Acta Chemica Scandinavica B 30 (1976) 383—390

Strained Heterocyclic Compounds 9.* Synthesis of 2-Hydroxy-β-lactams and Oxazolidin-4-ones by Photocyclization of 2-Oxoamides

NILS GUNNAR JOHANSSON [a,**] BJÖRN ÅKERMARK [a] and BERNDT SJÖBERG [b]

[a] Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm 70, Sweden and [b] Research and Development Laboratories, Astra Läkemedel AB, S-151 85 Södertelje, Sweden

The 6-hydroxypenam system (*12*) has been synthesized by photolysis of (−)-3-(oxophenylacetyl)thiazolidine-4-carboxylic acid ethyl ester (*11*). 7-Hydroxy-8-oxo-1-azabicyclo[4.2.0]octanes (*2,7*) are similarly formed from oxophenylacetylpiperidine (*1*) and 2-oxopropionylpiperidine (*6*). 2,3-Dihydroxysuccinylpiperidines (*5, 10*) were also isolated from the photolysis of *1* and *6*. The major photoproducts were, however, fused oxazolidin-4-ones, tetrahydro-5*H*-oxazolo[3,2,-*a*]pyridin-3(2*H*)-ones (*3,4,8,9*) and two tetrahydro-3-oxo-7a*H*-thiazolo[2,3-*b*]oxazoles (*13,14*).

As part of a program for synthesis of penicillin analogs we have studied the photocyclizations of 2-oxoamides. In analogy to the formation of hydroxycyclobutanones from 2-oxoketones,[1–5] the amides gave hydroxy-β-lactams, but the yields were low (5−10 %). Unexpectedly, oxazolidin-4-ones were formed as major products. The results have been reported as a preliminary communication.[6]

Recently, Henery-Logan and Chen [7] confirmed the utility of this photocyclization approach when they obtained the 6-hydroxypenam compounds *16 a,b,c* by ultraviolet irradiation of the corresponding 2-oxoamides *15 a,b,c*.

Synthesis of 2-oxoamides. Condensation of oxophenylacetylchloride and the appropriate amines gave the oxophenylacetylamides *1* and *11*. Ethoxyoxoacetylpiperidine and methylmagnesium bromide at −80 °C gave 2-oxopropionylpiperidine (*6*). 2-Oxoamides can also be made by coupling of the acid and an amine with carbodiimide.[7]

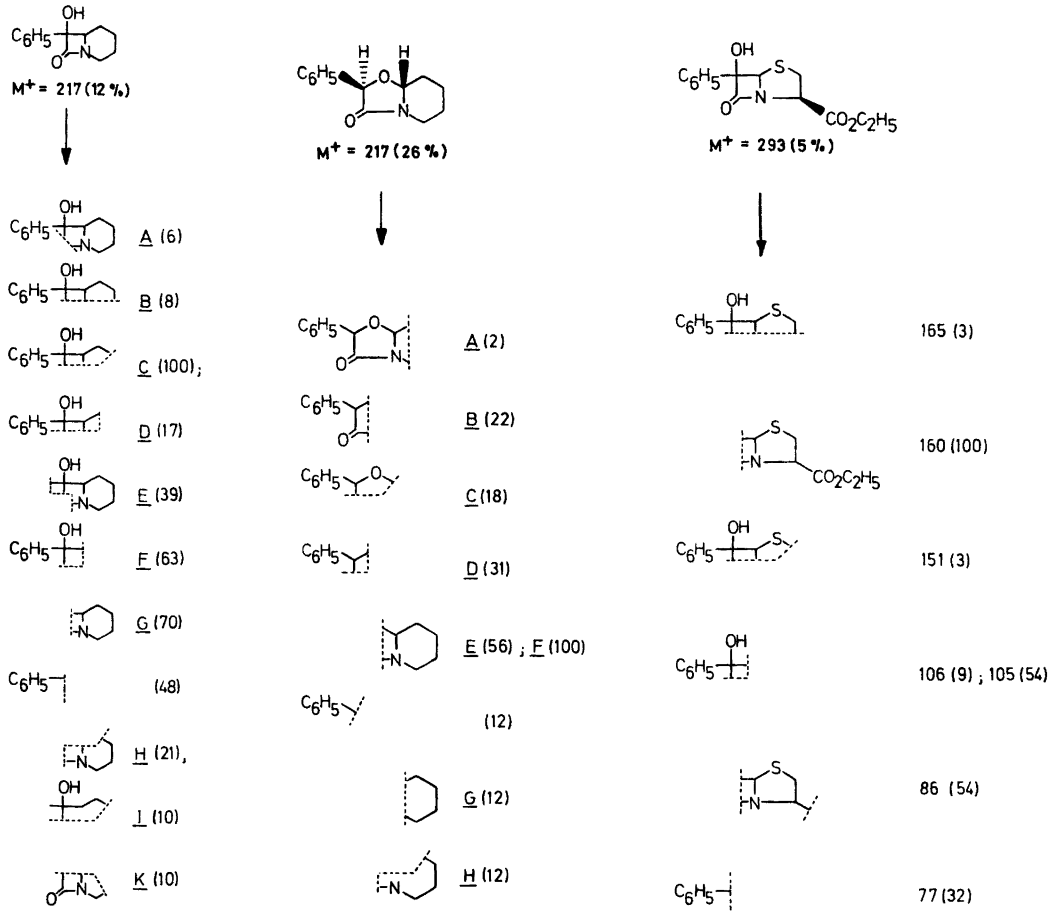
Photoproducts. The compounds *1*, *6* and *11* in dry benzene were irradiated by 3500 Å ultraviolet light for 19−40 h. Chromatography over silica gel and recrystallization gave the 7-hydroxy-1-azabicyclo[4.2.0]-octan-8-ones *2* and *7* in 8 % and 5 % yield, respectively, and (−)-6-hydroxy-7-oxo-6-phenyl-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid ethyl ester (*12*) in 8 % yield. The major products were the 6,7,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridin 3(2*H*)-ones *3* (21 %), *4* (15 %), *8* (25 %), and *9* (20 %) and (−)-tetrahydro-3-oxo-2-phenyl-7a*H*-thiazolo[2,3-*b*]oxazole-5-carboxylic acid ethyl esters (*13, 14*; 13 and 9 %). The 2,3-dihydroxysuccinylpiperidines *5* and *10* were also isolated (15 and 6 %), respectively).

From the photolysis of *1* an additional compound *A* (5 %; m.p. 97−100 °C) was isolated. Its ^{1}H NMR spectrum indicated that it contained phenyl groups and a rearranged piperidine moiety in the proportions 2:1, but it was not further characterized.

Spectroscopic data. The photolysis products were identified by their ^{1}H NMR, IR and MS data. The structure of compound *4* has been confirmed by an X-ray crystallographic analysis.[8] The main mass spectrometric fragments of compounds *2* and *4* were determined by high resolution mass spectrometry, and the frag-

* Part 8. Björn Åkermark, Margareta Bergström and Inger Lagerlund, *Acta Chem. Scand. B 29* (1975) 687.

** Present address: Research and Development Laboratories, Astra Läkemedel AB, S-151 85 Södertälje, Sweden.



Schemes 1–3. MS fragmentation of compound *2*, *4*, and *12*.

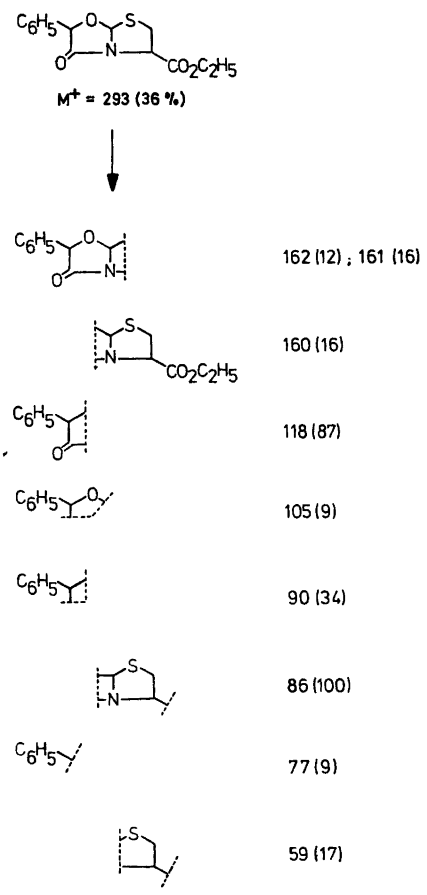
mentation patterns are illustrated in Schemes 1 and 2, respectively. The mass spectrometric fragmentations of compound *12* are depicted in Scheme 3 and of compound *13* in Scheme 4.

β-Lactams 2, 7 *and* 12. The β-lactam IR carbonyl absorptions for solids *2* and *7* are as low as 1725 and 1720 cm^{-1}, respectively, due to intermolecular hydrogen bonding. In dioxan solutions the absorptions are raised to 1750 and 1745 cm^{-1}. The carbonyl absorption of the β-lactam *12* is similarly raised from 1750 cm^{-1} in the solid state to 1770 cm^{-1} in dioxan. The carbonyl absorption of the ester group is not affected.

NMR signals were assigned to the *geminal* 2-CHα- and 2-CHβ-protons in *2* and *7* by consideration of the diamagnetic anisotropic effects of the β-lactam carbonyl groups,[9,10] and by comparison with the almost identical ^{1}H NMR signals of compounds *17a,b*, *18* and *19a,b*.[9,11]

^{1}H NMR signals were assigned to compound *12* after comparison between the ^{1}H NMR spectra of compound *12* and methyl 6-bromobisnorpenicillanate,[12] bisnorpenicillin V,[13] and other penicillins.[14]

The mass spectrometric fragmentation patterns of *2* (Scheme 1) and *7* are compatible with the suggested structures and are analogous to the fragmentations of unfused β-lactams [14] and penicillins.[14–17] Compound *12* (Scheme 3) behaves in the same principal manner as other penicillins,[14–17] with the thiazoline ion ($m/e = 160$) as a major characteristic peak.



Scheme 4. MS fragmentation of compound *13*.

Oxazolidin-4-ones 3, 4, 8, 9, 13 and 14. Oxazolidin-4-ones fused with a piperidine ring have previously been obtained by oxidation of the oxazolidine rings in Garrya alkaloids.[18,19]

Their IR carbonyl absorptions occur at 1700 – 1705 cm^{-1}. The carbonyl absorptions of *3*, *4*, *8* and *9* are similarly at 1695 – 1710 cm^{-1}. The oxazolidinones *13* and *14*, fused to a thiazolidine moiety, absorb at 1735 – 1740 cm^{-1}.

The high resolution mass spectrum of compound *4* is shown in Scheme 2. The mass spectra of *8*, *9*, *13* (Scheme 4) and *14* are analogous.

The *trans*-configuration of compound *4* has been established by X-ray crystallography.[8] Consequently, the isomeric compound *3* possesses *cis*-configuration. The NMR chemical shift of the 2-C hydrogen atom of the *trans*-compound *4* is at lower field (δ 5.13) than the corresponding shift of the *cis*-isomer *3* (δ 5.08).

This relative resonance of the 2-C protons is analogous to shifts observed for stereoisomers of thiazolidines[20] and 1,3-dioxolans.[21–23] In thiazolidines the 4-C proton resonance occurred at lower field when *cis* to an alkyl substituent at 2-C, compared to compounds in which the 4-C proton was *cis* to a hydrogen at 2-C.[20]

The 2-C acetal proton of 1,3-dioxolans has also been shown to be deshielded by *cis*-alkyl substituents at 3-C or 4-C.[21–23]

In the same way, the stereochemistry assigned to the isomers *8* and *9* is deduced from the relative NMR shifts of their 2-C protons. The 2-C proton of the *trans*-compound *9* absorbs at lower field (δ 4.28) than the corresponding proton of the *cis*-compound *8* (δ 4.17).

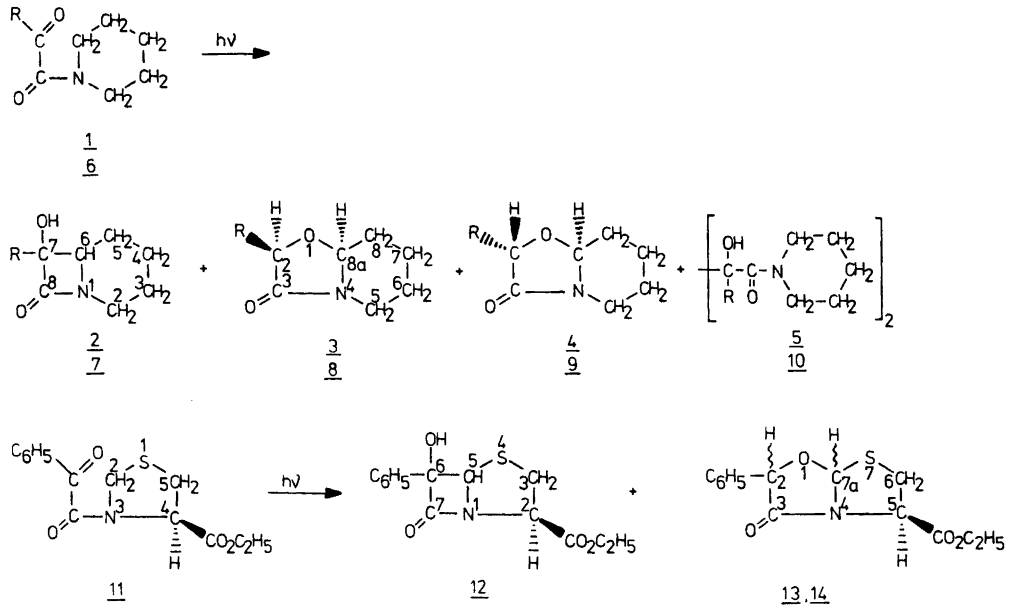
Pinacol formation. The mass spectra of *5* and *10* are indicative of pinacol structures. The molecular ion peaks are small (< 1 %) but peaks corresponding to the loss of one piperidine carbonyl moiety are prominent. The NMR spectrum of *5* exhibits absorptions of the aromatic protons (δ 6.84 – 7.11), the hydroxyl proton (δ 7.40, s) and the piperidine moiety (δ 3.25 – 3.55 and 0.8 – 1.6) in the proportion 5:1:10. The NMR spectrum of *10* is analogous.

No dimer was isolated from the photoproducts of *11*. It might have been formed in small amounts (< 5 %) but escaped detection since the photolysis mixture of *11* was more difficult to separate than those of *1* and *6*.

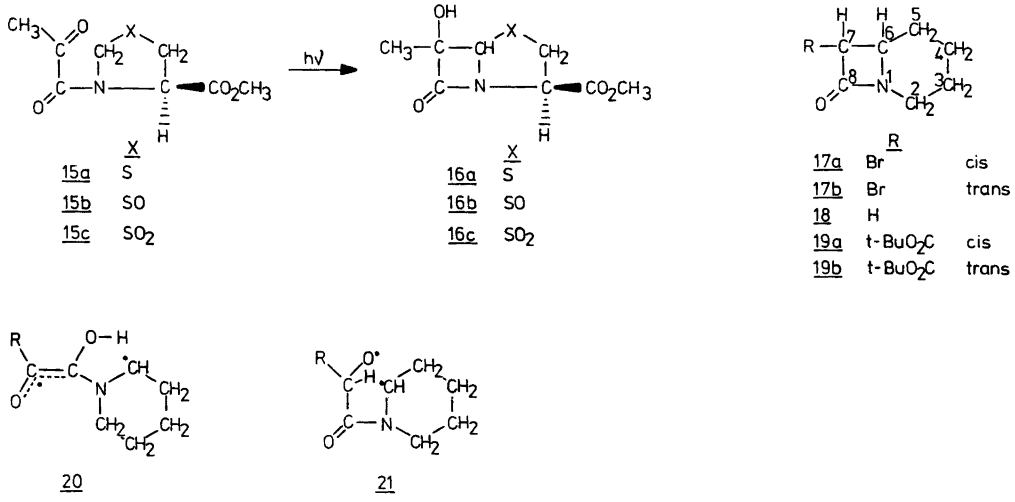
DISCUSSION

On photolysis of the α-oxoamides *1*, *6* and *11* hydroxy-β-lactams were formed. Although the formation of this type of compounds (hydroxy cyclobutanones) is a major photoreaction of 1,2-diketones,[1–5] only 5 – 10 % yields of hydroxy-β-lactams were obtained from α-oxoamides. In analogy to the cyclization of octane-4,5-dione and decane-5,6-dione [1] the reaction would be expected to yield two stereoisomeric cyclic products. However, only one isomer was isolated in each case (*2*, *7* and *12*). It is possible that small amounts of the other stereoisomeric hydroxy-β-lactams were formed but escaped detection.

The major photoproducts from the α-oxoamides *1*, *6* and *11* were the oxazolidinones *3*, *4*, *8*, *9*, *13*, and *14*. This type of photocyclization



Scheme 5. *1 – 5*, R = C_6H_5; *6 – 10*, R = CH_3.



	X
15a	S
15b	SO
15c	SO_2

	X
16a	S
16b	SO
16c	SO_2

	R	
17a	Br	cis
17b	Br	trans
18	H	
19a	t-BuO_2C	cis
19b	t-BuO_2C	trans

does not appear to have any precedents in the photochemistry of α-oxoesters or ketones.[24] A reasonable hypothesis is that some hydrogen abstraction occurs *via* a 5-membered transition state to yield an intermediate diradical *20*, which would cyclize either to an unstable hydroxyaziridine or an oxazolidinone. The intermediate *21* is also possible but hydrogen abstraction by the carbon of an excited carbonyl function has little precedent.

Finally, pinacols could be isolated from the photolysis of the oxoamides *1* and *6*. Analogous products have been isolated from photolysis of alkyl 2-oxopropionates and a number of other α-oxocarbonyl compounds [25–31] when the reactions were performed in solvents that were

good hydrogen donors. Since benzene is a poor donor, the α-oxoamides *1* and *6* probably serve themselves as hydrogen donors.

EXPERIMENTAL

Melting points were determined on a micro hot stage and are uncorrected. When recording infrared spectra solids were measured in KBr discs and liquids as films between NaCl discs. IR spectra were also recorded on dioxan solutions. The data are given in cm^{-1}. Proton magnetic resonance spectra were recorded on a Varian A-60 instrument. The chemical shifts are given as δ-values relative to TMS as an internal standard. Mass spectra were recorded on an LKB-9000 instrument and high-resolution mass spectra on an SM-1, Atlas-MAT-Bremen instrument (Ionization energy 70 eV). A Rayonet photochemical Reactor No. 100 equipped with 3500 Å lamps (24 W) was used for photolysis. Column chromatography was performed over silica gel (Kebo 0.15–0.30 mm) using increasing amounts of diethyl ether in light petroleum (b.p. 40–60 °C) as eluent.

TLC was performed on silica gel G (Merck) and on silica gel PF-254 (Merck) plates using mixtures of diethyl ether and light petroleum as eluent. Spots were located by UV illumination and by iodine vapor or by spraying the plates with chromic acid solutions.

1-(Oxophenylacetyl)piperidine (*1*). Oxophenylacetic acid (15 g) in 50 ml of dry diethyl ether was slowly added to freshly distilled thionylchloride (13 g) and pyridine (8.7 g) in 150 ml of dry, ice-cold diethyl ether. The precipitated pyridine hydrochloride was removed by filtration and the solution was slowly added to piperidine (18.7 g) in 150 ml of dry, ice-cold diethyl ether. The precipitate was filtered off, washed with ether and the combined ether solutions were washed with 0.2 N HCl and H_2O. The solvent was evaporated to give 1-(oxophenylacetyl)piperidine (14.7 g, 68 %) m.p. 107–108 °C. (Found: C 72.03; H 6.94; O 14.03. Calc. for $C_{13}H_{15}NO_2$: C 71.87; H 6.96; O 14.73.) ^1H NMR ($CDCl_3$): δ 1.50–1.70 (m, 3-CH_2, 4-CH_2, 5-CH_2); 3.23 (t, J=5 Hz, 2-CH, 6-CH); 3.65 (t, J=5 Hz, 2-CH, 6-CH); 7.4–7.6 (m, arom.); 7.8–8.0 (m, arom). MS, *m/e* (%): 217 (M^+, 6); 112 ($M-C_6H_5CO$, 100).

IR, KBr (dioxan): 1665 (1675), 1635, (1635) C=O. TLC (ether-light petroleum, 80–20) R_F=0.50.

Ethoxyoxoacetylpiperidine. Ethoxyoxoacetylchloride [32] (130 g) was added dropwise to piperidine (170 g) in 1500 ml of ice-cold diethyl ether. The precipitate was filtered off and the ether solution was washed with 0.5 N HCl, 0.5 N $NaHCO_3$ and H_2O. Distillation in vacuum gave ethoxyoxoacetylpiperidine (121 g, 68 %) b.p. 158 °C/12 mmHg. Lit. b.p.[33] 158–159 °C/11 mmHg.

N-(2-Oxopropionyl)piperidine (*6*). Methylmagnesium bromide (prepared from 13 Mg and 100 g CH_3Br) in 600 ml of dry diethyl ether was vigourously stirred at −80 °C and ethoxyoxoacetylpiperidine (50 g) in 200 ml of dry ether was added over a period of 3 h. The temperature was raised to −20 °C and kept at −20 °C for 70 min, after which 2 N HCl (250 ml) was slowly added. Chromatography on silica gel and distillation gave *N*-(2-oxopropionyl)piperidine (*6*) (29 g, 70 %) b.p. 138 °C/15 mm. (Found: C 61.79; H 8.38; O 20.78. Calc. for $C_8H_{13}NO_2$: C 61.91; H 8.44; O 20.62.) ^1H NMR ($CDCl_3$): 1.50–1.65 (m, 3-CH_2, 4-CH_2, 5-CH_2); 2.35 (s, CH_3); 3.22–3.60 (m, 2-CH_2, 6-CH_2). MS, *m/e* (%): 155 (M^+, 7); 112 ($M-CH_3CO$, 100). IR, neat (dioxan): 1710 (1710), 1640 (1640) C=O. TLC (diethyl ether): R_F=0.60.

(−)-Thiazolidine-4-carboxylic acid ethyl ester. Prepared in the same way as the corresponding methyl ester,[34] b.p. 91 °C/1 mmHg.

(−)-3-(Oxophenylacetyl)thiazolidine-4-carboxylic acid ethyl ester (*11*). Oxophenylacetylchloride, prepared from the acid (15 g, see above), in 125 ml of dry diethyl ether was slowly added to thiazolidine-4-carboxylic acid ethyl ester (17.8 g) and pyridine (8.7 g) in 200 ml of dry, ice-cold diethyl ether. The reaction mixture was worked up as described for *1*. Chromatography on silica gel gave (−)-3-(oxophenylacetyl)thiazolidine-4-carboxylic acid ethyl ester (24.8 g, 85 %), as a viscous liquid. $[\alpha]_D^{20}$ −80° (*c*, 0.64, $CHCl_3$). (Found: C 57.28; H 5.33; O 21.97. Calc. for $C_{14}H_{15}NO_4S$: C 57.32; H 5.15; O 21.82.) ^1H NMR ($CDCl_3$): δ 0.95–1.4 (m, C-CH_3); 3.23–3.38 (2 d, 5-CH_2); 3.9–4.4 (m, O-CH_2); 4.5 (d, J=4.5 Hz, 2-CH); 4.75 (d, J=2 Hz, 2-CH); 4.95–5.25 (m, 4-CH); 7.40–7.55 and 7.95–8.15 (m, arom.). IR, KBr (dioxan): 1735 (1735), 1670 (1675), 1640 (1645). C=O. TLC (diethyl ether-light petroleum, 60-40): R_F=0.42.

Photolysis of N-(oxophenylacetyl)piperidine (*1*). *N*-(Oxophenylacetyl)piperidine (*1*) (8.2 g) was dissolved in benzene (200 ml, distilled from Na) in a 4×50 cm pyrex tube. The solution was saturated with N_2 and the stoppered tube was irradiated with 3500 Å light for 19 h. Column chromatography over silica gel (400 g) gave a total recovery of 6.7 g and recrystallization from diethyl ether-light petroleum gave the compounds *2*–*5*. 1–2 % of the starting material was also recovered.

7-Hydroxy-7-phenyl-1-azabicyclo[4.2.0]octan-8-one (*2*). (0.6 g, 8 %) m.p. 148–150 °C. (Found: C 71.14; H 6.94; N 6.84; O 15.21. Calc. for $C_{13}H_{15}NO_2$: C 71.87; H 6.96; N 6.45; O 14.73.) MS, *m/e* (Letters refer to mass fragments in Scheme 1):

Found: 189.1156 (*A*). Calc. for $C_{12}H_{15}NO$: 189.1154.
Found: 146.0729 (*B*). Calc. for $C_{10}H_{10}O$: 146.0732.
Found: 133.0645 (*C*). Calc. for C_8H_9O: 133.0653.
Found: 120.0569 (*D*). Calc. for C_8H_8O: 120.0575.
Found: 112.0760 (*E*). Calc. for $C_6H_{10}NO$: 112.0762.
Found: 105.0335 (*F*). Calc. for C_7H_5O: 105.0340.
Found: 84.0809 (*G*). Calc. for $C_5H_{10}N$: 84.0813.
Found: 56.0514 (*H*). Calc. for C_3H_6N: 56.0500.
Found: 56.0268 (*I*). Calc. for C_3H_4O: 56.0262.
Found: 56.0150 (*K*). Calc. for C_2H_2NO: 56.0136.

^{1}H NMR ($CDCl_3$): δ 1.2–1.7 (m, 3-CH_2, 4-CH_2, 5-CH_2); 2.75 (m, 2-CH_α); 3.58 (dd, $J=4$ and 10 Hz, 6-CH); 3.80 (broad dd, $J=4$ and 13 Hz, 2-CH_β); 5.28 (s, OH); 7.32 (s, arom). IR, KBr (dioxan): 3215 (3340) OH; 1725 (1750) C=O. TLC (ether-light petroleum, 80–20): $R_F=0.28$.

*6,7,8,8aα-Tetrahydro-2β-phenyl-5*H*-oxazolo-[3,2-a]pyridin-3(2*H*)-one* (*3*) (1.7 g, 21 %) m.p. 83–84 °C. (Found: C 71.69; H 7.02; N 6.61; O 14.69. Calc. for $C_{13}H_{15}NO_2$: C 71.87; H 6.96; N 6.45; O 14.73.)
MS, *m/e* (%): 217 (M^+, 17); 161 (2); 118 (14); 105 (16); 90 (27); 84 (53); 83 (100); 77 (11); 55 (25). ^{1}H NMR ($CDCl_3$): δ 1.18–2.10 (m, 5-CH_2, 6-CH_2, 7-CH_2); 2.65 (m, 5-CH_α); 3.98 (broad dd, $J=3.5$ and 14 Hz); 4.85 (broad m, 8a-CH); 5.08 (s, 2-CH); 7.3 (m, arom). IR, KBr (dioxan): 1695 (1700) C=O. TLC (ether-light petroleum, 80–20): $R_F=0.28$.

*6,7,8,8aα-Tetrahydro-2α-phenyl-5*H*-oxazolo-[3,2-a]pyridin-3-(2*H*)-one* (*4*). (1.2 g, 15 %) m.p. 78–80 °C. (Found: C 71.84; H 6.68; N 6.54; O 14.76. Calc. for $C_{13}H_{15}NO_2$: C 71.87; H 6.96; N 6.45; O 14.73.)
MS, *m/e* (Letters refer to mass fragments in Scheme 2):

Found: 161.0470 (*A*). Calc. for $C_9H_7NO_2$: 161.0477.
Found: 118.0413 (*B*). Calc. for C_8H_6O: 118.0419.
Found: 105.0332 (*C*). Calc. for C_7H_5O: 105.0340.
Found: 90.0461 (*D*). Calc. for C_7H_6: 90.0469.
Found: 84.0820 (*E*). Calc. for $C_5H_{10}N$: 84.0813.
Found: 83.0736 (*F*). Calc. for C_5H_9N: 83.0735.
Found: 55.0528 (*G*). Calc. for C_4H_7: 55.0547.
Found: 55.0398 (*H*). Calc. for C_3H_5N: 55.0421.

^{1}N NMR ($CDCl_3$): 1.15–2.10 (m, 5-CH_2, 6-CH_2, 7-CH_2); 2.65 (m, 5-CH_α); 4.01 (broad dd, $J=$ 4 and 13 Hz, 5-CH_β); 5.08 (broad m, 8a-CH); 5.13 (d, $J=1.8$ Hz, 2-CH); 7.3 (m, arom). IR, KBr (dioxan): 1695 (1700) C=O. TLC (ether-light petroleum, 80–20): $R_F=0.41$.

2,3-Dihydroxy-2,3-diphenylsuccinylpiperidine (*5*). (1.2 g, 15 %) m.p. 163–166 °C. (Found: C 71.35; H 7.03; N 6.82; O 15.32. Calc. for $C_{26}H_{33}N_3O_4$: C 71.53; H 7.39; N 6.42; O 14.66.) ^{1}H NMR ($CDCl_3$): δ 0.8–1.6 (m, CH_2-CH_2-CH_2); 3.25–3.55 (m, CH_2-N-CH_2); 6.84–7.11 (m, arom.); 7.40 (s, OH). MS *m/e* (%): 436 (M^+, 1); 324 (36); 219 (100); 112 (74); 105 (77); 86 (95). IR, KBr (dioxan): 3220 (3260) OH; 1590 (1600) C=O. TLC (ether–light petroleum, 80–20): $R_F=0.70$.

Photolysis of N-(2-oxopropionyl)piperidine (*6*). *N*-(2-Oxopropionyl)piperidine (*6*) (10.0 g) in benzene (150 ml, distilled from NaH) was irradiated with 3500 Å light for 27 h in the same fashion as for compound *1*. Column chromatography over silica gel (550 g) gave a total recovery of 8.3 g. The compounds *7–10* were identified. 1.4 g (15 %) of the starting material was also recovered.

7-Hydroxy-7-methyl-1-azabicyclo[4.2.0]octan-8-one (*7*). The crude material (0.4 g, 5 %) was rechromatographed over silica gel, m.p. 138–139 °C. (Found: C 61.13; H 8.49; O 21.01. Calc. for $C_8H_{13}NO_2$: C 61.91; H 8.44; O 20.62.) MS, *m/e* (%): 155 (M^+, 1); 127 (12); 112 (25); 84 (32); 71 (100); 58 (10); 56 (19); 55 (11). ^{1}H NMR ($CDCl_3$): δ 1.2–1.9 (m, 3-CH_2, 4-CH_2, 5-CH_2); 1.29 (s, CH_3); 2.85 (m, 2-CH_α); 3.52 (broad, 6-CH); 3.82 (broad, 2-CH_β); 4.92 (s, OH). IR, KBr (dioxan): 3250 (3400) OH; 1720 (1745) C=O. TLC (diethyl ether): $R_F=$ 0.35.

*6,7,8,8aα-Tetrahydro-2β-methyl-5*H*-oxazolo-[3,2-a]pyridin-3(2*H*)-one* (*8*). (2.5 g, 25 %) colorless liquid. n_D^{20} 1.4853. (Found: C 61.90; H 8.51; N 8.97. Calc. for $C_8H_{13}NO_2$: C 61.91; H 8.44; N 9.03.) MS, *m/e* (%): 155 (M^+, 25); 154 (45); 153 (18); 127 (17); 116 (17); 100 (37); 99 (48); 98 (26); 84 (100); 83 (44); 82 (25). ^{1}H NMR ($CDCl_3$): δ 1.2–2.2 (m, 5-CH_2, 6-CH_2, 7-CH_2); 1.25 (d, $J=6$ Hz, CH_3); 2.75 (m, 5-CH_α); 3.85 (broad dd, $J=2.5$ and 11 Hz, 5-CH_β); 4.17 (m, $J=6$ Hz, 2-CH); 4.87 (broad m, 8a-CH). IR, neat (dioxan): 1710 (1710) C=O. TLC (diethyl ether): $R_F=0.47$.

*6,7,8,8aα-Tetrahydro-2α-methyl-5*H*-oxazolo-[3,2-a]pyridin-3(2*H*)-one* (*9*). (*Ca.* 2 g, 20 %) colorless liquid. n_D^{20} 1.4931. (Found: C 61.60; H 8.29. Calc. for $C_8H_{13}NO_2$: C 61.91; H 8.44.) MS, *m/e* (%): 155 (M^+, 28); 154 (72); 153 (46); 127 (29); 116 (35); 100 (52); 99 (75); 98 (43); 84 (33); 83 (75); 82 (39). ^{1}H NMR ($CDCl_3$): δ 1.2–2.2 (m, 5-CH_2, 6-CH_2, 7-CH_2); 1.38 (d, $J=6$ Hz, CH_3); 2.75 (m, 5-CH_α); 4.07 (broad dd, $J=3$ and 11 Hz, 5-CH_β); 4.28 (m, $J=6$ Hz, 2-CH); 4.87 (broad m, 8a-CH). IR, neat (dioxan): 1710 (1710) C=O. TLC (diethyl ether): $R_F=0.43$.

2,3-Dihydroxy-2,3-dimethylsuccinylpiperidine (*10*). (0.6 g, 6 %). Recrystallized from diethyl ether-light petroleum, m.p. 129–131 °C. (Found: C 61.03; H 8.79; O 21.23. Calc. for $C_{16}H_{28}N_2O_4$: C 61.51; H 9.03; O 20.49.) ^{1}H NMR ($CDCl_3$): δ 1.43 (s, CH_3); 1.60 (broad s, CH_2-CH_2-CH_2); 3.5 and 4.05 (two broad s, CH_2-N-CH_2); 6.3 (s, OH). MS, *m/e* (%) 312 (M^+, 1); 201 (12); 200 (98); 157 (37); 113 (12); 112 (100); 86 (50). IR, KBr (Dioxan): 3260 (3300) OH; 1585 (1590) C=O. TLC (diethyl ether): $R_F=$ 0.75.

Photolysis of (–)-3-(oxophenylacetyl)thiazolidine-4-carboxylic acid ethyl ester (*11*). 3-(Oxo-

phenylacetyl)thiazolidine-4-carboxylic acid ethyl ester (*11*) (11.0 g) in benzene (250 ml, dried over Na) was irradiated at 3500 Å for 40 h in the same way as for compound *1*. Column chromatography over silica gel gave a total recovery of 7.8 g. The compounds *12* – *14* were identified and recrystallized from diethyl ether-light petroleum. 2.0 g (18 %) of the starting material was also recovered.

(–)-6-Hydroxy-7-oxo-6-phenyl-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid ethyl ester (*12*). (0.7 g, 8 %) m.p. 109 – 111 °C. $[\alpha]_D^{20}$ – 305° (*c*, 0.67, $CHCl_3$). (Found: C 57.24; H 5.18; N 4.89; O 21.93. Calc. for $C_{14}H_{15}NO_4S$: C 57.32; H 5.15; N 4.78; O 21.82.) ^1H NMR ($CDCl_3$): δ 1.15 – 1.4 (C-CH_3); 3.05 – 3.35 (m, 3-CH_2); 4.0 – 4.3 (O-CH_2); 4.3 – 4.6 (broad, OH); 4.85 – 5.05 (m, 2-CH); 5.31 (s, 5-CH) 7.16 – 7.40 (m, arom.). MS, *m/e* (%): 293 (M^+, 5); 294 (M + 1, 0.17 × 5. Calc. for M + 1: 0.167 × 5); 295 (M + 2, 0.06 × 5. Calc. for M + 2: 0.063 × 5). IR, KBr (dioxan): 3400 (3600 – 3300) OH; 1735 (1735), 1750 (1770) C=O. TLC (diethyl ether-light petroleum, 60 – 40): R_F = 0.42.

*(–)-Tetrahydro-3-oxo-2-phenyl-7a*H*-thiazolo[2,3-*b*]oxazole-5-carboxylic acid ethyl ester* (*13*). (1.3 g, 13 %) m.p. 54 – 57 °C. $[\alpha]_D^{20}$ – 145° (*c*, 0.75, $CHCl_3$). (Found: C 57.52; H 5.11; N 4.87; O 21.75. Calc. for $C_{14}H_{15}NO_4S$: C 57.32; H 5.15; N 4.78; O 21.82.) ^1H NMR ($CDCl_3$): δ 1.2 (t, J = 7 Hz, C-CH_3); 3.25 and 3.33 (two d, J = 0.8 Hz and J = 4.0 Hz, respectively, 6-CH_2); 4.14 (q, J = 7 Hz, O-CH_2); 5.12 – 5.28 (m, 5-CH); 5.31 (s, 2-CH); 7.11 (s, 7a-CH); 7.25 – 7.40 (m, arom.). MS, *m/e* (%): 293 (M^+, 36); 294 (M + 1, 0.18 × 36. Calc. for M + 1: 0.16 × 36); 295 (M + 2, 0.07 × 36. Calc. for M + 2: 0.063 × 36). IR, KBr (dioxan): 1735 (1740), 1740 (1740) C=O. TLC (diethyl ether-light petroleum, 60 – 40): R_F = 0.61.

*(–)-Tetrahydro-3-oxo-2-phenyl-7a*H*-thiazolo[2,3-*b*]oxazole-5-carboxylic acid ethyl ester* (*14*). (0.9 g, 9 %) m.p. 103 – 106 °C. $[\alpha]_D^{20}$ – 100° (*c*, 0.68, $CHCl_3$). (Found: C 57.44; H 5.17; N 4.88; O 21.83. Calc. for $C_{14}H_{15}NO_4S$: C 57.32; H 5.15; N 4.78; O 21.82.) ^1H NMR ($CDCl_3$): δ 1.3 (t, C-CH_3); 3.11 and 3.18 (two d, J = 4.2 Hz and J = 0.9 Hz, respectively, 6-CH); 4.17 (q, O-CH_2); 5.11 – 5.31 (m, 5-CH); 5.43 (s, 2-CH); 7.0 (s, 7a-CH); 7.2 – 7.4 (m, arom.). MS, *m/e* (%): 293 (M^+, 34); 294 (M + 1, 0.17 × 34. Calc. for M + 1: 0.16 × 34); 295 (M + 2, 0.07 × 34. Calc. for M + 2: 0.063 × 34); 162 (8); 161 (9); 160 (6); 118 (47); 105 (8); 90 (28); 86 (100). IR, KBr (dioxan): 1735 (1735) C=O. TLC (diethyl ether-light petroleum, 60 – 40): R_F = 0.58.

Acknowledgements. We thank Professor T. Norin for valuable stereochemical discussions. The high-resolution mass spectra were recorded by Mr. Rolf Hjelm and other spectra by Miss Gurli Hammarberg. This work has been supported by The Swedish Board for Technical Development and by Astra Läkemedel AB.

REFERENCES

1. Urry, W. H. and Trecker, D. J. *J. Am. Chem. Soc. 84* (1962) 118.
2. Urry, W. H., Trecker, D. J. and Winey, D. A. *Tetrahedron Lett.* (1962) 609.
3. Turro, N. J. and Lee, T.-J. *J. Am. Chem. Soc. 91* (1969) 5651.
4. Turro, N. J. and Lee, T.-J. *J. Am. Chem. Soc. 92* (1970) 7467.
5. Zepp, R. G. and Wagner, P. J. *J. Am. Chem. Soc. 92* (1970) 7466.
6. Åkermark, B., Johansson, N.-G. and Sjöberg, B. *Tetrahedron Lett.* (1969) 371.
7. Henery-Logan, K. R. and Chen, C. G. *Tetrahedron Lett.* (1973) 1103.
8. Malmros, G. and Wägner, A. *To be published.*
9. Brunwin, D. M., Lowe, G. and Parker, J. *J. Chem. Soc. C* (1971) 3756.
10. Bohlmann, F. and Schumann, D. *Tetrahedron Lett.* (1965) 2435.
11. Johansson, N.-G. and Åkermark, B. *Acta Chem. Scand. 25* (1971) 1927.
12. Johansson, N.-G. *Acta Chem. Scand. B 30* (1976) 377.
13. Hoogmartens, J., Claes, P. J. and Vanderhaeghe, H. *J. Med. Chem. 17* (1974) 389.
14. Demarco, P. V. and Nagarajan, R. In Flynn, E. H., Ed., *Cephalosporins and Penicillins*, Academic, New York 1972, p. 311.
15. Richter, W. and Biemann, K. *Monatsh. Chem. 95* (1964) 766.
16. Bochkarev, V. N., Ovchinnikova, N. S., Vul'fson, N. S., Kleiner, E. M. and Khokhlov, A. S. *Dokl. Akad. Nauk. SSSR 172* (1967) 1079.
17. Moll, F. and Hannig, M. *Arch. Pharm. (Weinheim) 303* (1970) 321.
18. Wiesner, K., Armstrong, R., Bartlett, M. F. and Edwards, J. A. *J. Am. Chem. Soc. 76* (1954) 6068.
19. Wiesner, K., Taylor, W. I., Figdor, S. K., Bartlett, M. F., Armstrong, J. R. and Edwards, J. A. *Chem. Ber. 86* (1953) 800.
20. McMillan, I. and Stoodley, R. J. *Chem. Commun.* (1968) 11.
21. Bagget, N., Buck, K. W., Foster, A. B., Randall, M. H. and Webber, J. M. *J. Chem. Soc.* (1965) 3394.
22. Bagget, N., Buck, K. W., Foster, A. B. and Webber, J. M. *J. Chem. Soc.* (1965) 3401.
23. Bagget, N., Duxburry, J. M., Foster, A. B. and Webber, J. M. *J. Chem. Soc. C* (1966) 208.
24. Monroe, B. M. *Adv. Photochem. 8* (1971) 77.
25. Bentrude, W. G. and Darnall, K. R. *Chem. Commun.* (1968) 810.
26. Cohen, W. D. *Chem. Weekblad 13* (1916) 590; *Chem. Abstr. 10* (1916) 2092.
27. Leermakers, P. A. and Vesley, G. F. *J. Am. Chem. Soc. 85* (1963) 3776.

28. Kendall, D. S. and Leermakers, P. A. *J. Am. Chem. Soc. 88* (1966) 2766.
29. Yang, N. C. and Morduchowitz, A. *J. Org. Chem. 29* (1964) 1654.
30. Schönberg, A., Latif, N., Moubasher, R. and Sina, A. *J. Chem. Soc.* (1951) 1364.
31. Huyser, E. S. and Neckers, D. C. *J. Org. Chem. 29* (1964) 276.
32. Southwick, P. L. and Seivard, L. L. *J. Am. Chem. Soc. 71* (1949) 2532.
33. Wallach, O. and Lehmann, F. *Justus Liebigs Ann. Chem. 237* (1887) 245.
34. Ratner, S. and Clarke, H. T. *J. Am. Chem. Soc. 59* (1937) 200.

Received October 4, 1975.