Cycloadditions in Syntheses. Part 28.[1] 2-Azabicyclo[2.2.0]hexane-3,5-dione and its Derivatives: Synthesis and Transformation to Azetidin-2-ones[2]

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2-Azabicyclo[2.2.0]hexane-3,5-dione has been synthesized *via* photopyridone formation from 4-(dimethyl-t-butylsiloxy)- or 4-alkoxy-2-pyridones followed by mild acid hydrolysis. The title compound and its derivatives react with a variety of nucleophiles (ROH, RR'NH, RSH, or RMgBr) to give azetidin-2-ones having an acetic acid or acylmethyl side-chain at the 4-position, and hence serve as new building blocks for carbapenem nuclei.

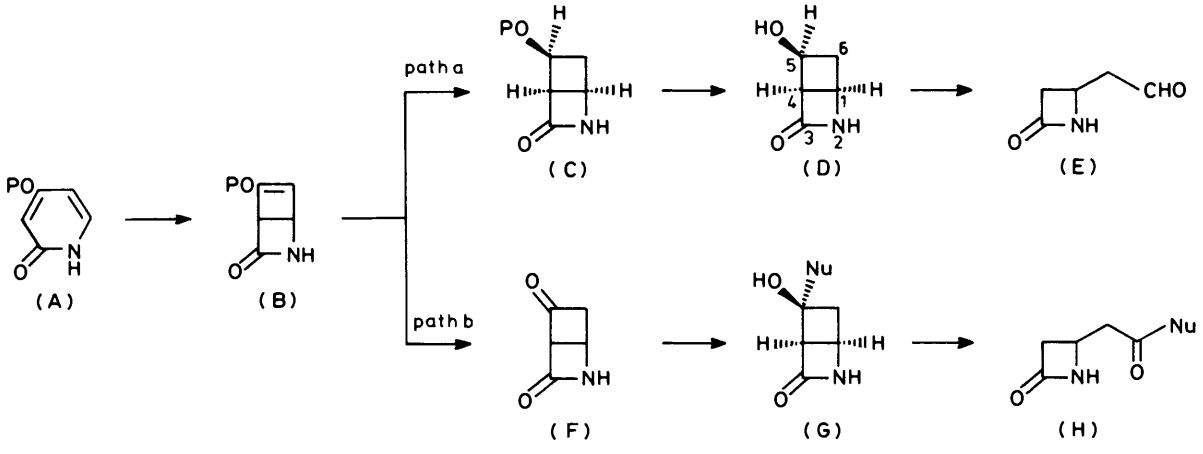
2-Pyridones (A) having an oxygen functional group at the 4-position do not dimerize under ordinary irradiation conditions, but give the photopyridones {2-azabicyclo[2.2.0]hex-5-en-3-ones (B)} *via* the S_1 state in good yield.[3] Now since the photopyridones consist of fused β-lactam and cyclobutene rings, selective cleavage of the cyclobutane ring would produce β-lactams. From this point of view, Brennan[4] and Kametani *et al.*[5] reported independently the synthesis of 3,4-disubstituted azetidin-2-ones by ozonolysis of the olefinic bond in the photopyridones (B). If the C-4–C-5 bond of compounds (B) can be cleaved selectively, it is expected that azetidin-2-ones having a two-carbon unit at the 4-position should be obtained, and these compounds should be more versatile key intermediates for carbapenem nuclei. In the preceding paper,[1] we reported the synthesis of 5-hydroxy-2-azabicyclo[2.2.0]hexan-3-one (D) from these photopyridones (B) *via* intermediate (C), and its ready retro-aldol-type C-4–C-5 bond cleavage to give β-lactams, and demonstrated its chemical equivalence to 4-(2-oxoethyl)azetidin-2-one (E) (Scheme 1, path a). It is obvious that if the 5-oxo derivative of (D) can be synthesized, it would react with nucleophiles ($Nu:^-$) to give the azetidin-2-ones (H) *via* formation of the adduct (G) followed by similar C–C bond cleavage (Scheme 1, path b).

In this paper, we report the conversion of photopyridones (B) into 2-azabicyclo[2.2.0]hexane-3,5-diones [*e.g.* (F)] and their reaction with nucleophiles to give the 4-substituted azetidin-2-ones (H).

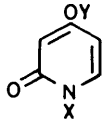
First, we achieved the synthesis of 2-azabicyclo[2.2.0]hexane-3,5-dione (**3a**) by using the 4-siloxy-2-pyridone (**1a**) as the starting material. Thus, 5-(dimethyl-t-butylsiloxy)-2-azabicyclo[2.2.0]hex-5-en-3-one (**2a**)[1] prepared by irradiation (≥ 300 nm) of pyridone (**1a**) in ether was treated with trifluoroacetic acid (TFA) in aqueous tetrahydrofuran (THF) to give the azabicyclohexanedione (**3a**) in 62% yield. Similar removal of the silyl group from compound (**2a**) also proceeded in aqueous THF in the presence of toluene-*p*-sulphonic acid (PTSA), Dowex 50W (H^+-form), or even 10% hydrochloric acid, instead of TFA. The stability of dione (**3a**) under acidic conditions prompted us to investigate a simpler synthesis of this compound. Thus, treatment of the photopyridones (**2b** and **c**)[1,3] in aqueous THF in the presence of a small amount of 10% hydrochloric acid gave dione (**3a**) in 51 and 72% yield, respectively. Similarly, the *N*-alkylated photopyridones (**2d**—**f**) derived from the 2-pyridones (**1d**—**f**) were transformed to the corresponding azabicyclohexanediones (**3b**—**d**), all in high yield.

Compound (**3a**), when treated with sodium borocyanohydride in a mixture of THF and acetic acid, gave *rel*-(1*R*,4*R*,5*S*)-5-hydroxy-2-azabicyclo[2.2.0]hexan-3-one (**4**) in 41% yield. Identity of compound (**4**) with that reported in the preceding paper[1] indicates that the reduction of the keto function in dione (**3a**) has occurred from the less hindered side. Though oxidation of ketol (**4**) with pyridinium chlorochromate in dichloromethane gave dione (**3a**) in 35% yield and hence provides another route to this dione *via* path a, the present method (path b) for the synthesis of dione (**3a**) is far superior in its short steps and high overall yield.

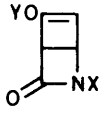
Next, we investigated the reaction of dione (**3a**) with a variety of nucleophiles with the intention of obtaining β-lactams. When



Scheme 1. P is an appropriate protecting group

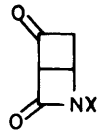


(1)

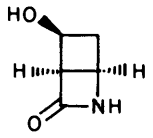


(2)

a; X = H, Y = $SiMe_2Bu^t$
b; X = H, Y = Me
c; X = H, Y = CH_2Ph
d; X = Me, Y = CH_2Ph
e; X = CH_2Ph, Y = CH_2Ph
f; X = $CH_2CO_2CH_2Ph$, Y = CH_2Ph
g; X = Me, Y = $SiMe_2Bu^t$

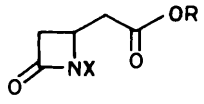


(3)



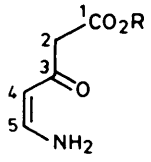
(4) ≡(D)

a; X = H
b; X = Me
c; X = CH_2Ph
d; X = $CH_2CO_2CH_2Ph$



(5)

a; X = H, R = Me
b; X = H, R = Et
c; X = H, R = CH_2Ph
d; X = Me, R = Me
e; X = Me, R = CH_2Ph
f; X = $CH_2CO_2CH_2Ph$, R = Me

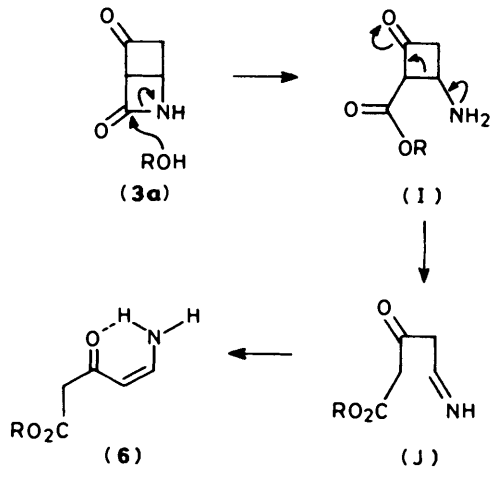


(6)

a; R = Me
b; R = Et
c; R = CH_2Ph

a solution of compound (**3a**) in absolute methanol was refluxed for 1 h, 4-(methoxycarbonylmethyl)azetidin-2-one (**5a**) was obtained in 77% yield, together with a trace of the β-keto ester (**6a**). The same type of compound, (**6b** and **c**), was obtained as the major product, when dione (**3a**) was heated in absolute ethanol or in THF containing benzyl alcohol. The formation of these compounds (**6a**—**c**) may be explained by assuming an initial N-2–C-3 bond cleavage of dione (**3a**), followed by subsequent ring opening [intermediates (I) and (J)] as depicted in Scheme 2.

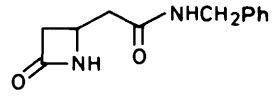
The desired azetidinones (**5a**—**c**) were all obtained in satisfactory yields when dione (**3a**) was treated with these alcohols in the presence of pyridine, and the reactions proceeded even at room temperature. Similarly, treatment of the *N*-alkylated 2-azabicyclohexanes (**3b**—**d**) with methanol or benzyl alcohol containing pyridine afforded *N*-alkylazetidin-2-ones (**5d**—**f**) in the respective yields of 80, 90, and 77%. By analogy with the reaction with alcohols, benzylamine or toluene-α-thiol also reacted with dione (**3a**) to give the amide (**7**) or thioester (**8a**) in 34 and 51% yield, respectively. Similarly, reaction of dione (**3b**) with toluene-α-thiol produced thioester (**8b**) in 61% yield. In the above experiments, it was shown that dione (**3a**)



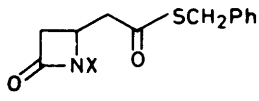
(3a) (I) (J) (6)

Scheme 2.

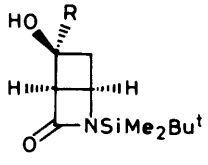
and its derivatives reacted successfully with *O*-, *N*-, and *S*-nucleophiles to give azetidin-2-one derivatives (**5**), (**7**), and (**8**). Hence, we then extended these reactions to those using Grignard reagents as *C*-nucleophiles. First, we examined the reaction of dione (**3a**) with methylmagnesium bromide in ether, but obtained a complicated mixture which was inseparable by chromatography. Since the above failure may be due to the presence of the unprotected NH group in dione (**3a**), we next employed the *N*-silylated 2-azabicyclohexanedione (**3**; X = $SiMe_2Bu^t$) as the starting material. The silylated dione was readily prepared by direct treatment of the photopyridone (**2a**) with dimethyl-t-butylsilyl chloride(TBDSC)–imidazole in



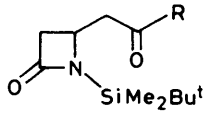
(7)



(8) **a**; X = H
b; X = Me



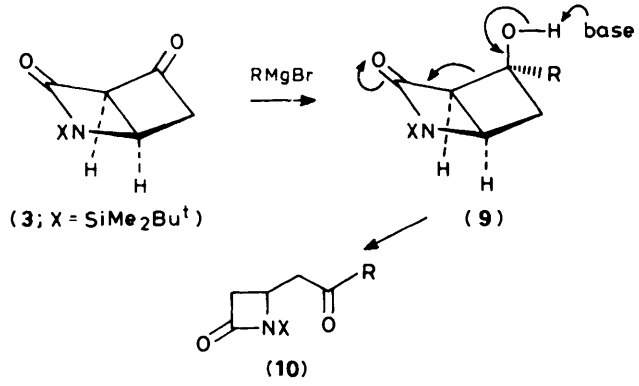
(9) **a**; R = Me
b; R = Et
c; R = Ph



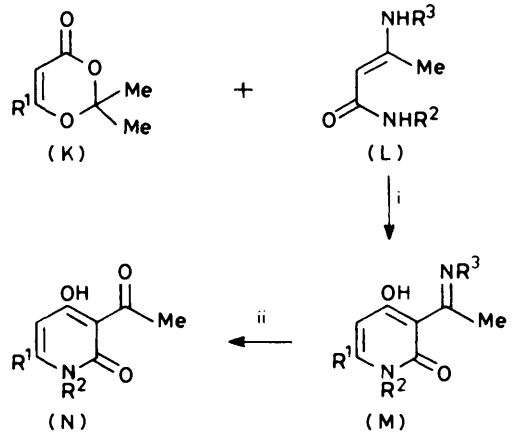
(10) **a**; R = Me
b; R = Et

dimethylformamide (DMF). Deprotection of the *O*-silyl group and *N*-silylation take place in compound enone (**2a**) simultaneously. Compound (**3**; X = $SiMe_2Bu^t$) was treated with 1.2 mol equiv. of methylmagnesium bromide in ether under ice-cooling to give the adduct (**9a**) in 40% yield as the sole detectable product. The i.r. spectrum of adduct (**9a**) showed absorption bands at 3 375 and 1 720 cm^{-1}, indicating the presence of hydroxy and β-lactam carbonyl groups, respectively. As detailed in the Experimental section, the n.m.r. spectrum of adduct (**9a**) also supports the assigned structure. Although the configuration of adduct (**9a**) is not clear at present, the *exo*-configuration of the methyl group is a reasonable deduction, because attack of the reagent on the carbonyl group should occur from the less hindered side (Scheme 3).

Similar reaction of compound (**3**; X = $SiMe_2Bu^t$) with ethyl- or phenyl-magnesium bromide gave the corresponding adducts



Scheme 3.



Scheme 4. *Reagents/conditions*: i, heat; ii, H_3O^+

(**9b** and **c**). Since these adducts (**9**) may be cleaved between the C-4 and C-5 positions just as in 5-hydroxy-2-azabicyclo-[2.2.0]hexan-3-one (**4**),[1] we then investigated the reaction of adducts (**9**) with a variety of bases and found that 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) is effective for this reaction. When a solution of adduct (**9a**) in benzene containing DBU was kept at room temperature, the azetidinone (**10a**) was obtained in 47% yield. Though the same reaction also proceeded for adduct (**9b**), compound (**9c**) was inert under these conditions and was recovered quantitatively.

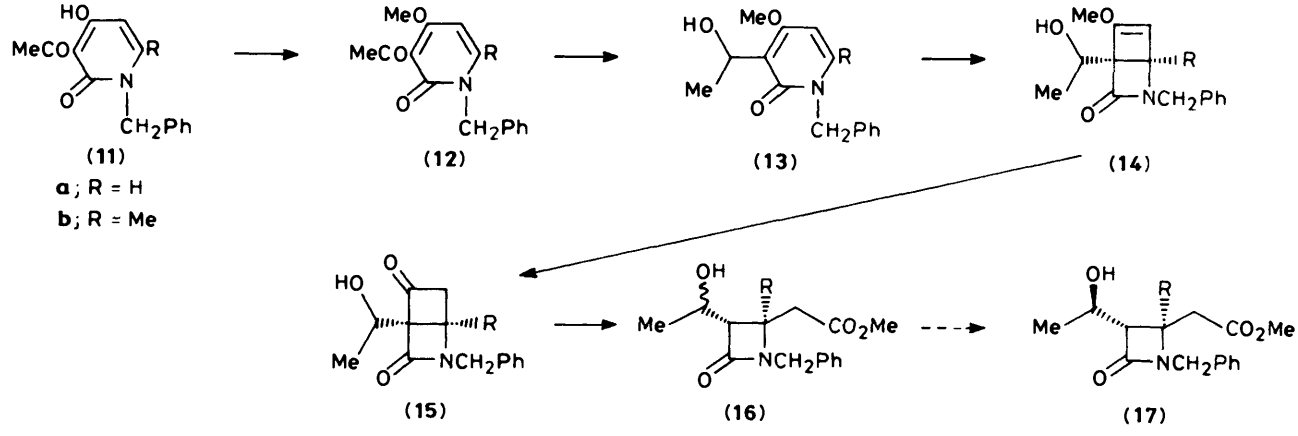
Thus, we have accomplished the synthesis of 2-azabicyclo-[2.2.0]hexane-3,5-dione (**3a**) and its successful conversion into azetidin-2-ones having a β-oxoethyl side-chain at the 4-position (H; Nu = OR, NRR′, SR, and R in Scheme 1). This synthetic method is also applicable to a variety of substituted derivatives of azetidinone (H) by use of an appropriately substituted 4-hydroxy-2-pyridone as starting material.

In order to demonstrate a wide applicability of the above method, we then applied it to the synthesis of 3-(1-hydroxyethyl)azetidnones [*e.g.* (**17**)]. In the synthesis of thienamycin derivatives from the azetidinones (H), it is necessary to introduce the 1-hydroxyethyl side-chain at the 3-position of the azetidinone ring at some stage. For this purpose, acetaldehyde is condensed with an azetidinone ring under strongly basic conditions.[6] If our method can be applied successfully for this purpose, 3-(1-hydroxyethyl)-4-methoxy-2-pyridones [*e.g.* (**13**)] are the choice for the starting material. Very recently, we have found that a 2,2-dimethyl-1,3-dioxin-4-one (K) reacts with 3-aminobut-2-enamides (L) when heated in an aprotic solvent, to give 3-(1-iminoethyl)-4-hydroxy-2-pyridones (M), which by subsequent acid hydrolysis give the acetyl derivatives (N) (Scheme 4).[7]

The 6-methyl derivative of (N) was also synthesized by the same procedure, but using diketene instead of the dioxinone (K).

Based on these facts, we have synthesized 1-benzyl-3-(1-hydroxyethyl)-4-methoxy-2-pyridone (**13a**) and its 6-methyl derivative (**13b**) from 3-acetyl-4-hydroxy-2-pyridones (**11a,b**), by initial methylation to give the methyl ethers (**12a,b**), followed by reduction with sodium borohydride. 1-Benzyl-3-(1-hydroxyethyl)-4-methoxy-2-pyridone (**13a**) was converted into 1-benzyl-3-(1-hydroxyethyl)-4-(methoxycarbonylmethyl)azetidin-2-one (**16a**) in three steps in 35% overall yield (Scheme 5). Since we have used racemic pyridone (**13a**) as the starting material, all of the products (**14a**), (**15a**), and (**16a**) obtained after photo-pyridone formation were mixtures of stereoisomers at the 1-position of the hydroxyethyl chain. However, it is obvious that the configuration between the 3- and 4-position in compound (**16a**) is *trans*, as evidenced by a small coupling constant (J 3 Hz) between the protons at C-3 and C-4. Though we did not succeed in our attempts at stereospecific synthesis of the desired azetidinone (**17a**) having the correct *R*-configuration at the 1′-position, compound (**17a**) can be synthesized readily from the above stereoisomeric mixture (**16a**) by the application of Karady's method.[8] The fact that the same transformation was also successful for the 6-methyl derivative (**13b**) indicates that the present method is also applicable to the synthesis of (**16**)-type azetidinones.

In conclusion, we have succeeded in the synthesis of 2-azabicyclo[2.2.0]hexane-3,5-dione (**3a**), from 2-pyridones having an appropriately protected 4-hydroxy group, in two



Scheme 5.

steps, both of which can be carried out on a multigram scale. Also, compound (**3a**) and its derivatives obtained by the present method were found to react with a variety of nucleophiles under mild conditions to give azetidin-2-ones (**5**), (**7**), (**8**), (**10**), and (**16**). Hence, we believe that dione (**3a**) and its derivatives can serve as equivalents of the latter azetidinones and provide new building blocks for carbapenem nuclei.

Experimental

M.p.s were determined on a Yanaco micromelting point apparatus (MP-S2) and are uncorrected. I.r. spectra were recorded on a JASCO A-102 spectrophotometer. ^{1}H N.m.r. spectra were recorded using tetramethylsilane as internal standard on JEOL JNM PMX-60 and FX-100 spectrometers at 60 MHz and 100 MHz, respectively. Mass spectra were recorded on a Hitachi model M-52, and high-resolution mass spectra on a JEOL-01SG-2 system. U.v. spectra were recorded on a Hitachi 320 spectrophotometer. The irradiation source used for photoreactions was a high-pressure mercury lamp (Ushio 450 W or Riko UVL 400HA, Pyrex filter) or Rayonet photochemical reactor lamps (Cat. No. RPR-3000 Å). Wakogel (C-200) was employed for silica gel column chromatography. Merck Kieselgel 60F 254 was employed for t.l.c.

4-Benzyloxy-1-methyl-2-pyridone (**1d**).—A suspension of 4-benzyloxy-2-pyridone (**1c**)[9] (2.59 g, 12 mmol) and dimethyl sulphate (1.76 g, 14 mmol) in 1M-aqueous NaOH (14 ml) was shaken at room temperature for 1 h. The mixture was made alkaline with 1M-aqueous NaOH, and then extracted with chloroform. The extract was dried over anhydrous sodium sulphate, and the solvent was evaporated off under reduced pressure to give the *product* (**1d**) (1.8 g, 65%) as needles (from ether), m.p. 96—98 °C (Found: C, 72.4; H, 6.15; N, 6.25. $C_{13}H_{13}NO_2$ requires C, 72.55; H, 6.1; N, 6.5%); δ_H ($CDCl_3$) 3.52 (3 H, s, Me), 5.02 (2 H, s, CH_2Ph), 5.92 (1 H, d, *J* 6.5 Hz, 5-H), 6.05 (1 H, s, 3-H), 7.10 (1 H, d, *J* 6.5 Hz, 6-H), and 7.40 (5 H, s, Ph).

1-Benzyl-4-benzyloxy-2-pyridone (**1e**).—A suspension of 4-benzyloxy-2-pyridone (**1c**)[9] (1.01 g, 5 mmol), benzyl bromide (4.3 g, 25 mmol), powdered NaOH (1.4 g, 25 mmol), and tetra-n-butylammonium hydrogen sulphate (680 mg, 2 mmol) in benzene (180 ml) was stirred and refluxed for 1 h. The solvent was evaporated off under reduced pressure, and the residue was dissolved in a mixture of chloroform (15 ml) and water (15 ml). The chloroform layer was washed with water, and dried over anhydrous sodium sulphate. The solvent was evaporated off under reduced pressure to give the *product* (**1e**) (1.4 g, 90%) as needles (from ethyl acetate), m.p. 133—134 °C (Found: C, 78.55; H, 5.85; N, 4.6. $C_{19}H_{17}NO_2$ requires C, 78.35; H, 5.9; N, 4.8%); $\nu_{max.}$ ($CHCl_3$) 1 645 cm^{-1}; δ_H ($CDCl_3$) 5.00 (2 H, s, NCH_2Ph), 5.09 (2 H, s, OCH_2Ph), 5.80—6.15 (2 H, m, 3- and 5-H), 7.14 (1 H, d, *J* 7 Hz, 6-H), 7.33 (5 H, s, NCH_2*Ph*), and 7.42 (5 H, s, OCH_2*Ph*).

4-Benzyloxy-1-benzyloxycarbonylmethyl-2-pyridone [*Benzyl* (*4-Benzyloxy-2-oxo-1,2-dihydropyridin-1-yl*)*acetate*] (**1f**).—Sodium hydride (60% dispersion) (0.29 g, 0.012 mol) was added to a stirred, ice-cooled solution of compound (**1c**)[9] (2.01 g, 0.01 mol) in hexamethylphosphoramide (25 ml). The mixture was stirred at room temperature until the sodium salt of compound (**1c**) had formed completely. Benzyl bromoacetate (2.75 g, 0.012 mol) was added to the mixture, and the resulting mixture was stirred for 2 h at room temperature, and then poured into ice–water; the precipitated crystals were collected by suction, dried, and subjected to silica gel column chromatography. Elution with chloroform gave the *product* (**1f**) (2.62 g, 75%) as needles (from hexane–chloroform), m.p. 119—120 °C (Found: C, 72.15; H, 5.25; N, 3.7. $C_{21}H_{19}NO_4$ requires C, 72.2; H, 5.5; N, 4.0%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 660 cm^{-1}; δ_H ($CDCl_3$) 4.63 (2 H, s, NCH_2), 5.00 (2 H, s, 4-OCH_2Ph), 5.22 (2 H, s, CO_2CH_2Ph), 5.90—6.20 (2 H, m, 3- and 5-H), 7.09 (1 H, d, *J* 8 Hz, 6-H), 7.35 (5 H, s, Ph), and 7.38 (5 H, s, Ph).

5-Benzyloxy-2-methyl-2-azabicyclo[2.2.0]*hex-5-en-3-one* (**2d**).—A solution of 4-benzyloxy-1-methyl-2-pyridone (**1d**) (1.6 g, 7.4 mmol) in ether (800 ml) was irradiated by high-pressure mercury lamp (Ushio 450 W, Pyrex filter) for 11 h. The solvent was evaporated off under reduced pressure to give a crystalline residue, which was recrystallized from hexane–chloroform (2:1) to give the *product* (**2d**) (1.44 g, 90%) as needles (from hexane–ether), m.p. 73—74 °C (Found: C, 72.35; H, 6.1; N, 6.5. $C_{13}H_{13}NO_2$ requires C, 72.55; H, 6.1; N, 6.5%); $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 615 cm^{-1}; δ_H ($CDCl_3$) 2.75 (3 H, s, 2-Me), 4.20 (2 H, br s, 1- and 4-H), 4.80 (2 H, s, CH_2Ph), 5.05 (1 H, s, 6-H), and 7.25 (5 H, s, Ph).

2-Benzyl-5-benzyloxy-2-azabicyclo[2.2.0]*hex-5-en-3-one* (**2e**).—A solution of compound (**1e**) (873 mg, 3 mmol) in a mixture of ether (350 ml) and acetonitrile (30 ml) was irradiated under argon by a Rayonet photoreactor (3 000 Å lamp) for 6 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the *product* (**2e**) (700 mg, 80%) as an oil (Found: M^+, 291.1251. $C_{19}H_{17}NO_2$ requires *M*, 291.1258); $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 615 cm^{-1}; δ_H ($CDCl_3$) 3.95—4.95 (7 H, m, NCH_2, 1-, 4-, and 6-H, and OCH_2Ph), and 7.15—7.55 (10 H, m, 2 × Ph).

5-Benzyloxy-2-benzyloxycarbonylmethyl-2-azabicyclo[2.2.0]-*hex-5-en-3-one* {*Benzyl* (*5-Benzyloxy-3-oxo-2-azabicyclo*[2.2.0]-*hex-5-en-2-yl*)*acetate*} (**2f**).—A solution of compound (**1f**) (1.05 g, 0.03 mol) in ether (350 ml) and acetonitrile (30 ml) was irradiated under argon by a Rayonet photoreactor lamp (3 000 Å) for 6 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with chloroform gave the *product* (**2f**) as plates (from hexane–ether), m.p. 50 °C (Found: C, 71.95; H, 5.4; N, 3.7. $C_{21}H_{19}NO_2$ requires C, 72.2; H, 5.5; N, 4.0%); $\nu_{max.}$ ($CHCl_3$) 1 740 and 1 615 cm^{-1}; δ_H ($CDCl_3$) 3.48—4.47 (4 H, m, NCH_2 and 1- and 4-H), 4.84 (2 H, s, CO_2CH_2Ph), 5.11 (1 H, m, 6-H), 5.18 (2 H, s, OCH_2Ph), 7.35 (5 H, s, 5-OCH_2*Ph*), and 7.38 (5 H, s, CO_2CH_2*Ph*).

5-(Dimethyl-t-butylsiloxy)-2-methyl-2-azabicyclo[2.2.0]*hex-5-en-3-one* (**2g**).—A solution of compound (**1g**)* (956 mg, 4 mmol) in ether (350 ml) was irradiated under argon by a Rayonet photoreactor lamp (3 000 Å) for 6 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (5:1) gave the *product* (**2g**) (800 mg, 84%) as an oil (Found: M^+, 239.1341. $C_{12}H_{21}NO_2Si$ requires *M*, 239.1340); $\nu_{max.}$ ($CHCl_3$) 1 740 and 1 615 cm^{-1}; δ_H ($CDCl_3$) 0.23 (6 H, s, $SiMe_2$), 0.93 (9 H, s, $SiBu^t$), 2.78 (3 H, s, NMe), 4.03 (1 H, d, *J* 3 Hz, 4-H), 4.16 (1 H, m, 1-H), and 5.13 (1 H, d, *J* 2 Hz, 6-H).

2-Azabicyclo[2.2.0]*hexane-3,5-dione* (**3a**).—(i) A mixture of 5-(dimethyl-t-butylsiloxy)-2-azabicyclo[2.2.0]hex-5-en-3-one (**1a**)[1] (350 mg, 1.53 mmol) and TFA (40 mg) in THF (7.8 ml)–

* Compound (**1g**) was prepared by silylation of 4-hydroxy-1-methyl-2-pyridone with TBDSC according to the procedure for the synthesis of compound (**1a**).[1]

water (3 ml) was kept at room temperature for 6 h. Pyridine (35 mg) and chloroform (30 ml) were added successively to the reaction mixture. The resulting mixture was dried over anhydrous sodium sulphate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**3a**) (105 mg, 62%) as needles (from hexane–ethyl acetate), m.p. 70 °C (Found: C, 53.75; H, 4.55; N, 12.55. $C_5H_5NO_2$ requires C, 54.05; H, 4.55; N, 12.6%); $\nu_{max.}$ ($CHCl_3$) 1 800 and 1 760 cm^{-1}; δ_H ($CDCl_3$) 3.20 (2 H, d, *J* 3.0 Hz, CH_2), 4.48 (1 H, q, *J* 3.0 Hz, 1-H), 4.68 (1 H, t, *J* 3.0 Hz, 4-H), and 6.70 (1 H, br s, NH).

(ii) A solution of 5-methoxy-2-azabicyclo[2.2.0]hex-5-en-3-one (**2b**)[3] (468 mg) in THF (4 ml) containing water (0.5 ml) and 10% hydrochloric acid (one drop) was kept at room temperature for 50 min. After neutralization with Dowex 1X4 (base form), dichloromethane (80 ml) was added to the mixture. The resulting mixture was dried over anhydrous sodium sulphate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the product (**3a**) (210 mg, 51%), which was identical in every respect with an authentic sample obtained from compound (**1a**) by the procedure described above.

(iii) By the same procedure as described above, compound (**3a**) was obtained in 72% yield from 5-benzyloxy-2-azabicyclo-[2.2.0]hex-5-en-3-one (**2c**).

2-*Methyl*-2-*azabicyclo*[2.2.0]*hexane*-3,5-*dione* (**3b**).—A solution of 5-benzyloxy-2-methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (**2d**) (1.8 g, 8.4 mmol) and PTSA monohydrate (180 mg) in a mixture of THF (10 ml)–water (3 ml) was kept at room temperature overnight. The mixture was neutralized with pyridine, and chloroform (80 ml) was added to the resulting mixture. After the mixture had been dried over anhydrous sodium sulphate, the solvent was evaporated off under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**3b**) (0.98 g, 95%) as an oil (Found: M^+, 125.0488. $C_6H_7NO_2$ requires *M*, 125.0476); $\nu_{max.}$ ($CHCl_3$) 1 800 and 1 740 cm^{-1}; δ_H ($CDCl_3$) 2.90 (3 H, s, Me), 3.09 (2 H, d, *J* 3 Hz, 6-H_2), 4.33 (1 H, m, 1-H), and 4.69 (1 H, d, *J* 2 Hz, 4-H).

2-*Benzyl*-2-*azabicyclo*[2.2.0]*hexane*-3,5-*dione* (**3c**).—By the same procedure as described above for the synthesis of compound (**3b**), the 3,5-*dione* (**3c**) was obtained as an oil in 84% yield from 2-benzyl-5-benzyloxy-2-azabicyclo[2.2.0]hex-5-en-3-one (**2e**) (Found: M^+, 201.0780. $C_{12}H_{11}NO_2$ requires *M*, 201.0788); $\nu_{max.}$ ($CHCl_3$) 1 795 and 1 750 cm^{-1}; δ_H ($CDCl_3$) 2.84 (2 H, d, *J* 3 Hz, 6-H_2), 4.00—4.80 (4 H, m, 1- and 4-H, and NCH_2), and 7.30 (5 H, m, Ph).

2-*Benzyloxycarbonylmethyl*-2-*azabicyclo*[2.2.0]*hexane*-3,5-*dione* {Benzyl (3,5-*Dioxo*-2-*azabicyclo*[2.2.0]*hexan*-2-*yl*)*acetate*} (**3d**).—A solution of compound (**2f**) (349 mg, 1 mmol) and PTSA monohydrate (20 mg) in a mixture of water (1 ml)—THF (4 ml) was stirred for 3 h. The mixture was neutralized with pyridine (one drop), and diluted with chloroform (30 ml). The resulting mixture was dried over anhydrous sodium sulphate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the *product* (**3d**) (233 mg, 90%) as an oil (Found: M^+, 259.0811. $C_{14}H_{13}NO_4$ requires *M*, 259.0843); $\nu_{max.}$ ($CHCl_3$) 1 810, 1 775, and 1 760 cm^{-1}; δ_H ($CDCl_3$) 3.17 (2 H, d, *J* 3 Hz, 6-H_2), 3.70—4.50 (2 H, *J* 18 Hz, NCH_2), 4.57 (1 H, m, 1-H), 4.73 (1 H, d, *J* 3 Hz, 4-H), 5.20 (2 H, s, CH_2Ph), and 7.37 (5 H, s, Ph).

2-(*Dimethyl-t-butylsilyl*)-2-*azabicyclo*[2.2.0]*hexane*-2,5-*dione* (**3**; X = $SiMe_2$ Bu^t).—A solution of compound (**1a**) (225 mg, 1 mmol), TBDSC (150 mg, 1 mmol), and imidazole (170 mg, 2.5 mmol) in DMF (5 ml) was kept at room temperature for 16 h. The reaction mixture was poured into ice–water, and extracted with ether. The extract was dried over anhydrous sodium sulphate, and the solvent was evaporated off under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3:1) gave the *product* (**3**; X = $SiMe_2$ Bu^t) (120 mg, 52%) as an oil (Found: M^+, 225.1185. $C_{11}H_{19}NO_2Si$ requires *M*, 225.1183): $\nu_{max.}$ ($CHCl_3$) 1 790 and 1 735 cm^{-1}; δ_H ($CDCl_3$) 0.20 (3 H, s, SiMe), 0.30 (3 H, s, SiMe), 0.98 (9 H, s, $SiBu^t$), 3.19 (2 H, m, 6-H_2), 4.33 (1 H, m, 4-H), and 4.72 (1 H, m, 1-H).

4-(*Methoxycarbonylmethyl*)*azetidin*-2-*one* [*Methyl* (4-*Oxoazetidin*-2-*yl*)*acetate*] (**5a**).—A solution of compound (**3a**) (49 mg, 0.44 mmol) in absolute methanol (5 ml) was refluxed for 1 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the product (**5a**)[10] (48 mg, 77%) as an oil, $\nu_{max.}$ ($CHCl_3$) 3 420, 1 755, and 1 730 cm^{-1}; δ_H 2.4—3.4 (4 H, m, 3-H_2 and CH_2CO_2), 3.72 (3 H, s, OMe), 3.92 (1 H, m, 4-H), and 6.33 (1 H, br s, NH). Further elution with the same solvent gave the *product* (**6a**) as an oil (Found: M^+, 143.0580. $C_6H_9NO_3$ requires *M*, 143.0582); $\nu_{max.}$ ($CHCl_3$) 3 350, 1 725, 1 685, and 1 640 cm^{-1}; δ_H ($CDCl_2$) 3.37 (2 H, s, 2-H_2), 3.77 (3 H, s, OMe), 4.47 (1 H, d, *J* 9 Hz, 4-H), 4.70 (1 H, d, *J* 16 Hz, NH), 6.96 (1 H, m, 5-H), and 8.79 (1 H, br s, NH).

4-(*Ethoxycarbonylmethyl*)*azetidin*-2-*one* [*Ethyl* (4-*Oxoazetidin*-2-*yl*)*acetate*] (**5b**).—A solution of compound (**3a**) (20 mg, 0.18 mmol) in absolute ethanol (5 ml) in the presence of pyridine (one drop) was set aside at room temperature for 16 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the product (**5b**)[11] (20 mg, 71%) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 760 and 1 740 cm^{-1}; δ_H ($CDCl_3$) 2.34 (3 H, t, *J* 8 Hz, OCH_2Me), 2.70 (1 H, dd, *J* 6 and 3 Hz, 3-H), 2.59—2.94 (2 H, m, CH_2CO_2), 3.21 (1H, dd, *J* 18 and 3 Hz, 3-H), 3.92 (1 H, m, 4-H), 4.25 (2 H, q, *J* 8 Hz, OCH_2Me), and 6.60 (1 H, br s, NH).

4-(*Benzyloxycarbonylmethyl*)*azetidin*-2-*one* [*Benzyl* (4-*Oxoazetidin*-2-*yl*)*acetate*] (**5c**).—A solution of compound (**3a**) (286 mg, 2.58 mmol) in benzyl alcohol (1.43 g, 13.24 mmol) was kept at room temperature for 4 h. The reaction mixture was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the product (**5c**) (322 mg, 57%) as leaves (from hexane–benzene), m.p. 98—99 °C (lit.,[12] 93—94 °C) (Found: C, 65.8; H, 5.95; N, 6.3. Calc. for $C_{12}H_{13}NO_3$: C, 65.75; H, 6.0; N, 6.4%); $\nu_{max.}$ ($CHCl_3$) 3 420, 1 760, and 1 730 cm^{-1}; δ_H ($CDCl_3$) 2.5—3.5 (4 H, m, 3-H_2 and CH_2CO_2), 3.97 (1 H, m, 4-H), 6.25 (1 H, br s, NH), 5.20 (2 H, s, CH_2Ph), and 7.44 (5 H, s, Ph).

4-*Methoxycarbonylmethyl*-1-*methylazetidin*-2-*one* [*Methyl* (1-*Methyl*-4-*oxoazetidin*-2-*yl*)*acetate*] (**5d**).—By the same procedure as described above for the synthesis of compound (**5a**), the *azetidin*-2-*one* (**5d**) was obtained as an oil in 79% yield from compound (**3b**) (Found: M^+, 157.0735. $C_7H_{11}NO_3$ requires *M*, 157.0738); $\nu_{max.}$ ($CHCl_3$) 1 745 and 1 735 cm^{-1}; δ_H ($CDCl_3$) 2.4—3.3 (4 H, m, 3-H_2 and CH_2CO_2), 2.79 (3 H, s, 1-Me), 3.73 (3 H, s, OMe), and 3.83 (1 H, m, 4-H).

4-*Benzyloxycarbonylmethyl*-1-*methylazetidin*-2-*one* [*Benzyl* (1-*Methyl*-4-*oxoazetidin*-2-*yl*)*acetate*] (**5e**).—A solution of compound (**3b**) (167 mg, 1.33 mmol) and benzyl alcohol (300 mg, 2.8

mmol) in anhydrous THF (2.5 ml) containing triethylamine (one drop) was kept at room temperature for 16 h. The reaction mixture was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the *product* (**5e**) (200 mg, 64%) as an oil (Found: M^+, 233.1039. $C_{13}H_{15}NO_3$ requires M, 233.1051); $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}; δ_H ($CDCl_3$) 2.75 (3 H, s, 1-Me), 2.2—3.5 (4 H, m, 3-H_2 and CH_2CO_2), 3.6—4.2 (1 H, m, 4-H), 5.15 (2 H, s, CH_2Ph), and 7.30 (5 H, s, Ph).

1-*Benzyloxycarbonylmethyl*-4-(*methoxycarbonylmethyl*)-*azetidin*-2-*one* [*Benzyl* (2-*Methoxycarbonylmethyl*-4-*oxoazetidin*-1-*yl*)*acetate*] (**5f**).—A solution of compound (**3d**) (259 mg, 1 mmol) in absolute methanol (5 ml) was refluxed for 6 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**5f**) (224 mg, 77%) as an oil (Found: M^+, 291.1095. $C_{15}H_{17}NO_5$ requires M, 291.1105); $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}; δ_H ($CDCl_3$) 2.50—2.82 (3 H, m, 3-H and 4-CH_2), 3.20 (1 H, dd, J 5 and 15 Hz, 3-H), 3.60 (3 H, s, OMe), 3.80—4.30 (1 H, m, 4-H), 4.10 (2H, s, NCH_2), 5.12 (2 H, s, CO_2CH_2Ph), and 7.32 (5 H, s, Ph).

Ethyl 5-*Amino*-3-*oxopent*-4-*enoate* (**6b**).—A solution of compound (**3a**) (20 mg, 0.18 mmol) in absolute ethanol (3 ml) was refluxed for 3 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3:1) gave the *product* (**6b**) (5 mg, 18%) as an oil (Found: M^+, 157.0732. $C_7H_{11}NO_3$ requires M, 157.0738); $\nu_{max.}$ ($CHCl_3$) 3 330, 1 720, 1 685, and 1 640 cm^{-1}; δ_H ($CDCl_3$) *inter alia* 3.36 (2 H, s, 2-H_2), 4.48 (1 H, d, J 9 Hz, 4-H), 4.70 (1 H, d, J 16 Hz, NH), 6.98 (1 H, m, 5-H), and 8.74 (1 H, br s, NH).

Benzyl 5-*Amino*-3-*oxopent*-4-*enoate* (**6c**).—A solution of compound (**3a**) (20 mg, 0.18 mmol) and benzyl alcohol (39 mg, 0.36 mmol) in anhydrous THF (5 ml) was refluxed for 5 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (4:1) gave the *product* (**6c**) (8 mg, 20%) as an oil (Found: M^+, 219.0890. $C_{12}H_{13}NO_3$ requires M, 219.0895); $\nu_{max.}$ ($CHCl_3$) 3 340, 1 725, 1 685, and 1 640 cm^{-1}; δ_H ($CDCl_3$) *inter alia* 3.40 (2 H, s, 2-H_2), 4.47 (1 H, d, J 9 Hz, 4-H), 4.69 (1 H, d, J 16 Hz, NH).

4-(N-*Benzylcarbamoylmethyl*)*azetidin*-2-*one* [N-*Benzyl*-(4-*oxoazetidin*-2-*yl*)*acetamide*] (**7**).—Benzylamine (34 mg, 0.32 mmol) was added to a stirred solution of compound (**3a**) (30 mg, 0.27 mmol) in anhydrous THF (2 ml). The mixture was kept for 1.5 h, and the solvent was then evaporated off under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with ethyl acetate gave the *product* (**7**) (20 mg, 34%) as prisms (from hexane–chloroform), m.p. 93—94 °C (Found: C, 66.1; H, 6.45; N, 12.85. $C_{12}H_{14}N_2O_4$ requires C, 66.05; H, 6.45; N, 12.85%); $\nu_{max.}$ ($CHCl_3$) 1 755 and 1 665 cm^{-1}; δ_H ($CDCl_3$) 2.18—2.59 (2 H, m, 4-CH_2), 2.64 (1 H, m, 3-H), 3.09 (1 H, ddd, J 15, 6, and 4 Hz, 3-H), 3.92 (1 H, m, 4-H), 4.40 (2 H, d, J 8 Hz, NCH_2Ph), 6.06 (1 H, br s, $NHCH_2$), 6.22 (1 H, br s, β-lactam NH), and 7.25 (5 H, s, Ph).

4-(*Benzylthiocarbonylmethyl*)*azetidin*-2-*one* [*Benzyl* (4-*Oxoazetidin*-2-*yl*)*thioacetate*] (**8a**).—A solution of compound (**3a**) (40 mg, 0.36 mmol) and toluene-α-thiol (200 mg, 1.6 mmol) in anhydrous THF containing triethylamine (one drop) was kept at room temperature for 16 h. The reaction mixture was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the *product* (**8a**) (43 mg, 51%) as prisms (from hexane–chloroform), m.p. 95—96 °C (Found: C, 61.2; H, 5.65; N, 5.9. $C_{12}H_{13}NO_2S$ requires C, 61.25; H, 5.55; N, 5.95%): $\nu_{max.}$ ($CHCl_3$) 3 410, 1 755, and 1 675 cm^{-1}; δ_H ($CDCl_3$) 2.5—3.5 (4 H, m, 3-H_2 and CH_2COS), 4.05 (1 H, m, 4-H), 4.20 (2 H, s, CH_2Ph), 6.25 (1 H, br s, NH), and 7.40 (5 H, s, Ph).

4-[(*Benzylthio*)*carbonylmethyl*]-1-*methylazetidin*-2-*one* [S-*Benzyl* (1-*Methyl*-4-*oxoazetidin*-2-*yl*)*thioacetate*] (**8b**).—A mixture of compound (**3b**) (190 mg, 1.52 mmol), toluene-α-thiol (520 mg, 4.19 mmol), and triethylamine (one drop) was kept at room temperature for 16 h. The reaction mixture was then subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**8b**) (223 mg, 61%) as an oil (Found: M^+, 249.0799. $C_{13}H_{15}NO_2S$ requires M, 249.0822); $\nu_{max.}$ ($CHCl_3$) 1 745 and 1 680 cm^{-1}; δ_H ($CDCl_3$) 2.75 (3 H, s, 1-Me), 2.3—3.4 (4 H, m, 3-H_2 and CH_2CO), 3.85 (1 H, m, 4-H), 4.15 (2 H, s, CH_2Ph), and 7.25 (5 H, s, Ph).

2-(*Dimethyl*-*t*-*butylsilyl*)-5-*hydroxy*-5-*methyl*-2-*azabicyclo*-[2.2.0]*hexan*-3-*one* (**9a**).—A solution of methylmagnesium bromide (0.2 ml, 0.6 mmol) in ether was added dropwise to a stirred, ice-cooled solution of compound (**3**; X = $SiMe_2$ Bu^t) (136 mg, 0.6 mmol) in anhydrous ether (4 ml) under argon, and the mixture was stirred for 15 min. Acetic acid was added to the mixture, and the resulting mixture was extracted with ether. The ethereal extract was dried over anhydrous sodium sulphate, and the solvent was evaporated off under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (2:1) gave the *product* (**9a**) (53 mg, 40%) as needles (from hexane), m.p. 82—83 °C (Found: C, 59.35; H, 9.65; N, 5.65. $C_{12}H_{23}NO_2Si$ requires C, 59.7; H, 9.6; N, 5.8%); $\nu_{max.}$ ($CHCl_3$) 3 400 and 1 720 cm^{-1}; δ_H ($CDCl_3$) 0.20 (3 H, s, SiMe), 0.30 (3 H, s, SiMe), 0.91 (9 H, s, Bu^t), 1.45 (3 H, s, 5-Me), 2.10 (1 H, d, J 14 Hz, 6-H), 2.34 (1 H, ddd, J 14, 5, and 2 Hz, 6-H), 2.84 (1 H, s, OH), and 3.53—3.73 (2 H, m, 1- and 4-H).

2-(*Dimethyl*-*t*-*butylsilyl*)-5-*ethyl*-5-*hydroxy*-2-*azabicyclo*-[2.2.0]*hexan*-3-*one* (**9b**).—By the same procedure as described above for the synthesis of compound (**9a**), *compound* (**9b**) was obtained as leaves in 37% yield from compound (**3**: X = $SiMe_2$ Bu^t) and ethylmagnesium bromide, m.p. 91—92 °C (from hexane) (Found: C, 60.85; H, 10.0; N, 5.0. $C_{13}H_{25}NO_2Si$ requires C, 61.15; H, 9.85; N, 5.5%); $\nu_{max.}$ ($CHCl_3$) 3 400 and 1 720 cm^{-1}; δ_H ($CDCl_3$) *inter alia* 0.93 (3 H, t, J 8 Hz, CH_2Me), 1.65 (2 H, q, J 8 Hz, CH_2Me), 2.04 (1 H, d, J 15 Hz, 6-H), 2.33 (1 H, ddd, J 15, 4, and 2 Hz, 6-H), 2.53 (1 H, s, OH), and 3.48—3.73 (2 H, m, 1- and 4-H).

2-(*Dimethyl*-*t*-*butylsilyl*)-5-*hydroxy*-5-*phenyl*-2-*azabicyclo*-[2.2.0]*hexan*-3-*one* (**9c**).—By the same procedure as described above for the synthesis of compound (**9a**), *compound* (**9c**) was obtained as prisms in 32% yield from compound (**3**: X = $SiMe_2$ Bu^t) and phenylmagnesium bromide, m.p. 113—114 °C (from hexane) (Found: C, 67.2; H, 8.3; N, 4.65. $C_{17}H_{25}NO_2Si$ requires C, 67.3; H, 8.3; N, 4.6%); $\nu_{max.}$ ($CHCl_3$) 3 350 and 1 720 cm^{-1}; δ_H ($CDCl_3$) *inter alia* 2.50 (1 H, dd, J 15 and 1.5 Hz, 6-H), 2.82 (1 H, dd, J 15 and 6 Hz, 6-H), 2.93 (1 H, s, OH), 3.84 (1 H, m, 1-H), 4.14 (1 H, d, J 4 Hz, 4-H), and 7.23—7.45 (5 H, m, Ph).

4-*Acetonyl*-1-(*dimethyl*-*t*-*butylsilyl*)*azetidin*-2-*one* (**10a**).—A solution of compound (**9a**) (110 mg, 0.49 mmol) and DBU in dry benzene (5 ml) was stirred for 3 h at room temperature. The mixture was neutralized with acetic acid, and condensed under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3:1) gave the *product* (**10a**) (52 mg, 47%) as needles (from hexane), m.p. 43—44 °C (Found: C, 59.3; H, 10.0; N, 5.45. $C_{12}H_{23}NO_2Si$ requires C, 59.7; H, 9.6; N, 5.8%); $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 710sh cm^{-1}; δ_H ($CDCl_3$) *inter alia* 2.17 (3 H, s, COMe), 2.56 (1

H, dd, *J* 18 and 4 Hz, 4-CH_aH$_b$), 2.61 (1 H, dd, *J* 18 and 6 Hz, 4-CH$_a$$H_b$), 3.00 (1 H, dd, *J* 18 and 4 Hz, 3-H), 3.33 (1 H, dd, *J* 18 and 6 Hz, 3-H), and 3.86 (1 H, m, 4-H).

1-(*Dimethyl-t-butylsilyl*)-4-(2-*oxobutyl*)*azetidin*-2-*one* (**10b**).—By the same procedure as described above for the synthesis of compound (**10a**), *compound* (**10b**) was obtained as plates in 53% yield from compound (**9b**), m.p. 69—70 °C (from pentane) (Found: C, 61.0; H, 10.0; N, 5.2. $C_{13}H_{25}NO_2Si$ requires C, 61.15; H, 9.85; N, 5.5%); δ_H ($CDCl_3$) *inter alia* 1.06 (3 H, t, *J* 8 Hz, CH_2Me), 2.42 (2 H, q, *J* 8 Hz, CH_2Me), 2.61 (1 H, dd, *J* 20 and 12 Hz, 4-CH_aH$_b$), 2.63 (1 H, dd, *J* 16 and 4 Hz, 3-H), 2.96 (1 H, dd, *J* 20 and 5 Hz, 4-CH$_a$$H_b$), 3.40 (1 H, dd, *J* 16 and 6 Hz, 3-H), and 3.91 (1 H, m, 4-H).

3-*Acetyl*-1-*benzyl*-4-*hydroxy*-6-*methyl*-2-*pyridone* (**11b**).—A solution of *N*-benzyl-3-benzamidocrotonamide (14 g, 50 mmol), diketene (8.4 g, 100 mmol), and triethylamine (505 mg, 5 mmol) in dichloromethane (180 ml) was kept overnight at room temperature. The solvent was evaporated off under reduced pressure, and the residue was dissolved in methanol (160 ml). Conc. hydrochloric acid (40 ml) was added to the solution, and the mixture was heated under reflux for 1.5 h. The solvent was evaporated off under reduced pressure, and the residue was washed with water and recrystallized from ethyl acetate to give the product (**11b**) (10.87 g, 85%) as needles, m.p. 141—142 °C (lit.,[13] m.p. 137—138 °C); $\nu_{max.}$ ($CHCl_3$) 1 655 and 1 615 cm^{-1}; δ_H ($CDCl_3$) 2.27 (3 H, s, COMe), 2.73 (3 H, s, 6-Me), 5.27 (2 H, s, CH_2Ph), 5.85 (1 H, s, 5-H), 7.0—7.58 (5 H, m, Ph), and 15.65 (1 H, s, OH).

3-*Acetyl*-1-*benzyl*-4-*methoxy*-2-*pyridone* (**12a**).—A mixture of 3-acetyl-1-benzyl-4-hydroxy-2-pyridone (**11a**)[7] (1.9 g, 7.8 mmol), methyl iodide (15.6 ml, 250 mmol), and silver oxide (15.6 g, 67 mmol) in acetone (230 ml) was stirred and refluxed for 75 min. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel (60 g) column chromatography. Elution with hexane–ethyl acetate (1:2) gave the *product* (**12a**) (1.3 g, 65%) as needles (from hexane–dichloromethane), m.p. 121—122 °C (Found: C, 69.95; H, 5.9; N, 5.2. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.45%); $\nu_{max.}$ ($CHCl_3$) 1 690 and 1 645 cm^{-1}; δ_H ($CDCl_3$) 2.52 (3 H, s, COMe), 3.83 (3 H, s, OMe), 5.05 (2 H, s, CH_2Ph), 6.02 (1 H, d, *J* 8 Hz, 5-H), 7.27 (5 H, s, Ph), and 7.32 (1 H, d, *J* 8 Hz, 6-H).

3-*Acetyl*-1-*benzyl*-4-*methoxy*-6-*methyl*-2-*pyridone* (**12b**).—By the same procedure as described for the synthesis of compound (**12a**), the *pyridone* (**12b**) was obtained from 3-acetyl-1-benzyl-4-hydroxy-6-methyl-2-pyridone (**11b**)[13] in 86% yield as needles (from hexane–dichloromethane), m.p. 127—128 °C (Found: C, 70.5; H, 6.05; N, 4.95. $C_{16}H_{17}NO_3$ requires C, 70.85; H, 6.3; N, 5.15%); $\nu_{max.}$ ($CHCl_3$) 1 680 and 1 640 cm^{-1}; δ_H ($CDCl_3$) 2.32 (3 H, s, COMe), 2.55 (3 H, s, 6-Me), 3.86 (3 H, s, OMe), 5.32 (2 H, s, CH_2Ph), 6.00 (1 H, s, 5-H), and 7.03—7.53 (5 H, m, Ph).

1-*Benzyl*-3-(1-*hydroxyethyl*)-4-*methoxy*-2-*pyridone* (**13a**).—A solution of compound (**12a**) (643 mg, 2.5 mmol) and $NaBH_4$ (94 mg, 2.5 mmol) in ethanol (40 ml) was stirred overnight at room temperature. The solvent was evaporated off under reduced pressure, and water was added to the residue. The mixture was extracted with dichloromethane. The extract was dried over anhydrous sodium sulphate, and concentrated under reduced pressure to give the *product* (**13a**) (556 mg, 86%) as needles (from hexane–dichloromethane), m.p. 107—108 °C (Found: C, 69.3; H, 6.35; N, 5.05. $C_{15}H_{17}NO_3$ requires C, 69.5; H, 6.6; N, 5.4%); $\nu_{max.}$ ($CHCl_3$) 3 400 and 1 640 cm^{-1}; δ_H ($CDCl_3$) 1.48 (3 H, d, *J* 6 Hz, *Me*CHOH), 3.83 (3 H, s, OMe), 4.87—5.47 (3 H, m, CH_2Ph and MeC*H*OH), 5.53—5.83 (1 H, br, OH), 6.12 (1 H, d, *J* 7.4 Hz, 5-H), and 7.03—7.50 (6 H, m, Ph and 6-H).

1-*Benzyl*-3-(1-*hydroxyethyl*)-4-*methoxy*-6-*methyl*-2-*pyridone* (**13b**).—By the same procedure as described above for the synthesis of compound (**13a**), the *pyridone* (**13b**) was obtained as needles in 74% yield from dione (**12b**), m.p. 124—125 °C (from hexane–dichloromethane) (Found: C, 70.5; H, 6.9; N, 5.0. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); $\nu_{max.}$ ($CHCl_3$) 3 440 and 1 720 cm^{-1}; δ_H ($CDCl_3$) 1.48 (3 H, d, *J* 6 Hz, *Me*CHOH), 2.30 (3 H, s, 6-Me), 3.85 (3 H, s, OMe), 4.90—5.67 (3 H, m, CH_2Ph and MeC*H*OH), 5.83 (1 H, br s, OH), 6.00 (1 H, s, 5-H), and 6.93—7.50 (5 H, m, Ph).

2-*Benzyl*-4-(1-*hydroxyethyl*)-5-*methoxy*-2-*azabicyclo*[2.2.0]-*hex*-5-*en*-3-*one* (**14a**).—A solution of the pyridone (**13a**) (648 mg, 2.5 mmol) in acetonitrile (340 ml) was irradiated by a high-pressure mercury lamp (Riko UVL 400 HA, Pyrex filter) for 100 min. The solvent was evaporated off under reduced pressure at room temperature to give the *product* (**14a**) (647 mg, 100%) as an oil (Found: M^+, 259.1225. $C_{15}H_{17}NO_3$ requires M, 259.1209); $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 730 cm^{-1}; δ_H ($CDCl_3$) 1.34 ($\frac{1}{3}$ × 3 H, d, *J* 7 Hz, *Me*CHOH), 1.39 ($\frac{2}{3}$ × 3 H, d, *J* 7 Hz, *Me*CHOH), 2.70 (1 H, br s, OH), 3.57 ($\frac{1}{3}$ × 3 H, s, OMe), 3.58 ($\frac{2}{3}$ × 3 H, s, OMe), 3.98 ($\frac{2}{3}$ H, s, 1-H), 4.01 ($\frac{1}{3}$ H, s, 1-H), 4.04—4.53 (3 H, m, MeC*H*OH and CH_2Ph), 4.73 (1 H, s, 6-H), and 7.03—7.43 (5 H, m, Ph).

2-*Benzyl*-4-(1-*hydroxyethyl*)-5-*methoxy*-1-*methyl*-2-*azabicyclo*[2.2.0]*hex*-5-*en*-3-*one* (**14b**).—A solution of the pyridone (**13b**) (410 mg, 1.5 mmol) in a mixture of acetonitrile (210 ml) and ether (70 ml) was irradiated by a high-pressure mercury lamp (Riko UVL 400 HA, Pyrex filter) for 13 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel (15 g) column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**14b**) (305 mg, 74%) as an oil (Found: M^+, 273.1352. $C_{16}H_{19}NO_3$ requires *M*, 273.1364); $\nu_{max.}$ ($CHCl_3$) 3 400 and 1 735 cm^{-1}; δ_H ($CDCl_3$) 1.43 (3 H, d, *J* 7 Hz, *Me*CHOH), 1.43 (3 H, s, 1-Me), 2.40 (1 H, br s, OH), 3.50 ($\frac{1}{3}$ × 3 H, s, OMe), 3.51 ($\frac{2}{3}$ × 3 H, s, OMe), 4.0—4.57 (3 H, CH_2Ph and MeC*H*OH), 4.56 ($\frac{1}{3}$ H, s, 6-H), 4.59 ($\frac{2}{3}$ H, s, 6-H), and 7.09—7.51 (5 H, m, Ph).

2-*Benzyl*-4-(1-*hydroxyethyl*)-2-*azabicyclo*[2.2.0]*hexane*-3,5-*dione* (**15a**).—A solution of compound (**14a**) (140 mg, 0.54 mmol) and PTSA monohydrate (20 mg, 0.105 mmol) in THF–water (6:1) (2 ml) was stirred at room temperature for 1 h. The reaction mixture was neutralized with saturated aqueous $NaHCO_3$, and extracted with chloroform. The extract was dried over magnesium sulphate, and concentrated under reduced pressure. The residue was subjected to silica gel (5 g) column chromatography. Elution with hexane–ethyl acetate (3:1) gave the *product* (**15a**) (66 mg, 50%) as an oil (Found: M^+, 245.1046. $C_{14}H_{15}NO_3$ requires *M*, 245.1051); $\nu_{max.}$ ($CHCl_3$) 1 780 and 1 740 cm^{-1}; δ_H ($CDCl_3$) 1.39 ($\frac{2}{3}$ × 3 H, d, *J* 7 Hz, *Me*CHOH), 1.41 ($\frac{1}{3}$ × 3 H, d, *J* 7 Hz, *Me*CHOH), 2.54 (1 H, br s, OH), 2.54—2.98 (2 H, m, 6-H_2), 4.08—4.72 (4 H, m, CH_2Ph, 1-H, and MeC*H*OH), and 7.03—7.57 (5 H, m, Ph).

2-*Benzyl*-4-(1-*hydroxyethyl*)-1-*methyl*-2-*azabicyclo*[2.2.0]-*hexane*-3,5-*dione* (**15b**).—By the same procedure as described above for the synthesis of compound (**15a**), the 3,5-*dione* (**15b**) was obtained as an oil in 46% yield from enone (**14b**) (Found: M^+, 259.120 82. $C_{15}H_{17}NO_3$ requires *M*, 259.120 74); $\nu_{max.}$ ($CHCl_3$) 3 500, 1 783, and 1 740 cm^{-1}; δ_H ($CDCl_3$) 1.47 ($\frac{1}{4}$ × 3 H, d, *J* 6.4 Hz, *Me*CHOH), 1.52 ($\frac{3}{4}$ × 3 H, d, *J* 6.4 Hz, *Me*CHOH), 1.59 ($\frac{3}{4}$ × 3 H, s, 1-Me), 1.61 ($\frac{1}{4}$ × 3 H, s, 1-Me),

2.01 (1 H, br s, OH), 2.66 ($\frac{1}{4}$ × 2 H, s, 6-H_2), 2.67 ($\frac{3}{4}$ × 2 H, s, 6-H_2), 4.09—4.56 (3 H, m, CH_2Ph and MeC*H*OH), and 7.1—7.5 (5 H, m, Ph).

1-*Benzyl*-3-(1-*hydroxyethyl*)-4-(*methoxycarbonylmethyl*)-*azetidin*-2-*one*{*Methyl* [1-*Benzyl*- 3-(1-*hydroxyethyl*)-4-*oxo*-*azetidin*-2-*yl*]*acetate*} (**16a**).—A solution of dione (**15a**) (40 mg, 0.163 mmol) and a catalytic amount of pyridine in absolute methanol (2 ml) was stirred at room temperature for 3 h. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel (3 g) column chromatography. Elution with hexane–ethyl acetate (1:1) gave the *product* (**16a**) (30 mg, 67%) as an oil (Found: M^+, 277.1253. $C_{15}H_{19}NO_4$ requires M, 277.1253); $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 740 cm^{-1}; δ_H ($CDCl_3$) 1.39 ($\frac{1}{3}$ × 3 H, d, J 6 Hz, *Me*CHOH), 1.42 ($\frac{2}{3}$ × 3 H, d, J 6 Hz, *Me*CHOH), 2.04 (1 H, br s, OH), 2.36—3.00 (2 H, m, CH_2CO_2), 3.22 ($\frac{1}{3}$ × H, t, J 5 Hz, 3-H), 3.26 ($\frac{2}{3}$ × H, dd, J 3 and 5 Hz, 3-H), 3.56 ($\frac{1}{3}$ × 3 H, s, OMe), 3.58 ($\frac{2}{3}$ × 3 H, s, OMe), 3.86—4.56 (4 H, m, CH_2Ph, MeC*H*OH and 4-H), and 7.00—7.30 (5 H, m, Ph).

1-*Benzyl*-3-(1-*hydroxyethyl*)-4-*methoxycarbonylmethyl*-4-*methylazetidin*-2-*one* {*Methyl* [1-*Benzyl*-3-(1-*hydroxyethyl*)-2-*methyl*-4-*oxoazetidin*-2-*yl*]*acetate*} (**16b**).—A solution of dione (**15b**) (54 mg, 0.21 mmol) and a catalytic amount of pyridine in absolute methanol (2 ml) was stirred overnight at room temperature. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel (4 g) column chromatography. Elution with hexane–ethyl acetate (3:1) gave the *product* (**16b**) (27 mg, 44%) as an oil (Found: M^+, 291.1447. $C_{16}H_{21}NO_4$ requires M, 291.1469); $\nu_{max.}$ ($CHCl_3$) 3 470 and 1 738 cm^{-1}; δ_H ($CDCl_3$) 1.16—1.54 (6 H, m, 4-Me and *Me*CHOH), 2.32 (1 H, d, J 15 Hz, C*H*HCO$_2$Me), 2.55 (1 H, d, J 15 Hz, CH*H*CO$_2$Me), 3.05 (1 H, d, J 10 Hz, 3-H), 3.64 (3 H, s, OMe), 3.90—4.63 (3 H, m, CH_2Ph and MeC*H*OH), 7.23 ($\frac{1}{4}$ × 5 H, s, Ph), and 7.27 ($\frac{3}{4}$ × 5 H s, Ph).

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