Lead Tetra-acetate Oxidation of Tetrahydrobenzazepine Enamides: The Synthesis of *N*-Acyl Substituted Tetrahydro-3-benzazocin-2(1*H*)-ones. A Chemical and Crystallographic Study

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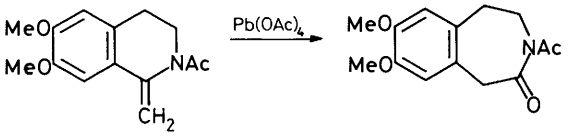
Oxidation with lead tetra-acetate of various *N*-acetyl, *N*-benzoyl and *N*-alkoxycarbonyl enamides derived from dihydrobenzazepines leads to a convenient synthesis of *N*-acyltetrahydrobenzazocinones. Unexpected rate decreases were observed for the *N*-acetyl and *N*-benzoyl derivatives with 7,8,9-trimethoxy substitution. Based on crystallographic analysis, these are attributed to conformational effects determining the extent of double bond conjugation with the aromatic ring and, primarily, the nitrogen lone pair. A comparison of oxidation and subsequent cleavage of the various *N*-alkoxycarbonyltetrahydrobenzazocinones demonstrated that the *N*-t-butoxycarbonyl group gives the highest overall yield of the tetrahydrobenzazocinone from the dihydrobenzazepine.

The study of the chemical reactivity of enamides, *N*-vinyl amides, and urethanes, has yielded many synthetically useful photochemical and thermal reactions.[1–3] As an adjunct of our interest in the photochemistry of enamides, we have been investigating their reactions with various oxidizing species.[4–6] Osmium tetraoxide oxidation of the enamide bond results in glycol formation both in simple and isoquinoline enamides,[7–8] while ruthenium tetraoxide results in cleavage of the double bond.[9] Thallium(III) causes an oxidative rearrangement with a simple enamide.[10] Lead tetra-acetate (LTA) with simple enamides bis-acetoxylates the double bond which can then undergo subsequent reactions.[11] Our studies on the reaction of isoquinoline enamides with LTA have demonstrated that the products can be a function of solvent and the type of *N*-acyl group, and are a result of trapping of the intermediate by solvent, enamide carbonyl or the isoquinoline aromatic ring.[4–6] For instance, LTA oxidation of the 1-methyleneisoquinoline enamide (**1**) readily causes an oxidative ring expansion to form the *N*-acyltetrahydrobenzazepinone (**2**) (Scheme 1).[12] We were

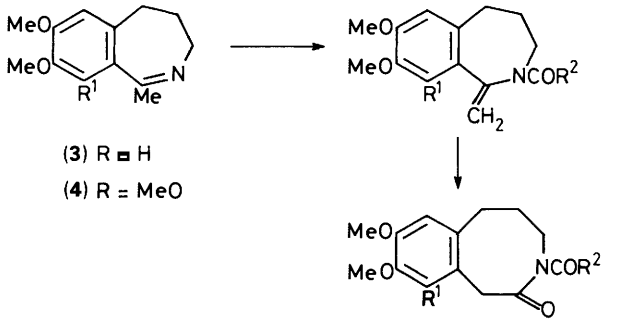


(**1**) (**2**)

Scheme 1.

interested in extending this last oxidative reaction to the next higher homologue because it would allow ready access to the fairly inaccessible and little described tetrahydrobenzazocinone ring system,[13] and convenient syntheses of the requisite dihydrobenzazepines have recently been described.[14–16] This report describes the successful implementation of this approach, together with some unexpected reaction rate decreases and their explanation. Also reported is an optimization study for removing various *N*-protecting groups from the resultant *N*-carbonyl substituted tetrahydrobenzazocinones to form the parent heterocycle.

The known acetyl[14,15] (**5**) and (**7**), and the corresponding benzoyl (**9**) and (**11**), enamides were prepared from the corresponding anhydrides and the dihydrobenzazepines (**3**) and (**4**) (Scheme 2). The carbamates were prepared from the same benzazepines and ethyl and t-butyl carbonic anhydrides [(**13**), (**19**), and (**21**)],[17] chloroformate esters [(**23**) and (**25**)],[18] and a hydroxyimide based benzyloxycarbonyl transfer reagent [(**15**) and (**17**)].[8] Oxidation of the acetyl and benzoyl enamides (**5**) and (**9**) in the 7,8-dimethoxy series with lead tetra-acetate[19] in acetic acid rapidly formed the tetrahydrobenzazocines (**6**) and (**10**) in excellent yield. The structure of the benzazocine (**6**) was assigned on the basis of analogy with the benzazepinones formed from isoquinoline enamides,[12] and ultimately by conversion of (**20**) into the known tetrahydrobenzazocinone (**27**).[13] In distinct contrast to the dimethoxy case, oxidation of the corresponding trimethoxy enamides (**7**) and (**11**) proceeded very slowly, requiring several hours at room temperature for (**11**) and 40 °C for (**7**). The resultant tetrahydrobenzazocines (**8**) and (**12**)



(**3**) R = H
(**4**) R = MeO

Benzazepine enamide (Yield %)	R^1	R^2	Benzazocinone (Yield %)
(**5**), [a]	H	Me	(**6**), 76
(**7**), [b]83	OMe	Me	(**8**), 28
(**9**), 84	H	Ph	(**10**), 83
(**11**), 77	OMe	Ph	(**12**), 19
(**13**), 70	H	OEt	(**14**), 60
(**15**), 22	H	OCH_2Ph	(**16**), 78
(**17**), 53	OMe	OCH_2Ph	(**18**), 52
(**19**), 86	H	OBu^t	(**20**), 75
(**21**), 86	OMe	OBu^t	(**22**), 73
(**23**), 75	OMe	OCH_2CCl_3	(**24**), 56
(**25**), 23	H	$OC(CH_3)_2CCl_3$	(**26**), 85

[a] Ref. 14. [b] Ref. 15.

Scheme 2.

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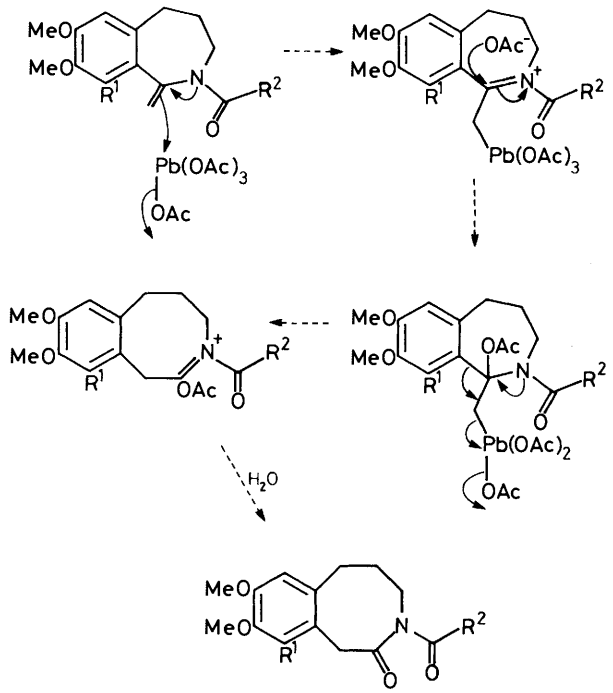


Scheme 3. Proposed mechanism of oxidative ring expansion

were formed in low yield, together with a large number of unidentified polar by-products. The urethanes, however, in both the 7,8-dimethoxy and 7,8,9-trimethoxy series rapidly ring expanded to the tetrahydrobenzazocines in good to excellent yield (Scheme 2).

In an attempt to determine the factors responsible for the dramatic rate decrease observed in the oxidation of the enamides (**7**) and (**11**) compared to the urethanes (**17**), (**21**), and (**23**), single crystal *X*-ray structures were obtained for (**11**) and (**21**). (For structural parameters see Tables 2—7 after the Experimental Section). The benzoyl derivative (**11**) was found to exist in two equally populated conformations in the crystal, differing only in the puckering of the C(4)–C(5) portion of the molecule. ORTEP representations of one conformation of (**11**) and of (**21**) are presented in Figures 1 and 2.

Dihedral angles between π systems were defined using planes constructed through the three bonded substituents of C(1) [C(10), C(9a), and N(2)], N(2) [C(1), C(3), and C(11)], and C(9a) [C(5a), C(9), and C(1)] for both (**11**) and (**21**). Lone pairs or π orbitals on each of these atoms were assumed to be perpendicular to the corresponding π-system plane. Angles between adjacent planes, as well as the out-of-plane deviation of N(2) in (**11**) and (**21**) are presented in Table 1.

From these dihedral angles it can be clearly seen that overlap between the lone pair on N(2) and the C(1)-C(10)π system is much greater in (**21**) (29.9°) than in (**11**) (83.3°). The resulting delocalization in (**21**) manifests itself as a greater electron density at C(10), allowing a more facile oxidation of (**21**) compared to (**11**). A proposed mechanism for the oxidative ring expansion is presented in Scheme 3, illustrating the importance of delocalization of the N(2) lone pair in stabilizing the developing positive charge at C(1) during the initial step of the reaction pathway. The lack of such stabilization in the oxidation of (**11**) apparently allows undesired reaction pathways to intervene before the desired interception of the intermediate cation by solvent can occur.

Participation by the electron-rich aromatic ring in stabilization of an incipient cation at C(1) is also expected to be slightly greater in (**21**) (39.3°) than in (**11**) (46.8°). This influence is probably minor compared to the conjugation of the nitrogen lone pair.

The two crystal structures also show a difference in the orientation of the amide carbonyl relative to the olefinic bond. While this difference might result in some minor long-range electronic effects, these are not likely to be a significant factor in the differing reactivity of (**11**) and (**21**), especially in comparison with lone pair/olefin interactions.

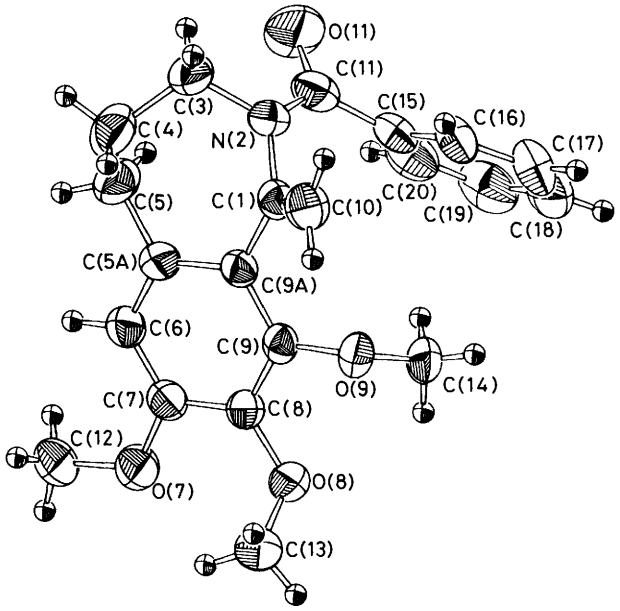


Figure 1. ORTEP representation of the enamide (**11**)

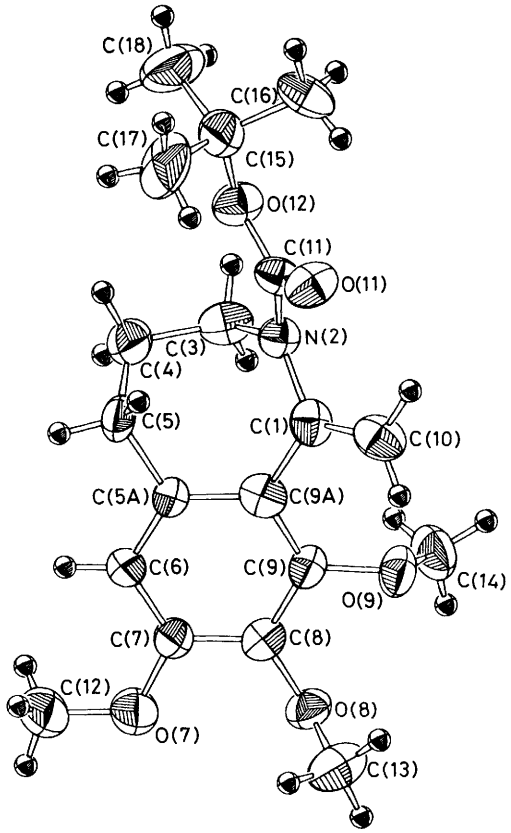
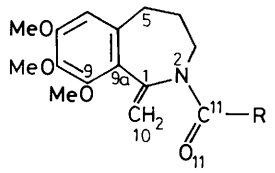


Figure 2. ORTEP representation of the enamide (**21**)

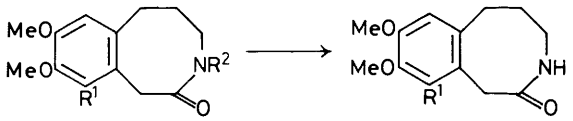
Table 1. Structural features of the enamides (**11**) and (**21**)



Central atoms of π-planes*		Dihedral angle (°) (**11**)	(**21**)
N(2)	C(1)	83.3	29.9
C(1)	C(9a)	46.8	39.3
Out-of-plane deviation of N(2), (Å)		0.13	0.11

* For definition of planes see text.

The cleavage of the various *N*-alkoxycarbonyltetrahydrobenzazocinones, with the exception of the ethoxy derivative (**14**),* was investigated to determine the optimum method of preparing the parent tetrahydrobenzazocinones (**27**) and (**28**) (Scheme 4). The t-butoxycarbonyl group in compounds (**20**)



Protected benzazocine	R^1	R^2	Deprotection method	Benzazocine (Yield %) (Overall Yield %)*
(**20**)	H	CO_2Bu^t	CF_3CO_2H	(**27**), 92 (59)
(**22**)	OMe	CO_2Bu^t	CF_3CO_2H	(**28**), 83 (52)
(**16**)	H	CO_2CH_2Ph	H_2/Pd/C	(**27**), 69 (12)
(**18**)	OMe	CO_2CH_2Ph	H_2/Pd/C	(**28**), 86 (24)
(**26**)	H	$CO_2C(CH_3)_2CCl_3$	Zn/Pb	(**27**), 91 (18)
(**24**)	OMe	$CO_2CH_2CCl_3$	Zn/Pb	(**28**), 76 (32)

Scheme 4. * Overall yield is for the sequence: enamide formation⟶benzazocine formation⟶urethane cleavage.

and (**22**) was readily removed by solvolysis with trifluoroacetic acid to form the parent tetrahydrobenzazocinones (**27**) and (**28**) respectively in excellent yield.[20] The benzyloxycarbonyl group in (**16**) and (**18**) was readily removed by catalytic hydrogenation.[8] The dimethyltrichloroethoxycarbonyl derivative[21] (**26**) and the trichloroethoxycarbonyl compound (**24**) could be readily removed using activated zinc under neutral conditions.[22,23] In summary, all of these protecting groups could be readily removed.

The differentiation occurs when the entire sequence of enamide formation, oxidation, and cleavage is considered. For the entire sequence, the t-butoxycarbonyl derivative is best overall for preparing the tetrahydrobenzazocinones (**27**) and (**28**). The benzyloxycarbonyl derivatives, which work very well in the isoquinoline series,[8,12] suffer from inefficient enamide formation. The trichloroethyl compounds suffer from a modest yield for oxidation to the tetrahydrobenzazocinone (**24**) for the trichloroethyl group, or from inefficient formation of the enamide (**25**) from the reaction of dihydrobenzazepine (**3**) with dimethyltrichloroethyl chloroformate.

In summary, the LTA oxidative ring expansion of tetrahydrobenzazepine enamides to tetrahydrobenzazocinones is general, with *N*-acyl, aroyl, and alkoxycarbonyl enamides undergoing the reaction. We have observed significant rate decreases in the oxidation of the *N*-acetyl and *N*-benzoyl 7,8,9-trimethoxy enamides which we have attributed to conformational effects on the double bond overlap with the aromatic ring and primarily the nitrogen lone pair. Of the various *N*-alkoxycarbonyl groups, the t-butoxy gave the highest overall yield going from the starting dihydrobenzazepine to the parent tetrahydrobenzazocinone.

Experimental

General Methods.—M.p.s were obtained on a Thomas-Hoover Unimelt capillary apparatus and are uncorrected. I.r. spectra were recorded in KBr pellets on a Perkin-Elmer 683 i.r. spectrometer or, alternatively, an f.t.-i.r. spectrum was obtained using a Digilab FTS-60 spectrometer. N.m.r. spectra were recorded on an IBM AF-270 spectrometer and were run in deuteriochloroform with tetramethylsilane as an internal standard. U.v. spectra were recorded in methanol on a Cary-Varian 2200 spectrophotometer. *X*-Ray analyses were obtained on a Rigaku AFC-5S diffractometer. Electron impact mass spectra were recorded on a Hewlett–Packard 5995 GC-MS using a direct insertion probe. High resolution mass spectra were obtained by VG Instruments using a VG Model 70—250 SEQ mass spectrometer with electron impact ionization at 70 eV. Microanalyses were determined by the BOC Group Technical Center Microanalytical Service under the direction of Allan Ellgren.

General Procedure for Oxidation of the Enamides (**5**), (**9**), (**13**), (**15**), (**17**), (**19**), (**21**), (**23**), *and* (**25**).—A 0.2—0.4M solution of the enamide in dichloromethane was added to a stirred suspension of lead tetra-acetate (1.1—5.0 equiv.) in an equal volume of glacial acetic acid. After the mixture had been stirred for 15—45 min, glycerol (propane-1,2,3-triol) (0.2 ml) was added to quench the excess of lead tetra-acetate, and the mixture was stirred for an additional 10 min. It was then diluted with dichloromethane, washed with water and saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified as described below for the individual product.

3-Acetyl-8,9-dimethoxy-3,4,5,6-tetrahydro-3-benzazocin-2(1H)-one (**6**). The known enamide[15] (**5**) (500 mg, 1.91 mmol) was oxidized according to the General Procedure with lead tetra-acetate (1.5 g, 3.5 mmol). The residue was recrystallized from ether to afford the *benzazocinone* (**6**) (402 mg, 76%), m.p. 128—130 °C (Found: C, 64.9; H, 6.8; N, 4.9. $C_{15}H_{19}NO_4$ requires C, 65.0; H, 6.9; N, 5.05%); $\nu_{max.}$ 1 711, 1 690, 1 516, 1 118, and 1 105 cm^{-1}; δ_H 1.86 (2 H, br s, 5-H), 2.17 (3 H, s, CH_3CO), 2.88 (2 H, t, 6-H), 3.86 (3 H, s, CH_3O), 3.87 (3 H, s, CH_3O), 3.89 (2 H, s, 1-H), 3.99 (2 H, br s, 4-H), 6.65 (1 H, s, 7-H), and 6.81 (1 H, s, 10-H).

3-Acetyl-8,9,10-trimethoxy-3,4,5,6-tetrahydro-3-benzazocin-2(1H)-one (**8**). A solution of the enamide[14] (**7**) (582 mg, 2 mmol) and lead tetra-acetate (1.24 g, 2.8 mmol) in acetic acid (5 ml) and dichloromethane (5 ml) was stirred under nitrogen for 20 h. An additional portion of lead tetra-acetate (0.44 g, 1 mmol) was added, and the mixture was warmed to 40 °C for 5 h. Propane-1,2,3-triol (0.2 ml) was added and the mixture was stirred 15 min. It was then diluted with dichloromethane (50 ml), washed with water (50 ml) and saturated aqueous sodium carbonate (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure.

* The corresponding ethoxycarbonyltetrahydrobenzazepinone derivative[12] is hydrolysed exclusively at the benzazepinone carbonyl group (G. R. Lenz, unpublished).

The residue was flash chromatographed[24] on silica gel. Elution with 30% ethyl acetate in hexane afforded the *benzazocinone* (**8**) (170 mg, 28%) as a viscous oil; $\nu_{max.}$ 1 744 and 1 696 cm^{-1}; δ_H 1.87 (2 H, m), 2.22 (3 H, s), 2.83 (2 H, t), 3.8—4.0 (13 H, m), and 6.46 (1 H, s); *m/z* 307 (70%, M^+), 265 (5), 248 (37), 233 (47), 195 (55), and 43 (100); *m/z* (high resolution) 307.1420 ($C_{16}H_{21}NO_5$ requires 307.1420).

2-*Benzoyl*-7,8-*dimethoxy*-1-*methylene*-2,3,4,5-*tetrahydrobenzazepine* (**9**). A solution of (**3**) (0.60 g, 2.7 mmol), benzoic anhydride (1.0 g, 4.4 mmol), and pyridine (4 ml) in dry benzene (90 ml) was heated at reflux for 2 h. After cooling to room temperature, the mixture was washed with saturated aqueous sodium hydrogen carbonate (50 ml) and water (2 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from ether–hexane to afford the *enamide* (**9**) (0.77 g, 84%), m.p. 95—96.5 °C (Found: C, 74.1; H, 6.5; N, 4.3. $C_{20}H_{21}NO_3$ requires C, 74.3; H, 6.55; N, 4.3%); $\nu_{max.}$ 1 645, 1 604, and 1 514 cm^{-1}; δ_H 2.05 (2 H, m, 4-H), 2.90 (2 H, m, 5-H), 3.75 (3 H, s, CH_3O), 3.82 (2 H, m, 3-H), 3.90 (3 H, s, CH_3O), 4.90 (1 H, s, CH_2=C), 5.20 (1 H, s, CH_2=C), 6.47 (1 H, s, 6-H), 6.65 (1 H, s, 9-H), and 6.97 (5 H, s).

3-*Benzoyl*-8,9-*dimethoxy*-3,4,5,6-*tetrahydro*-3-*benzazocin*-2(1H)-*one* (**10**). The enamide (**9**) (150 mg, 0.46 mmol) was oxidized according to the General Procedure with lead tetra-acetate (1.0 g, 2.3 mmol). The residue was flash chromatographed on silica gel. Elution with 6% ethyl acetate in dichloromethane afforded the *benzazocinone* (**10**) (130 mg, 83%), m.p. 153—154 °C (Found: C, 70.8; H, 6.2; N, 4.1. $C_{20}H_{21}NO_4$ requires C, 70.65; H, 6.3; N, 4.1%); $\nu_{max.}$ 1 705, 1 663, and 1 603 cm^{-1}; δ_H 1.94 (2 H, m), 3.02 (2 H, m), 3.89 (3 H, s), 3.90 (2 H, s), 3.92 (3 H, s), 4.19 (2 H, m), 6.80 (2 H, d), 6.80 (1 H, s), 6.81 (1 H, s), 7.16 (2 H, t), and 7.34 (1 H, t); *m/z* 339 (M^+, 24%), 218 (56), 217 (22), 165 (48), 105 (100, PhCo), and 77 (73).

2-*Benzoyl*-7,8,9-*trimethoxy*-1-*methylene*-2,3,4,5-*tetrahydrobenzazepine* (**11**). A solution of (**4**) (1.0 g, 4 mmol), benzoic anhydride (1.13 g, 5 mmol), and pyridine (7 ml) in benzene (30 ml) was heated at reflux under nitrogen for 3 h. The mixture was washed with saturated aqueous sodium hydrogen carbonate (50 ml) and water (2 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from ethyl acetate–hexane to afford the *enamide* (**11**) (1.06 g, 77%), m.p. 107—108.5 °C (Found: C, 71.3; H, 6.5; N, 3.9. $C_{21}H_{23}NO_4$ requires C, 71.4; H, 6.6; N, 4.1%); $\nu_{max.}$ 1 640, 1 622, and 1 591 cm^{-1}; δ_H 2.07 (2 H, m), 2.90 (2 H, t), 3.30 (3 H, s), 3.76 (3 H, s), 3.86 (3 H, s), 3.90 (2 H, t), 5.47 (1 H, s), 5.64 (1 H, s), 6.46 (1 H, s), and 7.2—7.35 (5 H, m); *m/z* 353 (M^+, 87%), 324 (96), 310 (33), 294 (37), 234 (29), 206 (98), 105 (92), and 77 (100).

3-*Benzoyl*-8,9,10-*trimethoxy*-3,4,5,6-*tetrahydro*-3-*benzazocin*-2(1H)-*one* (**12**). Lead tetra-acetate (561 mg, 1.27 mmol) was suspended in acetic acid (5 ml) and cooled in an ice–water bath. A solution of the enamide (**11**) (352 mg, 1 mmol) in dichloromethane (6 ml) was added dropwise. The cooling bath was removed, and the mixture was stirred for 5 h. Propane-1,2,3-triol (0.1 ml) was added and the mixture was stirred 15 min. The mixture was then diluted with dichloromethane (40 ml), washed with water (50 ml) and saturated aqueous sodium hydrogen carbonate (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was flash chromatographed on silica gel. Elution with 30% ethyl acetate in hexane containing 1% triethylamine followed by crystallization from dichloromethane afforded the *benzazocinone* (**12**) (69 mg, 19%), m.p. 167—169.5 °C (Found: C, 68.2; H, 6.4; N, 3.7. $C_{21}H_{23}NO_5$ requires C, 68.3; H, 6.3; N, 3.8%); $\nu_{max.}$ 1 693 and 1 676 cm^{-1}; δ_H 1.97 (2 H, m), 2.97 (2 H, t), 3.80 (3 H, s), 3.89 (3 H, s), 3.91 (3 H, s), 3.99 (2 H, s), 4.17 (2 H, m), 6.60 (1 H, s), 6.92 (2 H, d), 7.19 (2 H, t), and 7.33 (1 H, t); *m/z* 369 (M^+, 100%), 248 (40), 233 (28), 105 (71), and 77 (54).

Ethyl 7,8-*dimethoxy*-1-*methylene*-2,3,4,5-*tetrahydrobenzazepine*-2-*carboxylate* (**13**). A solution of 7,8-dimethoxy-1-methyl-4,5-dihydro-3*H*-2-benzazepine (**3**) (1.7 g, 7.8 mmol) and diethyl oxydiformate (1.5 g, 9.3 mmol) in dichloromethane (40 ml) was stirred under nitrogen for 18 h. Solvent was removed under reduced pressure and the residue was flash chromatographed on silica gel. Elution with 5% ethyl acetate in dichloromethane afforded the *enamide* (**13**) (1.6 g, 70%) as a viscous oil, b.p. 137 °C (0.01 mmHg) (Found: C, 66.1; H, 7.2; N, 4.7. $C_{16}H_{21}NO_4$ requires C, 65.95; H, 7.3; N, 4.8%); $\nu_{max.}$ 1 705, 1 610, and 1 520 cm^{-1}; $\lambda_{max.}$ 263 (ε 9 100) and 293 nm (4 800); δ_H 1.23 (3 H, t), 1.93 (2 H, m), 2.68 (2 H, m), 3.57 (2 H, t), 3.85 (3 H, s), 3.87 (3 H, s), 4.15 (2 H, q), 5.17 (1 H, s), 5.38 (1 H, s), 6.55 (1 H, s), and 6.94 (1 H, s).

Ethyl 8,9-*dimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-1H-3-*benzazocine*-3-*carboxylate* (**14**). The enamide (**13**) (1.35 g, 4.6 mmol) was oxidized according to the General Procedure with lead tetra-acetate (3.0 g, 6.8 mmol), the reaction mixture evaporated to a small volume, and the residue diluted with ether. After the product had crystallized it was filtered off and dried to afford the *benzazocinone* (**14**) (0.86 g, 60%); m.p. 119—120 °C (Found: C, 62.2; H, 6.9: N, 4.5. $C_{16}H_{21}NO_5$ requires C, 62.5; H, 6.9; N, 4.6%); $\nu_{max.}$ 1 775 and 1 725 cm^{-1}; $\lambda_{max.}$ 295 nm (ε 4 000); δ_H 1.22 (3 H, t), 1.90 (2 H, m), 2.85 (2 H, m), 3.7—4.0 (4 H, m), 3.85 (6 H, s), 4.15 (2 H, q), 6.60 (1 H, s), and 6.75 (1 H, s).

Benzyl 7,8-*dimethoxy*-1-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**15**). A solution of 7,8-dimethoxy-1-methyl-4,5-dihydro-3*H*-benzazepine (**3**) (1.0 g, 4.67 mmol), *N*-methylmorpholine (2 ml), and *N*-benzyloxycarbonyloxy-5-norbornene-2,3-dicarboximide (1.61 g, 5.14 mmol) in dichloromethane (40 ml) was stirred for 24 h with exclusion of moisture. The mixture was washed with 30% aqueous potassium carbonate (2 × 30 ml) and water (3 × 30 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was flash chromatographed on silica gel. Elution with 10% ethyl acetate in hexane containing 1% triethylamine afforded the *enamide* (**15**) (612 mg, 22%) as a viscous oil; $\nu_{max.}$ 1 709 cm^{-1}; δ_H 1.93 (2 H, m), 2.73 (2 H, t), 3.64 (2 H, t), 3.84 (3 H, s), 3.88 (3 H, s), 5.15 (2 H, s), 5.24 (1 H, s), 5.42 (1 H, s), 6.59 (1 H, s), 6.96 (1 H, s), and 7.25—7.4 (5 H, m); *m/z* 353 (M^+, 2.5%), 262 (100, M − $PhCH_2$), and 91 (59); *m/z* (high resolution) 353.1631 ($C_{21}H_{23}NO_5$ requires 353.1627), 262.1078 (Calc. for M^+ − $PhCH_2$: 262.1076).

Benzyl 8,9-*dimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**16**). The enamide (**15**) (430 mg, 1.22 mmol) was oxidized according to the General Procedure with lead tetra-acetate (647 mg, 1.46 mmol). After evaporation, the residue was flash chromatographed on silica gel. Elution with 30% ethyl acetate in hexane afforded the *benzazocinone* (**16**) (352 mg, 78%) as a viscous oil; $\nu_{max.}$ 1 769 and 1 711 cm^{-1}; δ_H 1.90 (2 H, m), 2.86 (2 H, t), 3.84 (3 H, s), 3.86 (3 H, s), 3.87 (2 H, s), 3.95 (2 H, t), 5.13 (2 H, s), 6.64 (1 H, s), 6.79 (1 H, s), 7.3 (2 H, m), and 7.4 (3 H, m); *m/z* 369 (M^+, 39%), 234 (100), 206 (11), 165 (24), and 91 (76); *m/z* (high resolution) 369.1584 ($C_{21}H_{23}NO_5$ requires 369.1576), 234.1129 (Calc. for $M - CO_2CH_2Ph$, 234.1128).

Benzyl 7,8,9-*Trimethoxy*-1-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**17**).—A solution of (**4**) (2.0 g, 8 mmol) in dichloromethane (20 ml) was treated with *N*-methylmorpholine (1.1 ml) and *N*-benzyloxycarbonyloxynorborn-5-ene-2,3-dicarboximide (2.51 g, 8 mmol) and the mixture stirred under nitrogen at room temperature for 24 h. An additional portion of the dicarboximide (0.6 g, 2 mmol) was added, and the mixture was then heated at reflux for 6 h. After this it was diluted with dichloromethane (50 ml) and washed with 30% aqueous potassium carbonate (2 × 50 ml) and water (2 × 50 ml), dried (Na_2SO_4), and evaporated under reduced

pressure. The residue was flash chromatographed on silica gel, elution with 15% ethyl acetate in hexane affording the *enamide* (**17**) (1.62 g, 53%) as a viscous oil: $\nu_{max.}$ 1 709 cm^{-1}; δ_H 1.94 (2 H, m), 2.76 (2 H, t), 3.71 (3 H, s), 3.68—3.75 (2 H, m), 3.83 (3 H, s), 3.86 (3 H, s), 5.09 (2 H, s), 5.49 (1 H, s), 5.65 (1 H, s), 6.43 (1 H, s), 7.16 (2 H, m), and 7.25 (3 H, m); *m/z* 292 (100%, $M^+ - PhCH_2$), 221 (18), and 91 (70); *m/z* (high resolution) 383.1724 ($C_{22}H_{25}NO_5$ requires 383.1731), 292.1187 (Calc. for $M - PhCH_2$: 292.1185).

Benzyl 8,9,10-*Trimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**18**).—The enamide (**17**) (1.35 g, 3.5 mmol) was oxidized according to the General Procedure with lead tetra-acetate (1.72 g, 3.85 mmol). After evaporation of the reaction mixture the residue was flash chromatographed on silica, elution with 20% ethyl acetate in hexane followed by recrystallization from dichloromethane—hexane affording the *benzazocinone* (**18**) (0.73 g, 52%), m.p. 92.5—94.5 °C (Found: C, 66.1; H, 6.3; N, 3.5. $C_{22}H_{25}NO_6$ requires C, 66.15; H, 6.3; N, 3.5%); $\nu_{max.}$ 1 715 and 1 705 cm^{-1}; δ_H 1.91 (2 H, m), 2.81 (2 H, t), 3.82 (3 H, s), 3.84 (6 H, s), 3.88 (2 H, t), 3.96 (2 H, s), 5.12 (2 H, s), 6.46 (1 H, s), and 7.15—7.35 (5 H, m); *m/z* 399 (M^+, 21%), 264 (100), 233 (16), 221 (13), 218 (15), 195 (16), and 91 (96).

t-Butyl 7,8-*Dimethoxy*-1-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**19**).—A solution of 7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-2-benzazepine (**3**) (0.6 g, 2.7 mmol) and di-t-butyl oxydiformate (1.1 g, 5 mmol) in dichloromethane (20 ml) was heated at reflux for 3 h. Solvent was removed under reduced pressure, and the residual solid was flash chromatographed on silica gel. Elution with 10% ethyl acetate in hexane followed by crystallization from dichloromethane–hexane afforded the *enamide* (**19**) (0.64 g, 73%), m.p. 140—143 °C (Found: C, 67.5; H, 8.1; N, 4.4. $C_{18}H_{25}NO_4$ requires C, 67.7; H, 7.9; N, 4.4%); $\nu_{max.}$ 1 693 cm^{-1}; δ_H 1.43 (9 H, s), 1.93 (2 H, m), 2.71 (2 H, t), 3.55 (2 H, t), 3.88 (3 H, s), 3.89 (3 H, s), 5.17 (1 H, s), 5.35 (1 H, s), 6.59 (1 H, s), and 6.97 (1 H, s); *m/z* 319 (M^+, 6%), 262 (100, $M - C_4H_9O$), 218 (16, $M - CO_2C_4H_9$), and 57 (84, C_4H_9).

t-Butyl 8,9-*Dimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**20**).—The enamide (**19**) (168 mg, 0.53 mmol) was oxidized according to the General Procedure with lead tetra-acetate (257 mg, 0.58 mmol). After evaporation of the reaction mixture the residue was recrystallized from dichloromethane–hexane to afford the *benzazocinone* (**20**) (133 mg, 75%), m.p. 124.5—127.5 °C (Found: C, 64.2; H, 7.6; N, 4.1. $C_{18}H_{25}NO_5$ requires C, 64.5; H, 7.5; N, 4.2%); $\nu_{max.}$ 1 701 cm^{-1}; δ_H 1.38 (9 H, s), 1.91 (2 H, m), 2.83 (2 H, t), 3.8—3.9 (10 H), 6.64 (1 H, s), and 6.80 (1 H, s); *m/z* 335 (M^+, 6%), 279 (64, $M - C_4H_8$), 235 (66, $M - CO_2C_4H_9$), 220 (43, $M - NHCO_2C_4H_9$), 165 (51), and 57 (100).

t-Butyl 7,8,9-*Trimethoxy*-2-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**21**).—A solution of (**4**) (1.67 g, 6.7 mmol) and di-t-butyl oxydiformate (1.72 g, 7.9 mmol) in dichloromethane (35 ml) was refluxed for 4 h. Additional oxydiformate (0.2 g) was added and refluxing continued for a further 2 h. The mixture was cooled to room temperature, washed with saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was flash chromatographed on silica gel. Elution with 10% ethyl acetate in hexane containing 1% triethylamine followed by recrystallization from hexane afforded the *enamide* (**21**) (2.01 g, 86%), m.p. 69.5—71 °C (Found: C, 65.3; H, 7.9; N, 4.0. $C_{19}H_{27}NO_5$ requires C, 65.3; H, 7.9; N, 4.0%); $\nu_{max.}$ 1 703 and 1 591 cm^{-1}; δ_H 1.39 (9 H, s), 1.89 (2 H, m), 2.73 (2 H, t), 3.60 (2 H, t), 3.85 (3 H, s), 3.86 (3 H, s), 3.87 (3 H, s), 5.31 (1 H, s), 5.64 (1 H, s), and 6.42 (1 H, s); *m/z* 349 (M^+, 1%), 292 (100, $M - C_4H_9$), 278 (36), 234 (21), and 57 (32).

t-Butyl 8,9,10-*Trimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**22**).—The enamide (**21**) (1.18 g, 3.38 mmol) was oxidized according to the General Procedure with lead tetra-acetate (1.65 g, 3.7 mmol). After evaporation, of the reaction mixture the residue was flash chromatographed on silica gel, elution with 20% ethyl acetate in hexane followed by recrystallization from hexane affording the *benzazocinone* (**22**), m.p. 85.5—88 °C (Found: C, 62.25; H, 7.6; N, 3.8. $C_{19}H_{27}NO_6$ requires C, 62.45; H, 7.45; N, 3.8%); $\nu_{max.}$ 1 713 and 1 709 cm^{-1}; δ_H 1.36 (9 H, s), 1.91 (2 H, m), 2.77 (2 H, t), 3.80 (2 H, t), 3.84 (6 H, s), 3.90 (3 H, s), 3.95 (2 H, s), and 6.47 (1 H, s); *m/z* 365 (M^+, 4%), 309 (41), 265 (34), 250 (41), 195 (29), and 57 (100).

2,2,2-*Trichloroethyl* 7,8,9-*Trimethoxy*-1-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**23**).—A solution of 1-methyl-7,8,9-trimethoxy-3,4-dihydro-3*H*-2-benzazepine (**4**) (1.0 g, 4 mmol) and pyridine (2 ml) in dichloromethane (15 ml) was cooled under a nitrogen atmosphere to 5 °C in an ice–water bath. A solution of 2,2,2-trichloroethyl chloroformate (0.7 ml, 5.1 mmol) in dichloromethane (5 ml) was added dropwise with stirring. The cooling bath was removed, and the mixture was allowed to warm to room temperature over 15 min. The mixture was diluted with dichloromethane (20 ml), washed with saturated aqueous sodium hydrogen carbonate (30 ml) and water (2 × 30 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was flash chromatographed on silica gel, elution with 10% ethyl acetate in hexane containing 1% triethylamine affording the *enamide* (**23**) (1.27 g, 75%) as an oil: $\nu_{max.}$ 1 720 cm^{-1}; δ_H 1.97 (2 H, m), 2.79 (2 H, t), 3.75 (2 H, t), 3.85 (3 H, s), 3.87 (3 H, s), 3.89 (3 H, s), 4.76 (2 H, s), 5.52 (1 H, s), 5.76 (1 H, s), and 6.44 (1 H, s); *m/z* 423 (15%), 425 (14), 427 (4.5), 429 (0.5) (Cl isotope cluster for M^+), 408 (100), 410 (98), 412 (32), 414 (4, $M^+ - CH_3$), 292 (51), and 278 (16); *m/z* (high resolution) 423.0398 (Calc. 423.0407), 425.0353 (Calc. 425.0377), and 427.0340 (Calc. 427.0348).

2,2,2-*Trichloroethyl* 8,9,10-*Trimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**24**).—The enamide (**23**) (1.27 g, 3 mmol) was oxidized according to the General Procedure with lead tetra-acetate (1.45 g, 3.27 mmol). After evaporation of the reaction mixture, the residue was crystallized from ethyl acetate–hexane to afford the *benzazocinone* (**24**) (0.74 g, 56%), m.p. 99—100.5 °C (Found: C, 46.4; H, 4.6; N, 3.2. $C_{17}H_{20}Cl_3NO_6$ requires C, 46.3; H, 4.6; N, 3.2%); $\nu_{max.}$ 1 730 and 1 717 cm^{-1}; δ_H 1.98 (2 H, m), 2.83 (2 H, t), 3.84 (6 H, s), 3.92 (3 H, s), overlaid with *ca.* 3.9 (2 H, m), 4.01 (2 H, s), 4.70 (2 H, s), and 6.47 (1 H, s); *m/z* 439 (100%), 441 (99), 443 (35), 445 (5), (Cl isotope cluster for M^+), 291 (37), 264 (13), 248 (34), and 221 (73).

2,2,2-*Trichloro*-1,1-*dimethylethyl*7,8-*Dimethoxy*-1-*methylene*-2,3,4,5-*tetrahydro*-2-*benzazepine*-2-*carboxylate* (**25**).—A solution of (**3**) (1.74 g, 7.95 mmol) in dichloromethane (15 ml) and pyridine (2 ml) was cooled to 0 °C in an ice–water bath under a nitrogen atmosphere. A solution of 2,2,2-trichloro-1,1-dimethylethyl chloroformate (2.29 g, 9.54 mmol) in dichloromethane (8 ml) was added dropwise to the stirred solution. The cooling bath was removed, and the mixture was allowed to warm to room temperature over 15 min. The mixture was diluted with dichloromethane (20 ml), washed with water (3 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was flash chromatographed on silica gel, elution with 10% ethyl acetate in hexane containing 1% triethylamine followed by

crystallization from dichloromethane–hexane affording the *enamide* (**25**) (0.74 g, 22%), m.p. 73–74 °C (Found: C, 51.3; H, 5.3; N, 3.2. $C_{18}H_{22}Cl_3NO_4$ requires C, 51.1; H, 5.25; N, 3.3%); $\nu_{max.}$ 1 708 cm^{-1}; δ_H 1.94 (6 H, s), 1.98 (2 H, m), 2.74 (2 H, t), 3.61 (2 H, t), 3.88 (3 H, s), 3.90 (3 H, s), 5.27 (1 H, s), 5.44 (1 H, s), 6.59 (1 H, s), and 6.99 (1 H, s); *m/z* 423 (M^+, 1%), 262 (100, $M - C_4Cl_3H_6$), and 246 (4).

2,2,2-*Trichloro*-1,1-*dimethylethyl* 8,9-*Dimethoxy*-2-*oxo*-3,4,5,6-*tetrahydro*-3-*benzazocine*-3-*carboxylate* (**26**).—The enamide (**25**) (211 mg, 0.5 mmol) was oxidized according to the General Procedure with lead tetra-acetate (243 mg, 0.55 mmol). After evaporation of the reaction mixture, the resulting solid was recrystallized from dichloromethane–hexane to afford the *benzazocinone* (**26**) (187 mg, 85%), m.p. 149—151 °C (Found: C, 48.9; H, 5.0; N, 3.15. $C_{18}H_{22}Cl_3NO_5$ requires C, 49.3; H, 5.05; N, 3.2%); $\nu_{max.}$ 1 769 and 1 689 cm^{-1}; δ_H 1.81 (6 H, s), 1.95 (2 H, m), 2.83 (2 H, t), 3.85 (3 H, s), 3.855 (3 H, s), 3.89 (2 H, s), 3.97 (2 H, t), 6.65 (1 H, s), and 6.79 (1 H, s); *m/z* 437 (25%), 439 (26), 441 (8), 443 (1) (Cl_3 isotope cluster for M^+), 279 (15, $M - C_4Cl_3H_6$), 235 (100, $M - CO_2C_4Cl_3H_6$), 191 (35), and 163 (84).

8,9-*Dimethoxy*-3,4,5,6-*tetrahydro*-3-*benzazocin*-2-*one* (**27**).—(a) *From the t-butyl oxobenzazocinecarboxylate* (**20**). A solution of the benzazocinecarboxylate (**20**) (169 mg, 0.5 mmol) in dichloromethane (5 ml) was cooled to 5 °C in an ice–water bath, and then treated with trifluoracetic acid (0.3 ml) with stirring. The mixture was further stirred at 5 °C for 30 min and then allowed to warm to room temperature over an additional 1 h. The mixture was diluted with dichloromethane (20 ml), washed with saturated aqueous sodium hydrogen carbonate (2 × 20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from dichloromethane–hexane to afford the *benzazocinone* (**27**) (109 mg, 92%), m.p. 210—212 °C (lit.,[13] 215 °C) (Found: C, 66.25; H, 7.3; N, 5.9. $C_{13}H_{17}NO_3$ requires C, 66.4; H, 7.3; N, 5.95%); $\nu_{max.}$ 1 663 cm^{-1}; δ_H 1.5—1.7 (1 H, m), 1.95—2.1 (1 H, m), 2.8—3.0 (2 H, m), 3.2—4.0 (4 H, m), 3.86 (3 H, s), 3.88 (3 H, s), 5.6—5.7 (1 H, br s), 6.64 (1 H, s), and 6.89 (1 H, s); *m/z* 235 (M^+, 31%), 218 (48), and 165 (100).

(b) *From the* 3-(2,2,2-*trichloro*-1,1-*dimethylethyl*) *oxobenzazocinonecarboxylate* (**26**). A solution of the benzazocinone (**26**) (110 mg, 0.25 mmol) in tetrahydrofuran (4 ml) was treated with zinc–lead couple (0.3 g) followed by 0.5M aqueous ammonium acetate (0.25 ml). After being stirred for 10 min at room temperature, the mixture was diluted with tetrahydrofuran (5 ml) and filtered through Celite. The solids were washed with ethyl acetate (2 × 10 ml) and dichloromethane (2 × 10 ml) and the filtrate was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was recrystallized from dichloromethane–hexane to afford (**27**) (54 mg, 91%).

(c) *From the benzyl oxobenzazocinecarboxylate* (**16**). The benzazocinecarboxylate (**16**) (290 mg, 0.79 mmol) was dissolved in ethyl acetate (15 ml), 10% palladium on carbon (50 mg) was added, and the mixture was hydrogenated at 40 p.s.i. for 90 min. The mixture was filtered through Celite, and the hydrogenation vessel and solids were washed with dichloromethane (3 × 15 ml). Solvent was removed under reduced pressure and the residue was recrystallized from dichloromethane–hexane to afford (**27**) (128 mg, 69%).

8,9,10-*Trimethoxy*-3,4,5,6-*tetrahydro*-3-*benzazocin*-2-*one* (**28**).—(a) *From the t-butyl oxobenzazocinecarboxylate* (**22**). The benzazocinecarboxylate (**22**) (365 mg, 1 mmol) was deprotected with trifluoroacetic acid as described above for the deprotection of (**20**). After evaporation, the residue was recrystallized from dichloromethane–hexane to afford *benzazocinone* (**28**) (224 mg, 83%), m.p. 161—162.5 °C (Found: C. 63.2; H, 7.3; N, 5.3. $C_{14}H_{19}NO_4$ requires C, 63.4; H, 7.2; N, 5.3%); $\nu_{max.}$ 1 655 cm^{-1}; δ_H 1.6—2.1 (2 H, m), 2.8—3.0 (2 H, m), 3.3—4.0 (4 H, m), 3.84 (3 H, s), 3.86 (3 H, s), 3.97 (3 H, br s), 5.70 (1 H, br s), and 6.46 (1 H, s); *m/z* 265 (M^+, 100%), 250 (17), 248 (16), 233 (28), and 195 (22).

(b) *From the* 3-(2,2,2-*trichloroethyl*) *oxobenzazocinecarboxylate* (**24**). The benzazocinecarboxylate (**24**) (441 mg, 1 mmol) was deprotected with zinc–lead couple (1.0 g) as described above for the deprotection of (**26**). After evaporation, the residue was flash chromatographed on silica. Elution with 3% methanol in chloroform followed by recrystallization from dichloromethane–hexane afforded (**28**) (202 mg, 76%).

(c) *From the benzyl oxobenzazocinecarboxylate* (**18**). The benzazocinecarboxylate (**18**) (399 mg, 1 mmol) was deprotected by catalytic hydrogenation as described above for the deprotection of (**16**). After evaporation, the residue was recrystallized from dichloromethane–hexane to afford (**28**) (228 mg, 86%).

Table 2. Fractional atomic co-ordinates with estimated standard deviations of the least significant figure in parentheses for the enamide (**11**)

Atom	*x*	*y*	*z*
O(7)	0.529 3(2)	0.138 2(2)	0.998 2(3)
O(8)	0.469 8(2)	0.128 9(2)	0.630 6(3)
O(9)	0.337 4(2)	0.268 7(2)	0.473 8(3)
O(11)	−0.078 7(3)	0.330 4(3)	0.735 2(4)
N(2)	0.126 9(2)	0.424 7(2)	0.728 3(3)
C(1)	0.242 5(3)	0.420 1(2)	0.678 8(4)
C(3)	0.157 1(4)	0.513 9(3)	0.901 6(5)
C(4)	0.280(1)	0.513 2(7)	1.067(1)
C(4*)	0.199 4(6)	0.462 3(6)	1.071 7(8)
C(5)	0.279(1)	0.398 4(9)	1.076(1)
C(5*)	0.346 2(7)	0.461 7(7)	1.098(1)
C(5A)	0.345 8(3)	0.349 3(3)	0.956 6(4)
C(6)	0.416 4(3)	0.280 5(3)	1.034 4(4)
C(7)	0.458 7(3)	0.207 1(2)	0.929 8(4)
C(8)	0.431 2(3)	0.202 8(2)	0.740 1(4)
C(9)	0.359 4(3)	0.270 7(2)	0.660 1(4)
C(9A)	0.314 2(3)	0.344 2(2)	0.764 4(4)
C(10)	0.283 6(3)	0.490 4(3)	0.576 7(4)
C(11)	0.005 1(3)	0.336 1(3)	0.658 3(5)
C(12)	0.566 1(4)	0.144 6(3)	1.193 5(5)
C(13)	0.610 8(4)	0.166 1(4)	0.663 4(5)
C(14)	0.241 0(3)	0.160 1(3)	0.345 7(4)
C(15)	−0.030 1(3)	0.247 1(3)	0.478 7(4)
C(16)	−0.029 1(3)	0.281 4(3)	0.315 9(5)
C(17)	−0.079 4(4)	0.198 3(3)	0.146 1(5)
C(18)	−0.129 5(4)	0.078 4(4)	0.141 5(6)
C(19)	−0.128 3(4)	0.043 3(3)	0.302 8(6)
C(20)	−0.081 7(3)	0.127 3(3)	0.469 8(5)

Table 3. Selected bond lengths (Å) with estimated standard deviations of the least significant figure in parentheses, enamide (**11**)

Atom	Atom	Distance	Atom	Atom	Distance
O(7)	C(7)	1.361(4)	C(3)	C(4*)	1.545(7)
O(7)	C(12)	1.423(4)	C(4)	C(5)	1.40(1)
O(8)	C(8)	1.376(3)	C(4*)	C(5*)	1.57(1)
O(8)	C(13)	1.422(4)	C(5)	C(5A)	1.488(9)
O(9)	C(9)	1.380(3)	C(5*)	C(5A)	1.612(8)
O(9)	C(14)	1.427(4)	C(5A)	C(6)	1.384(4)
O(11)	C(11)	1.225(4)	C(5A)	C(9A)	1.407(4)
N(2)	C(1)	1.445(3)	C(6)	C(7)	1.377(4)
N(2)	C(3)	1.470(4)	C(7)	C(8)	1.393(4)
N(2)	C(11)	1.352(4)	C(8)	C(9)	1.390(4)
C(1)	C(9A)	1.486(4)	C(9)	C(9A)	1.399(4)
C(1)	C(10)	1.317(4)	C(11)	C(15)	1.492(4)
C(3)	C(4)	1.57(1)	C–C phenol		1.378(7)

Table 4. Selected bond angles (°) with estimated standard deviations of the least significant figure in parentheses, enamide (**11**)

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(7)	O(7)	C(12)	118.0(2)	C(5A)	C(6)	C(7)	122.1(3)
C(8)	O(8)	C(13)	115.0(2)	O(7)	C(7)	C(6)	124.8(3)
C(9)	O(9)	C(14)	114.3(2)	O(7)	C(7)	C(8)	116.0(3)
C(1)	N(2)	C(3)	115.5(2)	C(6)	C(7)	C(8)	119.2(3)
C(1)	N(2)	C(11)	123.9(2)	O(8)	C(8)	C(7)	120.7(3)
C(3)	N(2)	C(11)	118.2(3)	O(8)	C(8)	C(9)	120.0(3)
N(2)	C(1)	C(10)	118.4(3)	C(7)	C(8)	C(9)	119.3(3)
N(2)	C(1)	C(9A)	116.5(2)	O(9)	C(9)	C(8)	118.5(2)
C(9A)	C(1)	C(10)	124.8(3)	O(9)	C(9)	C(9A)	119.4(2)
N(2)	C(3)	C(4)	112.3(4)	C(8)	C(9)	C(9A)	122.0(3)
N(2)	C(3)	C(4*)	109.3(3)	C(1)	C(9A)	C(5A)	120.8(3)
C(3)	C(4)	C(5)	113.4(8)	C(1)	C(9A)	C(9)	121.5(2)
C(3)	C(4*)	C(5*)	106.8(5)	C(5A)	C(9A)	C(9)	117.7(3)
C(4)	C(5)	C(5A)	114.0(8)	O(11)	C(11)	N(2)	121.3(3)
C(4*)	C(5*)	C(5A)	112.3(5)	O(11)	C(11)	C(15)	119.5(3)
C(5)	C(5A)	C(6)	114.2(4)	N(2)	C(11)	C(15)	119.2(3)
C(5*)	C(5A)	C(6)	117.1(4)	C(11)	C(15)	C(16)	121.5(3)
C(5)	C(5A)	C(9A)	124.1(4)	C(11)	C(15)	C(20)	118.9(3)
C(5*)	C(5A)	C(9A)	120.1(4)	C–C–C phenol			120.0(9)
C(6)	C(5A)	C(9A)	119.8(3)				

Table 5. Fractional atomic co-ordinates with estimated standard deviations of the least significant figure in parentheses for the enamide (**21**)

Atom	*x*	*y*	*z*
O(7)	0.614 7(7)	0.453 6(7)	0.2572
O(8)	0.450 3(7)	0.558 3(7)	0.351 5(7)
O(9)	0.402 8(7)	0.463 2(7)	0.502 2(7)
O(11)	0.632 5(6)	0.137 5(7)	0.719 5(7)
O(12)	0.606 2(7)	−0.062 1(7)	0.659 7(7)
N(2)	0.547 6(8)	0.118 8(9)	0.592 9(7)
C(1)	0.541(1)	0.257(1)	0.578 2(8)
C(3)	0.526(1)	0.029(1)	0.523 3(9)
C(4)	0.635(1)	0.002(1)	0.474 3(8)
C(5)	0.711(1)	0.126(1)	0.469 9(9)
C(5A)	0.642 4(9)	0.244(1)	0.440 3(7)
C(6)	0.662(1)	0.292(1)	0.361 6(9)
C(7)	0.600(1)	0.398(1)	0.334 7(9)
C(8)	0.514(1)	0.455(1)	0.381 2(8)
C(9)	0.492(1)	0.404(1)	0.459 3(8)
C(9A)	0.556(1)	0.300(1)	0.490 9(8)
C(10)	0.520(1)	0.343(1)	0.636 9(8)
C(11)	0.599(1)	0.070(1)	0.662(1)
C(12)	0.696(1)	0.396(1)	0.205(1)
C(13)	0.489(1)	0.684(1)	0.378(1)
C(14)	0.293(1)	0.422(1)	0.480(1)
C(15)	0.670(1)	−0.133(1)	0.724(1)
C(16)	0.610(1)	−0.116(1)	0.804 6(9)
C(17)	0.794(1)	−0.089(1)	0.725(1)
C(18)	0.659(2)	−0.275(1)	0.695(1)

Table 6. Selected bond lengths (Å) with estimated standard deviations of the least significant figure in parentheses, enamide (**21**)

Atom	Atom	Distance	Atom	Atom	Distance
O(7)	C(7)	1.40(1)	C(1)	C(10)	1.32(1)
O(7)	C(12)	1.40(1)	C(3)	C(4)	1.51(2)
O(8)	C(8)	1.36(1)	C(4)	C(5)	1.53(2)
O(8)	C(13)	1.41(1)	C(5)	C(5A)	1.52(1)
O(9)	C(9)	1.38(1)	C(5A)	C(6)	1.39(1)
O(9)	C(14)	1.38(1)	C(5A)	C(9A)	1.41(1)
O(11)	C(11)	1.23(1)	C(6)	C(7)	1.37(1)
O(12)	C(11)	1.34(1)	C(7)	C(8)	1.38(1)
O(12)	C(15)	1.47(1)	C(8)	C(9)	1.40(1)
N(2)	C(1)	1.42(1)	C(9)	C(9A)	1.39(1)
N(2)	C(3)	1.48(1)	C(15)	C(16)	1.49(2)
N(2)	C(11)	1.37(1)	C(15)	C(17)	1.49(2)
C(1)	C(9A)	1.50(2)	C(15)	C(18)	1.52(2)

Crystal Data.—Enamide (**11**), $C_{21}H_{23}NO_4$, M = 353.42, Triclinic, a = 11.028(2), b = 12.118(3), c = 7.700(1) Å, α = 98.66(2)°, β = 106.68(1)°, γ = 106.71(2)°, V = 913.1(3) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred high angle reflections, λ = 1.541 78 Å), space group $P\bar{1}$, Z = 2, D_x = 1.29 g/cm^3. Clear parallelepiped. Crystal dimensions 0.23 × 0.20 × 0.45 mm, μ = 6.83 cm^{-1}.

Data Collection and Processing.—Rigaku AFC5S diffractometer, $\omega/2\theta$ mode with ω scan width = 1.575 + 0.300 tanθ, ω scan speed 8—32° min^{-1}, graphite monochromated Cu-K_α radiation; 3033 reflections measured ($0° < 2\theta < 120°$, $+h$, $+-k$, $+-l$), 2 717 unique [merging R = 0.045 after absorption correction (max., min. transmission factors = 1.00, 0.94)], giving 1 900 with $I > 3\sigma(I)$. Three standards monitored every 150 reflections. No significant decay.

Structure Analysis and Refinement.—Direct methods and Fourier difference methods. Full-matrix least squares refinement of the position and anisotropic temperature factors of all non-hydrogen atoms. The hydrogens assigned calculated positions. All the hydrogens assigned calculated isotropic temperature factors 1.2 times the equivalent isotropic temperature factor of the associated non-hydrogen atom. The alternate atom sets C(4), C(5) and C(4*), C(5*) were assigned 50% occupancies to account for disorder in the structure. The accuracy of the positions of these atoms is less than that of the other atoms. Calculated parameters updated every two refinement cycles. The weighting scheme $w = [1/\sigma^2(F_o) + 0.000625F_o^2]$ with $\sigma(F_o)$ from counting statistics gave satisfactory agreement between F_o and F_c, with GOF = 1.71. The final R and R_w values were 0.048, 0.070. Programs and computers used and sources of scattering factor data are given in ref. 25.

Crystal Data.—Enamide (**21**), $C_{19}H_{27}NO_5$, M = 349.43, Orthorhombic, a = 11.533(4), b = 10.135(8), c = 16.344(6) Å, V = 1 910(3) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred high angle reflections, λ = 1.541 78 Å), space group $Pac2_1$, Z = 4, D_x = 1.21 g/cm^3. Clear

Table 7. Selected bond angles (°) with estimated standard deviations of the least significant figure in parentheses, enamide (**21**)

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(7)	O(7)	C(12)	117.9(8)	C(6)	C(7)	C(8)	122(1)
C(8)	O(8)	C(13)	114.2(9)	O(8)	C(8)	C(7)	121(1)
C(9)	O(9)	C(14)	114.8(9)	O(8)	C(8)	C(9)	121(1)
C(11)	O(12)	C(15)	120(1)	C(7)	C(8)	C(9)	118(1)
C(1)	N(2)	C(3)	117.9(9)	O(9)	C(9)	C(8)	116(1)
C(1)	N(2)	C(11)	122(1)	O(9)	C(9)	C(9A)	122(1)
C(3)	N(2)	C(11)	119(1)	C(8)	C(9)	C(9A)	122(1)
N(2)	C(1)	C(9A)	116(1)	C(1)	C(9A)	C(5A)	121(1)
N(2)	C(1)	C(10)	123(1)	C(1)	C(9A)	C(9)	121(1)
C(9A)	C(1)	C(10)	121(1)	C(5A)	C(9A)	C(9)	117(1)
N(2)	C(3)	C(4)	112(1)	O(11)	C(11)	O(12)	124(1)
C(3)	C(4)	C(5)	111(1)	O(11)	C(11)	N(2)	124(1)
C(4)	C(5)	C(5A)	111.7(9)	O(12)	C(11)	N(2)	112(1)
C(5)	C(5A)	C(6)	119(1)	O(12)	C(15)	C(16)	110(1)
C(5)	C(5A)	C(9A)	120(1)	O(12)	C(15)	C(17)	110(1)
C(6)	C(5A)	C(9A)	121(1)	O(12)	C(15)	C(18)	101(1)
C(5A)	C(6)	C(7)	119(1)	C(16)	C(15)	C(17)	114(1)
O(7)	C(7)	C(6)	123(1)	C(16)	C(15)	C(18)	110(1)
O(7)	C(7)	C(8)	115(1)	C(17)	C(15)	C(18)	111(1)

parallelepiped. Crystal dimensions 0.25 × 0.18 × 0.38 mm, μ = 6.80 cm^{-1}.

Data Collection and Processing.—Rigaku AFC5s diffractometer, $\omega/2\theta$ mode with ω scan width = 1.575 + 0.300 tanθ, ω scan speed 4 − 16° min^{-1}, graphite monochromated Cu-K_α radiation; 1 668 reflections measured ($0° < 2\theta < 120°$, $+h$, $+k$, $+l$), all of which are unique, giving 766 with $I > 3\sigma(I)$. Three standards monitored every 150 reflections. No significant decay or absorption.

Structure Analysis and Refinement.—Direct methods and Fourier difference methods. Full-matrix least squares refinement of the position and anisotropic temperature factors of all non-hydrogen atoms. The hydrogens assigned calculated positions. All the hydrogens assigned calculated isotropic temperature factors 1.2 times the equivalent isotropic temperature factor of the associated non-hydrogen atom. Calculated parameters updated every two refinement cycles. The weighting scheme $w = 1/[\sigma^2(F_o) + 0.000\,625\,F_o^2]$ from counting statistics gave satisfactory agreement between F_o and F_c, with GOF = 1.45. The final R and R_w values were 0.053 and 0.062. Programs and computers used and sources of scattering factor data are given in ref. 25. Thermal parameters and H-atom co-ordinates for compounds (**11**) and (**21**) are available on request from The Cambridge Crystallographic Data Centre.*

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References

1 A. Campbell and G. R. Lenz, *Synthesis*, 1987, 421.
2 G. R. Lenz, *Synthesis*, 1978, 489.
3 I. Ninomiya and T. Naito, *Alkaloids (N.Y.)*, 1983, **22**, 189.
4 C. R. Dorn, F. J. Koszyk, and G. R. Lenz, *J. Org. Chem.*, 1984, **49**, 2642.
5 G. R. Lenz and C. Costanza, *J. Org. Chem.*, 1988, **53**, 1176.
6 G. R. Lenz, *J. Org. Chem.*, 1988, **53**, 4447.
7 M. Narisada, F. Watanabe, and W. Nagata, *Tetrahedron Lett.*, 1971, 3681.
8 G. R. Lenz, *Heterocycles*, 1987, **26**, 721.
9 S. Torii, T. Inokuchi, and K. Kondo, *J. Org. Chem.*, 1985, **50**, 4980.
10 T. G. Back, O. E. Edwards, and G. A. McAlpine, *Tetrahedron Lett.*, 1977, 2651.
11 R. B. Boar, J. F. McGhie, M. Robinson, and D. H. R. Barton, *J. Chem. Soc. Perkin Trans. 1*, 1975, 1242.
12 G. R. Lenz, *J. Org. Chem.*, 1988, **53**, 5791.
13 Y. Okuno, K. Hemmi, and O. Yonemitsu, *J. Chem. Soc., Chem. Commun.*, 1971, 745; T. Iwakuma, H. Nakai, O. Yonemitsu, and B. Witkop, *J. Amer. Chem. Soc.*, 1974, **96**, 2564.
14 R. Alonso, K. Takahashi, B. Schönenberger, and A. Brossi, *Heterocycles*, 1987, **26**, 1595.
15 R. Alonso and A. Brossi, *Heterocycles*, 1987, **26**, 2209.
16 W. Meise and G. Schluter, *Liebigs Ann. Chem.*, 1987, 639.
17 G. R. Lenz, C-M. Woo, and B. L. Hawkins, *J. Org. Chem.*, 1982, **47**, 3049.
18 M. P. Cava, P. Stern, and K. Wakisaka, *Tetrahedron*, 1973, **29**, 2245; G. R. Lenz and F. J. Koszyk, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1273.
19 M. L. Mihailović, Z. Ceković, and L. Lorenc, *Org. Syn. Oxid. Met. Compds.*, 1986, 741. G. M. Rubottom, *Org. Chem. (N.Y.)*, 1982, **5**, 1.
20 L. A. Carpino, *Acc. Chem. Res.*, 1973, **6**, 191.
21 H. Eckert, M. Listl, and I. Ugi, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 361.
22 T. B. Windholz and D. B. R. Johnston, *Tetrahedron Lett.*, 1967, 2555.
23 G. Just and K. Grozinger, *Synthesis*, 1976, 457.
24 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
25 S. M. Evans, E. F. Ezell, and S. J. Sondheimer, *J. Cryst. Spectroscopy Res.*, 1989, **19**, 415.

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