Tetrahedron. Vol. 31, pp. 1671 to 1676. Pergamon Press 1975 Printed in Great Britain

MOLECULAR DESIGN BY CYCLOADDITION REACTIONS—XVIII

FORMATIONS OF HIGHLY STRAINED HETEROCYCLES

T. Sasaki,* K. Kanematsu and K. Iizuka
Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Chikusa, Nagoya 464, Japan

(*Received in Japan* 2 *December* 1974; *Received in UK for publication* 25 *February* 1975)

Abstract—Reactions of pentacyclo[$7.6.1.0^{2\,8}0^{3\,5}0^{10.15}$]hexadecatetraen-4-yl acetic acids (**3a**, **b**), azatricyclo-[$5.3.0^{3\,9}0^{4\,6}$]decaen-5-yl acetic acid (**3c**), and its alcohol derivatives (**12a**, **b**) with bromine gave bromocyclization products (**10a**, **b**, **c**) and (**13a**, **b**), respectively.

The Curtius reaction of the carboxylic acids (**3a**, **b**, **c**) with diphenylphosphoryl azide gave the corresponding urethanes (**19a**, **b**, **c**) together with compound **20** as a by-product. The cyclization reaction of **23**, which was easily prepared from reduction of the urethane (**19a**) followed by chlorination with N-chlorosuccinimide, in refluxing methanol in the presence of silver nitrate gave mainly the parent amine compound (**22**) accompanied with a small amount of the cyclized product (**24**).

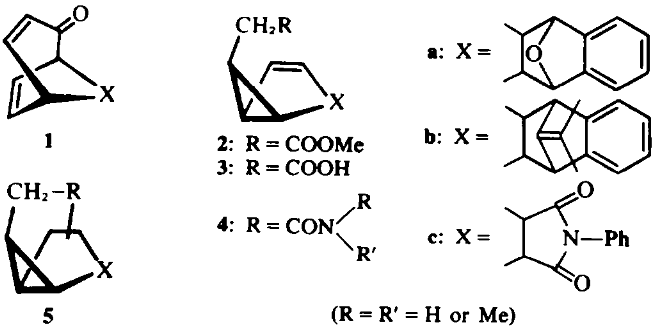
We have previously reported that the pentacyclo-[$7.6.1.0^{2\,8}0^{3.5}0^{10.15}$]-hexadecatetraen-4-yl acetates (**2a**, **b**)[2,3] and its acetamides (**4a**, **b**)[3] were easily prepared from compounds containing the bicyclo[3.2.2]nonadiene derivatives (enone-π-methane system) in the presence of nucleophilic reagents.

These photoproducts have a vinycyclopropyl acetyl group with *cis* configuration in a 6-membered ring, and thus, they are expected to cyclize intramolecularly to afford novel, highly strained heterocycles (**5**).

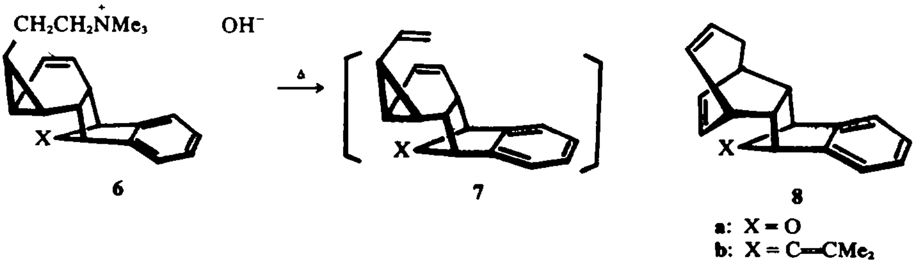
In this connection, we have recently reported transformation of the ammonium salts (**6a**, **b**) by the Hofmann degradation followed by thermal Cope rearrangement via divinylcyclopropane intermediate (**7**)[3] as shown in Scheme 2.

The present paper describes the cyclization of the photoproducts with some electrophilic reagents such as bromine, and a solvolytic cyclization of the chloramines using silver ion. Treatment of the carboxylic acids (**3a**, **b**, **c**) prepared from tropone adducts (**1a**, **b**, **c**), with bromine afforded the cyclized products (**10a**, **b**, **c**) in 66–79% yields. These products showed common characteristic IR bands at 1720–1730 cm^{-1} due to a 6-membered lactone moiety. The NMR spectra of **10a** and **10c** exhibited signals at δ 5·28 (1H, m, H-1) and 4·70 (1H, dd, H-2), and 5·55 (1H, m, H-1) and 4·73 (1H, t, H-2), respectively. On the other hand, the spectrum of **10b** exhibited signals at δ 5·20 (1H, m, H-1), but no signals due to a H-2 proton indicating the structures of **10a** and **10c**. Furthermore, two Me protons in **10b** exhibited at δ 1·24 (6H) as a singlet, which shifted to higher field region compared with that of two Me protons at δ 1·56 (s) and 1·63 (s) in the carboxylic acid **3b**, and no NMR signals of olefinic protons. From these results, the structures of compounds **10a**, **10b** and **10c** were assigned as depicted in Scheme 3.

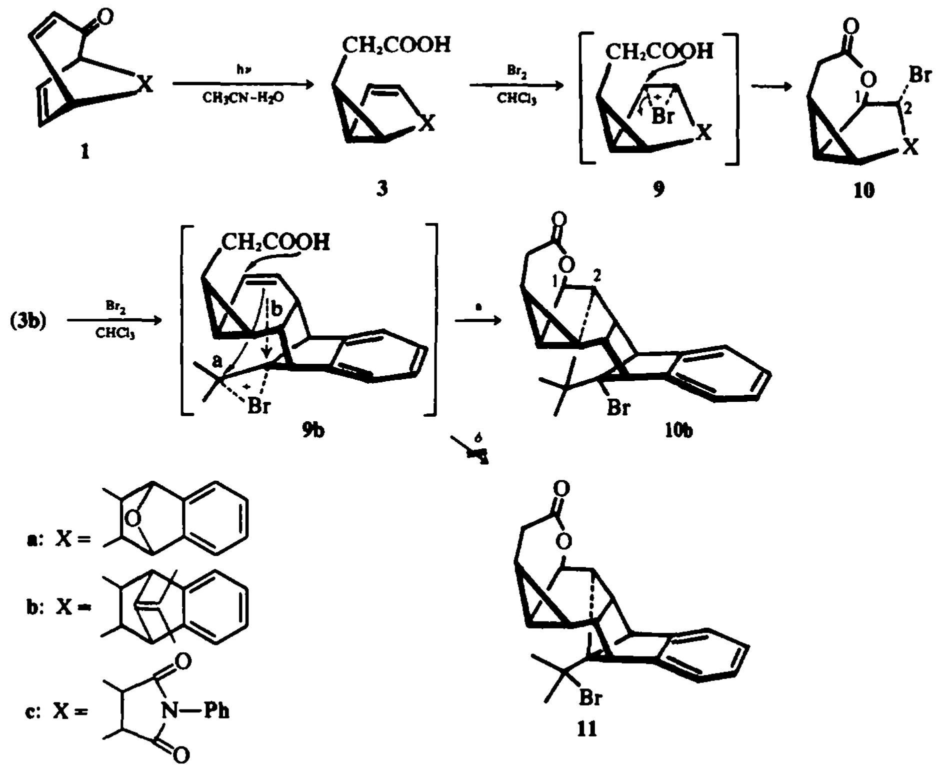
It is concluded that the bromolactones (**10a** and **10c**) were formed via bromonium ion intermediates (**9a**, **c**) followed by a nucleophilic attack of the carboxyl group.



Scheme 1



Scheme 2



Scheme 3

By contrast, the bromolactone (**10b**) was formed through initially produced bromonium ion intermediate (**9b**) by an attack of the isopropylidene group with bromine via path **a** rather than path **b** affording more strained compound (**11**). An examination of stereomodels and the chemical shifts of the Me protons (δ 1·24) also support this conclusion.

Reduction of the methylesters (**2a**, **b**) with LAH gave the corresponding alcohols (**12a**, **b**) in 92% yield. Similar reduction of **2c** was unsuccessful; treatment of the ester (**2c**) with LAH gave a mixture of compounds under even milder conditions which could not be purified. Similar bromolactonizations of the alcohols (**12a**, **b**) gave the corresponding cyclized products (**13a**, **b**) in 26–57% yield. The structure of **13a** and **13b** were determined by spectral evidence in comparison with the NMR spectra of **12a** and **12b**, and by elemental analyses (Experimental).

The amines (**14a**, **b**), prepared from **4a**, **b** (R=R'=H), on treatment with bromine afforded a mixture of compounds, from which cyclization products (**15a**, **b**) could only with difficulty be isolated.

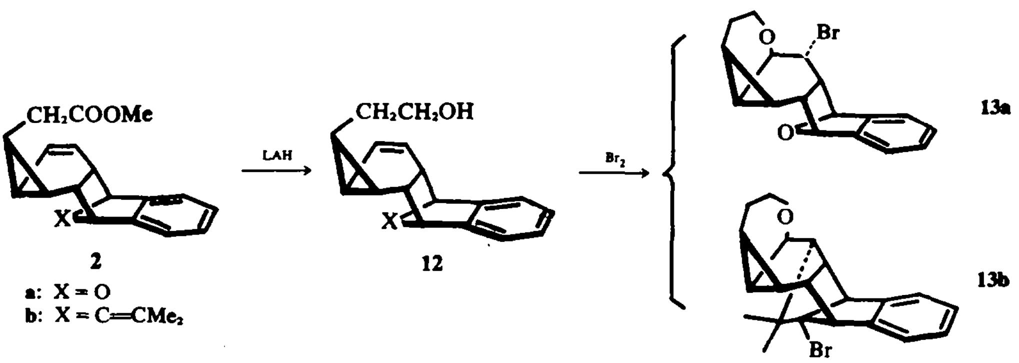
On the other hand, the carboxylic acids (**3a**, **b**, **c**) were inert to mercuric acetate because the bulky reagent could not attack the strained ring olefin.†

The cyclization[4] of the chloramine (**17**) by treatment of (**4a**) (R=H, R' = Me) with LAH gave the amine (**16**) in a quantitative yield. Then, chlorination of the amine (**16**) afforded the chloramine (**17**) in 90% yield. However, treatment of **17** in refluxing methanol in the presence of silver nitrate gave only the parent amine (**16**) and an expected cyclization product (**18**) could not be isolated. This result suggests that H-abstraction proceeds rather than the cyclization.

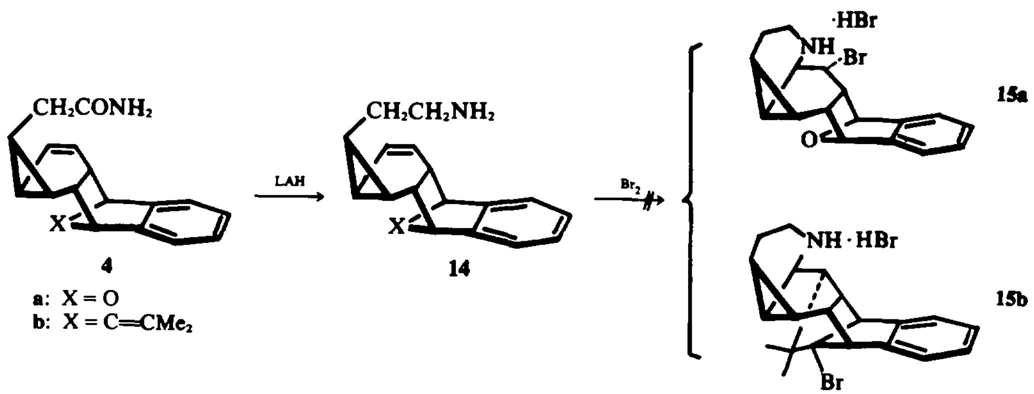
Further similar cyclization of the chloramine (**23**) by treatment of the acids (**3a**, **c**) with equimolar diphenylphosphoryl azide[5] gave the urethanes (**19a** and **19c**) in 71

---

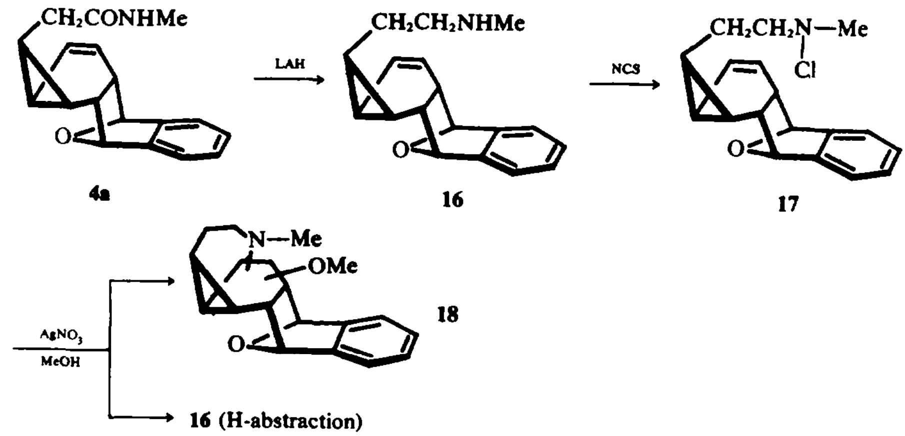
†The olefin was also found to be inert to hydrogenation over 10%-palladium on charcoal indicating the sterically hindered olefin.



Scheme 4



Scheme 5



Scheme 6

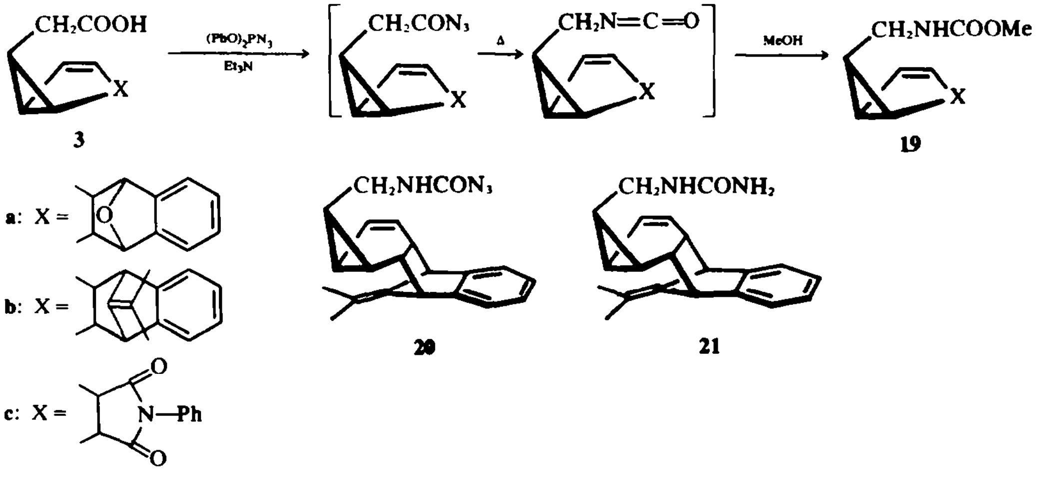
and 77% yields, respectively.† Surprisingly, the reaction of **3b** with diphenylphosphoryl azide gave the urethane (**19b**) in 41% besides a stable acyl azide (**20**) in 29% yield. Structural proofs of these urethanes (**19a**, **b**, **c**) and the acyl azide (**22**) were based on elemental analyses, spectral inspections and chemical transformation; catalytic hydrogenation of **20** over 10% Pd-C gave urea derivative (**21**).

The spectral data of these compounds are summarized in Table 1.

Reduction of the urethane (**19a**) with LAH gave the corresponding amine (**22**) in almost quantitative yield. Finally, treatment of the chlorinated amine (**23**) in refluxing methanol in the presence of silver nitrate for 10 hr gave the cyclized product **24** (picrate m.p. 205° (dec)) (6·5%) and the parent amine (**22**) (24%).

---

†The Curtius reaction of the carboxylic acid (**3a**) is unfavorable under acidic conditions since the molecules have a labile bridged O atom. Further the reaction of **3a** with thionyl chloride gave a lactone and no acid chloride. However, the reactions with diphenylphosphoryl azide proceed under neutral conditions[5] and thus the reagent was used for the reaction of the acids (**3a**, **b**, **c**).



Scheme 7

Table 1. NMR spectra of Curtius rearrangement products (δ values; J in Hz)

Compound No.	OMe	NH	Olefinic-H	Aromatic-H	$CONH_2$
19a*	3.53 (3H,s)	4.65(brs,1H)	5.85(m, 2H)	7.12(m, 4H)	
19b*	3.58 (3H,s)	4.50(brs,1H)	5.72(m, 2H)	7.10(m, 4H)	
19c**	3.65 (3H,s)	5.07(brs,1H)	5.7-6.3(m,2H)	7.40(m,4H)	
20*		4.95(brs,1H)	5.70(m, 2H)	7.05(m, 4H)	
21**		5.75(brs, 1H)	5.75(m, 2H)	6.90-7.30(m, 4H)	5.26(s, 2H)

* Solvent: in $CDCl_3$ ** in DMSO-d_6

The NMR spectra of the product (**24**) exhibited signals at δ 3·44 (s, 3H, OMe), 2.20 (s, 3H, N-Me) and 3·56 (m, 1H, H̱C-OMe), and the absence of olefinic proton signals indicating the cyclized structure (**24**) rather than **25**† as depicted in Scheme 8.

However, similar attempts for the bromocyclization of the amine (**22**) were unsuccessful and gave only tarry materials.

On the other hand, the synthesis of bridged azacycles by nitrenoid reaction of δ-ϵ unsaturated amines with lead tetraacetate and/or N-chlorosuccinimide has been shown by Nagata.[6] However, similar attempts to cyclize the amines (**14a**, **b**) were unsuccessful and only tarry materials were obtained. This is probably because of the initially producing highly strained aziridine rings might be polymerized during the reactions. Gassman *et al.*[7] have claimed that nitrenium ions are important in a variety of chloramine solvolyses in hot polar solvents. Mechanisms for homolytic cyclization of unsaturated chloramines in neutral medium was reported by Edwards *et al.*[8] in the course of our present work. From a reexamination of the cyclizations of the chloramines, they concluded that the nitrenium ions are not formed from simple aliphatic chloramines and possible homolytic mechanisms can be written for other reactions considered to involve nitrenium ions. Thus, the solvolytic reactions of **17** and **23** might be explained to proceed in a homolytic fashion, since the major products are the corresponding parent amines (the H-abstraction products) (**16** and **22**) as described above.

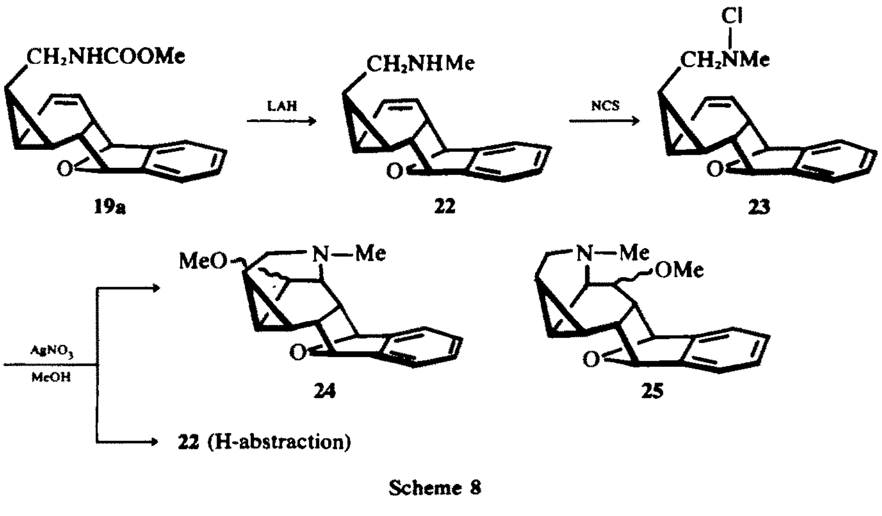
EXPERIMENTAL

Microanalyses were performed with a Perkin–Elmer 240 elemental analyser. NMR spectra were taken with a JEOL C-60-XL spectrometer with TMS as internal standard. IR spectra were taken with a JASCO-IR-S spectrophotometer. Mass spectra were obtained with a Hitachi RMU-D double-focusing spectrometer operating at an ionization potential of 70 eV. The solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 100–150°C.

General procedure for photolysis. A soln of the tropone adduct in the corresponding solvent was irradiated by a high pressure 100 W mercury lamp through a Pyrex filter under N_2 at room temp. The photolyses were monitored by TLC. The solvent was removed under reduced pressure and the residue was purified by recrystallization and then analysed by NMR.

Photolysis of **1a**. A soln of **1a** (500 mg) in acetonitrile-water (1:1) (80 ml) was irradiated for 1 hr. Work-up as described above gave **3a** (510 mg, 95%) as prisms; m.p. 177–178° (EtOH-n-hexane); δ ($CDCl_3$) 1·2–1·75 (3H, m, cyclopropane-H), 1·9-2·25 (4H, m), 4·95 (1H, s, benzyl-H), 5·20 (1H, s, benzyl-H), 5·84 (2H, m, olefinic-H), 7·15 (4H, m, aromatic-H) and 9·65 (1H, brs, COOH) (Found: C, 76·2; H, 6·1. $C_{17}H_{16}O_3$ requires: C, 76·1; H, 6·0%).

Photolysis of **1b**. A soln of **1b** (1·0 g) in acetonitrile-water (1:1) (90 ml) was irradiated fro 2 hr. Work-up gave **3b** (1·01 g, 95%) as prisms; m.p. 165–167° (benzene-*n*-hexane); ν_{max}(KBr) 1750 and 1460 cm^{-1}; δ ($CDCl_3$) 1·1–1·5 (3H, m, cyclopropane-H), 1·56 (3H, s, Me), 1·63 (3H, S, Me), 1·82 (2H, brs, CH_2–CO_2H), 2·1 (2H, m, bridgehead-H), 3·41 (1H, d, J = 1·5 Hz, benzyl-H), 3·62 (1H, d,



Scheme 8

---

†An examination of stereomodels supports the structure **24** since **25** consists of the 5-, 3- and 6-membered ring systems suggesting more highly strained molecule.

J = 1·5 Hz, benzyl-H), 5·67 (2H, m, olefinic-H), 7·05 (4H, m, aromatic-H) and 10·35 (1H, brs COOH) (Found: C, 82·3; H, 7·2. $C_{21}H_{22}O_2$ requires: C, 82·3; H, 7·25%).

Photolysis of **1c** *in methanol.* A soln of **1c** (500 mg) in MeOH (80 ml) was irradiated for 45 min. Work-up gave **2c** (500 mg) as needles; m.p. 106–108° (MeOH); ν_{max}(KBr) 1770, 1740, 1710, and 1600 cm^{-1}; *m/e* 311 and 279; δ ($CDCl_3$) 1·50–2·02 (3H, m, cyclopropane-H), 2·24 (2H, m, $C\underline{H}_2COO$), 3·37 (2H, m, bridgehead-H), 3·68 (3H, s, OMe), 5·76 (1H, dd, J = 10·2 and 2·0 Hz, olefinic-H), 6·08 (1H, dd, J = 10·2 and 5·5 Hz, olefinic-H), and 7·36 (5H, m, aromatic-H) (Found: C, 69·25; H, 5·3; N, 4·4. $C_{18}H_{17}O_4N$ requires: C, 69·45; H, 5·5; N, 4·5%).

Photolysis of **1c** *in acetonitrile-water.* A soln of **1c** (300 mg) in acetonitrile-water (1 : 1) (60 ml) was irradiated fro 45 min. Work-up gave **3c** (300 mg) as prisms; m.p. 185–187° (MeOH); ν_{max} (KBr) 3240–2930, 1770, 1730, 1700 and 1600 cm^{-1}; *m/e* 297 (parent); δ ($CDCl_3$) 1·53–1·88 (3H, m, cyclopropane-H), 2·33 (2H, m, $C\underline{H}_2COOH$), 3·36 (2H, m, bridgehead-H), 5·80 (1H, dd, J = 8·8 and 2·0 Hz, olefinic-H), 6·09 (1H, dd, J = 8·8 and 4·5 Hz, olefinic-H), and 7·34–7·42 (6H, m, aromatic-H and COOH) (Found: C, 68·55; H, 5·1; N, 4·8. $C_{17}H_{15}O_4N$ requires: C, 68·65; H, 5·1, N, 4·7%).

General procedure for bromolactonization. To a soln of carboxylic acid in chloroform was added dropwise a 0·1 M solution of Br_2 in chloroform. Then the mixture was stirred at room temp. and concentrated under reduced pressure. The residue was purified by chromatography on silica gel column.

Bromolactonization of **3a**. To a soln of **3a** (100 mg) in chloroform (20 ml) was added dropwise a 0·1 M soln of Br_2 in chloroform (4 ml). After addition the mixture was stirred for 3 hr, and then the solvent was removed. The residue was subjected to silica gel chromatography using benzene-chloroform to give **10a** (85 mg, 66%) as leaflets; m.p. 178–178·5° (ether); ν_{max} (KBr) 1730, 1460, 1390 and 1355 cm^{-1}; δ ($CDCl_3$) 1·1–2·2 (5H, m), 2·35 (1H, d, J = 18·0 Hz, $\underline{H}CCOO$), 2·70 (1H, d-m, J = 18·0 Hz, $\underline{H}CCOO$), 4·70 (1H, dd, J = 4·0 and 6·0 Hz, $\underline{H}CBr$), 5·17 (1H, s, benzyl-H), 5·32 (1H, s, benzyl-H), 5·28 (1H, m, $COOC\underline{H}$), and 7·02 (4H, m, aromatic-H) (Found: C, 58·9; H, 4·25. $C_{17}H_{15}O_3Br$ requires: C, 58·8; H, 4·35%).

Bromolactonization of **3b**. To a soln of **3b** (100 mg) in chlroform (20 ml) was added deopwise a 0·1 M soln of Br_2 in chlorform (3·5 ml). Work-up gave **10b** (90 mg, 72%) as needles; m.p. 206–207° (ether); ν_{max} (KBr) 1720, 1460 and 1395 cm^{-1}; δ ($CDCl_3$) 1·24 (6H, s, 2 Me), 1·3–3·0 (8H, m, cyclopropane-H, bridgehead-H and $C\underline{H}_2COO$), 3·20 (1H, d, J = 1·5 Hz, benzyl-H), 3·54 (1H, t, J = 1·5 Hz, benzyl-H), 5·20 (1H, m, $COOC\underline{H}$) and 7·1 (4H, m, aromatic-H) (Found: C, 65·2; H, 5·4; Br, 20·8. $C_{21}H_{21}O_2Br$ requires: C, 65·45; H, 5·5; Br, 20·75%).

Bromolactonization of **3c**. To a soln of **3c** (100 mg) in chloroform (20 ml) was added dropwise a 0·1 M soln of Br_2 in chloroform (3·6 ml). Work-up gave **10c** (100 mg, 79%) as needles; m.p. 231–233° (dec) (chlorform); ν_{max} (KBr) 1785, 1730, 1715, 1600, 1500 and 1395 cm^{-1}; δ (DMSO-d_6) 1·5–2·0 (3H, m, cyclopropane-H), 2·50 (2H, m, $C\underline{H}_2COO$), 2·8–3·3 (2H, m, bridgehead-H), 4·73 (1H, t, J = 4·0 Hz, $BrC\underline{H}$), 5·55 (1H, m, $COOC\underline{H}$), and 7·15–7·7 (5H, m, aromatic-H) (Found: C, 54·3; H, 3·5; N, 3·7. $C_{17}H_{14}O_4NBr$ requires: C, 54·25; H, 3·75; N, 3·7%).

Reduction of methyl ester (**2a**). To a stirred suspension of LAH (400 mg) in dry ether (30 ml) was added a soln of **2a** (400 mg) in dry ether (50 ml) at room temp. After the mixture was refluxed for 2 hr, the usual work-up gave **12a** (330 mg, 92%) as needles; m.p. 138–139° (ether-*n*-hexane); ν_{max} (KBr) 3480, 1460, 1440 and 1415 cm^{-1}; δ ($CDCl_3$) 1·0–1·55 (5H, m, cyclopropane-H and $C\underline{H}_2CH_2OH$), 1·70 (1H, brs, OH), 2·0 (2H, m, bridgehead-H), 3·50 (2H, t, J = 6·0 Hz, $C\underline{H}_2OH$), 4·91 (1H, s, benzyl-H), 5·18 (1H, s, benzyl-H), 5·80 (2H, m, olefinic-H) and 7·15 (4H, m, aromatic-H) (Found: C, 80·25; H, 7·1. $C_{17}H_{18}O_2$ requires: C, 80·3; H, 7·15%).

Reduction of methyl ester (**2b**). To a stirred suspension of LAH (300 mg) in dry ether (30 ml) was added a soln of **2b** (300 mg) in dry ether (50 ml) at room temp. After the mixture was refluxed for 2 hr, the usual work-up gave **12b** (250 mg, 92%) as needles; m.p. 106–107° (ether-*n*-hexane); ν_{max} (KBr) 3300, 1465, 1450 and 1375 cm^{-1}; δ ($CDCl_3$) 1·0–1·6 (6H, m, cyclopropane-H and $C\underline{H}_2CH_2O\underline{H}$, 1H exchangeable by D_2O), 1·58 (3H, s, Me), 1·66 (3H, s, Me), 1·87 (2H, m, bridgehead-H), 3·43 (1H, d, J = 1·5 Hz, benzyl-H), 3·56 (1H, t, J = 7·0 Hz, $C\underline{H}_2OH$), 3·65 (1H, d, J = 1·5 Hz, benzyl-H), 5·75 (2H, m, olefinic-H) and 7·15 (4H, m, aromatic-H) (Found: C, 86·05; H, 8·4. $C_{21}H_{24}O$ requires: 86·25; H, 8·25%).

Bromocyclization of **12a**. To a soln of **12a** (210 mg) in chloroform (20 ml) was added dropwise a 0·1 M soln of Br_2 in chloroform (9 ml). After addition the mixture was stirred at room temp. for 1 hr. Evaporation to dryness and chromatography on silica gel using benzene gave **13a** (70 mg, 26%) as needles; m.p. 167–169° (benzene-*n*-hexane); ν_{max} 1460 cm^{-1}; δ ($CDCl_3$) 1·1–2·2 (7H, m), 2·8–3·6 (2H, m, $CH_2C\underline{H}_2O$), 4·33 (1H, t, J = 4·0 Hz, $CH_2OC\underline{H}$), 4·60 (1H, dd, J = 4·0 and 7·0 Hz, $\underline{H}CBr$), 5·17 (1H, s, benzyl-H), 5·36 (1H, s, benzyl-H) and 7·15 (4H, m, aromatic-H) (Found: C, 64·3; H, 5·45. $C_{17}H_{17}OBr$ requires: C, 64·35; H, 5·4%).

Bromocyclization of **12b**. To a soln of **12b** (90 mg) in chloroform (10 ml) was added dropwise a 0·1 M soln of Br_2 in chloroform (3.5 ml). Work-up gave **13b** (65 mg, 57%) as needles; m.p. 202–206° (benzene-*n*-hexane); ν_{max} (KBr) 1460 cm^{-1}; δ ($CDCl_3$) 1·25 (6H, s, 2Me), 1·0–2·2 (7H, m), 3·15 (1H, d, J = 2·0 Hz, benzyl-H), 3·4 (2H, m, $C\underline{H}_2O$), 3·57 (1H, t, J = 2·0 Hz, benzyl-H), 4·53 (1H, m, $CH_2OC\underline{H}$) and 7·15 (4H, m, aromatic-H) (Found: C, 67·95; H, 6·2. $C_{21}H_{23}OBr$ requires: C, 67·9; H, 6·25%).

Reduction of carboxamide (**4a**). To a stirred suspension of LAH (200 Mg) in dry ether (50 ml) was added a soln of **4a** (250 mg) in dry ether-THF (3 : 2) (50 ml) at room temp. After the mixture was refluxed for 12 hr, usual work-up gave **16** (235 mg) as an oil; ν_{max} (neat) 3300 and 1460 cm^{-1}; δ ($CDCl_3$) 0·9–1·6 (5H, m, cyclopropane-H and $C\underline{H}_2CH_2NHMe$), 1·70 (1H, s, NH), 2·00 (2H, m, bridgehead-H), 2·32 (3H, s, NMe), 2·50 (2H, t, J = 6·0 Hz, $CH_2C\underline{H}_2NHMe$), 4·95 (1H, s, benzyl-H), 5·20 (1H, s, benzyl-H), 5·84 (2H, m, olefinic-H), and 7·17 (4H, m, aromatic-H) (Found: C, 80·7; H, 8·0; N, 5·3. $C_{18}H_{21}ON$ requires: C, 80·85; H, 7·9; N, 5·25%).

N-Chlorination of **16**. To a soln of **16** (235 mg) in methylene chloride (50 ml) was added N-chlorosuccinimide (NCS) (110 mg). After the mixture was stirred at room temp for 2 hr, and evaporation to dryness and chromatography on silica gel using chloroform gave **17** (240 mg, 90%) as colorless crystals; m.p. 115–118°; ν_{max} ($CHCl_3$) 1460 cm^{-1}; δ ($CDCl_3$) 0·8–1·7 (5H, m, cyclopropane-H and $C\underline{H}_2CH_2N$), 2·0 (2H, m, bridgehead-H), 2·73 (2H, t, J = 7·0 Hz, $CH_2C\underline{H}_2N$), 2·77 (3H, s, NMe), 4·86 (1H, s, benzyl-H), 5·11 (1H, s, benzyl-H), 5·75 (2H, m, olefinic-H), and 7·05 (4H, m, aromatic-H) (Found: C, 71·5; H, 6·65; N, 4·6. $C_{18}H_{20}ONCl$ requires: C, 71·65; H, 6·7; N, 4·65%).

Reaction of N-chloramine (**17**) *with silver nitrate in methanol.* To a soln of **17** (240 mg) in MeOH (50 ml) was added a soln of $AgNO_3$ (210 mg) in MeOH (20 ml). The mixture was refluxed for 10 hr in the dark. After cooling, the mixture was filtered and then dil HCl was added the filtrate to remove the excess of Ag ion and again filtered. The filtrate was concentrated under reduced pressure and then K_2CO_3aq was added to neutralize. The extract with ether was dried over K_2CO_3 and evaporated. Chromatography on alumina using chlorform gave **16** (100 mg, 47%) as light brownish oil.

General procedure for Curtius reaction with diphenylphosphoryl azide. A soln of carboxylic acid, triethyl amine and diphenylphosphoryl azide in dry benzene was refluxed for 1 hr, and then absolute MeOH (excess) was added and refluxed for 15 hr. The mixture was washed with water and dried. Then the solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel column and then analysed by NMR (Table 1).

Curtius reaction of **3a**. A soln of **3a** (1·58 g), triethylamine (0·7 g), and diphenylphosphoryl axide (1·8 g) in dry benzene (40 ml) was refluxed for 1 hr, and then abs. MeOH (15 ml) was added and refluxed for 15 hr. Work-up gave **19a** (1·24 g, 71%) as prisms; m.p. 155·5–156·5° (ether); ν_{max} (KBr) 3320, 1705, 1680 and 1540 cm^{-1} (Found: C, 72·8; H, 6·5; N, 4·7. $C_{18}H_{19}O_3N$ requires: C, 72·7; H, 6·45; N, 4·7%).

Curtius reaction of **3b**. A soln **3b** (450 mg), triethylamine (202 mg) and diphenylphosphoryl azide (550 mg) in dry benzene (30 ml) was refluxed for 1 hr, and then abs. MeOH (10 ml) was added and refluxed for 15 hr. The mixture was washed with water and dried. The solvent was then removed under reduced pressure and the residue was subjected to silica gel chromatography using benzene. The first fraction gave **20** (150 mg, 29%) as needles; m.p. 106–108° (ether-*n*-hexane); ν_{max} (KBr) 3300, 2155, 1710, 1680 and 1540 cm^{-1} (Found: C, 72·85; H, 6·5; N, 16·05. $C_{21}H_{22}ON_4$ requires: C, 72·8; H, 6·4; N, 16·15%). The second fraction gave **19b** (200 mg, 41%); m.p. 165–167° (ether); ν_{max} (KBr) 3325, 1705, 1680 and 1540 cm^{-1} (Found: C, 78·75; H, 7·8; N, 4·3. $C_{22}H_{25}O_2N$ requires: C, 78·75; H, 7·5; N, 4·2%).

Curtius reaction of **3c**. A soln of **3c** (297 mg), triethylamine (116 mg) and diphenylphosphoryl azide (320 mg) in dry benzene was refluxed for 1 hr, and then abs. MeOH (5 ml) was added and refluxed for 15 hr. Work-up gave **19c** (250 mg, 77%) as crystals; m.p. 137–138° (ether); ν_{max} (KBr) 3360, 1780, 1725, 1700, 1600 and 1540 cm^{-1} (Found: C, 66·0; H, 5·55; N, 8·8. $C_{18}H_{18}O_4N_2$ requires: C, 66·25; H, 5·55; N, 8·6%).

Catalytic hydrogenation of **20**. A soln of **20** (40 mg) in MeOH (60 ml) was hydrogenated over 10% Pd–C (50 mg) under atm. press. to give **21** (25 mg) as needles; m.p. 146–147° (MeOH-ether); ν_{max} (KBr) 3400, 1640, 1600 and 1560 cm^{-1} (Found: C, 78·55; H, 7·65; N, 8·8. $C_{21}H_{24}ON_2$ requires: C, 78·7; H, 7·55; N, 8·75%).

Reduction of **19a**. To a stirred suspension of LAH (400 mg) in dry ether (20 ml) was added a soln of **19a** (500 mg) in dry ether (30 ml) at room temp. After the mixture was refluxed for 15 hr, the usual work-up gave **22** (410 mg) as colorless oil; ν_{max} (neat) 3320 and 1465 cm^{-1}; δ ($CDCl_3$) 1·1–1·7 (3H, m, cyclopropane-H), 2·04 (2H, m, bridgehead-H), 2·1–2·7 (2H, m, $C\underline{H}_2$NHMe), 2·29 (3H, s, NMe), 3·04 (1H, brs, NH), 4·95 (1H, s, benzyl-H), 5·20 (1H, s, benzyl-H), 5·90 (2H, m, olefinic-H), and 7·16 (4H, m, aromatic-H); picrate, m.p. 208° (dec) (MeOH) as yellow needles; ν_{max} (KBr) 1630, 1610, 1570 and 1545 cm^{-1} (Found: C, 57·1; H, 4·5; N, 11·55. $C_{23}H_{22}O_8N_4$ requires: C, 57·25; H, 4·6; N, 11·6%).

N-Chlorination of **22**. To a soln of **22** (410 mg) in methylene chloride (50 ml) was added NCS (267 mg). After the mixture was stirred at room temp for 2 hr, and evaporation to dryness and chromatography on silica gel using methylene chloride gave **23** (370 mg, 80%) as colorless oil; ν_{max} (neat) 1460 cm^{-1}; δ ($CDCl_3$) 1·1–1·75 (3H, m, cyclopropane-H), 2·03 (2H, m, bridgehead-H), 2·78 (3H, s, NMe), 2·6–3·0 (2H, m, $C\underline{H}_2$NMeCl), 4·93 (1H, s, benzyl-H), 5·18 (1H, s, benzyl-H), 5·86 (2H, m, olefinic-H) and 7·15 (4H, m, aromatic-H) (Found: C, 70·8; H, 6·45; N, 4·95. $C_{17}H_{18}ONCl$ requires: C, 70·95; H, 6·3; N, 4·85%).

Cyclization of chloramine (**23**) *with silver nitrate in methanol*. To a soln of **23** (370 mg) in MeOH (50 ml) was added a soln of $AgNO_3$ (330 mg) in MeOH (20 ml). The mixture was refluxed for 10 hr in the dark. After cooling, the mixture was filtered and then dil. HCl was added to remove the excess of Ag ion and filtered. The filtrate was concentrated under reduced pressure and then K_2CO_3aq was added to neutralize. The extract with ether was dried and evaporated. The residue was dissolved with MeOH (10 ml). The soln was added with a satd soln of picric acid in MeOH to give picrate **24** (40 mg, 6·5%) as yellow prisms; m.p. 205° (dec) (MeOH); ν_{max} (KBr) 1630, 1615, 1565, 1500 and 1440 cm^{-1}; δ ($CDCl_3$) (free amine **24**) 1·1–1·7 (3H, m, cyclopropane-H), 2·0 (2H, m, bridgehead-H), 2·20 (3H, s, NMe), 2·1–2·9 (3H, m, $C\underline{H}_2NC\underline{H}$), 3·44 (3H, s, OMe), 3·56 (1H, m, $\underline{H}$COMe), 5·04 (1H, s, benzyl-H), 5·26 (1H, s, benzyl-H), and 7·15 (4H, m, aromatic-H) (Found: C, 56·5; H, 4·8; N, 10·9. $C_{24}H_{24}O_9N_4$ requires: C, 56·25; H, 4·7; N, 10·95%). The mother liquor was concentrated under reduced pressure and then KOHaq was added. The soln was then extracted with ether. Evaporation to dryness and chromatography on alumina using chloroform gave **22** (150 mg 24% as picrate).

REFERENCES

[1] Part XVII of this series, see T. Sasaki, K. Kanematsu, A. Kondo and Y. Nishitani, *J. Org. Chem.* **39**, 3569 (1974).
[2] T. Sasaki, K. Kanematsu and K. Hayakawa, *J. Chem. Soc.* Perkin I, 1951 (1972).
[3] T. Sasaki, K. Kanematsu and K. Iizuka, *Ibid.* Perkin I, 933 (1974).
[4] P. G. Gassman, F. Hoyda and J. Dygos, *J. Am. Chem. Soc.* **90**, 2716 (1968).
[5] T. Shioiri and S. Yamada, *J. Syn. Org. Chem. Japan* **31**, 666 (1973); and refs cited.
[6] W. Nagata, *Lectures in Heterocyclic Chemistry* **1**, 29 (1972); and refs cited.
[7] P. G. Gassman, *Accounts Chem. Res.* **3**, 26 (1970).
[8] O. E. Edwards, G. Bernath, J. Dixon, J. M. Paton and D. Vocelle, *Can. J. Chem.* **52**, 2123 (1974).