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STUDIES IN PHEROMONE CHEMISTRY

ANALOGS OF A HETEROCYCLIC INSECT SEX PHEROMONE

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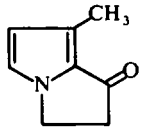
Abstract—A group of structural analogs of the male butterfly pheromone I has been prepared for biological testing. Some conformational and stereochemical features of these compounds are discussed.

INTRODUCTION

MALE butterflies of the species *Lycorea ceres ceres* and *Danaus gilippus berenice* possess extrusible organs, called hairpencils, which secrete the pyrrolizidinone I along with other compounds.[1,2] Behavioral studies have shown that I plays an essential role in the courtship of the latter species.[3] Independently, electroantennograms have indicated that this compound is the active pheromone in hairpencil secretion.[4,5]



I

The characterization of this unusual heterocyclic pheromone provides a good opportunity to examine the relationship between chemical constitution and biological activity. It has been suggested in connection with a recent study of ant alarm pheromones that biological activity is chiefly a function of molecular shape.[6] In the case of a moth sex pheromone, a very high degree of stereochemical specificity has been demonstrated; competitive inhibition was found between geometrical isomers.[7] Since so little is known about the chemical nature of receptor sites, no detailed explanation of these findings can be expected at present.[8] In order to extend our knowledge of the structural specificity of pheromone activity, we have prepared a number of analogs (compounds II–VI and X) of the natural heterocyclic ketone I, which will be subjected to biological testing. The first two of these are chemically very similar to I, but represent *seco* analogs in which the pyrrolidinone ring is opened, providing greater conformational mobility. The three saturated bicyclic analogs represent a considerable change in functionality, since the relatively non-basic pyrrole ring is replaced by the basic pyrrolidine moiety. However, in these, the molecular shape is closer to that of the pheromone (I), and is also better defined.

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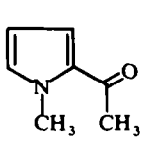

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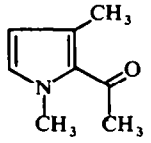

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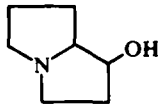

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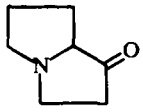

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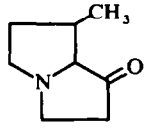


VI

The known compound X is simply a *des*-methyl analog of I. Many other variants of I can be imagined, but we hope to be guided in our further work by the biological results obtained from this first set of analogs.

DISCUSSION

1-Methylpyrrole, prepared by alkylation of the potassium salt of pyrrole[9] with methyl iodide,[10] was converted into II by acetylation using acetic anhydride and boron trifluoride etherate.[11] This product, which proved to be unstable in air, is a colorless liquid showing the expected spectral properties.

2-Acetyl-1, 3-dimethylpyrrole (III), a similarly unstable liquid with a characteristic pleasant odor, was conveniently synthesized as outlined in Chart 1.

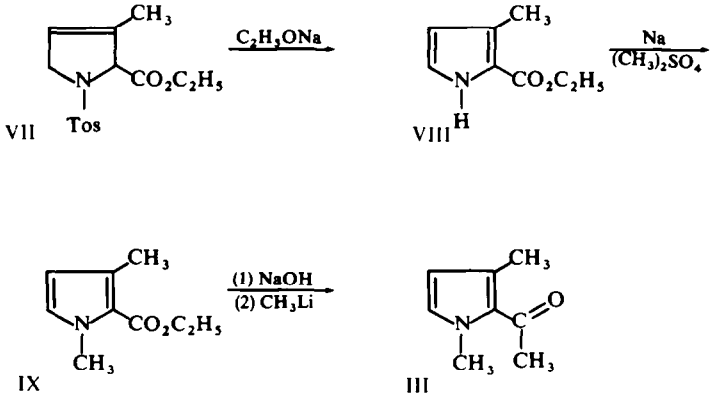
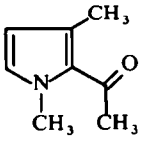


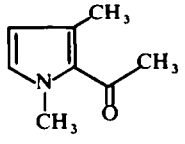
CHART 1

2-Ethoxycarbonyl-3-methylpyrrole (VIII) was prepared in 50% overall yield from N-tosylglycine ethyl ester and methyl vinyl ketone *via* the dihydropyrrole VII as described previously.[12] Methylation of VIII using sodium and dimethylsulfate gave IX,[13] which was hydrolyzed to the corresponding acid, characterized by elemental analysis and the usual spectral data. Methyl lithium converted the acid into the desired methyl ketone (III) in 60% yield.

Since the theory of Amoore *et al.*[6] places special weight on the shape of molecules which interact with chemoreceptors, we gave some attention to the conformational situation which obtains in the case of III. From a resonance point of view, either of two planar conformations might be the most stable: an *s–cis* (III A) or an *s–trans* (III B). On the other hand, both of these planar forms can be seen to suffer serious non-bonded interactions, which would tend to force the acetyl group to rotate out of the plane of the aromatic ring. We have attempted to determine the preferred conformation of III both experimentally and theoretically, in order to ascertain how closely this model compound resembles the actual pheromone.*



IIIA



IIIB

In an attempt to apply the nuclear Overhauser effect[14] to this problem we had first to assign the three Me group absorptions (τ 6.13, 7·58 and 7·62) in the NMR spectrum of III. Base-catalyzed deuterium exchange of the acetyl protons caused the disappearance of the τ 7·58 resonance. From NMR spectral comparison with I, it was clear that the 1-Me group and the 3-Me group give rise to the singlets at τ 6·13 and 7·62 respectively. Unfortunately, irradiation of either of these Me groups failed to enhance the intensity of the Ac signal, so that no answer was provided by this technique. We were similarly unsuccessful in deriving useful information from chemical shift data, since both the N-Me and the 3-Me groups in III were shifted downfield by about 0·3 ppm compared with their positions in 1,3-dimethylpyrrole (prepared from IX by hydrolysis and decarboxylation).

An extended Hückel-theory calculation indicated that a twisted version of conformation III B, with a 40° angle between the planes of the pyrrole ring and the Ac group, should be the most stable (ΔE_{AB} = 18 kcal/Mol, barrier to rotation through plane = 23 kcal/Mol). This result is in agreement with the suggestion of Jones *et al.*,[15,16,17] who proposed that 1-alkyl-2-formylpyrroles prefer *s-trans* conformations.

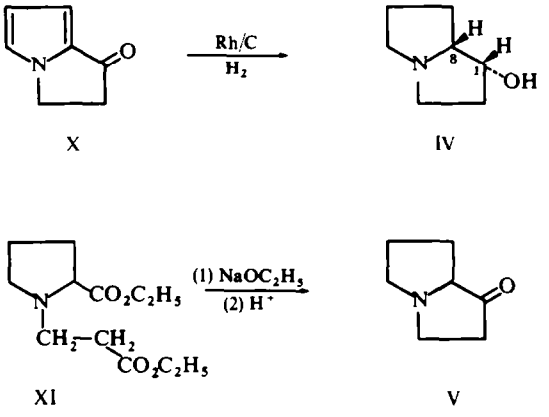
A space-filling model of III, built by combining a Kendrew-type skeletal model with Courtauld's atomic models,† also suggested a non-planar conformation, with a

* Of course, since ketone III is far from rigid, these considerations really do not indicate what conformation III might adopt when interacting with a receptor. This limitation applies even more strongly to the acyclic pheromones studied previously (Ref 6).

† For a description of this space-filling model see J. A. Rupley and T. C. Bruice, *J. Mol. Biol.* **37**, 521 (1968). If III is actually non-planar, it should be a chiral molecule. If the barrier of rotation through the plane of the pyrrole ring, $\Delta G^{\ddagger}$ were greater than 10 kcal/Mol, then the enantiomers would be sufficiently stable [*cf* H. Kessler, *Angew Chem.* **82**, 237 (1970); *Int. Ed.* **9**, 219 (1970)] to be distinguished in an appropriate chiral solvent [*cf* W. H. Pirkle and S. D. Beare, *J. Am. Chem. Soc.* **91**, 5150 (1969)]. Toward this end the NMR spectrum of III, dissolved in fluorotrichloromethane and (−)2,2,2-trifluorophenylethanol (kindly provided by Dr. W. H. Pirkle), was studied. However, neither at 25°, nor at − 60° were there any observable chemical shift differences, indicating that the barrier to rotation must be considerably lower than our EHT calculations indicate. (These calculations give ΔE values very close to $\Delta G^{\ddagger}$ values).

minimum angle of *ca* 25° between the Ac group and the ring. This value agrees well with a torsional angle of 22° obtained from UV data by application of the Braude equation.[18] Overall, it would appear from these considerations that the conformation of III is less close to that of the original pheromone than was originally anticipated; the chief differences are the interchange of the positions of the CO oxygen and the attached carbon residue, and the non-planarity of the isolated molecule.

2,3-Dihydro-1*H*-pyrrolizin-1-one* (X Chart 2) was prepared from pyrrole by N-cyanoethylation, followed by intramolecular Friedel-Crafts ring closure, as described previously.[19,20] Hydrogenation over rhodium-on-carbon, as described by Adams *et al.*[21] gave 1-hydroxypyrrolizidine (IV). (This reduction is reported to be stereospecific. Since hydrogenation generally involves *cis* donation of hydrogen from the catalyst to the substrate,[22] it is likely that IV has the OH substituent *trans* to the C_8-bridgehead H atom, as shown, rather than *cis* as previously assigned.[21])†



X IV

XI V

CHART 2

We were unable to oxidize alcohol IV to the corresponding saturated ketone V by the Oppenauer method;[21] chromium trioxide[23] and silver carbonate on Celite[24] oxidations were similarly unsuccessful. However, the desired ketone was obtained by Dieckmann cyclization of the diester XI, prepared by Michael addition of (−)-proline ethyl ester to ethyl acrylate.[25]

Finally, as outlined on Chart 3, we were able to prepare VI, the tetrahydro derivative of I, by a considerably shorter route than had been employed previously.[26] Adams and Leonard had obtained the ethyl ester of 3-methylproline (XIII) in eight steps from 4-methylpyridine.[26] Starting from the dihydropyrrole VII, hydrogenation over rhodium-on-carbon gave the homogeneous pyrrolidine ester XII; saponification yielded the corresponding *cis* acid.[27] Acid-catalyzed removal of the N-*p*-tosyl group gave the ethyl ester XIII. (The pathway represents a convenient new route to *cis*-3-methylproline.[27]) Michael addition of XIII to ethyl acrylate gave the diester XIV, which was converted into the desired bicyclic ketone (VI) *via* the Dieckmann route.

* Unpublished observations of Prof. Dietrich Schneider indicate that this compound gives a positive response in electroantennogram studies.

† A referee has pointed out that the more stable *cis* product could result. We have no additional evidence to settle this point.

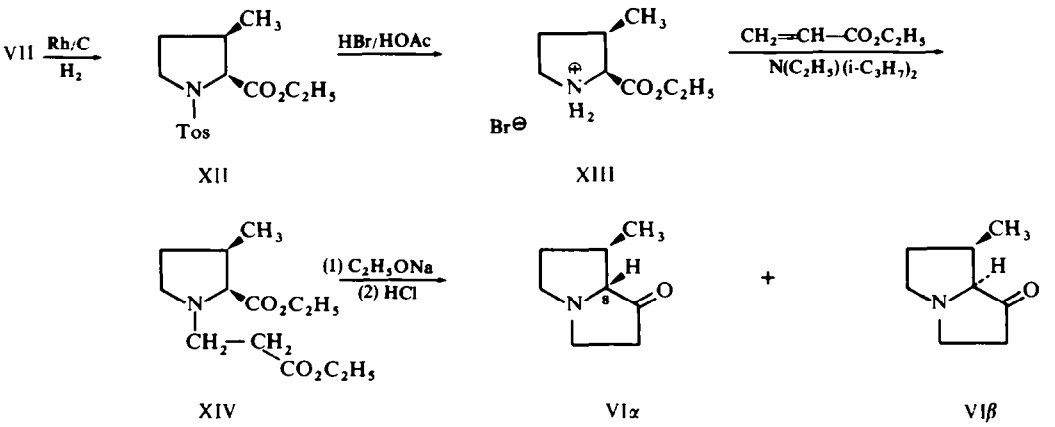


CHART 3

The properties of the final ketone (VI) agree well with those previously described.[26] GLPC analysis, however, revealed that the major component (95%) is accompanied by a minor component (5%) of longer retention time. These compounds could be separated by preparative GLPC; they had nearly identical NMR spectra and mass spectral fragmentation patterns, while their IR spectra differed only in the fingerprint region. On this basis, it appeared quite certain that these products were epimeric at C_8, and this supposition was supported by the observation that the pure, major isomer could be epimerized photochemically to a mixture containing 20% of the minor epimer. (This minor isomer is much more labile than its diastereoisomer; the free base polymerizes within a few hours, even when stored in an inert atmosphere at $-20°$.)

We do not have definitive evidence on the stereochemistry of these isomers. However, Culvenor *et al.*[28] have reported that for an analogous 1-ethoxycarbonyl compound, sodium methoxide treatment brings about total epimerization of the substituent from the less stable *endo* position to the favored *exo* position. If we assume that the C_8 bridgehead proton is similarly activated by the adjacent CO function, then the major (stable) product from this sequence should be assigned the stereochemistry shown in formula VIα (*exo*-methyl), and the minor component VIβ. In this event, it is the minor product which has the stereochemistry implied by the trivial name "retronecanone", while the major one corresponds to the stereochemistry of the alkaloids hastanecine or turneforcedine.[28, 29]

Plans are now being made for behavioral and neurophysiological studies of these compounds.

EXPERIMENTAL

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. M.ps were determined on a Hoover capillary m.p. apparatus and are corrected. TLC was carried out on Eastman 6060 chromatogram sheets (silica gel); compounds were visualized with iodine. IR spectra were recorded using a Perkin–Elmer 257 grating infrared spectrophotometer, and UV spectra were measured on a Cary Model 14. NMR spectra were taken with a Varian A-60A instrument in $CDCl_3$ using TMS as internal reference. The decoupling measurements were performed with a Varian HA-100 instrument. Mass spectra were

recorded with an A.E.I. MS-902 mass spectrometer at an ionizing voltage of 70 eV.* For coupled GLPC mass spectrometry, a Perkin–Elmer 270 instrument was used. The columns for GLPC were as follows: Column A, 5% carbowax 20M on chromosorb W 60–80 mesh (10 ft × $\frac{1}{8}$ in); Column B, 5% carbowax 20M on chromosorb W 60–80 mesh (8 ft × $\frac{3}{8}$ in); Column C, 10% SE-30 on chromosorb W 60–80 mesh (6 ft × $\frac{1}{8}$ in). Column D, 15% carbowax 20M on chromosorb W 60–80 mesh (20 ft × $\frac{3}{8}$ in); Column E, 1% SE-30 on chromosorb W 60–80 mesh (10 ft × $\frac{1}{8}$ in).

1-*Methyl*-2-*acetylpyrrole* (II). The procedure of Anderson was used.[11] To a previously chilled mixture of 8·0 g (0·10 mole) 1-methylpyrrole[9,10] and 12·0 g (0·10 mole) Ac_2O, 1·0 ml of BF_3 ethyl ether was added. The mixture was warmed to 80° and allowed to cool for 1 hr; it was then poured into 300 ml ice-water. After 1 h, the soln was steam-distilled. The distillate was then neutralized with Na_2CO_3 and saturated with salt before being extracted with ether. The combined ether layers were dried (Na_2SO_4), filtered, and the solvent removed. The residue was distilled to give 3·5 g (28%) of colorless liquid (b.p. 77–80° at 13 mm), which darkened in the air. The compound was stored at − 20° under argon.

On GLPC (column A at 220°) only one peak appeared with t_r 5·3 min; IR (CCl_4): 2810 (N-CH_3), 1655 cm^{-1} (C=O); UV: λ_{max}^{EtOH} 286 nm ($\varepsilon = 1{\cdot}46 \times 10^4$); NMR: τ 3·05 (q, 1, C_5—H), 3·30 (t, 1, C_3—H), 3·85 (q, 1, C_4—H), 6·12 (s, 3, N—CH_3), 7·63 (s, 3, $COCH_3$); mass spectrum principal peaks at *m/e* 123 (M^+), 108 (base peak, M—CH_3), 94 (M—C_2H_5), 80 (M—$COCH_3$), 53, 43, 38.

Ethyl N-p-*tosyl*-3-*methylpyrroline*-2-*carboxylate* (VII). This compound was prepared according to Terry *et al.*,[12] and showed on TLC (n-heptane-ethanol: 3–1) only one spot (R_f 0·62). The IR spectrum (CCl_4) showed characteristic absorptions at 1750, 1735 (C=O), and 1170 cm^{-1} (− SO_2N). Other properties agreed well with the literature report.

Ethyl 3-*methylpyrrole*-2-*carboxylate* (VIII). This compound was prepared from VII as reported.[12] On TLC (n-heptane-EtOH: 3–1) only one spot was visible; IR (CCl_4): 3475, 3460, 3300 (N—H), 1715, 1960 cm^{-1} (C=O); NMR τ 3·25 (t, 1, C_5—H), 3·95 (t, 1, C_4—H), 5·68 (q, 2, −$\underline{CH}_2$—CH_3), 7·67 (s, 3, C_3—CH_3), 8·68 (t, 3, —CH_2—$\underline{CH}_3$); mass spectrum: in agreement with reported spectrum.[30]

2-*Ethoxycarbonyl*-1,3-*dimethylpyrrole* (IX). To a soln of 5·48 g (35 mmoles) of VIII in 90 ml of dry toluene stirred under N_2 was added 1·24 g (54 mmoles) of small Na pieces. This mixture was refluxed for 4 hr, during which the Na salt of the pyrrole separated as a white curdy ppt. Then 5·2 ml (6·9 g, 55 mmol) of freshly distilled Me_2SO_4 was added dropwise; stirring and heating was continued for another hr. The $NaMeSO_4$ was filtered off and washed with toluene. The solvent was removed from the filtrate to give a dark brown oil. This was chromatographed on neutral alumina (Woelm activity 1) with hexane to give 3·74 g (65%) of IX as a colorless oil, which was stored at − 20° under argon. IR (CCl_4): 2810 (N-CH_3), and 1695 cm^{-1} (C=O); NMR τ 3·43 (d, 1, C_5—H), 4·10 (d, 1, C_4—H), 5·75 (q, 2, −$\underline{CH}_2$− CH_3), 6·18 (s, 3, N—CH_3), 7·69 (s, 3, C_3—CH_3), 8·67 (t, 3, —$CH_2\underline{CH}_3$); TLC (n-heptane-alcohol: 3–1) one spot (R_f 0·85).

1,3-*Dimethylpyrrole*-2-*carboxylic acid*. A soln of 3·44 g (20·6 mmoles) of IX and 5·6 g (100 mmoles) of KOH in a mixture of 30 ml MeOH and 10 ml water was refluxed for $\frac{1}{4}$ hr under an argon atmosphere. The yellow soln was allowed to cool and the solvent partly removed. The mixture was diluted with 50 ml water, washed twice with ether, and acidified with 6N HCl. The ppt was filtered off, washed with water and recrystallized from EtOH, yielding 2·3 g (81%) white crystals, m.p. 159–160°; IR (CCl_4): 1710, 1695 and 1655 cm^{-1} (C=O); NMR: τ 2·11 (s, 1, COOH), 3·29 (d, 1, C_5—H), 4·02 (d, 1, C_4—H), 6·11 (s, 3, N—CH_3), 7·61 (s, 3, C_3—CH_3). (Found: C, 60·36; H, 6·58; N, 9·96. Calcd for $C_7H_9NO_2$: C, 60·42; H, 6·52; N, 10·07%).

1,3-*Dimethyl*-2-*acetylpyrrole* (III). To a soln of 0·60 g (4·3 mmoles) of the above acid in 50 ml dry ethyl ether stirred under an argon atmosphere was added 5·2 ml (8·6 mmoles) MeLi soln (5·2%); the first half was added dropwise, the rest quickly. The reaction mixture was refluxed for 2 hr and 25 ml water was then added to the clear yellow soln dropwise. The organic layer was washed with water until neutral, dried (Na_2SO_4), filtered, and the ether removed, yielding 512 mg (87%) crude III as a yellow oil. This was purified by preparative GLPC (column B at 160°, carrier flow rate: 120 ml/min). One major component was eluted with t_r 7 min. The compound, which was a colorless oil with a very characteristic aromatic odor, decomposes quickly in the air. It crystallized when stored at − 20° under argon; its m.p. is below 0°.

IR (CCl_4) 1645 cm^{-1} (C=O); UV: λ_{max}^{EtOH} 288 nm ($\varepsilon = 1{\cdot}76 \times 10^4$); NMR: τ 3·40 (d, 1, C_5—H), 4·09 (d, 1, C_4—H), 6·17 (s, 3, N—CH_3), 7·62 (s, 3, —$COCH_3$), 7·66 (s, 3, C_3—CH_3); mass spectrum, principal peaks at *m/e* 137 (M^+), 122 (M—CH_3, acetyl; base peak), 94 (M—$COCH_3$), 67, 53, 43, 42, 41. (Found: C, 70·18; H, 8·20; N, 10·03. Calcd for $C_8H_{11}NO$: C, 70·04; H, 8·08; N, 10·21%).

* Mass spectra were determined by the Cornell High Resolution Mass Spectrometer Facility, supported by Grant BR-00355 from the National Institutes of Health.

Deuterium exchange. A soln was prepared containing 23 mg of III in 1 ml of CH_3OD; deuterated water was added until III just stayed in soln. To this clear soln. 23 mg Na_2CO_3 was added. The mixture was refluxed for 16 hr under an argon atmosphere. After removal of the solvent, the yellow oily remainder was dissolved in 1·0 ml $CDCl_3$, filtered, and used directly for NMR examination. The NMR spectrum showed only two singlets, besides the two aromatic protons: τ 6·17 (s, 3, N—CH_3), 7·66 (s, 3, C_3—CH_3); mass spectrum: principal peaks at *m/e* 140 (M^+), 122 (M—CD_3, base peak), 94 (M—$COCD_3$), 67, 53, 43, 42.

2,3-*Dihydro*-1H-*pyrrolizin*-1-*one* (X). This compound was prepared as described previously.[19,20] The crude product could conveniently be purified by vacuum sublimation (70° at 0·07 mm); IR (CCl_4): 1705 cm^{-1} (C=O). Other properties agreed well with literature reports.[1b,20]

1-*Hydroxypyrrolizidine* (IV). The procedure of Adams *et al.*[21] was used. A soln of 18·0 g (0·149 mole) X in 150 ml AcOH was reduced over 3·0 g of 5% rhodium-on-carbon catalyst at room temp and 50 psi. Absorption of H_2 (93% of the theoretical amount) was completed in 2·5 hr. The catalyst was removed by filtration and the solvent removed. To the residue, 200 ml saturated NaCl aq and 50 ml 20% NaOH aq were added. The mixture was extracted with ether, dried (Na_2SO_4), filtered, and the solvent removed. The remaining oil was distilled to give 15·9 g (78%) colorless oil, b.p. 94–95° at 1·6 mm. A picrate was formed in EtOH, m.p. 240–241° (dec.) lit.[21] m.p. 244–245; IR (CCl_4): 3360, 3100 cm^{-1} (—OH); NMR τ 3·54 (s, 1, —OH), 5·90 (q, 1, C<u>H</u>OH), 6·5–8·2 (mult, 11H); mass spectrum: principal peaks at *m/e* 127 (M^+), 108, 83 (M—C_2H_3OH, base peak), 70, 55, 42, 41.

Pyrrolizidin-1-*one* (V). This compound was prepared as described previously,[22] except that the hydrochloride of the proline ester was used (see preparation of XIV). The product is very unstable in the air, but can be stored under argon at − 20° for several months.

IR (CCl_4): 1750 cm^{-1} (C=O); NMR: very similar to the complex spectrum of IV, except for the disappearance of the signals at τ 3·54 and 5·90; mass spectrum: principal peaks at *m/e* 125 (M^+), 97 (M—CO, base peak), 96, 82, (M—$COCH_3$) 69, 68, 41, 40. Other properties are in good agreement with literature reports.[21,25]

N-p-*Tosyl*-cis-3-*methylproline ethyl ester* (XII). A soln of 49·5 g (0·16 mole) VII in 500 ml AcOH was reduced over 3·0 g of 5% rhodium-on-carbon catalyst at room temp and 50 psi. Absorption of the theoretical amount of H_2 was completed within 2 hr. The catalyst was removed by filtration (filter paper covered with Celite) and the solvent removed. After 100 ml added EtOH had been removed, the crystalline residue was dried in vacuum over KOH and finally recrystallized from EtOH-water to yield 40·0 g (89%) of XII, m.p. 99–101°. TLC (n-heptane-EtOH: 3–1) showed one spot with R_f 0·65; IR (CCl_4): 1740 (C=O), 1170 cm^{-1} (—SO_2N); NMR: similar to spectrum of VII, except for a shift of C_3—CH_3 from τ 8·35 (s) to 9·10 (d). On GLPC (column E at 200°) only one peak appeared, t_r 5·5 min.[27]

A sample of XII (300 mg, 1 mmole) was saponified with 5 ml AcOH-conc HCl (1:1) by refluxing for 1 hr. The solvent was removed, the residue dissolved in 2 ml of 100% NaOH aq and acidified with 6N HCl. The resultant acid was extracted with EtOAc, dried (Na_2SO_4), filtered, and the solvent removed. The crystalline residue could be recrystallized from EtOAc, to give the free acid, m.p. 178–180 (softening at 170); lit. m.p. of *cis*-isomer: 183–185°, *trans*-isomer: 113–115°.[27]

3-*Methylproline ethyl ester hydrobromide* (XIII). A soln of 18·0 g (58 mmoles) XII in 120 ml HBr in glacial AcOH (15%) was stirred for 40 hr at room temp. After removal of the solvent, dry ether was added and distilled off. The latter was repeated until XIII did not dissolve. The dark brown residue was then treated with ether until the solvent was only slightly yellow, and the residue was finally dried in vacuum over KOH. The product thus obtained could be used for the next step without further purification. TLC (n-butanol-AcOH-water 4:1:1); one spot, ninhydrin positive, r_f 0·63; IR (CCl_4): 3200–2500 (—N^+H_2), 1735 cm^{-1} (C=O).

Ethyl β-N-(3-*methyl*-2-*carbethoxypyrrolidyl*)-*propionate* (XIV). It is advisable to use the salt of the amino acid ester as starting material, and not the amine,[25,26] because the danger of diketopiperazine formation with proline esters is especially great. A soln of 13·8 g (58 mmoles) of XIII, 26 ml (150 mmoles) of N,N-diisopropylethylamine (Hünig base) and 32·5 ml (30·0 g, 300 mmoles) ethyl acrylate containing a trace of hydroquinone in 50 ml EtOH was refluxed for 17 hr under an argon atmosphere. The mixture was cooled, the solvent removed and 80 ml of ice-cold 30% NaOH aq was added. The soln was extracted rapidly twice with cold ether; the combined ether layers were dried (Na_2SO_4), filtered and the ether evaporated. The dark brown residue was distilled to give 7·5 g (50% from XII) of a colorless oil, b.p. 113–120°/1·4 mm (lit.[26] 126–127° at 4 mm). Lower boiling fractions showed strong absorptions in IR due to —NH, and were therefore discarded. TLC (n-BuOH–AcOH–water 4:1:1); one spot, ninhydrin negative, R_f 0·60. IR (CCl_4): 1730 cm^{-1} (broad, C=O).

1-*Methyl-7-ketopyrrolizidine* (VI). The Dieckmann condensation was performed as described previously for the homolog V.[25] Instead of refluxing, the azeotropic mixture of toluene and alcohol was slowly distilled off; whenever necessary new toluene was added to the mixture.

After distillation (b.p. 46–47°/0·8 mm, lit.[26] 79–80° at 8 mm), a colorless liquid which darkened rapidly on the air was collected in an acetone–Dry Ice cooled trap (yield 55%). It could be stored without decomposition at −20° under argon. A picrate, m.p. 189–190° (dec), was formed in ether. IR (CCl_4: 1745 cm^{-1} (C=O); NMR: τ 8·85 (d, 3, C_1—CH_3), 6·5–8·2 (mult, 10 H); mass spectrum: principal peaks at *m/e* 139 (M^+), 111 (M—CO), 96 (M—$COCH_3$), 83 (M—COC_2H_4), 57 (base peak), 41. On GLPC (column C at 125°) one major (T_r 4·0 min, 95%) and one minor peak (T_r 4·5 min, 5%) appeared. Both peaks showed the same fragmentation pattern in their mass spectra after separation by GLPC (column C, 120°, direct inlet into mass spectrometer).

Photochemical epimerization of VI. A 250 mg sample of VI was fractionated by preparative GLPC (column D at 175°). The two components were collected with T_r 28 min (144 mg) and 31 min (10 mg), respectively. A 90 mg sample of the major compound (VIα) was irradiated in 180 ml of ethyl ether with a 450W Hanovia lamp through Pyrex. One milliliter samples were taken after 1, 2, 6, and 10 hr, respectively. Analyses by GLPC (column C at 125°, injected 10 μl each time) showed only one peak (T_r 4·0 min) after 2 hr, whereas after 6 hr, a minor component (T_r 4·5 min) was eluted also. Finally after 10 hr irradiation the two compounds were observed in a ratio of 4:1; longer irradiation caused extensive formation of polymer.

The NMR spectrum of the minor component (VIβ, 10 mg, from preparative GLPC) was identical with the spectrum of the starting material; the IR spectrum showed only minor differences in the fingerprint region. Component VIβ seemed to decompose in ether solution. The GLPC of the supernatant (column C at 125°) showed that the major peak now had a retention time identical to that of component VIα, and gave only one major peak of the same retention time upon admixture with this starting material.

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