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SYNTHETIC STUDIES ON TERPENOIDS—III[1]

SYNTHETIC APPROACHES TO DITERPENE ALKALOIDS

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Abstract—A stereoselective synthetic route to the bicyclic keto ester **14** from octalin **4** is described. Ketoester **14** is converted to its azide **27** in several steps. Photolysis of **27** produced the lactam **2** whose transformation to lactam **3** is reported.

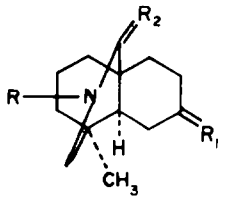
The fundamental skeleton of the great majority of C_{19} and C_{20} diterpene alkaloids[2] such as atisine, veatchine can be represented by the decalin **1**. The synthesis of diterpene alkaloids had been a challenge to the ingenuity of organic chemists for a long time owing to the lack of suitable methods for the construction of complex ring structures as present in atisine and related compounds. Extensive investigations in the last two decades towards diterpene alkaloids have led to the total synthesis of atisine, veatchine, versatile synthons and related model compounds.[3] The crucial problem in any synthesis of diterpene alkaloids is the construction of the hetero-bridged *trans*-decalin system as present in atisine or an oxazolidine bridge present in garrya alkaloids. Reactions to form such a bridge involving Me and another reactive group 1,3-diaxially situated in decalin and phenanthrene moiety have been extensively studied.[4] In connection with our studies on diterpene alkaloids[5,6] it was attempted[7] to synthesize the bicyclic ketoester **14** which on hydrolysis and by suitable photolysis would allow an entry to the desired lactams **2** and **3**, one of the major structural units of many diterpenoid alkaloids. Lactams **2** and **3** possess suitable structural and stereochemical characteristics for utilising the same for extending synthetic studies to more complicated molecular patterns as are found in the degradation products of these alkaloids. Here we describe our observations[8] concerning the synthesis of **14** and its transformation to **2** and **3**.

For the present investigation, octalin **4**, prepared and purified by the published procedure,[9] was chosen as reference material which can serve as a convenient relay intermediate. Hydroboration–oxidation of **4** under the standard condition[10] afforded a crystalline alcohol in 80% yield which was assigned to **5** in view of the expected preferential attack by the hydroborating agent from the less hindered α-face of double bond and on spectral evidence. In the NMR spectrum alcohol **5** exhibited a multiplet at δ 3.88 ppm ($W_{1/2}$ = 14 Hz), characteristic of the axial proton[11] at C-6 of **5**. Oxidation[12] of **5** with CrO_3 in hexamethylphosphoramide (HMPT) afforded ketone **6** which on attempted isomerisation with acid and base was recovered unchanged. The stability of ketone **6** under enolizing condition indicated that A/B ring fusion of **6** is in the more stable *trans*-configuration and therefore the hydrogen at C-5 is α-oriented. Hydroboration reaction involves a *cis* addition of the B–H moiety to the double bond and this would suggest that the C-6 OH group of **5** was also α-oriented. A by-product of the hydroboration reaction, that resulted in 4% yield was identified as hydrocarbon **7** by comparing (IR and tlc) with an authentic specimen, prepared by the published procedure.[13] The formation of **7** was presumably the outcome of hydrogenolysis[14] of the B–H moiety of **2** by boric acid, probably formed by the trace of water present in BF_3OEt_2. The boric acid hydrogenolysis of B–H moiety has also been recorded[15] to generate hydrocarbon[16] **9** during the hydroboration of olefin[17] **8**.

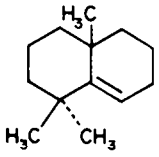
Reduction of **6** with LAH afforded a 6β-alcohol **10** in 82% yield whose configurational assignment was supported by its NMR spectrum which showed a multiplet δ 4.38 ppm ($W_{1/2}$ = 6 Hz) characteristic of an equatorial hydrogen.[11] Oxidation[17] of **10** in cyclohexane with $Pb(OAc)_4/I_2$ afforded the cyclic ether **11** (described below) and ketone **6** in yields 36% and 60% respectively. The cyclic ether **11** presented two spots of unequal intensity in tlc indicating the probable formation of a small amount of **12**, though no clear-cut evidence was available to support its structural assignment. Oxidation of **11** with CrO_3/AcOH yielded the crystalline ketoacid **13** in 70% yield. Treatment of the sodium salt of **13** with MeI in hexamethylphosphoramide[18,19] afforded ketoester **14** in 80% yield. Reduction of **14** with $NaBH_4$ in MeOH furnished a mixture of alcohols **15** whose tosyl derivative on heating with NaI and Zn in diglyme produced **16** in excellent yield. Ester **16** on heating with quinoline in AcOH[20] produced the crystalline acid **17** in 90% yield which was identical with an authentic specimen.[21] Thus the structure of the cyclic ether **11** remained established.

From the mother liquor of keto acid **13** was obtained an oily material which had molecular ion *m/e* 224 in the MS and showed bands at 1700 and 1710 cm^{-1} in the IR spectrum. Based on these spectroscopic data the structure of the oily material was assigned to **18** which possibly originated during CrO_3 oxidation of **12**. It is worthwhile to mention that owing to insufficient material the structure of **12** and **18** could not be definitely established.

Kinetic enolate of **14**, generated by $LiNCHMe_2$ in 1,2-dimethoxy ethane, reacted with Me_3SiCl affording as expected[22] the less highly substituted enol ether **19** in predominant amount along with some amount of the highly substituted enol ether **20**. Epoxidation of the



1: R = H, R_1 = R_2 = H, H
2: R = H, R_1 = R_2 = O
3: R = Ms, R_1 = O, R_2 = H, H



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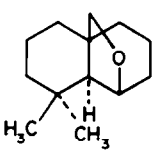
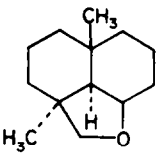


11



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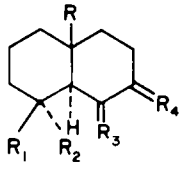

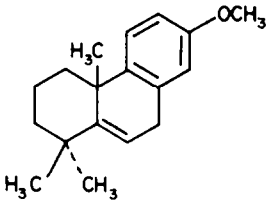

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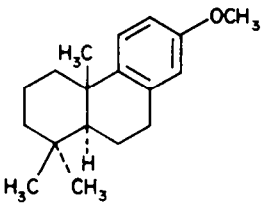
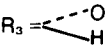
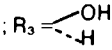


9

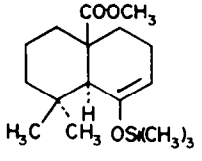
5: R = R_1 = R_2 = CH_3; R_3 =  , R_4 = H, H
6: R = R_1 = R_2 = CH_3; R_3 = O, R_4 = H, H
7: R = R_1 = R_2 = CH_3; R_3 = R_4 = H, H
10: R = R_1 = R_2 = CH_3; R_3 =  , R_4 = H, H
13: R = COOH, R_1 = R_2 = CH_3, R_3 = O, R_4 = H, H
14: R = $COOCH_3$, R_1 = R_2 = CH_3, R_3 = O, R_4 = H, H
15: R = $COOCH_3$, R_1 = R_2 = CH_3, R_3 = ~OH, R_4 = H, H
16: R = $COOCH_3$, R_1 = R_2 = CH_3, R_3 = R_4 = H, H
17: R = COOH, R_1 = R_2 = CH_3, R_3 = R_4 = H, H
18: R = R_2 = CH_3; R_1 = COOH, R_3 = 0, R_4 = H, H

Scheme 1.

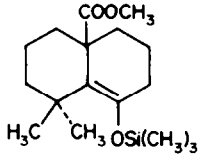
mixtures of silyl esters **19** and **20** in CH_2Cl_2 with *m*-chloroperbenzoic acid (MCPBA) followed by acid hydrolysis[23] of the crude product produced the oily hydroxy ketone **21** in 50% yield. Attempts to deoxygenate the C-6 CO group of **21** by drastic reduction procedures (Clemensen, Huang-Minlon modified Wolff-Kishner etc) without blocking the C-7 OH group gave poor and erratic results. It therefore became necessary to block the secondary OH function temporarily and after many trials the conversion of **21** to **22** was found suitable for such drastic reduction. Treatment of **21** with MeI and NaH in THF afforded **22** and **23** in yields 94% and 6% respectively. Clemmensen reduction[17] of **22** produced **24** which on demethylation[24] with BBr_3 followed by oxidation with Jones reagent[25] afforded ketoester **25**.

The next operation concerned the construction of the heterobridge in ring A of ketoester **25**. Treatment of **25** with ethylene glycol in refluxing benzene containing *p*-TsOH afforded the oily ketal **26** which was subjected to neutral hydrolysis[26] by heating under reflux with a mixture of Me_3SiCl and NaI in MeCN. The resulting acidic material on treatment with oxalyl chloride was converted to the corresponding acid chloride whose conversion to azide **27** was accomplished by adding a mixture of pyridine and N_3H in toluene.[27] After elimination of toluene under reduced pressure at 0°, azide was immediately taken in dry thiophen-free benzene. In order to avoid concomitant thermal rearrangement to isocyanate, no attempt was made to isolate azide **27** but its IR indicated the almost total absence of isocyanate contaminant.

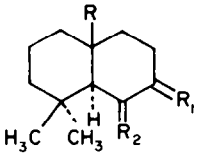
Photolysis[28] of azide **27** in benzene with Hanovia UV lamp 450 w at room temp followed by deketalization of the resulting product afforded lactam **2** in 7.8% yield which was identical (IR and tlc) with an authentic spe-



19



20



21: R = $COOCH_3$, R_1 = ~OH, H R_2 = O
22: R = $COOCH_3$, R_1 = ~OCH_3, H, R_2 = o
23: R = $COOCH_3$, R_1 = R_2 = OCH_3, H
24: R = $COOCH_3$, R_1 = ~OCH_3, H R_2 = H, H
25: R = $COOCH_3$, R_1 = O, R_2 = H, H
26: R = $COOCH_3$, R_1 =  , R_2 = H, H
27: R = CON_3, R_1 =  , R_2 = H, H

Scheme 2.

cimen.[29] Photolysis of azide without blocking the C-7 CO afforded only 3.8% yield of **2** and the yield was variable from run to run.

Lactam **2** on heating with excess LAH in dioxane followed by oxidation with pyridinum chlorochromate[30] afforded an oily carbonyl compound which on treatment with mesityl chloride yielded **3** whose mp. mixed with an authentic specimen[29] remained undepreseed. The IR spectra of **3** was indistinguishable from the IR spectra of an authentic specimen.

In conclusion the present approach for synthesis of **14** and its transformation to **2** and **3** constitutes an alternative approach for the construction of the fundamental skeleton of diterpenoid alkaloids.

EXPERIMENTAL

M.ps were determined on a Kofler hot-stage and are uncorrected. Unless otherwise stated IR spectra were taken on a Perkin–Elmer 337 spectrometer for KBr discs or liquid films and NMR spectra recorded on a Varian A-90 spectrometer were measured in $CDCl_3$ with TMS as internal standard. The chemical shifts are presented in terms of δ, s: singlet, d: doublet, t: triplet and m: multiplet. Column chromatography was carried out with Neutral Brockmann alumina and silica gel (BDH). Tlc plates were coated with silica gel G having a thickness of about 0.2 mm and the spots were located by exposing the dried plates in I_2 vapour. Unless otherwise stated all organic extracts were washed with brine, dried over anhyd $MgSO_4$ and evaporated under reduced pressure. Microanalyses were out in Microanalytical Laboratory, 5251 in Franz Pascher Microanalytiches Laboratorium at Bonn, West Germany. All compounds described here are racemic although the prefix (±) is omitted and only one enantiomer is depicted in structural formulas. All compounds in this paper are numbered by the steroid–terpenoid convention as depicted in Scheme 1, with gem substituted ring of decalins being ring A.

Hydroboration of octalin **4**

To a soln of B_2H_6 in THF at 0° prepared by the addition of BF_3Et_2O (5.12 g) to a suspension of $NaBH_4$ (1.41 g) in THF (60 ml) under N_2, was added **4** (2.82 g) dissolved in THF (40 ml) and the mixture was stirred at 0° for 16 hr. The mixture was allowed to warm to room temp. for 1 hr and then 10% NaOH aq (30 ml) was added followed immediately by 30% H_2O_2 (30 ml). The mixture was heated under reflux for 1 hr, cooled and diluted with ether. The organic layer was separated, washed, dried and evaporated to yield a gummy material which was chromatographed over alumina (80 g). Elution with hexane yielded **7** (110 mg; 4%), b.p. 106–112°/117 mm (bath), lit.[14] 100–105°/10 mm (bath); *m/e* 180 (M^+) (Calc. for $C_{13}H_{24}$: C, 86.58; H, 13.48. Found: C, 86.42; H, 13.11%). Elution with hexane: C_6H_6 (98:2) gave the crystalline **5** (2.48 g; 80%), m.p. 62–64° (aq MeOH), *m/e* 196 (M^+); IR (KBr) 3450 (OH) cm^{-1}; NMR δ 0.91 (3H, s), 0.99 (3H, s), 1.13 (3H, s) (4,4-CH_3 and 10-CH_3) and 3.88 (1H, m, $W_{1/2}$ = 16 Hz, H-6). (Calc. for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.16; H, 12.12%).

4,4,10-*Trimethyl*-6-*keto*-trans-*decalin* **6**

To a stirred soln of CrO_3 (160 mg) in dry HMPA (4 ml) was added **5** (150 mg) dissolved in HMPA (3 ml). The mixture was stirred at room temp. for 4 hr, diluted with water and extracted with ether. The extract was washed with $NaHCO_3$ aq, dried, evaporated and on distillation afforded **6** (140 mg; 95%); b.p. 98–105°/0.2 mm (bath *m/e* 194 (M^+); IR (film) 1725 (C=0) cm^{-1}; NMR δ 0.96 (3H, s), C.98 (3H, s), 1.23 (3H, s) (4,4-CH_3 and 10-CH_3) and 2.31 (1H, s, H-5). (Calc. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.11; H, 11.18%).

Attempted isomerization of ketone **6**

(a) Ketone **6** (110 mg) dissolved in C_6H_6 (20 ml) was refluxed for 8 hr with a catalytic amount of *p*-TsOH. After the usual workup **6** was recovered unchanged.

(b) Ketone **6** (110 mg) was heated under reflux with 5% methanolic KOH (30 ml) for 10 hr. After the usual workup **6** was recovered unchanged.

4,4,10-*Trimethyl*-6β-*hydroxy*-trans-*decalin* **10**

To LAH (1.91 g) in THF (40 ml) was added **6** (750 mg) dissolved in THF (10 ml). After heating the resulting mixture for 4 hr water was added. The ppt was filtered out and the filtrate was dried. Removal of solvent afforded a thick oily material which was chromatographed over alumina. Hexane eluted **5** (190 mg; 25%). Elution with hexane: C_6H_6 (95:5) yielded **10** (490 mg; 65%), m.p. 45–48° (aq CH_3OH); *m/e* 196 (M^-); IR (KBr) 3450 (OH) cm^{-1}; NMR δ 0.95 (3H, s), 1.20 (3H, s) 1.26 (3H, s) (4,4-CH_3 and 10-CH_3) and 4.38 (1H, m, $W_{1/2}$ = 6 Hz). Calc. for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.18; H, 12.08%).

Lead tetraacetate oxidation of alcohol **10**

A mixture of $Pb(OAc)_4$ (4.41 g) and anhyd $CaCO_3$ (4.41 g) suspended in cyclohexane (100 ml) was heated under reflux for 30 min. To the above suspension was added **10** (1.01 g) dissolved in cyclohexane (40 ml) followed immediately by I_2 (1.02 g) and the resulting mixture was heated under reflux for 1.5 hr with two Philips 250-W photo lamps. The cooled mixture was filtered and the filtered cake was washed thoroughly with ether. The combined filtrates were washed successively with NaOH aq, $NaHSO_3$ aq, brine and dried. On removal of solvent a dark oily material (1.24 g) was obtained. The same experiment was repeated twice. The total product (3.68 g) was chromatographed over alumina. Hexane eluted **11** (1.31 g; 36%); b.p. 122–132°/12 mm (bath); *m/e* 194 (M^+); NMR δ 0.95 (3H, s), 1.09 (3H, s) (4,4-CH_3) and 3.88 (2H, m, 10-H). (Calc. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.08; H, 11.18%). Elution with hexane: C_6H_6 (98:2) afforded **6** (1.45 g; 60%).

10β-*Carboxyl*-4,4-*dimethyl*-6-*keto*-trans-*decalin* **13**

A soln of CrO_3 (820 mg) in AcOH (5 ml) was added to a stirred soln of **11** (750 mg) in AcOH (10 ml) and the resulting soln was stirred for 65 hr at room temp. The soln was poured into water, extracted with ether and worked up. The semi-solid material obtained was chromatographed on silica gel. Ether: light petroleum (40:60) eluted **13** (610 mg; 70%), m.p. 130–132° (ether); *m/e* 224 (M^+) and 179 (M^+–COOH); IR (KBr) 1700 and 1725 (acid and ester CO) cm^{-1}; NMR δ 0.96 (3H, s) and 1.45 (3H, s) (4,4-CH_3). (Calc. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.28; H, 8.49%).

From the mother liquor of **13** was obtained the oily **18** (12 mg). *m/e* 224 (M^+); IR (film) 1710 and 1700 (acid and ketonic CO) cm^{-1}.

10β-*Carbomethoxyl*-4,4-*dimethyl*-6-*keto*-trans-*decalin* **14**

To a soln of **13** (610 mg) dissolved in HMPA (30 ml) was added NaOH (96 mg) in H_2O (5 ml) and after stirring the mixture for 1.2 hr at room temp. MeI (1.21 g) was added. The resulting soln was stirred at room temp for 1.8 hr, acidified and extracted with ether. The organic extract was washed, dried and evaporated to obtain the oily **14** (511 mg; 80%), b.p. 85–91°/0.25 mm (bath), *m/e* 238 (M^+); IR (film) 1745 (unresolved ketonic and ester CO) cm $^{-1}$; NMR δ 0.96 (3H, s) 1.45 (3H, s) (4,4-CH_3) and 3.75 (3H, s, OCH_3). (Calc. for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.18; H, 9.12%).

10β-*Carboxyl*-4,4-*dimethyl*-trans-*decalin* **17**

To **14** (510 mg) dissolved in MeOH (20 ml) and cooled to 0° was added $NaBH_4$ (85 mg). After stirring the mixture for 4 hr at 0°, water was added, extracted with ether and worked up. The residue was chromatographed over alumina. Fraction eluted by ether: C_6H_6 (1:1) afforded the oily **15** (517 mg; 98%); *m/e* 240 (M^+) and 222 (M^+–H_2O); IR (film) 3550 (OH) cm^{-1}.

A soln of **15** (510 mg) and *p*-TsCl (150 mg) in dry C_5H_5N (5 ml) was stirred at ambient temp. overnight. The mixture was poured into water and extracted with CH_2Cl_2. The extract was washed with 1% HCl, dried and concentrated to yield the oily tosyl derivative (820 mg; 99%) which without purification was dissolved in glyme (35 ml) followed by addition of NaI (520 mg) and

Zn powder (580 mg). The mixture was heated under reflux for 5 hr and filtered. The filtrate was diluted with water, extracted with ether, dried and evaporated to obtain the oily **16** (120 mg; 75%); *m/e* 224 (M^+); IR (film) 1740 (ester CO) cm^{-1}.

A mixture of **16** (120 mg), freshly distilled quinoline (3 ml) and AcOH (1 ml) was heated under reflux for 52 hr under a slow stream of N_2. The mixture was poured into ether (80 ml), washed with 6 N HCl and then with 10% NaOH aq. The alkaline extract was acidified, extracted with $CHCl_3$, washed with brine and dried. Solvent removal yielded **17** (110 mg; 90%), m.p. 93–96° (aq MeOH), lit.[21] 93–97°; m.m.p. 93–95°; *m/e* 210 (M^+) and 165 (M^+–COOH). (Calc. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 73.78; 10.18%).

*10β-Carbomethoxyl-4,4-dimethyl-7-keto-*trans*-decalin* **25**

Following the procedure of House *et al.*[22] triphenylmethane (8 mg) was added at 0°, under dry N_2, to MeLi (4 mmol in 1,2-dimethoxyethane) followed by dry freshly distilled diisopropylamine (400 mg, 4 mmole). To this cold soln was added **14** (714 mg, 3 mmole) dissolved in 1,2-dimethoxyethane (5 ml) and then a soln prepared from 1,2-dimethoxyethane (10 ml), Et_3N (200 mg) and Me_3SiCl (830 mg). The resulting mixture was stirred at room temp for 20 min at 0°. $NaHCO_3$ aq was added and extracted with ether. The dried ether extract afforded a mixture of **19** and **20**.

To the crude mixture (950 mg) of **19** and **20** dissolved in CH_2Cl_2 (10 ml), cooled to 0°, was added MCPBA (2 mmole) in CH_2Cl_2 during several min. After 1 hr, $NaHSO_3$ was added, stirred and filtered. The product, isolated by ether extraction from the filtrate was dissolved in diglyme (10 ml) followed by addition of 2N HCl (5 ml). The mixture was heated on water bath for 55 min, cooled, extracted with ether, washed, and dried. The extract yielded a dark oil which was chromatographed over silica gel. C_6H_6: ether (9:1) eluted **21** (378 mg, 50%) as a colourless oil; *m/e* 254 (M^+) and 236 (M^+–H_2O); IR (film) 3450 (OH), 1730 and 1710 (CO) cm^{-1}.

Alcohol **21** (378 mg) dissolved in THF (20 ml) was added dropwise to a suspension of NaH (350 mg) in THF under N_2. After warming the mixture for 10 min, MeI (4 ml) was added slowly and then heated under reflux for 6 hr. The mixture was cooled, diluted with water and extracted with ether. The dried extract was chromatographed over silica gel. C_6H_6: hexane (1:1) eluted **23** (23 mg, 6%); *m/e* 284 (M^+). Further elution with C_6H_6: hexane (8:2) yielded **22** (372 mg, 94%); *m/e* 268 (M^+); IR (film) 1735 and 1715 (C=O) cm^{-1}.

Ketoester **22** (372 mg) suspended in 20% HCl (20 ml) was heated under reflux for 8 hr in presence of amalgated mossy Zn (6 gm). After cooling, the mixture was extracted with $CHCl_3$ washed, dried and concentrated to obtain a dark oil which on distillation gave the oily **24** (246 mg, 75%), b.p. 162–166°/12 mm (bath), *m/e* 254 (M^+).

Ester **24** (240 mg) dissolved in CH_2Cl_2 (5 ml) was cooled to −35° followed by dropwise addition of BBr_3 (1 ml). The mixture was stirred for 10 min and allowed to attain room temp. Workup afforded a dark red material which was dissolved in acetone (5 ml), cooled to 0° followed by treatment with Jones reagent (2 ml). The mixture was stirred at room temp for 10 min and after the usual workup yielded a reddish oil which was chromatographed over silica gel. C_6H_6 eluted **25** (129 mg, 60%) as semi-solid material, *m/e* 238 (M^+); IR (film) 1730 (ester CO) cm^{-1}; NMR δ 0.98 (3H, s), 1.45 (3H, s) (4,4-CH_3), and 3.78 (3H, s, $COOCH_3$). (Calc. for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.21; H, 9.18%).

Lactam **2**

A soln of **25** (357 mg), *p*-TsOH,H_2O (6 mg) and ethylene glycol (3 ml) in C_6H_6 (20 ml) was refluxed under N_2 for 30 hr. The resulting dark yellow soln was washed with $NaHCO_3$ aq and with brine. Evaporation of the dried extract gave a yellow oil which when purified by silica gel preparative tlc, with 2% of ether in C_6H_6 as solvent afforded the oily **26** (380 mg, 90%), IR (film) 1730 cm^{-1}; *m/e* 282 (M^+); NMR δ 0.96 (3H, s) 1.42 (3H, s) (4,4-CH_3), 3.78 (3H, s, $COOCH_3$) and 3.92 (4H, s).

A mixture of **26** (250 mg), Me_3SiCl (314 mg) and NaI (450 mg) in dry CH_3CN (6 ml) was heated under reflux for 80 hr. The mixture was cooled, diluted with water, extracted with $CHCl_3$, washed successively with 10% $NaHSO_3$, brine and then dried. The dried extract afforded a gummy material (211 mg) which was almost free from **26** as evidenced by tlc, and this material in ether (6 ml) was treated with oxalyl chloride (1 ml) at room temp. Volatile materials were removed at 20°/6 mm. The residue was dissolved in toluene (6 ml), cooled to 0° followed by dropwise addition of a mixture of C_5H_5N (60 mg) and N_3H (40 mg) in toluene (3 ml). When the addition was complete, the mixture was stirred at room temp for 40 min and filtered. After elimination of toluene and excess N_3H, azide **27** was immediately taken in C_6H_6, IR (film) 1710 and 2130 (–CON_3) cm^{-1} and negligible absorption in the N–H, NCO or hydrazide regions.

The soln of azide **27** was irradiated using a Hanovia UV lamp 450 w at room temp in a 1-cm quartz cell with a capacity of 250 ml. The reaction was complete within 5 hr. The resulting dark soln was concentrated, treated with *p*-TsOH,H_2O (800 mg), heated for 10 hr and worked up to obtain a dark residue which was chromatographed twice over Florosil. $CHCl_3$ eluted **2** (15 mg, 7.8% based from the starting ketal **26**), m.p. 157–159° (CH_2Cl_2–hexane) which mixed with an authentic specimen[29] (m.p. 158.5–160.5°) did not exhibit any depression in m.p., IR (KBr) 3405, 1710, 1655 cm^{-1} and was indistinguishable from the IR spectra of authentic specimen.

Lactam **3**

To lactam **2** (22 mg) dissolved in dry dioxane (15 ml) was added LAH (76 mg) and heated under reflux for 26 hr. Water was added, the ppt was filtered out and the filtrate was dried. Removal of solvent afforded a mobile oily compound which dissolved in CH_2Cl_2 (4 ml) was added to pyridinium chlorochromate (32 mg) in CH_2Cl_2 (2 ml). The usual workup afforded a dark red oily carbonyl compound, IR (film) 1708 and 3365 cm^{-1}, which was dissolved in C_5H_5N (4 ml) followed by treatment of mesityl chloride (0.8 ml). Work up followed by filtering the residue over florosil (eluent $CHCl_3$) afforded **3** (15 mg; 55% based from the starting lactam), m.p. 181–183° (CH_2Cl_2–hexane) and its m.p. with authentic specimen[29] (m.p. 183.5–184.5°) remained unaltered, IR (KBr) 1705, 1318 and 1152 cm^{-1}, indistinguishable from the IR spectra of authentic specimen. (Calc. for $C_{14}H_{23}NO_3S$: C, 58.95; H, 8.07. Found: C, 58.76; H, 7.94%).

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REFERENCES

[1]Part II, A. K. Banerjee, *Tetrahedron* **35**, 1247 (1979).
[2]R. H. F. Manaske, *The Alkaloids* XII, p. 1. Academic Press, New York (1970).
[3]U. R. Ghatak and S. Chakrabarty, *J. Org. Chem.* **41**, 1089 (1976) and related Refs. cited.
[4]R. F. C. Brown, *Aust. J. Chem.* **17**, 47 (1964).
[5]A. S. Sarma, A. K. Banerjee and P. C. Dutta, *J. Chem. Soc.* Perkin 722 (1976).
[6]P. N. Chakravarty, A. K. Banerjee, P. R. Dutta, A. S. Sarma and P. C. Dutta, *Ind. J. Chem.* **12**, 948 (1974).
[7]Taken in part from M.Sc. Thesis of P. C. Caraballo, I.V.I.C., Caracas 1976.
[8]Preliminary communication, A. K. Banerjee, P. C. Caraballo, H. E. Hurtado and M. C. Carrasco, *Heterocycles* **3**, 315 (1980).
[9]J. A. Marshall and A. R. Hochstetler, *J. Am. Chem. Soc.* **91**, 648 (1969).
[10]H. C. Brown, K. J. Murray, L. J. Murray, J. A. Snover and G. Zweifel, *Ibid.* **82**, 4233 (1960).
[11]N. S. Bhaca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, p. 79. Holden-Day, San Francisco (1969).

[12]G. Gardillo, M. Orena and S. Sandri, *Synthesis* 394 (1976).
[13]B. Gaspert, T. G. Halsall and D. Wills, *J. Chem. Soc.* 624 (1958).
[14]H. C. Brown and K. J. Murray, *J. Org. Chem.* **26**, 631 (1961).
[15]A. K. Banerjee and M. S. Rizo, Unpublished observation.
[16]R. F. Church, R. E. Ireland and J. A. Marshall, *J. Org. Chem.* **31**, 2526 (1966).
[17]A. K. Banerjee, C. D. Ceballo, M. N. Vallejo and E. H. Bolívar, *Bull. Chem. Soc. Japan* **52**, 608 (1979).
[18]J. E. Shaw, D. C. Kunerth and J. J. Sherry, *Tetrahedron Letters* 689 (1973).
[19]Esterification of **13** with trimethyloxonium tetrafluoborate[8] afforded excellent yield of **14** but owing to the complicated experimental procedure was found inconvenient for repeated experiment.
[20]G. Aranda and M. Fetizon, *Synthesis* 330 (1975).
[21]W. L. Meyer and A. S. Levinson, *J. Org. Chem.* **28**, 2184 (1964).
[22]H. O. House, L. J. Czuba, M. Gall and H. D. Olmstead, *Ibid.* **34**, 2324 (1969).
[23]G. M. Rubottom, M. A. Vazquez and D. R. Pelegrina, *Tetrahedron Letters* 4319 (1974).
[24]L. Fieser and M. Fieser, *Reagents for Organic Synthesis* Vol. 1, p. 66. Wiley, New York (1967).
[25]A. Bowers, T. C. Halsall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.* 2548 (1953).
[26]G. A. Olah, S. C. Narang, B. G. B. Gupta and R. Malhotra, *J. Org. Chem.* **44**, 1247 (1979).
[27]J. W. Van Reijendam and F. Baardman, *Synthesis* 413 (1973).
[28]J. W. ApSimon and O. E. Edwards, *Can. J. Chem.* **40**, 896 (1962).
[29]W. L. Meyer, T. E. Goodwin, R. J. Hoff and C. W. Sigel, *J. Org. Chem.* **42**, 2761 (1977).
[30]E. J. Corey and J. W. Suggs, *Tetrahedron Letters* 2647 (1975).