-propanedithiol[12] to form the thioacetal which was not decomposed under the formylation condition. After preparation of **2b** from salicylaldehyde in 97% yield, the same reaction sequence was followed as for **2a**. In this manner, total yield was slightly improved (5% from salicylaldehyde), especially in the formylation and the cyclization step, compared with the synthesis from **2a**.

Although 2-acetyl-7-formylbenzofuran (**1a**) can be successfully prepared from **2b** with an acceptable yield, we continued to investigate other synthetic strategy because we needed to synthesize 2-acetyl-7-(formylmethyl)benzofuran (**1b**) and to improve the total yield for the large scale reaction to be useful. For this purpose, we employed the new approach of oxidative cleavage of alkenes to introduce desired formyl and methyformyl group in the aromatic ring (Scheme 2).

Thus, commercially available 2-allylphenol was used as a starting material for the synthesis of 2-acetyl-7-(formylmethyl)benzofuran (**1b**). The formylation of 2-allylphenol with $SnCl_4$/formaldehyde[11] resulted in 3-allylsalicylaldehyde (**5**) in 50% yield, and cyclization of **5** with chloroacetone[2b] afforded 2-acetyl-7-allylbenzofuran (**6**) in 60% yield. It was expected that the yields should be improved in both steps because the allyl group alleviates the involvement of polymerization. Direct oxidative cleavage of allyl group by ozonolysis[7c] was first tried to form the formylmethyl group for the synthesis of 2-acetyl-7-(formylmethyl)benzofuran (**1b**), but the five-membered ring-opened compound **7** was obtained. To overcome this problem, we have studied an indirect mild oxidative cleavage of alkenes to convert allyl group to formylmethyl group without opening the furan ring. As a result, the compound **6** was treated with a catalytic amount of osmium tetraoxide solution to form a diol adduct followed by adding sodium periodate in THF/water at room temperature to give the desired 2-acetyl-7-(formylmethyl)benzofuran (**1b**) in 61% yield with a very limited amount of polymer. Furthermore, 2-acetyl-7-formylbenzofuran (**1a**) was also successfully synthesized with 64% yield from **6** by rearrangement of the double bond under $RhCl_3 \cdot 3H_2O$/EtOH condition[13] followed by the catalytic oxidative cleavage of the resulting 2-acetyl-

7-(1-propenyl)benzofuran.

In summary, we present an efficient method for the preparations of 2-acetyl-7-formylbenzofuran as well as 2-acetyl-7-(formylmethyl)benzofuran from the common starting material, commercially available 2-allylphenol, in a good yield by utilizing a mild oxidative cleavage with osmium tetraoxide/sodium periodate system.

Experimental

2-(1,3-Dioxan-2-yl)phenol (2a). A mixture of salicylaldehyde (18.00 g, 0.147 mol), 1,3-propanediol (2.13 mL, 0.295 mol) and p-TsOH·H_2O (0.16 g) in 100 mL of toluene was refluxed with azeotropic removal of water with a Dean-Stark trap for 2 hours. After cooling to room temperature, the reaction mixture was washed with saturated aq. sodium bicarbonate solution, the aqueous layer was extracted with 200 mL of methylene chloride. The organic layer was washed with brine, dried over anhyd. sodium sulfate, filtered and evaporated to give a crude product. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 3) to give 22.00 g of product (83% yield). IR (KBr) 3300 (OH), 2950 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.51 (m, 1H, SCH_2CH_2, axial), 2.12-2.41 (m, 1H, SCH_2CH_2, equatorial), 3.90-4.12 (m, 2H, OCH_2), 4.21-4.38 (m, 2H, OCH_2), 5.65 (s, 1H, OCH(Ph)O), 6.85-6.96 (m, 2H, ArH), 7.25-7.32 (m, 2H, ArH), 7.90 (s, 1H, OH).

2-(1,3-Dithian-2-yl)phenol (2b). To a solution of salicylaldehyde (5.31 g, 43.4 mmol) in 150 mL of methylene chloride was added 1,3-propanedithiol (7.02 g, 65.1 mmol) followed by boron trifluoride etherate (12.30 g, 86.7 mmol) at 0 ℃. The reaction mixture was stirred for 1 h at 0 ℃, and then poured into a separatory funnel containing 100 mL of aq. saturated sodium bicarbonate solution. The aqueous layer was extracted with 200 mL of methylene chloride. The organic layer was washed with brine, dried over anhyd. sodium sulfate, filtered and evaporated to give the crude product. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 4) to give 9.00 g of product (97% yield). mp 131 ℃; IR (KBr) 3331 (OH), 2910 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.81-2.15 (m, 1H, SCH_2CH_2, axial), 2.15-2.25 (m, 1H, SCH_2CH_2, equatorial), 2.84-3.13 (m, 4H, SCH_2), 6.55 (s, 1H, OH), 6.85-6.92 (m, 2H, ArH), 7.16-7.34 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.79 (SCH_2CH_2), 31.56 ($SCH_2CH_2CH_2S$), 47.06 (SCH(Ph)S), 117.14, 120.72, 123.67, 129.05, 129.97, 154.21; MS (m/e) 212 (M^+), 177, 147, 138 (base peak), 119, 83, 45.

3-(1,3-Dioxan-2-yl)salicylaldehyde (3a). To a solution of **2a** (5.40 g, 0.03 mol) in 100 mL of benzene were added tin(IV) chloride (0.83 g, 0.003 mol) and tri-n-butylamine (0.87 g, 0.012 mol). The mixture was stirred for 20 minute at room temperature, and then paraformaldehyde (1.8 g, 0.06 mol) was added. The resulting mixture was heated at 100 ℃ for 8 h. After cooling, the reaction mixture was poured into cold water (100 mL), acidified to pH 2 with 2 N hydrochloric acid, and extracted with 100 mL of ether. The organic layer was washed with brine, dried over anhyd. sodium sulfate, filtered and evaporated. The residue was subjected to column chromatography on silica gel with ethyl acetate-hexane (1 : 4) to give 1.00 g of product (16% yield). IR (KBr) 3400 (OH), 2911, 1660 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.41-1.48 (m, 1H, SCH_2CH_2, axial), 2.22-2.32 (m, 1H, SCH_2CH_2, equatorial), 4.04 (m, 4H, OCH_2), 5.95 (s, 1H, OCH(Ph)O), 7.02-7.10 (m, 1H, ArH), 7.54-7.59 (m, 1H, ArH), 7.87-7.92 (m, 1H, ArH), 9.91 (s, 1H, CHO), 11.33 (s, 1H, OH).

3-(1,3-Dithian-2-yl)salicylaldehyde (3b). Compound **3b** was prepared from **2b** (2.0 g, 9.4 mmol) by the method described for **3a**. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 5) to give 0.5 g of product (22% yield). mp 183 ℃; IR (KBr) 3429 (OH), 2900, 1673 (aldehyde C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.59-1.97 (m, 1H, SCH_2CH_2, axial), 2.16-2.18 (m, 1H, SCH_2CH_2, equatorial), 2.86-2.97 (m, 2H, SCH_2), 3.08-3.22 (m, 2H, SCH_2), 5.72 (s, 1H, CHO), 7.02-7.12 (m, 1H, ArH), 7.53-7.58 (m, 1H, ArH), 7.83-7.90 (m, 1H, ArH), 9.88 (s, 1H, CHO), 11.33 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 25.02 (SCH_2CH_2), 32.25 ($SCH_2CH_2CH_2S$), 42.43 (SCH(Ph)S), 120.15, 124.10 136.60, 139.79, 157.96, 196.47 (ArCHO); MS (m/e) 240 (M^+), 212, 166, 138, 105, 73, 33 (base peak).

2-Acetyl-7-(1,3-dioxan-2-yl)benzofuran (4a). To a solution of **3a** (350 mg, 1.66 mmol) in 10 mL of absolute ethanol was added 150 mg of KOH pellet. The resulting suspension was warmed up until the suspension turned into clear solution. To this clear solution was added chloroacetone (0.25 g, 3.13 mmol) dropwise and then the resulting dark solution was refluxed for 15 min. After the cooling to room temperature, the reaction mixture was poured into 30 mL of ice-water, and ethanol was removed under reduced pressure. The aqueous layer was extracted with ether and the ether layer was dried over anhydrous magnesium sulfate, filtered and concentrated to give a reddish residue, which was purified by column chromatography on silica gel with ethyl acetate-hexane (1 : 3) to give 53 mg of product (13% yield). IR (Neat) 2911, 1680 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.47-1.60 (m, 1H, OCH_2CH_2, axial), 2.18-2.35 (m, 1H, OCH_2CH_2, equatorial) 2.60 (s, 3H, OCH_3), 4.05-4.18 (m, 2H, OCH_2), 4.27-4.35 (m, 2H, OCH_2), 6.14 (s, 1H, OCH(Ph)O), 7.30-7.37 (m, 1H, ArH), 7.50 (s, 1H, furan-H), 7.66-7.76 (m, 2H, ArH).

2-Acetyl-7-(1,3-dithian-2-yl)benzofuran (4b). Compound **4b** was prepared from **3b** (230 mg, 0.95 mmol) by the method described for **3a**. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 4) to give 72 mg of product (27% yield). mp 149 ℃; IR (KBr) 2900, 1680 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.85-2.12 (m, 1H, SCH_2CH_2, axial), 2.15-2.35 (m, 1H, SCH_2CH_2, equatorial), 2.60 (s, 3H, $COCH_3$), 2.85-3.15 (m, 2H, SCH_2), 3.15-3.31 (m, 2H, SCH_2), 5.95 (s, 1H, SCH(Ph)S), 7.25-7.36 (m, 1H, ArH), 7.51 (s, 1H, furan-H), 7.62-7.74 (m, 2H, ArH).

3-Allyl-salicylaldehyde (5). Compound **5** was prepared from 2-allylphenol (5.00 g, 0.037 mol) by the method described for **3a**. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 20) to give 3.05 g of product (50% yield). IR (Neat) 3098 (OH), 2844, 1684 (aldehyde C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.41 (d, 2H, $CH_2CH=CH_2$, J=6.4 Hz), 5.04-5.15 (m, 2H, $CH=CH_2$), 5.90-6.15 (m, 1H, $CH=CH_2$), 6.92-7.00 (m, 1H, Ar-H) 7.39-7.44 (m, 2H, ArH), 9.85 (s, 1H, CHO), 11.32 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.03 ($CH_2CH=CH_2$), 116.21, 119.55 ($CH=CH_2$), 131.86, 135.78, 137.11 ($CH=CH_2$),

196.65 (ArCHO).

2-Acetyl-7-allylbenzofuran (6). Compound **6** was prepared from **5** (3.0 g, 18.2 mmol) by the method described for **4a**. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 20) to give 2.18 g of product (60% yield). mp 45 ℃; IR (KBr) 3000, 1683 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.60 (s, 3H, $COCH_3$), 3.71 (d, 2H, $CH_2CH=CH_2$, J=6.6 Hz), 5.11-5.23 (m, 2H, $CH=CH_2$), 6.01-6.15 (m, 1H, $CH=CH_2$), 7.28-7.31 (m, 2H, ArH), 7.52 (s, 1H, furan-H), 7.54-7.59 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.12 ($COCH_3$), 33.35 ($CH_2CH=CH_2$), 112.70, 116.36 ($CH=CH_2$), 120.90, 123.81, 124.66, 126.66, 127.64, 135.08 ($CH=CH_2$), 152.35, 188.17 ($COCH_3$); MS (m/e) 200 (M^+), 159, 129 (base peak), 77, 51; Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.25; H, 5.97.

3-(Formylmethyl)salicylaldehyde (7). To a cooled (−78 ℃) solution of **6** (100 mg, 0.5 mmol) in 10 mL of methanol, O_3 was introduced until the colorless solution turned into blue color. The ozonizer was turned off and stirring was continued until the blue color turned into colorless. The solution was treated with dimethylsulfide (37 mg, 0.6 mmol) and stirred for 10 min at −78 ℃, and then allowed to come to room temperature. After the reaction was completed by checking on TLC, methanol was removed under reduced pressure. To the residue was added water, then extracted with ether. The organic layer was dried over anhyd. magnesium sulfate, filtered and concentrated to give a reddish oily residue, which was purified by column chromatography on silica gel with ethyl acetate-hexane (1 : 1) to give 81 mg of product (81% yield). IR (Neat) 3425, 2922, 2855, 1731 (aldehyde C=O), 1653 (aldehyde C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.82 (s, 2H, CH_2CHO), 7.05-7.13 (m, 1H, ArH), 7.45-7.50 (m, 1H, ArH), 7.55-7.62 (m, 1H, ArH), 9.82 (s, 1H, $ArCH_2CHO$), 9.92 (s, 1H, ArCHO), 11.31 (s, 1H, OH).

2-Acetyl-7-formylbenzofuran (1a) from 4a. A mixture of **4a** (50 mg, 0.20 mmol) and catalytic amount of p-TsOH in acetone (10 mL) and deionized water (30 mL) was refluxed for 3 hours. The solution was treated with saturated aq. sodium bicarbonate solution, and the acetone was removed *in vacuo*. The aqueous layer was extracted with 50 mL of ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated. The residue was subjected to column chromatography on silica gel with ethyl acetate-hexane (1 : 4) to give 34 mg of product (90% yield). mp 90 ℃; IR (KBr) 3122, 2864, 1693 (C=O), 1691 (C=O, and aldehyde C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.60 (s, 3H, $COCH_3$), 7.40-7.45 (m, 1H, ArH), 7.52 (s, 1H, furan-H) 7.90-7.95 (m, 1H, ArH), 10.53 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.57 ($COCH_3$), 111.72, 121.82, 124.08, 128.64, 129.41, 153.84, 154.55, 187.38 (ArCHO), 188.83 ($COCH_3$); MS (m/e) 188 (M^+), 173 (base peak), 159, 145, 117, 89, 77, 63, 50; Anal. Calcd for $C_{11}H_8O_3$: C, 70.21; H, 4.29. Found: C, 70.28; H, 4.15.

2-Acetyl-7-formylbenzofuran (1a) from 4b. A solution of **4b** (350 mg, 1.3 mmol) in THF (10 mL) was added a mixture of boron trifluoride etherate solution (0.8 mL) and HgO (690 mg, 3.2 mmol) in aqueous THF (15% H_2O, 20 mL) at room temperature. The reaction mixture was stirred for 30 min, diluted with ether, and extracted with ether. The extract was washed with brine, dried over anhyd. magnesium sulfate, filtered and evaporated. The residue was separated from column chromatography on silica gel with ethyl acetate to give 200 mg of product (83% yield).

2-Acetyl-7-formylbenzofuran (1a) from 6. To a solution of rhodium chloride trihydrate (380 mg) in 5 mL of absolute ethanol was added **6** (2.0 g, 10 mmol) in 1 mL of absolute ethanol. After heating at 70 ℃ for 8 h under nitrogen atmosphere, the mixture was cooled and filtered. The filterate was concentrated to give residue, which was subjected to column chromatography on silica gel with ethyl acetate-hexane (1 : 4) to give 1.5 g (75%) of rearranged product, 2-acetyl-7-(1-propenyl)benzofuran. IR (Neat) 2913, 1691 (C=O), 1564 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.99 (d, 3H, $CH=CHCH_3$, J=5.0 Hz), 2.61 (s, 3H, $COCH_3$), 6.73-6.75 (m, 2H, $CH=CHCH_3$), 7.47 (s, 1H, furan-H), 7.37-7.53 (m, 3H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.86 ($CH=CHCH_3$), 26.12 ($COCH_3$), 112.59, 120.89, 123.25, 123.76, 124.79, 125.48, 127.06, 129.85, 152.24, 152.54, 188.02 ($COCH_3$).

The oxidative cleavage of propenyl group was performed as follow: To a solution of 2-acetyl-7-(1-propenyl)benzofuran (1.5 g, 7.5 mmol) in 200 mL of THF/H_2O (3 : 1) was added 13 mL (10 mol %) of a 4 wt % solution of osmium tetraoxide in water. After the color of the solution turned black, sodium metaperiodate (4.8 g, 22.5 mmol) was added, and the resulting mixture was stirred for 1 h at room temperature. The mixture was filtered, and the filter cake was washed with three 50 mL portions of ether. The filtrate was washed with 50 mL of water and then 50 mL of brine. The ether layer was dried over anhydrous magnesium sulfate, filtered and evaporated to give a crude product. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 1) to give 1.2 g of **1a** (64% yield).

2-Acetyl-7-(formylmethyl)benzofuran (1b) from 6. Compound **1b** was prepared from **6** (2.0 g, 10 mmol) by the same oxidative cleavage method described for **1a**. Purification was performed by column chromatography on silica gel with ethyl acetate-hexane (1 : 1) to give 1.2 g of product (61% yield). mp 84 ℃; IR (KBr) 3133, 2897, 1723 (C=O), 1683 (aldehyde C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.60 (s, 3H, $COCH_3$), 4.02 (d, 2H, $ArCH_2CHO$, J=1.7 Hz), 7.29-7.48 (m, 2H, ArH), 7.52 (s, 1H, furan-H), 7.58-7.70 (m, 1H, ArH), 9.91 (t, 1H, $ArCH_2CHO$, J=1.7 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.33 ($COCH_3$), 44.06 ($ArCH_2CHO$), 113.08, 117.01, 122.55, 124.20, 127.09, 129.22, 152.69, 154.25, 188.24 ($COCH_3$), 197.54 ($ArCH_2CHO$); MS (m/e) 202 (M^+), 173 (base peak), 159, 131, 115, 102, 77, 51; Anal. Calcd for $C_{12}H_{10}O_3$: C, 71.30; H, 4.95. Found: C, 71.23; H, 4.97.

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Synthesis and Crystal Structure of 1,3-Diaza-5,6,6-trimethyltricyclo[5,2,1,0^{5,10}]decan-2,4-dione

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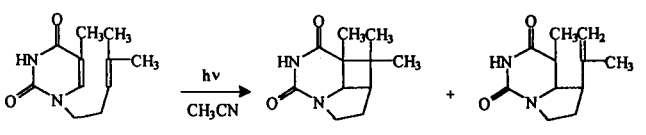
Intramolecular [2+2] photocycloaddition reaction of olefinic cycloenones are well-established synthetic methods of complex carbocyclic and heterocyclic compounds, since this simple reaction provides good regio- and stereospecificity in relatively high yield. The retro-ene reactions or chemical cleavages of cyclobutane ring of the photoadduct transform annelative two carbon ring or carbon hetero ring expansion of original cycloenones, otherwise those are difficult to obtain by ordinary synthetic methods.[1] Direct and/or pyrex filtered irradiation of N^1-(4-methyl-3-pentenyl) thymine (1) with a 12 W low pressure Hg lamp in CD_3CN at room temperature for 10 hr gave (2) and (3) in ratio 4.9 : 3.5.[2]



1 2 3

Experimental

1,3-Diaza-5,6,6-trimethyltricyclo[5,2,1,0^{5,10}]decan-2,4-dione (2) and 1,3-Diaza-5-methyl-7(1-methylethenyl)bicyclo[4,3,0]nonan-2,4-dione (3). A solution of 52 mg of **1** in 250 mL of acetonitrile was irradiated with a 12 W low pressure Hg lamp for 15 hr under nitrogen stream. The solvent was removed and the residue was submitted to preparative TLC (silica gel) using methanol-methylenechloride (1 : 9) as the eluents. The isolated yield was 17 mg (33%) of **2** and 21 mg (41%) of **3**. Compound **2**, mp 204-206 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.90 (s, 3H), 1.05 (s, 3H), 1.34 (s, 3H), 1.82-1.93 (m, 2H), 2.61 (td, J=6.1, 5.6 Hz, 1H), 3.16 (ddd, J=1 2.2, 8.7, 8.7 Hz, 1H), 3.55 (d, J=6.2 Hz, 1H), 4.06-4.19 (m, 1H), 7.20 (s, 1H); IR (KBr), 1703 cm^{-1} ($\nu_{c=o}$); EIMS m/z 208 (M^+). Compound **3**, mp 220-222 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (d, J=6.7 Hz, 3H), 1.67 (s, 3H), 1.90-2.18 (m, 2H), 2.32-2.42 (m, 1H), 2.89 (dd, J=6.3, 6.2 Hz, 1H), 3.45 (dd, J=12.7, 5.8 Hz, 1H), 3.54-3.62 (m, 2H), 4.70 (s, 1H), 4.86 (d, J=1.3 Hz, 1H), 7.17 (s, 1H); IR (KBr), 1721, 1691 cm^{-1} ($\nu_{c=o}$); EIMS m/z 208 (M^+).

Crystallographic Studies. Small plate-like crystal was selected for X-ray analysis. Preliminary examination and data collection were performed with MoKα$_1$ radiation (λ=0.71073 Å) on an MXC3 diffractometer (Mac Science) equipped with an incident beam graphite monochromator. The unit cell parameters and the orientation matrix for data collection were obtained from the least-squares refinement using the setting angles of 15 reflections in the range 20°<2θ(MoKα$_1$)<28°. The monoclinic cell parameters and calculated volumes are a=13.113 (6) Å, b=7.174 (3) Å, c=11.836 (6) Å, β=99.99° (4). The systematic extinctions ($0k0 : k=2n+1$, $h0l : h+l=2n+1$) were indicative of the space group C_{2h}^5-$P2_1/c$. Intensity data were collected with the ω-2θ scan techniques. The intensities of two standard reflections, measured every hundred reflections, showed no significant deviations during the data collection.

The initial positions for all non-hydrogen atoms were obtained by using direct methods of the SHELXS-86 program.[4] The structure was refined by full matrix least-squares technique with the use of the SHELXL-93 program.[5] Anisotropic thermal motion for non-hydrogen atoms and isotropic extinction parameters were included. The final cycle of refinement performed on Fo^2 with all 1715 unique reflections afforded residuals $wR2$=0.1126 and the conventional R index based on the reflections having $Fo>4\sigma(Fo)$ is 0.0496. Additional crystallographic data and details of the data collection are given in Table 1. Final atomic positions for non-hydrogen and hydrogen atoms are listed in Table 2. Table 3 shows bond lengths and angles.

Results and Discussion

A view of the new compound is given in Figure 1. Table 4 presents least-squares planes of rings in the compound. The title compound is structurally similar to the tricyclic compound reported earlier.[6] In this tricyclic system, the three rings (4,5,6-membered) are fused by the C5-C6, C7-C10, and N1-C10 bonds. The cyclobutane is a nearly ideal plane. The C6 atom in this ring deviates 0.401 Å from the least-squares plane defined by C5, C7, and C10 atoms. The thy-