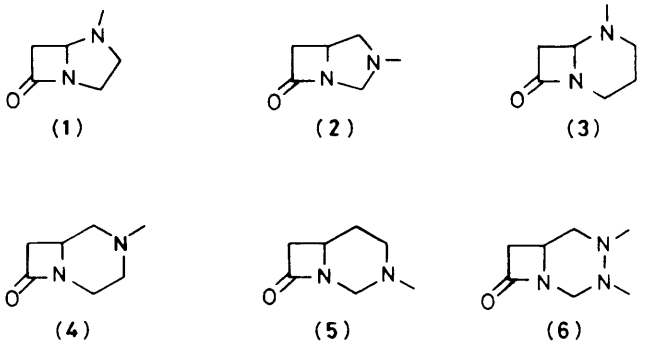
Synthesis of 1,2-Diazetidinones (Aza-β-lactams) by Photochemical Ring Contraction[1]

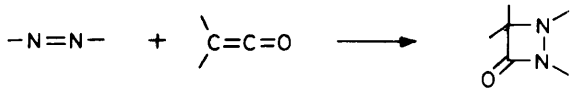
Geoffrey Lawton
Roche Products Ltd., P.O. Box 8, Welwyn Garden City, Hertfordshire, AL7 3AY
Christopher J. Moody* and Christopher J. Pearson
Department of Chemistry, Imperial College of Science and Technology, London SW7 2AY

Irradiation of 4-diazopyrazolidine-3,5-diones (**11**) in the presence of alcohols, diethylamine, or water gives 1,2-diazetidinones (**12**) formed by photochemical Wolff rearrangement with ring contraction followed by reaction of the resulting ketene with the nucleophile. In the case of the bicyclic diazo compound (**11d**) a fragmentation reaction competes with ring contraction. The aza-β-lactams (**12**) show the expected high frequency carbonyl stretch in their i.r. spectra. The acid (**12e**) readily decarboxylates to give the 4-unsubstituted 1,2-dibenzyldiazetidinone (**28**), the four-membered ring of which is cleaved by alkaline hydrolysis, lithium aluminium hydride or diborane to give (**29**), (**30**), and (**31**), respectively (Scheme 9). Attempts to modify the carboxy substituent of (**12e**) into an acylamino group were unsuccessful.

In the search for modified and improved antibacterial agents, the β-lactams continue to play a key role, and in recent years there has been considerable interest in the modification of the ring system of naturally occurring β-lactams such as the penicillins and cephalosporins. These nuclear analogues are primarily accessible only by total synthesis, and among these, the aza analogues, which incorporate one or more additional nitrogen atoms into the ring fused to the β-lactam, have been extensively studied. For examples, derivatives of the dethia 1-azapenam (**1**),[2] 2-azapenam (**2**),[3] 1-azacepham (**3**),[4] 2-azacepham (**4**),[5] 3-azacepham (**5**),[6] and 2,3-diazacepham (**6**)[7] ring systems have all been prepared and evaluated for their biological activity.

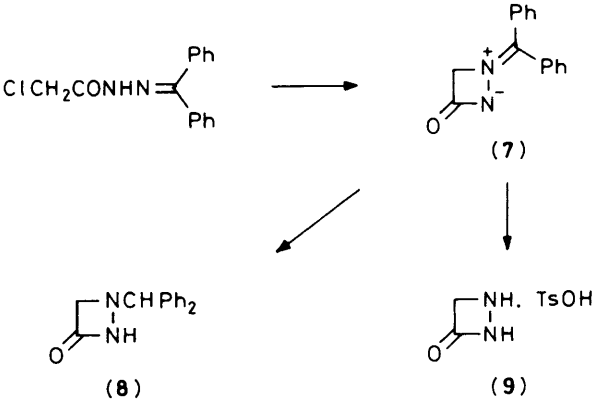


However, with the exception of some recent work by Taylor and co-workers,[8–13] aza-β-lactams based on 1,2-diazetidinones, in which the additional nitrogen is incorporated into the four-membered ring itself, have not been widely investigated. The only general route to 1,2-diazetidinones is the reaction between azo compounds and ketenes (Scheme 1), and although there are several examples of this reaction in the literature,[14] for the most part the resulting 1,2-diazetidinones are not suitable for further elaboration to β-lactam antibiotic analogues.



Scheme 1.

In contrast, the work by Taylor has provided versatile precursors to aza-β-lactams. The route is based on the cyclisation, under basic conditions, of benzophenone chloroacetylhydrazone to give the diazetidinium ylide (**7**) (Scheme 2) which can be converted into the 1,2-diazetidinones (**8**) and (**9**) by treatment with sodium borohydride and toluene-*p*-sulphonic acid (TsOH) with 1 mol equiv. of water respectively.



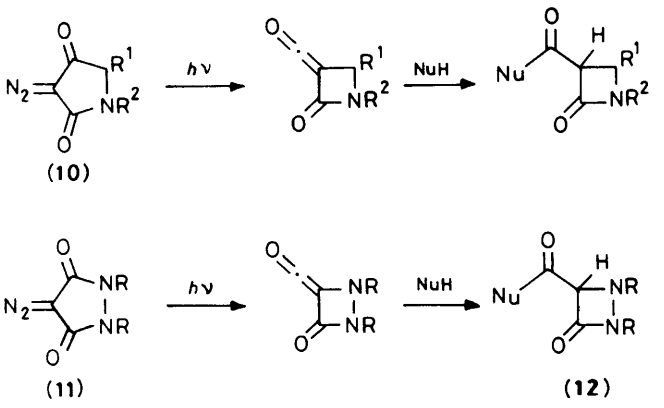
Scheme 2.

We have developed an alternative route to these structurally simple, but relatively rare aza-β-lactams, and we now report our results in detail.[1]

Results and Discussion

Among the many methods available for the preparation of β-lactams, several examples of the ring contraction of five-membered rings are known.[15–17] Of particular interest was the β-lactam synthesis developed independently by Lowe[16] and by Stork[17] in which the four-membered ring is formed by photochemical Wolff rearrangement of 3-diazopyrrolidine-2,4-diones (**10**) and subsequent trapping of the intermediate ketenes with nucleophiles (NuH) (Scheme 3). An analogous route (Scheme 3) to aza-β-lactams (**12**) seemed particularly attractive

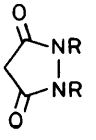
because the starting 4-diazopyrazolidine-3,5-diones (**11**) would be easily accessible by diazo-transfer[18] to pyrazolidine-3,5-diones, themselves readily available.[19,20]



Scheme 3.

However, it was by no means certain that in the photolysis of (**11**) the N–C bond would migrate to the electron deficient centre, since in the photolysis of (**10**) exclusive migration of C-5, rather than N-1, is observed.[16,17] The marked reluctance[16,17,21] of N–C bonds to migrate in the photochemical Wolff rearrangement is generally explained by participation of the nitrogen lone pair in amide resonance, especially in photoexcited states. Nevertheless, there are examples of nitrogen migration in the Wolff rearrangement,[22] and therefore the preparation and photochemical decomposition of symmetrical 4-diazopyrazolidine-3,5-diones (**11**) was investigated.

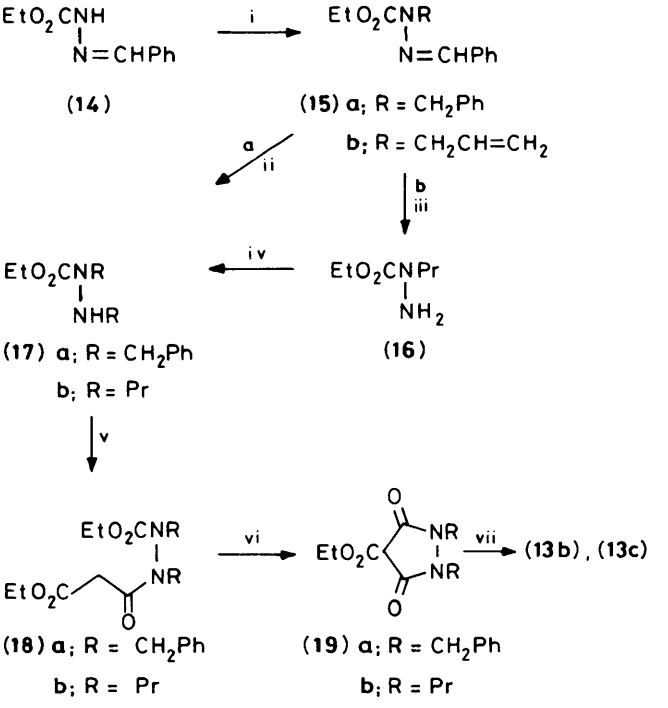
Preparation of 4-Diazopyrazolidine-3,5-diones.—The starting pyrazolidine-3,5-diones (**13**) were prepared by modification of literature procedures. Thus the known diphenyl derivative (**13a**)



(**13**) **a**; R = Ph
b; R = CH_2Ph
c; R = Pr
d; RR = $(CH_2)_4$

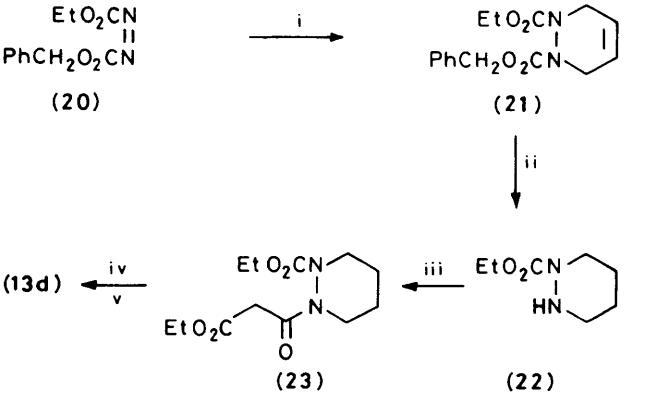
was prepared (50%) by monoacylation of hydrazobenzene with ethoxycarbonylacetyl chloride followed by base catalysed cyclisation.[23] The more direct procedure[24] involving reaction of hydrazobenzene with diethyl malonate in the presence of sodium ethoxide gave a much lower yield.

The 1,2-dialkylpyrazolidine-3,5-diones (**13b, c**) were prepared from ethyl 3-benzylidenecarbazate (**14**) by a modified literature procedure.[20] Alkylation with benzyl or allyl bromide under phase transfer conditions gave the expected products (**15**) in high yield (Scheme 4). Hydrogenation of (**15a**) gave the dibenzyl derivative (**17a**) (75%), whereas hydrogenation of the allyl derivative (**15b**) under acidic conditions resulted in saturation of the C=C and C=N bonds with concomitant hydrogenolysis to give (**16**). Reductive alkylation of (**16**) with propionaldehyde gave the dipropyl derivative (**17b**). Acylation of the dialkyl carbazates (**17**) with ethoxycarbonylacetyl chloride gave the diacyl hydrazines (**18**) which, without further purification, were cyclised under basic conditions to the pyrazolidinedione esters (**19**). Hydrolysis and decarboxylation of (**19**) occurred readily in wet acetonitrile to give the required pyrazolidinediones (**13b, c**).



Scheme 4. *Reagents:* i, RBr, C_6H_6, 40% NaOH–H_2O, $PhCH_2\overset{+}{N}Me_3Cl^-$; ii, H_2, Pd–C, EtOH; iii, H_2, Pd–C, EtOH, H^+; iv, EtCHO, H_2, Pd–C, EtOH; v, EtO_2CCH_2COCl, C_6H_6, Et_3N; vi, NaOEt, EtOH, reflux; vii, H_2O, MeCN, reflux

The bicyclic pyrazolidinedione (**13d**) was prepared as shown in Scheme 5. Although simple symmetrical azodicarboxylates have been widely used as reactive dienophiles,[25] unsymmetrical diesters such as (**20**) have not been used. The Diels–Alder reaction of (**20**) with buta-1,3-diene gave the tetrahydropyridazine (**21**) in high yield. Hydrogenation served to saturate the double bond and remove the benzyloxycarbonyl group to give (**22**). The literature preparation[26] of the monoester (**22**) involves the partial hydrolysis of the corresponding diethyl diester under vigorous conditions and in poor yield, and hence the use of the unsymmetrical azo diester (**20**) represents an improvement. Annelation of the five-membered ring proceeded as before by acylation with ethoxycarbonylacetyl chloride followed by cyclisation, hydrolysis and decarboxylation.



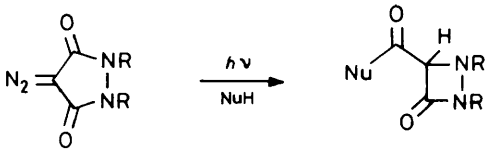
Scheme 5. *Reagents:* i, butadiene, C_6H_6; ii, H_2, Pd–C, EtOH; iii, EtO_2CCH_2COCl, C_6H_6, Et_3N; iv, NaH, toluene, reflux; v, H_2O, MeCN, reflux

Table. Aza-β-lactams (**12**) from 4-diazopyrazolidine-3,5-diones (**11**)

R	(11)	NuH	(12)	% Yield	$\nu_{max.}$ (cm^{-1})	δ (4-H)
Ph	**a**	EtOH	**a**	0		
$PhCH_2$	**b**	EtOH	**b**	45	1 785	4.47
$PhCH_2$	**b**	Bu^{t}OH	**c**	30	1 785	4.34
$PhCH_2$	**b**	Et_2NH	**d**	17	1 785	4.68
$PhCH_2$	**b**	H_2O	**e**	50	1 785	4.53
Pr	**c**	MeOH	**f**	48	1 785	4.32
Pr	**c**	H_2O	**g**	56	1 780	4.38
$-(CH_2)_4-$	**d**	EtOH	**h**	4	1 770	4.43

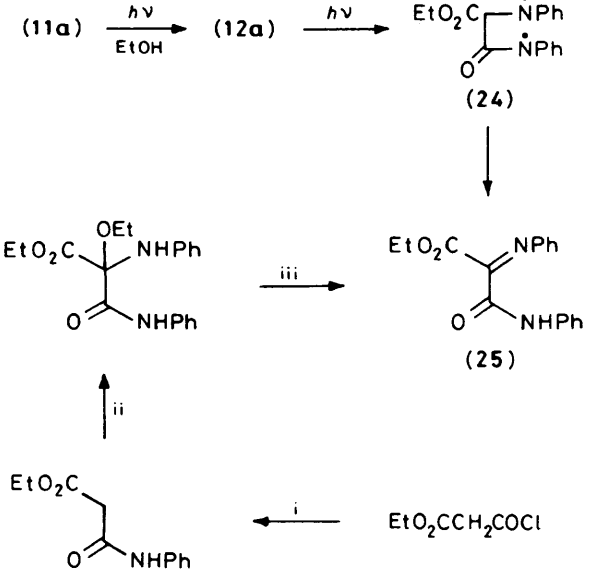
Subsequent diazo transfer to the pyrazolidine-3,5-diones (**13**) using tosyl azide in acetonitrile in the presence of triethylamine then gave the required 4-diazopyrazolidine-3,5-diones (**11**).

Photochemical Ring Contraction Reactions.—The diazo compounds (**11**) were irradiated in ether solution containing 5—10% (v/v) of a nucleophile to act as a ketene trap, and the results are summarised in Table 1.



(11) (12)

Irradiation of the diphenyl derivative (**11a**) in ether containing ethanol gave one major product (39%) together with a trace of azobenzene (2%). Although the major product had clearly incorporated ethanol (^{1}H n.m.r.), the lack of a high frequency carbonyl stretch in its i.r. spectrum indicated that it was not the required 1,2-diazetidinone (**12a**), and on the basis of its spectral properties it was assigned the structure (**25**). This structure was confirmed by an independent synthesis from ethoxycarbonylacetyl chloride by reaction with aniline, followed by condensation with nitrosobenzene (Scheme 6). It is likely that the product (**25**) does arise *via* the aza-β-lactam (**12a**), possibly by photochemical homolytic cleavage of the N–N bond to give the diradical (**24**) (Scheme 6), and since aryl substituents



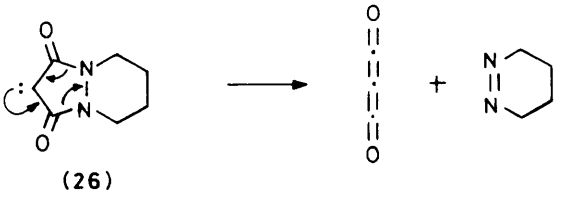
Scheme 6. *Reagents:* i, $PhNH_2$; ii, PhNO, Na_2CO_3, H_2O, EtOH; iii, TsOH, C_6H_6, reflux

would facilitate such a process by stabilising the diradical, attention was then turned to the dialkyl derivatives (**11b—d**).

The dibenzyl compound (**11b**) was irradiated in ether containing ethanol to give the required 1,2-diazetidinone (**12b**) (45%) as a colourless oil. The four-membered ring structure was supported by a high frequency carbonyl stretch at 1 785 cm^{-1} in the i.r. spectrum, and by the n.m.r. spectra which showed *inter alia* a singlet for 4-H at δ 4.47, AB quartets for the N-1 and N-2 benzylic protons at δ 3.85 (*J* 13 Hz) and 4.45 (*J* 15 Hz) respectively in the proton spectrum, and singlets for the ester and lactam carbonyls at δ 162.3 and 164.3 (assignment uncertain) and a doublet for C-4 at δ 78.1 in the off-resonance ^{13}C spectrum. Similarly irradiation of (**11b**) in the presence of t-butyl alcohol, diethylamine, or water gave the corresponding aza-β-lactams (**12c—e**) in moderate yields (Table 1), the particularly low yield of the amide (**12d**) being attributed to the repeated chromatography necessary to obtain a pure sample. In contrast the acid (**12e**) was easily isolated from the photolysis mixture simply by extraction into aqueous sodium hydrogen carbonate.

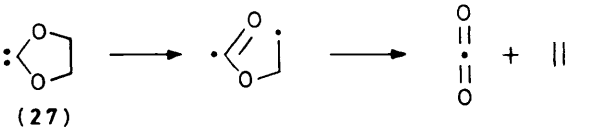
When the photolysis of (**11b**) was carried out in the absence of nucleophiles, some evidence for the intermediate ketene (*cf.* Scheme 3) was obtained. Thus a solution of the diazo compound (**11b**) in dry dichloromethane was irradiated, and the course of the reaction was monitored by i.r. spectroscopy. The spectra showed a gradual decrease in intensity of the band assigned to the diazo group ($\nu_{max.}$ 2 160 cm^{-1}) with the appearance of two new bands at 2 240 and 1 780 cm^{-1}. These are tentatively assigned to the ketene and four-membered ring carbonyl groups of the intermediate ketene.

The 1,2-dipropyl compound (**11c**) and the bicyclic diazo compound (**11d**) also underwent ring contraction to 1,2-diazetidinones on irradiation in the presence of a nucleophile (Table 1), although the yield of bicyclic aza-β-lactam (**12h**) was disappointingly low. The major product in the photolysis of (**11d**) in the presence of ethanol was diethyl malonate (41%), along with an unidentified hydrocarbon oil. Formation of the former product can be rationalised in terms of a fragmentation of the carbene intermediate (**26**). Whereas Wolff rearrangement would lead to ring contraction, a competing fragmentation [arrows in (**26**)] would give carbon suboxide (rapidly intercepted by ethanol to give diethyl malonate), and the azo compound, 3,4,5,6-tetrahydropyridazine (Scheme 7) which was not isolated.



Scheme 7.

Presumably a similar fragmentation accounts for the formation of small amounts of azobenzene in the photolysis of (**11a**). As written (Scheme 7) this fragmentation corresponds to a concerted $\sigma_2s + \sigma_2s + \omega_2s$ process from the singlet carbene, although a non-concerted pathway is also possible. Indeed in

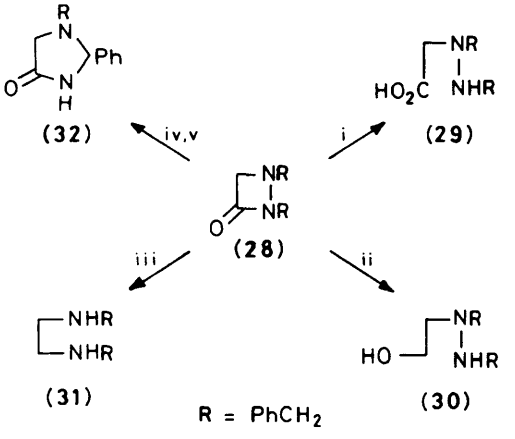


Scheme 8.

the related fragmentation of the carbene (**27**) to carbon dioxide and ethylene (Scheme 8), calculations suggest that a stepwise process involving a diradical is energetically more favourable than the concerted pathway.[27]

Properties of the 1,2-*Diazetidinones*.—The chemistry of these aza-β-lactams has been investigated in the dibenzyl series using the readily obtained acid (**12e**) as starting material. When heated, the acid (**12e**) is decarboxylated in high yield to give the 1,2-diazetidinone (**28**). The ^{1}H n.m.r. spectrum of (**28**) contains an AB quartet at δ 4.38 for the hydrogens on C-4, and indeed this is a characteristic feature of other C-4 unsubstituted 1,2-diazetidinones.[11,28] This quartet coalesced to a singlet at 390 K, giving a value[29] for the inversion barrier at N-1 of 19 kcal mol^{-1} (1 kcal = 4.19 kJ).

The aza-β-lactam ring in (**28**) is moderately stable to acidic hydrolysis requiring prolonged (>4 h) refluxing in aqueous THF containing hydrochloric acid to effect complete destruction of the ring, as monitored by the disappearance of the high frequency carbonyl in the i.r. spectrum. Alkaline hydrolysis of (**28**) gave the hydrazinoacetic acid derivative (**29**) in 67% yield (Scheme 9).

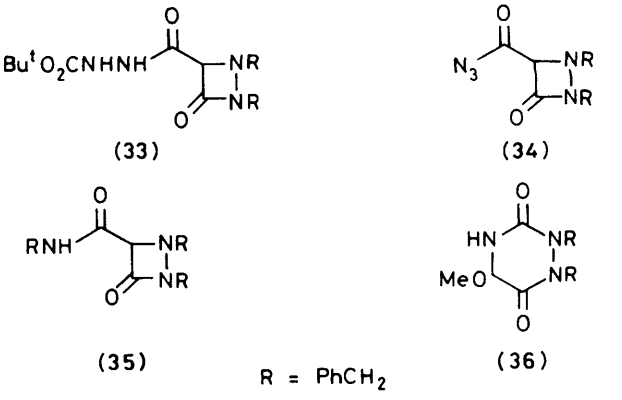


Scheme 9. *Reagents:* i, NaOH, H_2O, MeCN; ii, $LiAlH_4$, THF, reflux; iii, diborane–THF; iv, LDA, THF, −78 °C; iv, MeI, then aqueous work-up

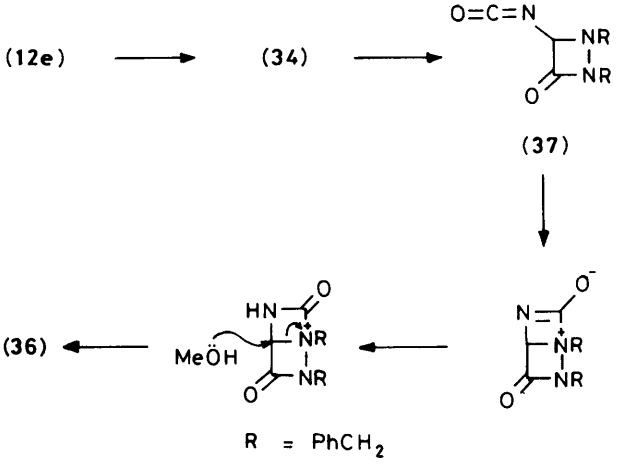
The 1,2-diazetidinone ring of (**28**) is also cleaved under reducing conditions. Thus treatment of (**28**) with lithium aluminium hydride in refluxing THF gave the hydrazino alcohol (**30**) in high yield. A similar reductive cleavage to 3-aminopropan-1-ols occurs when *N*-substituted β-lactams are treated with $LiAlH_4$.[30] Diborane reduction of β-lactams is however less selective and mixtures of amino alcohols and azetidines are often produced.[31] The aza-β-lactam (**28**) gave 1,2-dibenzylaminoethane (**31**) on treatment with diborane by reduction of the carbonyl and reductive cleavage of the N–N bond. Diborane is known to effect reductive cleavage of N–N bonds.[32] Attempted formation and alkylation of the anion at C-4 of (**28**) using lithium di-isopropylamide (LDA), followed by iodomethane, led to the unmethylated ring-expanded imidazolin-4-one (**32**) in 68% yield, presumably by rearrangement of the dipole stabilised anion formed by deprotonation of the N-2 benzyl group.[9,33]

Since one of the salient features of many β-lactam antibiotics is the presence of an acylamino group on the carbon atom adjacent to the β-lactam carbonyl, routes to 4-acylamino-1,2-diazetidinones were investigated. Again, the acid (**12e**) was chosen as starting material since standard methods are available for the conversion of a carboxy group into amino or acylamino functions, and such transformations are known in the β-lactam area.[34] Thus the acid (**12e**) was coupled with *t*-butyl carbazate in the presence of dicyclohexylcarbodi-imide to give the *t*-butoxycarbonylhydrazide (**33**) as a crystalline solid. However, attempted conversion of (**33**) into the corresponding acyl azide (**34**), the substrate required for Curtius rearrangement, by treatment with trifluoroacetic acid followed by sodium nitrite in aqueous acid, led only to complete decomposition.

Similarly, treatment of the acid (**12e**) with ethyl chloroformate, followed by sodium azide,[35] led to a red oil containing no trace of the required acyl azide (**34**). In a final attempt to prepare the acyl azide (**34**), the acid (**12e**) was treated with diphenylphosphoryl azide (DPPA)[36] and triethylamine in benzene at room temperature. After 1 h, t.l.c. indicated complete reaction and the appearance of a strongly u.v. active spot, presumed to be the acyl azide (**34**). The solution was then refluxed, before being quenched with methanol. Two products were isolated, only one of which retained the four-membered ring but had not incorporated methanol. This product was identified as the 1,2-diazetidinone (**35**), and arises by coupling of the acid (**12e**) with benzylamine mediated by DPPA. The origin of the benzylamine is uncertain, rigorous checks confirming that it was not an impurity in any of the reagents or starting material, but presumably it must be a decomposition product of the 1,2-dibenzyldiazetidinone itself.



The second product, which had incorporated an additional nitrogen atom and methanol was assigned structure (**36**) on the basis of its spectral data. One possible mechanism for its formation is shown in Scheme 10 and involves the required formation of, and Curtius rearrangement of, the acyl azide (**34**) to give the isocyanate (**37**), which is intercepted intramolecularly before the addition of methanol. Ring opening of the strained bicyclic system by methanol then leads to the observed product.



Scheme 10.

Experimental

I.r. spectra were recorded in the range 600—4 000 cm^{-1} on a Perkin-Elmer 257 or 298 spectrophotometer and were calibrated against polystyrene. U.v. and visible spectra were recorded on a Pye Unicam SP800 spectrophotometer. ^1H N.m.r. spectra were recorded at 60, 90, 250, and 300 MHz using Varian EM360, Perkin Elmer R32 or Jeol FX90Q, Bruker WM250, and Bruker WM300 instruments using tetramethylsilane as internal reference. ^{13}C N.m.r. spectra were recorded at 62.9 and 22.5 MHz using the Bruker WM250 and Jeol instruments. Low and high resolution mass spectra were recorded on A.E.I. MS12 and VG Micromass 7070B instruments at 70 eV. Light petroleum refers to that fraction with b.p. 60—80 °C. Ether refers to diethyl ether. All solvents were dried by standard procedures, and organic solutions were dried over magnesium sulphate. Column chromatography was carried out on Merck Kieselgel 60 (70—230 mesh) and flash chromatography on Kieselgel H (type 60). Photochemical reactions were carried out in a water-cooled Pyrex apparatus with external irradiation from a medium-pressure mercury lamp.

1,2-*Diphenylpyrazolidine*-3,5-*dione* (**13a**).—This was prepared by the literature method.[23]

Ethyl 3-*Benzylidene*-2-*benzylcarbazate* (**15a**).—Aqueous sodium hydroxide (40%; 18 ml) and trimethylbenzylammonium chloride (0.1 g) were added to a rapidly stirred mixture of ethyl 3-benzylidenecarbazate[37] (**14**) (3.0 g, 16 mmol) and benzyl bromide (4.65 g, 27.2 mmol) in benzene (90 ml). The two-phase mixture was stirred and heated under reflux for 17 h. The organic layer was separated, washed with saturated aqueous ammonium chloride and water, dried, and evaporated to give the *title compound* (**15a**) (4.3 g, 95%), m.p. 64—65 °C (Found: C, 72.5; H, 6.4; N, 9.9. $C_{17}H_{18}N_2O_2$ requires C, 72.3; H, 6.4; N, 9.9%); $\nu_{max.}$(Nujol) 1 700 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.4 (3 H, t), 4.4 (2 H, q), 5.23 (2 H, s), 7.2—7.5 (10 H, m), and 7.75 (1 H, s); *m/z* 282 (M^+), 150, and 91 (base).

Ethyl 2-*Allyl*-3-*benzylidenecarbazate* (**15b**).—Reaction of ethyl 3-benzylidenecarbazate (**14**) with allyl bromide using the conditions described above gave the *title compound* (**15b**) (87%), b.p. 115 °C at 0.7 mmHg (Found: C, 66.9; H, 6.9; N, 12.3. $C_{13}H_{16}N_2O_2$ requires C, 67.2; H, 6.9; N, 12.1%); $\nu_{max.}$(neat) 1 700 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.40 (3 H, t), 4.32 (2 H, q), 4.60 (2 H, m), 5.20 (2 H, m), 5.75 (1 H, m), 7.5 (5 H, m), and 7.75 (1 H, s); *m/z* 232 (M^+, base).

Ethyl 2,3-*Dibenzylcarbazate* (**17a**).—A solution of the carbazate (**15a**) (2.0 g) in ethanol (20 ml) was hydrogenated over 10% palladium-on-charcoal (0.3 g) until uptake of hydrogen ceased. Filtration, evaporation, and distillation gave the *title compound* (**17a**) (1.51 g, 75%), b.p. 163—167 °C at 0.1 mmHg (Found: C, 72.2; H, 7.3; N, 9.6. $C_{17}H_{20}N_2O_2$ requires C, 71.8; H, 7.1; N, 9.85%); $\nu_{max.}$(neat) 3 300 and 1 695 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.25 (3 H, t), 3.91 (2 H, s), 4.25 (2 H, q), 4.47 (2 H, s), and 7.32 (10 H, s), NH not observed; *m/z* 284 (M^+), 234, 194, and 91 (base).

Ethyl 2-*Propylcarbazate* (**16**).—A solution of the carbazate (**15b**) (10.0 g) in a mixture of ethanol (100 ml) and acetic acid (25 ml) was hydrogenated over 10% palladium–charcoal (1.5 g) until uptake of hydrogen ceased. Filtration, evaporation, and distillation gave the title compound (**16**) (4.2 g, 72%), b.p. 80—84 °C at 0.3 mmHg; $\nu_{max.}$(neat) 3 320, 3 210, and 1 670 cm^{-1}; δ (90 MHz; $CDCl_3$) 0.95 (3 H, t), 1.3 (3 H, t), 1.60 (2 H, m), 3.35 (2 H, t), 3.85 (2 H, br, D_2O exch.), and 4.15 (2 H, q); *m/z* 146 (M^+), 130 (base), and 117.

Ethyl 2,3-*Dipropylcarbazate* (**17b**).—A mixture of the carbazate (**16**) (4.0 g, 27 mmol), and propanal (1.6 g, 27 mmol) in ethanol (110 ml) was hydrogenated over 10% palladium–charcoal (0.3 g) for 24 h. Filtration, evaporation, and distillation gave the *title compound* (**17b**) (3.4 g, 70%), b.p. 75—80 °C at 0.3 mmHg (Found: C, 57.2; H, 10.5; N, 14.9. $C_9H_{20}N_2O_2$ requires C, 57.4; H, 10.7; N, 14.9%); $\nu_{max.}$(neat) 3 320 and 1 700 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.85 (3 H, t), 0.92 (3 H, t), 1.24 (3 H, t), 1.44 (2 H, m), 1.58 (2 H, m), 2.76 (3 H, t), 3.27 (2 H, t), and 4.13 (2 H, q); *m/z* 188 (M^+), 159, 113 (base), and 100.

Ethyl 2,3-*Dibenzyl*-3-(*ethoxycarbonylacetyl*)*carbazate* (**18a**).—A solution of ethoxycarbonylacetyl chloride (0.27 g, 1.8 mmol) in benzene (20 ml) and triethylamine (0.2 g, 1.9 mmol) were added dropwise to a stirred ice-cooled solution of the carbazate (**17a**) (0.51 g, 1.8 mmol) in benzene (20 ml). After the addition was completed, the mixture was stirred for a further 3 h, and then filtered. The filtrate was washed with water (50 ml), dried, and evaporated to give the title compound (**18a**) (0.52 g, 72%) as a yellow gum, $\nu_{max.}$(neat) 1 740, 1 720, and 1 680 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.10 (3 H, t), 1.21 (3 H, t), 2.95 (2 H, AB, *J* 16 Hz), 4.15 (4 H, 2 overlapping q), 4.75 (4 H, 2 × d), and 7.32 (10 H, ~ s); *m/z* 399 ($M^+ + 1$), 220, 178, 106, and 91 (base).

Ethyl 3-(*Ethoxycarbonylacetyl*)-2,3-*dipropylcarbazate* (**18b**).—The carbazate (**17b**) (3.6 g, 19 mmol) was acylated with ethoxycarbonylacetyl chloride (2.9 g, 19 mmol) as described above to give the title compound (**18b**) (5.3 g, 92%) as a yellow oil, $\nu_{max.}$(neat) 1 740, 1 710, and 1 670 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 0.9 (6 H, t), 1.2 (6 H, t), 1.5—2.0 (4 H, m), 3.3—3.8 (6 H, m), and 4.2 (2 H, m); *m/z* 303 ($M^+ + 1$), 267, 198, 159, and 105.

1,2-*Dibenzylpyrazolidine*-3,5-*dione* (**13b**).—A solution of the carbazate (**18a**) (0.45 g) in ethanol (5 ml) was added dropwise to a stirred solution of sodium ethoxide [from sodium (0.05 g)] in ethanol (10 ml), and the mixture was heated under reflux for 20 h. After being cooled, the solution was diluted with chloroform (20 ml), washed with hydrochloric acid (2M; 20 ml) and water (30 ml), dried, and evaporated to give ethyl 1,2-dibenzyl-3,5-dioxopyrazolidine-4-carboxylate (**19a**) as a yellow foam. Without purification, this material was refluxed in aqueous acetonitrile for 2 h. Evaporation of the solvent gave the *title compound* (**13b**) (0.25 g, 78%), m.p. 128.5 °C (Found: C, 72.9; H, 5.7; N, 10.0. $C_{17}H_{16}N_2O_2$ requires C, 72.8; H, 5.75; N, 10.0%); $\nu_{max.}$(Nujol) 1 690 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 3.34 (2 H, s), 4.75 (4 H, s), and 7.3 (10 H, m); *m/z* 280 (M^+) and 91 (base).

1,2-*Di-propylpyrazolidine*-3,5-*dione* (**13c**).—Following the procedure described above, the carbazate (**18b**) (5.3 g) was cyclised to the pyrazolidine ester (**19b**), which when heated in aqueous acetonitrile gave the title compound (**13c**) (1.3 g, 41%) as a yellow oily solid, $\nu_{max.}$(Nujol) 1 700 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 0.9 (6 H, t), 1.5 (4 H, m), 3.2 (2 H, s), and 3.58 (4 H, t); *m/z* 184 (M^+).

Benzyl Ethyl Diazene-1,2-*dicarboxylate* (**20**).—Benzyl ethyl hydrazine-1,2-dicarboxylate (40 g, 0.168 mol), prepared by acylation of ethyl carbazate with benzyl chloroformate, in ethyl acetate (150 ml) was treated with t-butyl hypochlorite (25 ml) at room temperature. After being stirred for 3 h, the solution was washed with aqueous sodium hydrogen carbonate (100 ml) and water (100 ml), dried, and evaporated to give the title compound (**20**) (38.2 g, 95%) as a red oil, δ_H (60 MHz; $CDCl_3$) 1.35 (3 H, t), 4.38 (2 H, q), 5.30 (2 H, s), and 7.30 (5 H, s), used without further purification.

Ethyl Hexahydropyridazine-1-*carboxylate* (**22**).—Butadiene was bubbled through a solution of benzyl ethyl diazene-1,2-

dicarboxylate (36 g) in benzene (150 ml) for 1 h. The solution was stirred for 24 h, during which time the red–orange colour of the diazene was discharged. Evaporation of the solvent gave benzyl ethyl 1,2,3,6-tetrahydropyridazine-1,2-dicarboxylate (**21**) (44.3 g, 100%) as a colourless oil, δ_H (60 MHz; $CDCl_3$) 1.15 (3 H, t), 3.57—3.82 (2 H, m), 4.2 (2 H, q), 4.5 (2 H, m), 5.08 (2 H, s), 5.65 (2 H, br), and 7.20 (5 H, s), used without further purification.

A solution of the tetrahydropyridazine (**21**) (19 g) in ethanol (150 ml) was hydrogenated over 10% palladium–charcoal (1.2 g) until uptake of hydrogen ceased. Filtration, evaporation, and distillation gave the title compound (**22**) (6.7 g, 71%), b.p. 80 °C at 0.2 mmHg (lit.,[26] 114—119 °C at 20 mmHg); $\nu_{max.}$(neat) 3 320 and 1 690 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.22 (3 H, t), 2.15 (4 H, m), 2.9 (2 H, t), 3.55 (2 H, t), 4.15 (2 H, q), and 6.05 (1 H, br, D_2O exch.).

*Hexahydro-*1H*-pyrazolo*[1,2-a]*pyridazine-*1,3*-dione* (**13d**).—A solution of ethoxycarbonylacetyl chloride (4.9 g, 32 mmol) in dry ether (30 ml) was added dropwise to a stirred solution of the hexahydropyridazine (**22**) (5.0 g, 32 mmol) and triethylamine (3.2 g, 32 mmol) in dry ether (200 ml). Stirring was continued for 2 h, after which the mixture was filtered, and the filtrate evaporated to give ethyl 2-(ethoxycarbonylacetyl)hexahydropyridazine-1-carboxylate (**23**) (8.2 g, 93%) as a yellow oil, $\nu_{max.}$(neat) 1 735 and 1 680 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.30 (3 H, t), 1.34 (3 H, t), 1.68 (4 H, m), 2.3—3.3 (4 H, m), 3.3 (2 H, AB *J* 17 Hz), 4.25 (5 H, m), and 4.60 (1 H, br), used without further purification.

A solution of the above compound (**23**) (2.0 g) in dry toluene (20 ml) was added to a stirred suspension of sodium hydride (80%; 0.20 g) in dry toluene (100 ml). After evolution of hydrogen had ceased, the mixture was heated under reflux for 6 h, cooled and poured into water (100 ml). The water layer was acidified and extracted with dichloromethane. The organic extract was dried and evaporated. The residue was dissolved in aqueous acetonitrile and heated under reflux for 3 h. Evaporation of the solvent and crystallisation of the residue from ethyl acetate–cyclohexane gave the *title compound* (**13d**) (0.6 g, 60%) as colourless plates, m.p. 119.5 °C (Found: C, 54.5; H, 6.5; N, 18.05. $C_7H_{10}N_2O_2$ requires C, 54.5; H, 6.5; N, 18.2%); $\nu_{max.}$(Nujol) 1 735 and 1 695 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.74 (4 H, m), 3.10 (2 H, s), and 3.50 (4 H, m); *m/z* 154 (M^+, base).

Diazo Transfer Reactions: General Procedure.—Triethylamine (6 mmol) was added dropwise to an ice cooled solution of the pyrazolidine-3,5-dione (**13**) (4.4 mmol) and toluene-*p*-sulphonyl azide[38] (1.70 g, 8.8 mmol) in acetonitrile (30 ml). The mixture was stirred at 0 °C for 1 h, and then at room temperature for 2 h, or until t.l.c. indicated that the reaction was complete. The solvent was evaporated, and the residue triturated with ether. The ether was washed with aqueous sodium hydroxide (5%) and water, dried, and evaporated, and the residue chromatographed on silica gel eluting with dichloromethane to give unchanged tosyl azide, followed by the diazo compound (**11**). The following compounds were thus prepared.

4-*Diazo-*1,2*-diphenylpyrazolidine-*3,5*-dione* (**11a**) (39%), m.p. 118—118.5 °C (from ethanol) (Found: C, 64.8; H, 3.6; N, 20.1. $C_{15}H_{10}N_4O_2$ requires C, 64.7; H, 3.6; N, 20.1%); $\nu_{max.}$(Nujol) 2 150 and 1 695 cm^{-1}; δ_H (60 MHz), 7.15 (m); *m/z* 278 (M^+, base).

4-*Diazo-*1,2*-dibenzylpyrazolidine-*3,5*-dione* (**11b**) (66%), m.p. 78 °C (from ethanol) (Found: 66.7; H, 4.6; N, 18.3. $C_{17}H_{14}N_4O_2$ requires C, 66.7; H, 4.6; N, 18.3%); $\nu_{max.}$(Nujol) 2 140 and 1 690 cm^{-1}; $\lambda_{max.}$(EtOH) 230 (log ε 4.3) and 280sh nm; δ_H (90 MHz; $CDCl_3$) 4.72 (4 H, s), and 7.25 (10 H, m); *m/z* 306 (M^+) and 91 (base).

4-*Diazo-*1,2*-dipropylpyrazolidine-*3,5*-dione* (**11c**) (55%), gum (Found: M^+, 210.2363. $C_9H_{14}N_4O_2$ requires 210.2361); $\nu_{max.}$(neat) 2 140, 1 720, and 1 690 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 0.98 (6 H, t), 1.6 (4 H, m), and 3.55 (4 H, t); *m/z* 210 (M^+).

2-*Diazotetrahydro-*1H*-pyrazolo*[1,2-a]*pyridazine-*1,3(2H)*-dione* (**11d**) (78%), m.p. 92—93 °C (from chloroform–light petroleum) (Found: C, 46.7; H, 4.4; N, 31.0. $C_7H_8N_4O_2$ requires C, 46.7; H, 4.5; N, 31.1%); $\nu_{max.}$(Nujol) 2 130, 1 710, and 1 675 cm^{-1}; $\lambda_{max.}$(EtOH) 225 (log ε 4.19), 270infl. and 320infl. nm; δ_H (60 MHz; $CDCl_3$) 2.85 (4 H, m) and 3.50 (4 H, m); *m/z* 180 (M^+).

Photolysis of the Diazo Compound (**11a**).—A solution of the diazo compound (**11a**) (0.12 g) in dry ether (100 ml) and ethanol (5 ml) was irradiated for 24 h. Evaporation of the solvents and flash chromatography of the residue gave (i) azobenzene (1.6 mg, 2%), m.p. 64—66 °C (lit.,[39] 67 °C), and (ii) 2-*phenyliminomalonic acid monoethyl ester* N-*phenylcarboxamide* (**25**) (49 mg, 39%) as a yellow oil (Found: M^+, 296.1159. $C_{17}H_{16}N_2O_3$ requires 296.1161); $\nu_{max.}$(neat) 3 350, 1 736, 1 685, and 1 600 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.09 (3 H, t), 4.20 (2 H, q), 6.9—7.8 (10 H, m), and 9.1 (1 H, br, D_2O exch.); *m/z* 296 (M^+).

Independent Synthesis of the Imine (**25**).—A solution of nitrosobenzene (0.57 g, 5.3 mmol) in aqueous ethanol (30 ml) was added dropwise to a stirred mixture of malonic acid monoethyl ester *N*-phenylcarboxamide (1.1 g, 5.3 mmol) and sodium carbonate (0.57 g, 5.3 mmol) in ethanol (30 ml). The mixture was stirred for 4 h, filtered, and the filtrate evaporated to leave a yellow oil, which was dissolved in ethanol (10 ml). On cooling, colourless needles of 2-*ethoxy-*2*-phenylaminomalonic acid monoethyl ester* N-*phenyl-carboxamide* (0.95 g, 59%) separated, m.p. 136 °C (Found: C, 66.75; H, 6.45; N, 8.2. $C_{19}H_{22}N_2O_4$ requires C, 66.65; H, 6.5; N, 8.2%); $\nu_{max.}$(Nujol) 3 390, 3 300, 1 740, 1 700, 1 680, 1 605, and 1 590 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.03 (3 H, t), 1.20 (3 H, t), 3.58 (2 H, q), 4.15 (2 H, q), 5.90 (1 H, br), 6.6—7.7 (10 H, m), and 8.95 (1 H, br).

A solution of the above compound (138 mg) and toluene-*p*-sulphonic acid (9 mg) in benzene (10 ml) was heated under reflux for 2 h. After being cooled, the solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give the imine (**25**) (120 mg, 100%).

Photolysis of Diazo Compound (**11b**).—(*a*) *In the presence of ethanol.* A solution of the diazo compound (**11b**) (370 mg) in dry ether (130 ml) and ethanol (5 ml) was irradiated for 1 h. Evaporation of the solvents and flash chromatography of the residue gave *ethyl* 1,2-*dibenzyl-*3-*oxo-*1,2-*diazetidine-*4-*carboxylate* (**12b**) (190 mg, 45%) as a colourless oil (Found: C, 70.7; H, 6.35; N, 8.7. $C_{19}H_{20}N_2O_3$ requires C, 70.35; H, 6.2; N, 8.6%); $\nu_{max.}$(neat) 1 785 and 1 742 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.18 (3 H, t), 3.85 (2 H, AB, *J* 13 Hz), 4.13 (2 H, q), 4.45 (2 H, AB, *J* 15 Hz), 4.47 (1 H, s), and 7.25 (10 H, m); δ_C (62.9 MHz; $CDCl_3$) 13.8 (q), 50.5 (t), 62.2 (t), 64.2 (t), 78.1 (d), 127.0—129.6 (several overlapping d), 134.7 (s), 135.1 (s), 162.3 (s), and 164.3 (s); *m/z* 324 (M^+), 251, 233, 117, 116, and 91 (base).

(*b*) *In the presence of t-butyl alcohol.* A solution of the diazo compound (**11b**) (283 mg) in dry ether (120 ml) and t-butyl alcohol (25 ml) was irradiated for 2 h. Evaporation of the solvents and chromatography of the residue gave *t-butyl* 1,2-*dibenzyl-*3-*oxo-*1,2-*diazetidine-*4-*carboxylate* (**12c**) (96 mg, 30%), m.p. 76 °C (from hexane–ethyl acetate) (Found: C, 71.6; H, 6.9; N, 7.9. $C_{21}H_{24}N_2O_3$ requires C, 71.6; H, 6.9; N, 7.95%); $\nu_{max.}$(Nujol) 1 785 and 1 744 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.35 (9 H, s), 3.83 (2 H, AB, *J* 13 Hz), 4.34 (1 H, s), 4.47 (2 H, AB, *J* 16 Hz), and 7.25 (10 H, m); *m/z* 352 (M^+), 296, 231, 107, 106, 105, 104, and 91 (base).

(*c*) *In the presence of diethylamine.* A solution of the diazo compound (**11b**) (240 mg) in dry ether (130 ml) and diethylamine (5 ml) was irradiated for 50 min. Evaporation of the solvents and flash chromatography of the residue gave a

yellow oil, which was rechromatographed to give 1,2-*dibenzyl*-N,N-*diethyl*-3-*oxo*-1,2-*diazetidine*-4-*carboxamide* (**12d**) (48 mg, 17%) as a yellow oil, which was not of analytical purity; $\nu_{max.}$(neat) 1 780 and 1 650 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 0.98 (3 H, t), 1.06 (3 H, t), 3.03 (1 H, m), 3.31 (3 H, m), 3.88 (2 H, AB, *J* 14 Hz), 4.52 (2 H, AB, *J* 17 Hz), 4.68 (1 H, s), and 7.26 (10 H, m); *m/z* 351 (M^+), 251, 218, 210, 132, 105, and 91 (base).

(*d*) *In the presence of water.* A solution of the diazo compound (**11b**) (415 mg) in ether saturated with water (175 ml) was irradiated for 45 min. The solution was concentrated to *ca.* 50 ml, and extracted with aqueous sodium hydrogen carbonate (50 ml). The hydrogencarbonate layer was washed with ether, acidified, and extracted with dichloromethane. The dichloromethane extract was dried, and evaporated to give 1,2-*dibenzyl*-3-*oxo*-1,2-*diazetidine*-4-*carboxylic acid* (**12e**) (200 mg, 50%), m.p. 108—119 °C (decomp.) which could not be obtained analytically pure due to its facile decarboxylation, $\nu_{max.}$(Nujol) 3 500—2 500, 1 785, and 1 720 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.85 (2 H, *J* 12 Hz), 4.40 (2 H, AB, *J* 16 Hz), 4.53 (1 H, s), 7.15 (10 H, m), and 9.40 (1 H, br, D_2O exch.); *m/z* 252 ($M^+ - CO_2$), 224, 161, 149, 117, and 91 base).

Photolysis of the Diazo Compound (**11c**).—(*a*) *In the presence of methanol.* A solution of the diazo compound (**11c**) (218 mg) in dry ether (120 ml) and methanol (20 ml) was irradiated for 1 h. Evaporation of the solvents and flash chromatography of the residue gave *methyl* 1,2-*dipropyl*-3-*oxo*-1,2-*diazetidine*-4-*carboxylate* (**12f**) (143 mg, 48%) as a pale yellow oil (Found: M^+, 214.1321. $C_{10}H_{18}N_2O_3$ requires *M*, 214.1327); $\nu_{max.}$(neat) 1 785 and 1 755 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.97 (3 H, t), 0.99 (3 H, t), 1.2—1.8 (4 H, m), 2.57 (1 H, m), 3.05 (1 H, m), 3.23—3.55 (2 H, m), 3.83 (3 H, s), and 4.32 (1 H, s); *m/z* 214 (M^+), 157, 130, 127, and 115.

(*b*) *In the presence of water.* A solution of the diazo compound (**11c**) (410 mg) in ether saturated with water (175 ml) was irradiated for 2 h. Work-up as described previously gave 1,2-*dipropyl*-3-*oxo*-1,2-*diazetidine*-4-*carboxylic acid* (**12g**) (200 mg, 56%) as a yellow gum, which could not be obtained analytically pure due to its facile decarboxylation; $\nu_{max.}$(neat) 3 500—2 400, 1 780, and 1 750 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.94 (3 H, t), 0.97 (3 H, t), 1.17—1.85 (4 H, m), 2.58 (1 H, m), 3.03 (1 H, m), 3.20—3.73 (2 H, m), 4.38 (1 H, s), and 9.45 (1 H, br); *m/z* 156 ($M^+ - CO_2$, base).

Photolysis of the Diazo Compound (**11d**).—A solution of the diazo compound (**11d**) (740 mg) in ether (300 ml) and ethanol (25 ml) was irradiated for 4 h. Evaporation of the solvents and chromatography of the residual orange oil gave (i) diethyl malonate (270 mg, 41%), (ii) an unidentified hydrocarbon oil (130 mg), and (iii) *ethyl hexahydro*-2-*oxo*[1,2]*diazeto*[1,2-a]-*pyridazine*-1-*carboxylate* (**12h**) (35 mg, 4%) as a colourless oil, which could not be obtained analytically pure; $\nu_{max.}$(neat) 1 770 and 1 740 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.33 (3 H, t), 1.72 (2 H, m), 1.86 (2 H, m), 2.4 (1 H, m), 3.24 (1 H, dt, *J* 13 and 6 Hz), 3.50 (1 H, m), 3.95 (1 H, m), 4.30 (2 H, qq), and 4.43 (1 H, s); *m/z* 198 (M^+), 170, 169, 125, 114, 97 (base), 86, 84, 70, 68, 55, and 41.

Decarboxylation of 1,2-*Dibenzyl*-3-*oxo*-1,2-*diazetidine*-4-*carboxylic Acid* (**12e**).—A solution of the acid (**12e**) (420 mg) in toluene (30 ml) was heated under reflux for 2 h. Evaporation of the solvent and chromatography gave 1,2-*dibenzyl*-1,2-*diazetidin*-3-*one* (**28**) (260 mg, 80%), as a colourless waxy solid, m.p. 38 °C (Found: C, 75.9; H, 6.5; N, 10.8. $C_{16}H_{16}N_2O$ requires C, 76.2; H, 6.4; N, 11.1%); $\nu_{max.}$(Nujol) 1 765 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.84 (2 H, AB, *J* 12.2 Hz), 4.07 (2 H, AB, *J* 13.7 Hz), 4.38 (2 H, AB, *J* 15.8 Hz, $\Delta\nu_{AB}$ 64.6 Hz, coalesces of warming to 390 K), and 7.25 (10 H, m); δ_C (62.9 MHz; $CDCl_3$) 50.2 (t), 66.9 (t), 77.2 (t), 127.3—129.3 (several overlapping d), 135.7 (s), and 166.7 (s); *m/z* 252 (M^+), 224, 145, 133, 128, 127, 105, and 91 (base), *m** (252 to 224) 199.5.

Alkaline Hydrolysis of the Diazetidinone (**28**).—A mixture of the diazetidinone (**28**) (70 mg), acetonitrile (10 ml), water (2.5 ml) and aqueous sodium hydroxide (1M; 0.3 ml) was stirred at room temperature for 20 h. The acetonitrile was evaporated, and the aqueous layer extracted with dichloromethane (30 ml). Evaporation of the dichloromethane gave the unchanged diazetidinone (**28**) (13 mg). The aqueous layer was acidified and re-extracted with dichloromethane. The dichloromethane extract was dried, and evaporated to give N,N′-*dibenzylhydrazinoacetic acid* (**29**) (50 mg, 67%), m.p. 145—146 °C (from ethanol) (Found: C, 71.15; H, 6.8; N, 10.35. $C_{16}H_{18}N_2O_2$ requires C, 71.1; H, 6.7; N, 10.4%); $\nu_{max.}$(Nujol) 3 400—2 500 and 1 610—1 530 cm^{-1}; δ_H [250 MHz; $(CD_3)_2SO$] 3.27 (2 H, s), 3.45 (2 H, br s, D_2O exch.), 3.83 (2 H, s), 3.95 (2 H, s), and 7.35 (10 H, m); *m/z* 270 (M^+).

Reduction of Diazetidinone (**28**).—(*a*) *With lithium aluminium hydride.* Lithium aluminium hydride (20 mg, 0.53 mmol) was added to a stirred solution of the diazetidinone (**28**) (128 mg, 0.51 mmol) in THF (5 ml). The mixture was stirred at room temperature for 0.25 h, then at reflux for 4 h. Aqueous work-up gave 2-(*N,N′-dibenzylhydrazino*)*ethanol* (**30**) (127 mg, 97%), b.p. 130 °C at 0.5 mmHg (Kugelrohr) (Found: M^+, 256.1572. $C_{16}H_{20}N_2O$ requires 256.1575); $\nu_{max.}$(neat) 3 700—3 150 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 2.61 (2 H, m), 3.40 (1 H, br s, D_2O exch.), 3.49 (1 H, t, D_2O exch.), 3.67 (2 H, m), 3.86 (2 H, s), 3.92 (2 H, s), and 7.30 (10 H, m); *m/z* 257 ($M^+ + H$), 224, 166, 136, 92 (base), and 65.

(*b*) *With diborane.* A solution of borane–THF complex (1M; 1.8 ml) was added to a stirred solution of the diazetidinone (**28**) (47 mg, 0.18 mmol) in THF (10 ml), and the mixture refluxed for 2 h. Work up gave 1,2-di(benzylamino)ethane (**31**) (38 mg, 85%), b.p. 115—120 °C at 0.3 mmHg (Kugelrohr) (lit.,[40] 184—186 °C at 2 mmHg); $\nu_{max.}$(neat) 3 300 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.79 (2 H, br s, D_2O exch.), 2.77 (4 H, s), 3.78 (4 H, s), and 7.31 (10 H, m); *m/z* 240 (M^+) and 91 (base).

Reaction of the Diazetidinone (**28**) *with Lithium Di-isopropylamide.*—Butyl-lithium (1.5M solution in hexane; 0.28 ml) was added to a stirred solution of di-isopropylamine (0.06 ml) in THF (2 ml), and the mixture cooled to −78 °C. A solution of the diazetidinone (**28**) (96 mg) in THF (1 ml) was added, and the resulting deep red solution was stirred at −78 °C for 0.25 h. Addition of iodomethane (0.03 ml), warming to room temperature, aqueous work-up, and chromatography gave 1-*benzyl*-2-*phenylimidazolin*-4-*one* (**32**) (65 mg, 68%), m.p. 167.5 °C (from light petroleum–ethyl acetate) (Found: M^+, 252.1258. $C_{16}H_{16}N_2O$ requires 252.1263); $\nu_{max.}$(Nujol) 3 200, 3 100, and 1 705 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.25 (2 H, qd, *J* 14.5, 2 Hz), 3.62 (2 H, AB, *J* 13.5 Hz), 5.03 (1 H, s), 6.83 (1 H, br s, D_2O exch.), 7.25 (5 H, m), 7.37 (3 H, m), and 7.52 (2 H, m); *m/z* 252 (M^+), 251, 175, 161, 120, 117, and 91 (base).

1,2-*Dibenzyl*-4-(3-*t-butoxycarbonylcarbazoyl*)-1,2-*diazetidin*-3-*one* (**33**).—Dicyclohexylcarbodi-imide (103 mg, 0.5 mmol) was added to a stirred solution of the carboxylic acid (**12e**) (150 mg, 0.5 mmol) and t-butyl carbazate (66 mg, 0.5 mmol) in dichloromethane at 0 °C. The mixture was stirred at 0 °C for 0.5 h and then at room temperature for 2 h. The resulting suspension was concentrated, and triturated with ether. The insoluble solid was filtrated off, the filtrate evaporated, and the residue chromatographed to give the *title compound* (**33**) (147 mg, 72%) (Found: C, 64.5; H, 6.3; N, 13.5. $C_{22}H_{26}N_4O_4$ requires C, 64.4; H, 6.4; N, 13.65%); $\nu_{max.}$(Nujol) 3 280, 1 785, 1 755, 1 715, and 1 690 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.46 (9 H, s), 3.94

(2 H, br s), 4.27 (2 H, AB, *J* 15 Hz), 4.55 (1 H, s), 6.24 (1 H, br s), 7.08—7.30 (10 H, m), and 7.84 (1 H, br s); *m/z* 252 ($M^+ - CO_2 - C_4H_8$), 224, 133, and 91 (base).

Attempted Synthesis of 1,2-*Dibenzyl*-4-(*methoxycarbonyl*)-*amino*-1,2-*diazetidin*-3-*one*.—Triethylamine (95 mg, 0.95 mmol) and diphenylphosphoryl azide (260 mg, 0.94 mmol) were added to a stirred solution of the acid (**12e**) (278 mg, 0.94 mmol) in benzene (7 ml) at room temperature. After being stirred for 1 h, the mixture was heated under reflux for 1 h, methanol (0.5 ml) was added, and the refluxing continued for a further 3 h. The benzene was evaporated, and the residue dissolved in ethyl acetate (30 ml), and washed successively with hydrochloric acid (1M), aqueous potassium hydrogen carbonate, and aqueous sodium chloride, dried, and evaporated. Chromatography gave (i) unchanged phosphoryl azide (15 mg), (ii) N-*benzyl*-3-*oxo*-1,2-*dibenzyl*-1,2-*diazetidine*-4-*carboxamide* (**35**) (41 mg, 11%), m.p. 128—129 °C (Found: C, 74.95; H, 5.9; N, 10.9. $C_{24}H_{23}N_3O_2$ requires C, 74.8; H, 6.0; N, 10.9%); $\nu_{max.}$(Nujol) 1 765 and 1 670 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.90 (2 H, AB, *J* 12 Hz), 4.14 (2 H, dq, *J* 15 and 15.7 Hz), 4.37 (2 H, AB, *J* 14.8 Hz), 4.49 (1 H, s), 6.50 (1 H, br s), and 6.91—7.35 (15 H, m); *m/z* 385 (M^+) 282, 252, 161, 149, 133, 118, 106, and 91 (base); and (iii) 1,2-*dibenzyl*-1,2-*dihydro*-5-*methoxy*-1,2,4-*triazine*-3,6(4H,5H)-*dione* (**36**) (55 mg, 18%), m.p. 164—165 °C (from ether–chloroform) (Found: C, 66.2; H, 5.8; N, 12.9. $C_{18}H_{19}N_3O_3$ requires C, 66.45; H, 5.9; N, 12.9%); $\nu_{max.}$(Nujol) 3 200, 3 090, and 1 675 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.31 (3 H, s), 4.70 (1 H, d, *J* 4.4 Hz, collapses to singlet with D_2O), 4.77 (2 H, AB, *J* 16 Hz), 4.79 (2 H, AB, *J* 16 Hz), 6.88 (1 H, d, *J* 4.4 Hz, D_2O exch.), 7.12 (2 H, m), and 7.28 (8 H, m); δ_C (62.9 MHz; $CDCl_3$), 49.9, 54.9, 65.7, 82.3, 127.4, 127.8, 128.1, 128.7, 129.0, 134.7, 135.1, 155.3, and 161.7; *m/z* 325 (M^+), 293 and 91 (base).

Acknowledgements

We thank the S.E.R.C. and Roche Products Ltd. for a CASE awared to C. J. P.

References

1 Preliminary communication, G. Lawton, C. J. Moody, and C. J. Pearson, *J. Chem. Soc., Chem. Commun.*, 1984, 754.
2 G. Johnson and B. C. Ross, *J. Chem. Soc., Chem. Commun.*, 1981, 1269; G. Johnson, P. M. Rees, and B. C. Ross, *ibid.*, 1984, 970; D. Davies and M. J. Pearson, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2539.
3 W. F. Huffman, K. G. Holden, T. F. Buckley, J. G. Gleason, and L. Wu, *J. Am. Chem. Soc.*, 1977, **99**, 2352; D. B. Bryan, R. F. Hall, K. G. Holden, W. F. Huffman, and J. G. Gleason, *ibid.*, 1977, **99**, 2353; C. L. Branch and M. J. Pearson, *J. Chem. Soc., Chem. Commun.*, 1981, 946.
4 S. Wolfe, J.-B. Ducep, G. Kannengiesser, and W. S. Lee, *Can. J. Chem.*, 1972, **50**, 2902; A. K. Bose, J. C. Kapur, and M. S. Manhas, *Synthesis*, 1974, 891; S. D. Sharma and U. Mehra, *Tetrahedron Lett.*, 1984, **25**, 1849.
5 T. W. Doyle, B.-Y. Luh, D. T.-W. Chu, and B. Belleau, *Can. J. Chem.*, 1977, **55**, 2719; M. J. Pearson, *J. Chem. Soc., Chem. Commun.*, 1981, 947.
6 J. G. Gleason, D. B. Bryan, and K. G. Holden, *Tetrahedron Lett.*, 1980, **21**, 3947; C. L. Branch and M. J. Pearson, *ibid.*, 1982, **23**, 3003.
7 J. Finkelstein, K. G. Holden, R. Sneed, and C. D. Perchonock, *Tetrahedron Lett.*, 1977, 1855.
8 E. C. Taylor, R. B. Greenwald, N. F. Haley, H. Yanagisawa, and R. J. Clemens, 'Organic Synthesis: Today Tomorrow,' (Proceedings of IUPAC Symposium Organic Synthesis), eds. B. M. Trost and C. R. Hutchinson, Pergamon, Oxford, 1980, p. 173.
9 E. C. Taylor, R. J. Clemens, H. M. L. Davies, and N. F. Haley, *J. Am. Chem. Soc.*, 1981, **103**, 7659.
10 E. C. Taylor, H. M. L. Davies, R. J. Clemens, H. Yanagisawa, and N. F. Haley, *J. Am. Chem. Soc.*, 1981, **103**, 7660.
11 E. C. Taylor, N. F. Haley, and R. J. Clemens, *J. Am. Chem. Soc.*, 1981, **103**, 7743.
12 E. C. Taylor, R. J. Clemens, and H. M. L. Davies, *J. Org. Chem.*, 1983, **48**, 4567.
13 E. C. Taylor, H. M. L. Davies, W. T. Lavell, and N. D. Jones, *J. Org. Chem.*, 1984, **49**, 2204.
14 *E.g.*, J. H. Hall and G. Krishnan, *J. Org. Chem.*. 1984, **49**, 2498, and references therein.
15 H. W. Moore, L. Hernandez, and A. Sing, *J. Am. Chem. Soc.*, 1976, **98**, 3728; D. H. Aue and D. Thomas, *J. Org. Chem.*, 1975, **40**, 2356; H. W. Moore and M. J. Arnold, *ibid.*, 1983, **48**, 3365.
16 G. Lowe and D. D. Ridley, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2024.
17 G. Stork and R. P. Szajewski, *J. Am. Chem. Soc.*, 1974, **96**, 5787.
18 M. Regitz, *Synthesis*, 1972, 351.
19 A. N. Khaletskii and B. L. Moldaver, *Russ. Chem. Rev.* (*Engl. Transl.*), 1963, **32**, 535.
20 P. Barraclough, A. G. Caldwell, C. J. Harris, and N. Whittaker, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2097.
21 E. Voigt and H. Meier, *Chem. Ber.*, 1975, **108**, 3326.
22 H. Chaimovich, R. J. Vaughan, and F. H. Westheimer, *J. Am. Chem. Soc.*, 1968, **90**, 4088; R. R. Rando, *ibid.*, 1970, **92**, 6706; N. T. Buu and J. T. Edward, *Can. J. Chem.*, 1972, **50**, 3719; E. Müller and P. Heinrich, *Chem.-Ztg.*, 1971, **95**, 567; *ibid.*, 1972, **96**, 112; H. Tomioka, M. Kondo, and Y. Izawa, *J. Org. Chem.*, 1981, **46**, 1090.
23 M. A. McGee, H. D. Murdoch, G. T. Newbold, J. Redpath, and F. S. Spring, *J. Chem. Soc.*, 1960, 1989.
24 H. Ruhkopf, *Chem. Ber.*, 1940, **73**, 820.
25 C. J. Moody, *Adv. Heterocycl. Chem.*, 1982, **30**, 1.
26 W. T. Hunter, U.S. P. 2,841,584 (1954) (*Chem. Abstr.*, 1962, **56**, 2460).
27 D. Feller, E. R. Davidson, and W. T. Borden, *J. Am. Chem. Soc.*, 1981, **103**, 2558.
28 E. Fahr, W. Fischer, A. Jung, L. Sauer, and A. Mannschreck, *Tetrahedron Lett.*, 1967, 161.
29 H. Gunther, 'NMR Spectroscopy,' Wiley, Chichester, 1980, p. 251.
30 A. K. Mukerjee and A. K. Singh, *Synthesis*, 1975, 547.
31 P. G. Sammes and S. Smith, *J. Chem. Soc., Chem. Commun.*, 1982, 1143, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2415.
32 D. S. Kemp, J. C. Chabala, and S. A. Marson, *Tetrahedron Lett.*, 1978, 543.
33 P. Beak and D. B. Reitz, *Chem. Rev.*, 1978, **78**, 275.
34 G. Lowe and H. Wing Yeung, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2907.
35 *Cf.* J. A. Gainor and S. M. Weinreb, *J. Org. Chem.*, 1982, **47**, 2833.
36 T. Shiori, K. Ninomiya, and S. Yamada, *J. Am. Chem. Soc.*, 1972, **94**, 6203; K. Ninomiya, T. Shiori, and S. Yamada, *Tetrahedron*, 1974, **30**, 2151.
37 J. Thiele and A. Lachman, *Liebigs Ann. Chem.*, 1895, **288**, 267.
38 M. Regitz, J. Hocker, and A. Liedhegener, *Org. Synth.*, Coll. Vol. 5, p. 179.
39 'Vogel's Textbook of Practical Organic Chemistry,' Longman, London, 1978, p. 724.
40 Z. Eckstein and A. Lukasiewicz, *Przem. Chem.*, 1960, **39**, 367.

Received 11*th April* 1986; *Paper* 6/711