Synthesis of 1,3-Dioxin-4-ones and Their Use in Synthesis. XVI.[1,2] 4-Oxo-1,3-dioxin-5-carboxylic Acids and Related Compounds: Versatile Synthetic Intermediates for the Synthesis of 6-Unsubstituted Six-Membered Heterocyclic Compounds

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A novel method for the synthesis of so far unknown 1,3-dioxin-4-ones having a carboxyl group at the 5-position is described. Reaction of formyl Meldrum's acid and an alcohol in an aprotic solvent at 50—60 °C gave the corresponding half esters of formylmalonic acid. Treatment of the latter with appropriate ketones in acetic anhydride containing a catalytic amount of *p*-toluenesulfonic acid gave the desired dioxinone-5-carboxylates.

Successful conversion of these 1,3-dioxin-4-ones either to 1,3-oxazine-2,4-dione or uracil derivatives having an alkoxycarbonyl group at the 5-position demonstrated that these dioxinones can serve as chemical equivalents for alkoxycarbonylformylketenes.

The fact that 5-benzyloxycarbonyl-1,3-dioxin-4-one can readily be transformed to the so far unknown 5-aminodioxinone derivative indicates further the importance of the dioxinone having a carboxyl group at the 5-position as a new building block for heterocyclic compounds.

Keywords 4-oxo-1,3-dioxin-5-carboxylic acid; formylmalonic acid half ester; formyl Meldrum's acid; 5-amino-1,3-dioxin-4-one; cycloaddition; 4-oxo-1,3-oxazine-5-carboxylate; 2-dimethylamino-1,3-oxazin-4-one; alkoxycarbonylformylketene

In previous paper of this series,[3] we reported a synthesis of 5-halo-1,3-dioxin-4-ones (B) from the corresponding 5,6-unsubstituted dioxinones[4] (A) and their transformation to the dioxinones having an appropriate alkyl group at the 5-position (C) by palladium-catalyzed cross-coupling reactions with a variety of alkenes and alkynes followed by catalytic hydrogenation. At the same time, we have demonstrated that these dioxinones (C) can serve as equivalents of alkylated formylketenes (D), which are potential synthons for various 5-alkylated six-membered heterocycles (E) as well as formylacetic acid derivatives (F).

In order to explore further the utilization of 1,3-dioxin-4-ones in organic synthesis, a study was undertaken to investigate a new method for synthesizing so far unknown 1,3-dioxin-4-ones having a carboxyl group at the 5-position (G: R=H). These dioxinones not only are expected to be valuable synthons for a variety of heterocycles having a carboxyl group at the 5-position, but also may serve as an equivalent of acetoxymethylenemalonate (H),[5] which we have successfully utilized as the dienophile in Diels–Alder reactions with furan and cyclopentadiene for the synthesis of *C*-nucleosides (I) and their carbocyclic analogues (J).[5,6]

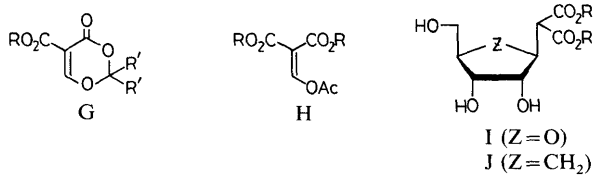


Fig. 1

In order to realize our plan mentioned above by the use of a general synthetic method for 6-unsubstituted dioxinones developed in our laboratory,[4] it was necessary to synthesize half esters of formylmalonic acid (**2** or **3**) as the starting material. This was accomplished from formyl Meldrum's acid[7] (**1**) in the following way. Thus, when **1** was reacted with an appropriate alcohol (methanol or benzyl alcohol) in benzene or chloroform at about 50—60 °C until all of the starting material (**1**) was consumed (*ca.* 0.5—1 h), the half ester (**2** or **3**) was obtained in a high yield as the sole product.[8]

The half ester (**2** or **3**) thus obtained, though recrystallizable in each case as a single stereoisomer [probably with a *cis* relationship (*cf.* the structure depicted in parenthesis) between the hydroxyl and carboxyl groups, see Experimental], was then subjected to the dioxinone formation reaction[4] (treatment of the half ester with an appropriate ketone in acetic anhydride containing a catalytic amount of *p*-toluenesulfonic acid at ambient tempera-

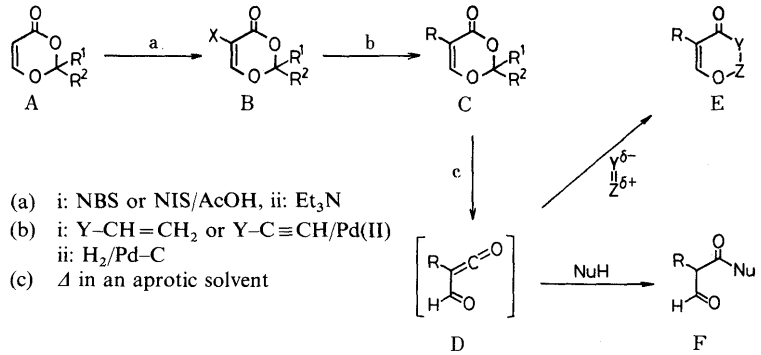
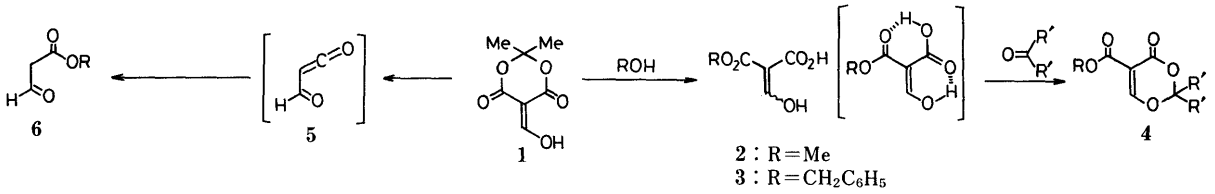


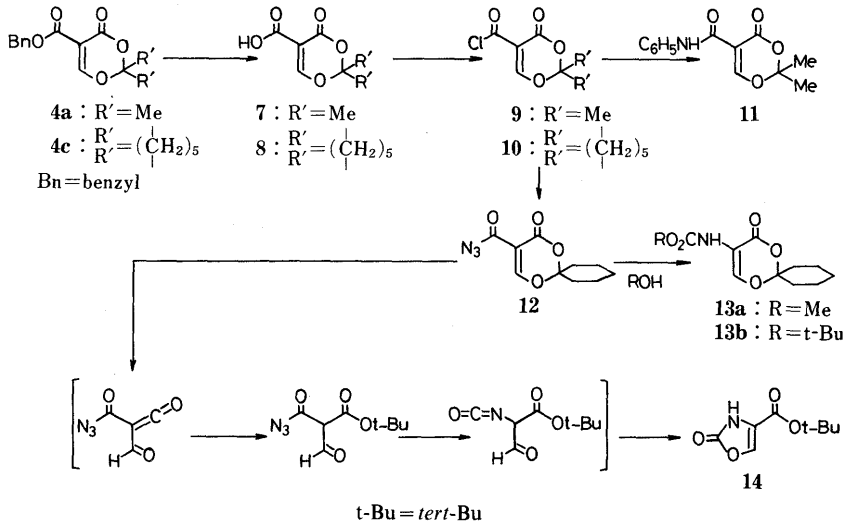
Chart 1



2 : R=Me
3 : R=$CH_2C_6H_5$

	R	R′
a	$CH_2C_6H_5$	CH_3
b	CH_3	$-(CH_2)_5-$
c	$CH_2C_6H_5$	$-(CH_2)_5-$
d	CH_3	CH_3

Chart 2



Bn=benzyl

t-Bu=*tert*-Bu

Chart 3

ture) to give the corresponding dioxinones (**4**) in satisfactory yields.

Though the dioxinones (**4**) thus obtained were all stable when they were crystallized from an appropriate aprotic solvent and could be stored indefinitely at room temperature under complete protection from moisture, it should be noted that the uncrystallizable dioxinones (such as **4d**) could not be isolated by silica gel column chromatography at room temperature due to facile decomposition by moisture, presumably because they are all good Michael acceptors (at the 6-position) and the Michael adducts thus formed have a very unstable acetal function. Such decomposition could be prevented, however, by carrying out the chromatography at a lower temperature (−20 °C) and the oily methyl ester (**4d**) was obtained in good yield.

In order to examine the chemical reactivity of **4** further, we first employed two compounds (**4a** and **4c**) as typical representatives. As expected, when **4a** was hydrogenated over palladium charcoal in ethyl acetate, the corresponding carboxylic acid (**7**) was obtained as the sole product. The structure of **7** was supported by satisfactory analytical and spectral data and by its conversion to **4d** by treatment with diazomethane.

The acid chloride (**9**) obtained by treatment of **7** with thionyl chloride was treated with aniline in tetrahydrofuran (THF) to give the corresponding anilide (**11**). The acid chloride (**10**) obtained from **4c** in the same manner, afforded the acyl azide (**12**) on treatment with sodium azide in aqueous acetonitrile. The azide (**12**) gave the urethanes (**13a**, **b**) when it was heated in appropriate alcohols. When *tert*-butyl alcohol was used in the above reaction, an appreciable amount of the oxazolone (**14**) was also obtained concomitantly. Since **13b** was recovered when it was refluxed in *tert*-butyl alcohol, it seems reasonable to assume that the formation of **14** occurred from **12** through initial ketene formation with retention of the acyl azide group (see the formulae shown in parenthesis in Chart 3), while initial rearrangement of acyl azide to isocyanate with retention of the dioxinone ring leads to the formation of **13b**.

Next, the dioxinone (**4a**) was subjected to thermal reaction. Thus, when **4a** was heated in boiling benzene (or toluene) containing dimethylcyanamide or phenyl isocyanate, the corresponding 1,3-oxazin-4-one (**15**) or 1,3-oxazine-2,4-dione (**16**) was obtained in good yield. These facts as well as the formation of the uracil derivative (**17**), when **4a** was reacted with 1,3-dimethylurea under comparable conditions, show clearly that **4a** upon heating even in benzene cycloreverts to the corresponding benzyloxycarbonylformylketene (**18**).

The ease of cycloreversion of 2,2-dimethyl-1,3-dioxin-4-ones to the corresponding acyl- or formyl-ketenes depends upon the presence of alkyl groups on the 5- and/or 6-positions. Thus, the temperature needed to cause this reaction in nonpolar solvents is 80—110 °C (*e.g.* reflux in

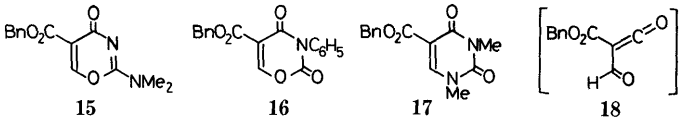


Fig. 2

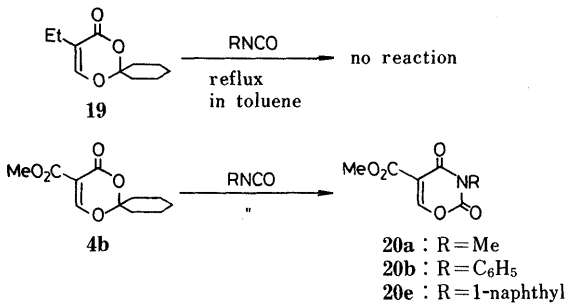


Chart 4

benzene or toluene) for 5,6-unsubstituted compounds, 110—140 °C (reflux in toluene or xylene) for 5- and 6-monoalkylated compounds, and 160—170 °C (reflux in mesitylene) for 5,6-dialkylated compounds.[9] The kind of substituent at the 2-position of the dioxinone ring also had significant effects upon the ease of the ring-opening reaction. Thus, 5-ethyl-4-oxo-1,3-dioxin-2-spirocyclohexane (**19**), previously synthesized in our laboratory,[3] was found to be stable in refluxing toluene, and hence an attempted reaction of **19** with an isocyanate resulted in complete recovery of the starting dioxinone. However, when **4b** was heated in toluene in the presence of isocyanates, the corresponding 1,3-oxazine-2,4-diones (**20**) were obtained in satisfactory yields. Though the reason is not clear at present, this fact shows that introduction of an electron-withdrawing alkoxycarbonyl group into the 5-position of the dioxinone ring facilitates the thermal ring opening to the corresponding ketene (*e.g.* **18**).

In conclusion, we have elaborated a novel method for the synthesis of 1,3-dioxin-4-ones having a carboxyl group at the 5-position (**4**) from formyl Meldrum's acid (**1**) *via* the half ester of formylmalonic acid (*e.g.* **2** or **3**). It has also been demonstrated by the present study that these dioxinone (**4**) can readily be converted to the alkoxycarbonylformylketenes under quite mild conditions irrespective of the kind of substituent at the 2-position. Since a carboxyl group can be transformed readily to an amino group (*e.g.* **13**), it is clear that the newly synthesized 5-alkoxycarbonyl-1,3-dioxin-4-ones (especially the benzylesters: **4a** and **4c**) not only represent the dioxinone having a one-carbon unit at the 5-position which could not be readily prepared by the previous method[4,9] (Chart 1), but also may serve as potential synthons for various 5-substituted six-membered heterocycles.

Use of these dioxinones (**4**) as well as the 1,3-oxazine-2,4-diones (**16** and **20**) derived from **4** as the dienophiles in Diels–Alder reaction is also in progress in our laboratories and the results will be reported in due course.

Experimental

All melting points were determined on a micro-hot stage (Yanagimoto) and are uncorrected. Infrared (IR) spectra were recorded on a JASCO A-102 spectrometer, ultraviolet (UV) spectra with a Hitachi 320 spectrometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra on a JEOL JNM-PMX60SI or JNM-FX-100 spectrometer (with tetramethylsilane as an internal standard). Mass spectra (MS) were taken either with a Hitachi M-52 spectrometer or with a JEOL JMS-01SG-2 spectrometer. Silica gel used for column chromatography was Wakogel C-200. Preparative thin-layer chromatography (PTLC) was performed on Merck Kieselgel 60 F254.

Methyl Hydrogen 2-Formylmalonate (2) A mixture of formyl Meldrum's acid (**1**,[7] 17.2 g, 0.1 mol), absolute methanol (6.4 g, 0.1 mol), and dry benzene (100 ml) was heated at 50—60 °C for 30 min with stirring. The solvent was evaporated off *in vacuo*. The residue was cooled in ice-water and washed with hexane to give crude **2** (13.9 g, 96%). A portion was recrystallized from dichloromethane–hexane to give prisms of mp 38—40 °C. IR ($CHCl_3$): 3400—2400, 1712, 1654, 1638, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.90 (3H, s, OMe), 8.46 (1H, s, =CH–), 13.4 (2H, br s, CO_2H and =CH–OH). *Anal.* Calcd for $C_5H_6O_5$: C, 41.10; H, 4.14. Found: C, 40.58; H, 3.99.

Benzyl Hydrogen 2-Formylmalonate (3) A mixture of **1** (17.2 g, 0.1 mol), benzyl alcohol (11.9 g, 0.11 mol), and chloroform (50 ml) was warmed at 40 °C for 7 h. The solvent was evaporated off *in vacuo*. The residue was washed with hexane to give crude **3** (17.8 g, 80%). A portion was recrystallized from ether–hexane to give needles of mp 54—56 °C. IR ($CHCl_3$): 3400—2400, 1710, 1605 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 5.33 (2H, s, CH_2), 7.40 (5H, s, C_6H_5), 8.48 (1H, s, =CH–), 12.23 (2H, br, CO_2H and =CH–OH). MS *m/z*: 222 (M^+). *Anal.* Calcd for $C_{11}H_{10}O_5$: C, 59.46; H, 4.54. Found: C, 59.30; H, 4.35.

Other alkyl hydrogen 2-formylmalonates were prepared from **1** and alcohols in a similar manner. Ethyl hydrogen 2-formylmalonate: yellowish oil. ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, t, J=7.5 Hz), 4.40 (2H, q, J=7.5 Hz), 8.53 (1H, s, =CH–), 13.40 (2H, br, CO_2H and =CH–OH). *tert*-Butyl hydrogen 2-formylmalonate: yellowish oil. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (9H, s, *tert*-Bu), 8.43 (1H, s, =CH–), 13.00 (2H, br, CO_2H and =CH–OH). Diphenylmethyl hydrogen 2-formylmalonate: needles of mp 85—87 °C (from ether–hexane). Yield, 65%. IR ($CHCl_3$): 3500—2400, 1710, 1650, 1605 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.06 [1H, s, $(C_6H_5)_2CH$], 7.35 (10H, s, 2×C_6H_5), 8.66 (1H, br s, =CH–), 12.65 (2H, br, CO_2H and =CH–OH). MS *m/z*: 297 (M^+-1), 254 (M^+-CO_2). *Anal.* Calcd for $C_{17}H_{14}O_5$: C, 68.45: H, 4.73. Found: C, 68.20; H, 4.51.

Benzyl 2,2-Dimethyl-4-oxo-1,3-dioxin-5-carboxylate (4a) A mixture of crude **3** (8.88 g, 40 mmol), acetone (4.68 g, 80 mmol), and acetic anhydride (8.17 g, 80 mmol) was stirred under ice-salt cooling. Concentrated sulfuric acid (784 mg, 8 mmol) was added to the mixture dropwise at below −5 °C. Then, the mixture was stirred at 0 °C for 4 h. Ice-water was added and precipitated crystals were collected by suction, washed with water and dried. The crude **4a** [7.37 g (70%)] was recrystallized from ether to give prisms of mp 78—80 °C. IR ($CHCl_3$): 1770, 1710, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (6H, s, 2×Me), 5.30 (2H, s, OCH_2-), 7.40 (5H, s, C_6H_5), 8.15 (1H, s, 6-CH). MS *m/z*: 261 (M^+-1), 204 (M^+−acetone). *Anal.* Calcd for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 63.87; H, 5.37.

Methyl 4-Oxo-1,3-dioxin-2-spirocyclohexane-5-carboxylate (4b) A mixture of crude **2** (18.9 g, 0.13 mol), cyclohexanone (25.5 g, 0.26 mmol), acetic anhydride (26.8 g, 0.26 mol), and *p*-toluenesulfonic acid (2.5 g, 13 mmol) was stirred at 0 °C for 30 min and then at room temperature for 3 h. The reaction mixture was poured onto ice-water with stirring. Separated crystals were collected by suction, washed with water, and dried. Recrystallization from ether gave 16.7 g (57%) of **4b** as prisms of mp 87—89 °C. IR ($CHCl_3$): 1769, 1712, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.70 (10H, m, C_5H_{10}), 3.80 (3H, s, OMe), 8.17 (1H, s, 6-CH). *Anal.* Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.27; H, 6.35.

Benzyl 4-Oxo-1,3-dioxin-2-spirocyclohexane-5-carboxylate (4c) A mixture of crude **3** (4.44 g, 20 mmol), cyclohexanone (3.93 g, 40 mmol), acetic anhydride (4.08 g, 40 mmol), and *p*-toluenesulfonic acid (380 mg, 2 mmol) was stirred at room temperature for 4 h. Separated crystals were collected by suction, washed with hexane and then with water, and dried. The crude **4c** (5.69 g, 94%) was recrystallized from ether to give prisms of mp 87.5—89 °C. IR ($CHCl_3$): 1780, 1710, 1605 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.70 (10H, m, C_5H_{10}), 5.30 (2H, s, $-OCH_2$) 7.40 (5H, m, C_6H_4), 8.16 (1H, s, 6-CH). MS *m/z*: 302 (M^+). *Anal.* Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.61; H, 5.88.

Methyl 2,2-Dimethyl-4-oxo-1,3-dioxin-5-carboxylate (4d) A mixture of crude **2** (438 mg, 3 mmol), acetone (348 mg, 6 mmol), and acetic anhydride (612 mg, 6 mmol) was stirred under ice-salt cooling. Concentrated sulfuric acid (100 mg) was added to the mixture at below −5 °C. The mixture was stirred for 1.5 h at 0 °C and directly subjected to silica gel

column chromatography at −20 °C. Elution with a mixture of hexane and ethyl acetate (2:1, v/v) gave **4d** as an oil. Yield, 377 mg (56%). IR ($CHCl_3$): 1775, 1710, 1605 cm^{-1}. ^{1}H-NMR (CCl_4) δ: 1.80 (6H, s, 2×Me), 3.85 (3H, s, OMe), 8.10 (1H, s, 6-CH). MS *m/z*: 186 (M^+), 127 (M^+ − acetone).

2,2-Dimethyl-4-oxo-1,3-dioxin-5-carboxylic Acid (7) Compound **4a** (1.31 g, 5 mmol) was hydrogenated over 10% Pd–C (100 mg) in ethyl acetate (25 ml) at room temperature under atmospheric pressure. The catalyst was filtered off. Evaporation of the solvent *in vacuo* gave **7**, 0.78 g (98%). Recrystallization from a mixture of ether and hexane gave prisms of mp 78—80 °C. IR ($CHCl_3$): 3350—2950, 1760, 1700, 1605 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (6H, s, 2×Me), 8.92 (1H, s, 6-CH), 11.62 (1H, br s, CO_2H). High-resolution MS *m/z*: M^+ Calcd for $C_7H_8O_5$: 172.0371. Found: 172.0372.

4-Oxo-1,3-dioxin-2-spirocyclohexane-5-carboxylic Acid (8) Following the procedure given for the preparation of **7**, compound **4c** (1.51 g, 5 mmol) was hydrogenated to give **8**, 1.06 g (100%). Recrystallization from a mixture of hexane and ether gave prisms of mp 102—103.5 °C. IR ($CHCl_3$): 3300—3000, 1755, 1695, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.30—2.40 (10H, m, C_5H_{10}), 8.35 (1H, s, 6-CH), 10.06 (1H, br s, CO_2H). MS *m/z*: 212 (M^+). *Anal.* Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.60; H, 5.62.

Methylation of 7 to Give 4d A slight excess of diazomethane was added to a solution of **7** (172 mg, 1 mmol) in ether under ice-cooling. Evaporation of the solvent gave **4d** as an oil, whose ^{1}H-NMR and IR data were identical with those of **4d** obtained by the condensation of **2** with acetone.

2,2-Dimethyl-5-(*N*-phenylcarbamoyl)-1,3-dioxin-4-one (11) A mixture of crude **7** (185 mg, 1.08 mmol) and thionyl chloride (3 ml) was stirred at room temperature for 1 h. Excess thionyl chloride was evaporated off *in vacuo* to give the crude chloride **9** as an oil. Aniline (300 mg) was added to a solution of **9** in dichloromethane with stirring under ice-cooling. The mixture was stirred for 30 min, diluted with dichloromethane and washed with 5% hydrochloric acid and brine successively. Purification of the organic layer by column chromatography (silica gel, 5 g) gave **11** as yellowish leaves of mp 103—104 °C (recrystallized from dichloromethane–hexane). Yield, 65 mg (24%). IR ($CHCl_3$): 3320, 1720, 1665, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.80 (6H, s, 2×Me), 6.83—7.90 (5H, m, C_6H_5), 8.36 (1H, s, 6-CH), 10.10 (1H, br s, NH). MS *m/z*: 247 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_5$: C, 63.14; H, 5.30; N, 5.67. Found: C, 63.02; H, 5.22; N, 5.58.

5-Azidocarbonyl-4-oxo-1,3-dioxin-2-spirocyclohexane (12) Compound **8** (3.12 g, 14.7 mmol) was stirred with thionyl chloride (30 ml) at room temperature for 30 min. Excess thionyl chloride was evaporated off and the acid chloride (**10**) was dissolved in acetonitrile (10 ml). A solution of sodium azide (4.78 g, 73.5 mmol) in water (20 ml) was added dropwise to the above solution over 10 min under ice-salt cooling. The mixture was stirred for an additional 30 min and extracted with ether. The extract was washed with brine, dried over magnesium sulfate, and evaporated *in vacuo* to give **12** as a solid. Recrystallization from ether gave pure **12** as yellowish prisms of mp 87—89 °C (dec.). Yield, 1.59 g (46%). IR ($CHCl_3$): 2150, 1765, 1675, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.25—2.25 (10H, m, C_5H_{10}), 8.26 (1H, s, 6-CH). MS *m/z*: 237 (M^+). *Anal.* Calcd for $C_{10}H_{11}N_3O_4$: C, 50.63; H, 4.67; N, 17.72. Found: C, 50.74; H, 4.51; N, 17.78.

Methyl 4-Oxo-1,3-dioxin-2-spirocyclohexane-5-carbamate (13a) A solution of **12** (24 mg, 0.1 mmol) in absolute methanol (2 ml) was heated at 50 °C for 2 h. The solvent was evaporated off *in vacuo* and the residue was purified by PTLC (hexane–ethyl acetate, 2:1, v/v) to give **13a** as an oil. Yield, 5.1 mg (21%). IR ($CHCl_3$): 3425, 1715, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.15—2.26 (10H, m, C_5H_{10}), 3.75 (3H, s, Me). 6.30 (1H, br s, NH), 7.76 (1H, s, 5-CH). High-resolution MS *m/z*: for $C_{11}H_{15}NO_5$: 241.0949. Found: 241.0940.

***tert*-Butyl 4-Oxo-1,3-dioxin-2-spirocyclohexane-5-carbamate (13b) and *tert*-Butyl 2,3-Dihydro-2-oxooxazole-4-carboxylate (14)** A solution of **12** (1.42 g, 6 mmol) in dry *tert*-butyl alcohol (50 ml) was heated at 50 °C for 2.5 h. The solvent was evaporated off *in vacuo* and the residue was chromatographed on a silica gel (75 g) column. Elution with a mixture of hexane and ethyl acetate (10:1, v/v) gave **13b** as prisms of mp 93.5—95 °C (recrystallized from hexane). Yield, 722 mg (42%). IR ($CHCl_3$): 3450, 1725, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.50 (9H, s, *tert*-Bu), 1.25—2.25 (10H, m, C_5H_{10}), 6.30 (1H, br s, NH), 7.75 (1H, s, 6-CH). MS *m/z*: 283 (M^+). *Anal.* Calcd for $C_{14}H_{21}NO_5$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.34; H, 7.61; N, 4.92. Further elution with a mixture of hexane and ethyl acetate (5:1, v/v) gave **14** as needles of mp 138.5—140 °C (recrystallized from hexane–ether). Yield, 420 mg (38%). IR ($CHCl_3$): 3450, 1805, 1770, 1717, 1628 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.55 (9H, s, *tert*-Bu), 7.30 (1H, s, 4-CH), 8.75 (1H, br, NH). MS *m/z*: 185 (M^+). *Anal.* Calcd for $C_8H_{11}NO_4$: C, 51.88; H, 5.99; N, 7.56. Found: C, 51.88; H, 5.84; N, 7.55.

Benzyl 2-Dimethylamino-4-oxo-1,3-oxazine-5-carboxylate (15) A solution of **4a** (262 mg, 1 mmol) and dimethylcyanamide (77 mg, 1.1 mmol) in dry benzene (3 ml) was refluxed for 15 min. The solvent was evaporated off *in vacuo* and the residue was washed with ether to give crystalline **15**. Yield, 228 mg (83%). Recrystallization from hexane–benzene gave needles of mp 101—103 °C. IR ($CHCl_3$): 1752, 1712, 1678, 1650, 1588 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.15 (6H, s, 2×Me), 5.31 (2H, s, CH_3), 7.40 (5H, s, C_6H_5), 8.13 (1H, s, 6-CH). High-resolution MS *m/z*: M^+ Calcd for $C_{14}H_{14}N_2O_2$: 274.0953. Found: 274. 0961.

Benzyl 2,4-Dioxo-3-phenyl-1,3-oxazine-5-carboxylate (16) A solution of **4a** (262 mg, 1 mmol) and phenyl isocyanate (119 mg, 1 mmol) in dry toluene (2 ml) was refluxed for 1 h. The solvent was evaporated off *in vacuo* and the crystalline residue was washed with ether to give **16**. Yield, 209 mg (65%). Recrystallization from acetone gave needles of mp 197—198 °C. IR ($CHCl_3$): 1785, 1755, 1735, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 5.35 (2H, s, CH_2), 7.37 (10H, m, 2×C_6H_5), 8.36 (1H, s, 6-CH). MS *m/z*: 323 (M^+). *Anal.* Calcd for $C_{18}H_{13}NO_5$: C, 66.87; H, 4.05; N, 4.33. Found: C, 67.08; H, 4.05; N, 4.41.

Benzyl 1,3-Dimethyl-2,4-dioxopyrimidine-5-carboxylate (17) A mixture of **4a** (52.4 mg, 0.2 mmol), powdered 1,3-dimethylurea (17.6 mg, 0.2 mmol), and dry benzene (1 ml) was refluxed for 15 min. The solvent was evaporated off and the residue was purified by PTLC [dichloromethane–methanol (50:1, v/v)] to give **17** as needles of mp 135—136 °C (recrystallized from ethyl acetate). Yield, 39.3 mg (72%). IR ($CHCl_3$): 1750, 1700, 1660, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.33 and 3.45 (each 3H, s, Me), 5.30 (2H, s, CH_2), 7.36 (5H, br s, C_6H_5), 8.18 (1H, s, 6-CH). MS *m/z*: 274 (M^+). *Anal.* Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21. Found: C, 61.39; H, 4.98; N, 10.21.

Methyl 3-Methyl-2,4-dioxo-1,3-oxazine-5-carboxylate (20a) A solution of **4b** (1.13 g, 5 mmol) and methyl isocyanate (0.57 g, 10 mmol) in dry toluene (10 ml) was refluxed for 5 h. The solvent was evaporated off and the residue was washed with ether to give **20a**, 538 mg (58%). Recrystallization from hexane–ethyl acetate gave needles of mp 104—106 °C. IR ($CHCl_3$): 1788, 1754, 1731, 1708, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.33 (3H, s, NMe), 3.86 (3H, s, OMe), 8.23 (1H, s, 6-CH). *Anal.* Calcd for $C_7H_7NO_5$: C, 45.41; H, 3.81; N, 7.57. Found: C, 45.81; H, 3.51; N, 7.53.

Methyl 2,4-Dioxo-3-phenyl-1,3-oxazine-5-carboxylate (20b) Following the procedure given for **20a**, **4b** (13.4 g, 59.3 mmol) was heated with phenyl isocyanate (8.5 g, 71.2 mmol) for 9 h to give crude **20b**, 13.5 g (92%). Recrystallization from ethyl acetate gave leaves of mp 180—182 °C. IR ($CHCl_3$): 1792, 1761, 1738, 1716, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.86 (3H, s, OMe), 7.42 (5H, m, C_6H_5), 8.13 (1H, s, 6-CH). *Anal.* Calcd for $C_{12}H_9NO_5$: C, 58.30; H, 3.67; N, 5.67. Found: C, 58.52; H, 3.84; N, 5.74.

Methyl 3-(1-Naphthyl)-2,4-dioxo-1,3-oxazine-5-carboxylate (20c) Following the procedure given for **20a**, **4b** (1.13 g, 5 mmol) was heated with 1-naphthyl isocyanate (3.30 g, 5 mmol) for 10 h to give crude **20c**, 2.25 g (50%). Recrystallization from ethyl acetate gave leaves of mp 198—200 °C. IR ($CHCl_3$): 1785, 1758, 1731, 1715, 1634, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.90 (3H, s, OMe), 7.67 (7H, m, naphthyl), 8.42 (1H, s, 6-CH). *Anal.* Calcd for $C_{16}H_{11}NO_5$: C, 64.14; H, 3.73; N, 4.71. Found: C, 64.38; H, 3.72; N, 4.63.

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