

## Total Synthesis of *N*<sub>a</sub>-Methylsecodine

Atta-ur-Rahman,\* Mumtaz Sultana, Ilfat Hassan, and (in part) Naeem M. Hasan  
H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-32, Pakistan

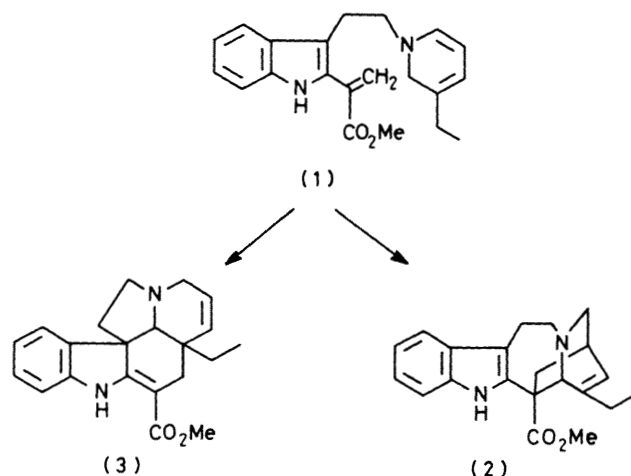
A short synthetic route to *N*<sub>a</sub>-methylsecodine is described involving a Friedel–Crafts acylation at the indole 2-position followed by a Wittig reaction to generate the acrylate moiety.

Dehydrosecodine (1) has been postulated as a key biosynthetic intermediate<sup>1,2</sup> which can undergo intramolecular Diels–Alder reactions in two different ways to afford either the *Iboga* alkaloid catharanthine (2) or the *Aspidosperma* alkaloid tabersonine (3) (Scheme 1). All attempts towards the synthesis of dehydrosecodine have met with failure, although *N*-benzyldehydrosecodine has recently been synthesized and was found to afford *N*-benzyl derivatives of catharanthine, carbomethoxycleavamine,<sup>†</sup> and  $\psi$ -vincadifformine.<sup>3</sup> Secodine has also been synthesized,<sup>4–6</sup> although by rather lengthy routes, and a number of approaches to indole alkaloids including the intermediacy of secodine have been studied.<sup>7,8</sup> We report here a short and high-yield synthesis of *N*-methylsecodine based on a ready Friedel–Crafts acylation at the indole 2-position which is followed by a Wittig reaction. 3-(2-Bromoethyl)-*N*-methylindole (7), the starting synthon for further elaboration, was prepared in good yield by methylation of indole-3-acetic acid to give the acid (4) [NaH, MeI, tetrahydrofuran (THF), 24 h, 30 °C], esterification to the methyl ester (5) (MeOH, H<sub>2</sub>SO<sub>4</sub>, 24 h), reduction to the alcohol (6) [lithium aluminium hydride (LAH), diethyl ether, 1 h; 30 °C], and bromination (PBr<sub>3</sub>, reflux in benzene, 2 h).

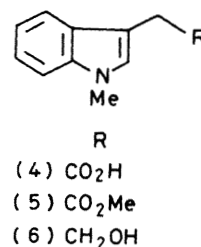
Model reactions were first explored in order to gain some insight into the experimental parameters for the synthesis of *N*-methylsecodine (15). Thus the de-ethyl analogue (10) of *N*-methylsecodine was prepared from 1,2,3,6 tetrahydropyridine (Scheme 2). Friedel–Crafts acylation of compound (7) was carried out using methoxalyl chloride and AlCl<sub>3</sub>. The reaction mixture, when kept overnight, afforded the ester (8). A characteristic feature of the compound was its u.v. spectrum which was typical of 2-acylindoles showing maxima at 212, 240, and 320 nm and minima at 275 and 230 nm. The <sup>1</sup>H n.m.r. spectrum showed two sharp singlets at  $\delta$  4.0 and  $\delta$  4.05 for the *N*-methyl and *O*-methyl protons, respectively.

Alkylation of the bromide (8) with 1,2,3,6 tetrahydropyridine afforded the diamine (9) in 45% yield. The u.v. spectrum of the product was characteristic of 2-acylindoles while the i.r. spectrum showed an absorption at 1 600 cm<sup>-1</sup> for the olefinic function. The mass spectrum showed the molecular ion at *m/z* 326.1620, consistent with that calculated for C<sub>19</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub> (326.1630). A multiplet at  $\delta$  5.77, integrating for two protons, was assigned to the olefinic protons.

The crucial step in this sequence was the Wittig reaction. Surprisingly, butyl-lithium, when used for the generation of the Wittig reagent, did not give the desired acrylate but afforded a product showing addition of 42 mass units.<sup>‡</sup> After a number of explorative experiments methyl-lithium was found to be the reagent of choice, and when added to a suspension of methyltriphenylphosphonium bromide and



Scheme 1.



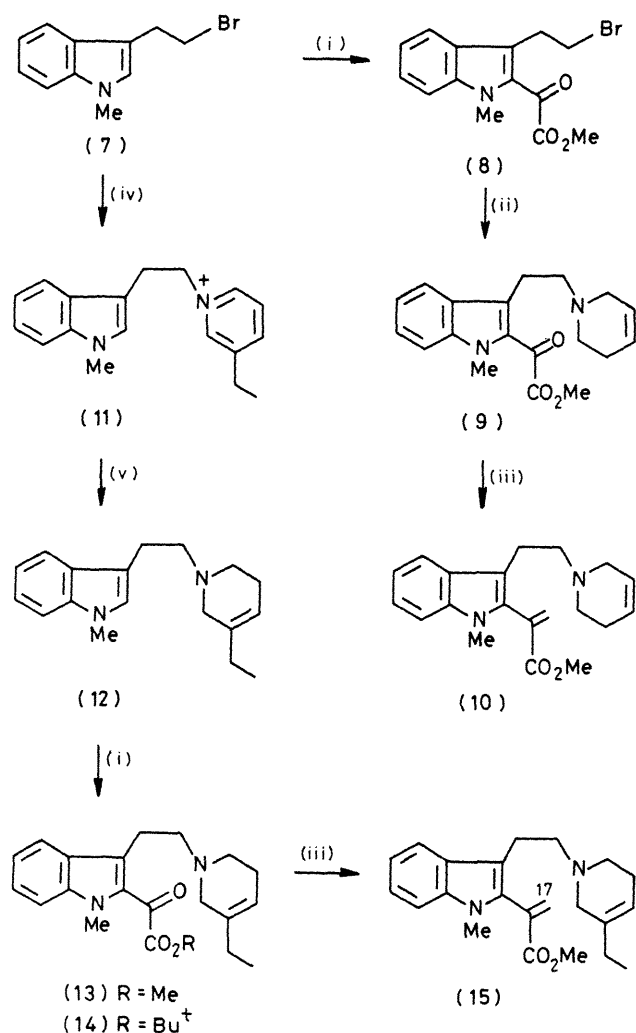
stirred for one hour, the Wittig reagent was formed. Subsequent addition of the  $\alpha$ -keto ester (9) afforded the acrylate (10) in 40% yield. Having the required methodology in hand for the model system we directed our efforts to applying it to the synthesis of *N*-methylsecodine (15).

3-(2-Bromoethyl)-*N*-methylindole (7) and 3-ethylpyridine when heated in a sealed tube at 120 °C afforded the corresponding quaternary salt (11), subsequent reduction of which with sodium borohydride in the presence of triethylamine afforded the tetrahydropyridine (12). Friedel–Crafts acylation of compound (12) with methoxalyl chloride was accomplished in an identical manner to that employed in the model reaction. The product (13) afforded a u.v. spectrum characteristic of 2-acylindoles. The i.r. spectrum exhibited carbonyl absorptions at 1 740 cm<sup>-1</sup> and 1 640 cm<sup>-1</sup> assigned to the ester carbonyl and keto function, respectively. The mass spectrum afforded the parent ion at *m/z* 354.3945, consistent with the molecular formula C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>. The n.m.r. spectrum showed two sharp singlets at  $\delta$  4.00 and  $\delta$  4.05 for the *N*-methyl and *O*-methyl protons, respectively.

The  $\alpha$ -methylene function was introduced by employing the Wittig reaction using methyltriphenylphosphonium bromide. Reaction with the pyruvate (13) at low temperature (–20 °C) for 72 h afforded the acrylate (15) in 45% yield.

<sup>†</sup> Methoxycarbonylclevamine.

<sup>‡</sup> A study of the spectral data for the compound indicated that it was the butyl ester (14) formed by reaction with butoxide present as an impurity in butyl-lithium.



**Scheme 2.** Reagents and conditions: (i)  $\text{ClC(=O)CO}_2\text{Me}$ ,  $\text{AlCl}_3$ ,  $\text{CH}_2\text{Cl}_2$ , 30 °C, 24 h; (ii) 1,2,3,6-tetrahydropyridine, ethyl acetate, reflux, 10 h; (iii)  $\text{CH}_3\text{P}(\text{C}_6\text{H}_5)_3\text{Br}^-$ ,  $\text{CH}_3\text{Li}$ , diethyl ether, -20 °C, 72 h; (iv) 3-ethylpyridine, ethyl acetate, 120 °C, 72 h; (v)  $\text{NaBH}_4$ ,  $\text{Et}_3\text{N}$ , MeOH, 0 °C, 1 h

The u.v. spectrum of compound (15) was characteristic of the 2-indol-2-yl)acrylic ester system, showing maxima at 220, 259, 275, and 295 nm and minima at 250, 260, and 280 nm. The mass spectrum showed the parent ion at  $m/z$  352.2153, in agreement with the molecular formula  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_2$  (352.2150). The formation of the product (15) was further confirmed by its characteristic n.m.r. spectrum which showed two doublets at  $\delta$  5.59 ( $J$  1.7 Hz) and 6.99 ( $J$  1.7 Hz) for the  $\text{C}=\text{CH}_2$   $\text{H}_a$  and  $\text{H}_b$  protons, respectively.

The synthesis of *N*-methylsecodine described here is the shortest route reported so far to the secodine system, and it is likely to facilitate experiments on the generation of dehydrosecodine derivatives for subsequent biomimetic transformations to the *Aspidosperma* and *Iboga* alkaloidal systems.

## Experimental

Mass spectra were recorded on Varian MAT 112-S mass spectrometer coupled to a Spectroscopy 188 computer. High-resolution mass spectra were recorded on a Varian MAT 312 mass spectrometer. I.r. spectra were recorded on Pye-Unicam SP-200G or Jasco-IRA-I i.r. spectrophotometers.

U.v. spectra were recorded on a Pye-Unicam SP-800A spectrophotometer or a Shimadzu U.V. 240 instrument. N.m.r. spectra were recorded on Jeol JNM-PMX 60 and Bruker-FT-WP100SY instruments using tetramethylsilane as internal standard. Light petroleum refers to that fraction boiling in the range 40–60 °C.

***N*-Methylindole-3-acetic Acid (4).**—Sodium hydride (5.0 g, 0.20 mol) was taken up in dry THF (250 ml), indole-3-acetic acid (5.0 g, 0.028 mol), was added in small portions to the resulting suspension of sodium hydride, and the mixture was stirred for 15 min. Methyl iodide (5.0 ml, 0.09 mol) was added dropwise to the reaction mixture which was then kept overnight at 25 °C. Excess of sodium hydride was carefully destroyed with water. The aqueous layer was acidified and extracted exhaustively with ethyl acetate and the extracts were dried over anhydrous sodium sulphate and evaporated to give the acid (4) a reddish brown gum (4.0 g, 75%),  $\lambda_{\text{max}}$  (MeOH) 225 and 285,  $\lambda_{\text{min}}$  (250 nm);  $\delta(\text{CDCl}_3)$  3.77 (3 H, s,  $\text{NCH}_3$ ) and 7.04 (4 H, m, ArH) (Found:  $M^+$ , 189.0789. Calc. for  $\text{C}_{11}\text{H}_{11}\text{NO}_2$ :  $M$ , 189.0779;  $m/z$  144, 71, and 57).

**Methyl *N*-Methylindole-3-acetate (5).**—*N*-Methylindole-3-acetic acid (4) (4.0 g, 0.021 mol) was dissolved in anhydrous methanol (200 ml) and sulphuric acid (2.0 ml) was added. The solution was stirred for 24 h at 25 °C and was then evaporated to give a brownish gum. The gum was dissolved in ethyl acetate (150 ml) and washed with aqueous sodium carbonate solution ( $2 \times 50$  ml). The ethyl acetate layer was dried with sodium sulphate and evaporated under reduced pressure to give a dark brown gum. Column chromatography of the gum on silica gel gave the pure ester (5) (3.98 g, 94%),  $\lambda_{\text{max}}$  (MeOH) 225 and 285,  $\lambda_{\text{min}}$  250 nm;  $\nu_{\text{max}}$  1720  $\text{cm}^{-1}$  (Found:  $M^+$ , 203.0911. Calc. for  $\text{C}_{12}\text{H}_{13}\text{NO}_2$ :  $M$ , 203.0911);  $m/z$  158 (2%), 148 (8), 144 (100), 102 (6), 83 (16), and 71 (10);  $\delta(\text{CDCl}_3)$  3.44 (3 H, s,  $\text{NCH}_3$ ), 3.55 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), 6.82 (1 H, s, indole 2-H), and 7.10–7.24 (4 H, m, ArH).

***N*-Methylindole-3-ethanol (6).**—The ester (5) (3.98 g, 0.019 mol) was dissolved in anhydrous diethyl ether (150 ml) and fresh LAH (2.0 g) was added to the magnetically stirred solution. The mixture was stirred at room temperature (30 °C) for 1 h and excess of LAH was carefully destroyed with drops of water. The lithium and aluminium salts were filtered off, and the ethereal filtrate was washed with water. The ether layer was separated, dried with anhydrous sodium sulphate, and evaporated to afford a pale brown gum. Flash chromatography of the crude gum over a silica column afforded the pure alcohol (6) (3 g, 88%),  $\lambda_{\text{max}}$  (MeOH) 225 and 285,  $\lambda_{\text{min}}$  250 nm (Found:  $M^+$ , 175.0911. Calc. for  $\text{C}_{11}\text{H}_{13}\text{NO}$ :  $M$ , 175.0997);  $m/z$  146 (8%), 145 (10), 144 (90), 128 (2), and 115 (4);  $\delta(\text{CDCl}_3)$  3.66 (3 H, s,  $\text{NCH}_3$ ) and 6.71 (1 H, s, indole 2-H).

**3-(2-Bromoethyl)-*N*-methylindole (7).**—The alcohol (6) (3.56 g, 0.20 mol) was dissolved in anhydrous benzene (100 ml). Phosphorus tribromide (2.6 ml, 0.033 mol) was added and the magnetically stirred solution was refluxed for 2 h. T.l.c. [light petroleum–ethyl acetate–dichloromethane (8 : 1 : 1)] showed complete conversion of the alcohol into a faster moving compound. The reaction mixture was cooled, washed with 10% aqueous sodium carbonate ( $2 \times 50$  ml), and the organic layer was dried over anhydrous sodium sulphate and evaporated to give a pale yellow gum. Rapid filtration of the gum over silica gel provided the pure bromide (7) (2.89 g, 72.25%),  $\lambda_{\text{max}}$  (MeOH) 225 and 285,  $\lambda_{\text{min}}$  250 nm (Found:  $M^+$ , 237.0155. Calc. for  $\text{C}_{11}\text{H}_{12}\text{NBr}$ :  $M$ , 237.0153);  $m/z$  239 (19%), 144 (100), 71 (20), and 69 (10);



$\delta(\text{CDCl}_3)$  3.25 (2 H, t,  $J$  6.4 Hz,  $\text{CH}_2\text{CH}_2\text{Br}$ ), 3.52 (2 H, t,  $J$  6.4 Hz,  $\text{CH}_2\text{CH}_2\text{Br}$ ), and 7.15–7.28 (4 H, m, ArH).

**Methyl 3-(2-Bromoethyl)-N-methylindole-2-pyruvate (8).**— $\text{AlCl}_3$  (1 g, 6 mmol) and dichloromethane (5.0 ml) was placed in a two-necked flask equipped with a magnetic stirrer bar and a rubber septum. The flask was flushed with nitrogen and charged with a slight positive pressure. Methoxalyl chloride (1.3 g, 10 mmol) was slowly injected through the septum. The reaction mixture was stirred for 15 min. The bromide (1.0 g, 4 mmol) was added and the reaction mixture was stirred overnight. The reaction was quenched with 20% aqueous sodium carbonate (50 ml) and the organic layer was separated, dried over anhydrous sodium sulphate, and concentrated to give a yellow gum. Flash column chromatography over silica gel afforded the pure pyruvate (8) (0.5 g, 38%),  $\lambda_{\text{max}}$  (MeOH) 212, 240, and 320,  $\lambda_{\text{min}}$  275 and 230 nm;  $\nu_{\text{max}}$  1 680 and 1 740  $\text{cm}^{-1}$  [Found:  $M^+$  (100%), 323.0150. Calc. for  $\text{C}_{14}\text{H}_{14}\text{NO}_3\text{Br}$ :  $M$ , 323.0157];  $m/z$  325 (46%), 266 (80), 264 (94), 239 (10), 238 (78), 230 (22), 220 (12), 202 (22), and 185 (32);  $\delta(\text{CDCl}_3)$  4.00 (3 H, s,  $\text{NCH}_3$ ), 4.025 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), and 7.50–7.68 (4 H, m, ArH).

**Methyl N-Methyl-3-[2-(1,2,3,6-tetrahydro-1-pyridyl)ethyl]-indole-2-pyruvate (9).**—The 2-acylindole (8) (250 mg, 0.07 mmol) was dissolved in ethyl acetate (15.0 ml), 1,2,3,6-tetrahydropyridine was added, and the solution was refluxed for 10 h. At the end of this period a salt was deposited which was filtered off. The reaction mixture was washed with 10% HCl (2  $\times$  50 ml) and the aqueous (acidic) layer was basified with 10% aqueous  $\text{Na}_2\text{CO}_3$  (20 ml) and extracted with ethyl acetate (60 ml). The extract was dried and evaporated to afford the diamino ester (9) as a yellow gum (100 mg, 45%),  $\lambda_{\text{max}}$  (MeOH) 212, 240, and 320,  $\lambda_{\text{min}}$  275 and 230 nm;  $\nu_{\text{max}}$  1 600, 1 680, and 1 740  $\text{cm}^{-1}$  [Found:  $M^+$ , 326.1620. Calc. for  $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_3$ :  $M$ , 326.1630];  $m/z$  213 (2%), 143 (3), 126 (2), 115 (3), 97 (9), 96 (50), and 69 (6);  $\delta(\text{CDCl}_3)$  4.00 (3 H, s,  $\text{NCH}_3$ ), 4.02 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), 5.77 (2 H, m,  $\text{HC}=\text{CH}$ ), and 7.42–7.68 (4 H, m, ArH).

**Methyl {N-Methyl-3-[2-(1,2,3,6-tetrahydro-1-pyridyl)ethyl]-indol-2-yl}acrylate (10).**—Methyl-lithium (1.6M; 0.1 ml; 5% in diethyl ether) was added to a suspension of methyltriphenylphosphonium bromide (0.3 g, 8.4 mmol) in dry diethyl ether (15 ml). The reaction mixture was stirred for 1 h under nitrogen. The pyruvate (9) (0.1 g) was quickly added to the reaction mixture and the reaction vessel was kept at  $-20^\circ\text{C}$  for 72 h. T.l.c. showed complete conversion of starting material into a slower moving compound. The mixture was filtered and the filtrate was subjected to preparative t.l.c. to afford the acrylate (10) (0.001 g, 40%),  $\lambda_{\text{max}}$  (MeOH) 220, 256, 279, and 298,  $\lambda_{\text{min}}$  250, 260, and 280 nm [Found:  $M^+$  324.18383. Calc. for  $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2$ :  $M$ , 324.1837];  $m/z$  215 (100%) and 214 (50);  $\delta(\text{CDCl}_3)$  3.20 (3 H, s,  $\text{NCH}_3$ ), 3.75 (3 H, s,  $\text{CO}_2\text{Me}$ ), 5.92 (1 H, d,  $J$  1.2 Hz,  $\text{C}=\text{CHH}$ ), and 6.78 (1 H, d,  $J$  1.2 Hz,  $\text{C}=\text{CHH}$ ).

**3-Ethyl-1-[2-(N-methylindol-3-yl)ethyl]pyridinium Bromide (11).**—The bromide (7) (2.1 g, 8.0 mmol) and 3-ethylpyridine (1.5 ml, 11.2 mmol) were dissolved in ethyl acetate (5.0 ml) and heated in a sealed tube at  $120^\circ\text{C}$  for 72 h. A brown gum, which was seen to deposit at the bottom of the tube, was thoroughly washed, first with ethyl acetate and then with diethyl ether, and was then crystallised from light petroleum–

ethyl acetate (1 : 1) to afford the salt (11) (1.8 g, 75%), m.p.  $75\text{--}76^\circ\text{C}$  (decomp.);  $\lambda_{\text{max}}$  (MeOH) 225 and 285,  $\lambda_{\text{min}}$  240 nm;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 2 880 and 1 630  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.04 (3 H, t,  $J$  7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 2.55 (2 H, q,  $J$  7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 3.48 (2 H, t,  $J$  6.4 Hz,  $\text{CH}_2\text{CH}_2\text{N}^+$ ), 3.69 (3 H, s,  $\text{NCH}_3$ ), 5.17 (2 H, t,  $J$  6.4 Hz,  $\text{CH}_2\text{CH}_2\text{N}^+$ ), and 7.04 (1 H, s, indole 2-H).

**3-[2-(3-Ethyl-1,2,5,6-tetrahydro-1-pyridyl)ethyl]-N-methylindole (12).**—Sodium borohydride (1.0 g) was added in small portions to a solution of the salt (11) (2.0 g, 7.9 mmol) in methanol (200 ml) containing triethylamine (4.0 ml). The mixture was stirred at  $0^\circ\text{C}$  for 1 h and the methanol was removed under reduced pressure. The concentrated mass was dissolved in 10% HCl, the pH was adjusted to 2, and the solution was stirred at  $25^\circ\text{C}$  for 10 min and then diluted with excess of 10% aqueous sodium carbonate (50 ml). The aqueous solution was extracted with dichloromethane (3  $\times$  20 ml), and the combined extracts (60 ml) were washed with water, dried with sodium sulphate, and concentrated under reduced pressure to afford a pale orange gum (1.5 g). T.l.c. of the gum showed two spots with very similar  $R_F$ -values. Careful column chromatography [light petroleum–chloroform (1 : 4) as eluant] on silica gel allowed the separation of the two products. The major faster moving compound was identified as the desired product (12) (1.0 g, 60%),  $\lambda_{\text{max}}$  (MeOH) 225 and 280,  $\lambda_{\text{min}}$  250 nm;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1 600  $\text{cm}^{-1}$  [Found:  $M^+$ , 268.1941. Calc. for  $\text{C}_{18}\text{H}_{24}\text{N}_2$ :  $M$ , 268.1939];  $m/z$  156 (1%), 155 (2), 154 (1), 149 (0.5), 144 (10), 124 (100), 95 (2), 77 (2), 67 (2), and 55 (6);  $\delta(\text{CDCl}_3)$  2.02 (2 H, q,  $J$  7.0 Hz,  $\text{CH}_2\text{CH}_3$ ), 3.72 (3 H, s,  $\text{NCH}_3$ ), 5.5 (1 H, m,  $\text{C}=\text{CH}$ ), and 6.8 (1 H, s, indole 2-H).

**Methyl 3-[2-(3-Ethyl-1,2,5,6-tetrahydro-1-pyridyl)ethyl]-N-methylindole-2-pyruvate (13).**—Methoxalyl chloride (0.9 ml, 9.6 mmol) was injected into a suspension of  $\text{AlCl}_3$  (1.0 mg, 7.4 mmol) in dichloromethane (10.0 ml). The mixture was stirred for 5 min and a solution of the tetrahydropyridine (12) (1.0 g, 3.7 mmol) in the minimum amount of dichloromethane (5.0 ml) was added to the reaction mixture which was then kept for 24 h. The reaction was quenched with 10% aqueous sodium carbonate (50 ml). The organic layer was separated, dried over anhydrous sodium sulphate, and evaporated to give the pure pyruvate (13) (0.5 g, 55%),  $\lambda_{\text{max}}$  (MeOH) 210, 240, and 322,  $\lambda_{\text{min}}$  235 and 270 nm;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1 640 and 1 740  $\text{cm}^{-1}$  [Found:  $M^+$ , 354.3945. Calc. for  $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_3$ :  $M$ , 354.3945];  $m/z$  335 (2%), 310 (2), 279 (1), 254 (8), 219 (4), 175 (14), 144 (70), 124 (100), and 95 (20);  $\delta(\text{CHCl}_3)$  1.03 (3 H, t,  $J$  7.7 Hz,  $\text{CH}_2\text{CH}_3$ ), 2.00 (2 H, q,  $J$  7.7 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.00 (3 H, s,  $\text{NCH}_3$ ), 4.05 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), and 5.47 (1 H, m,  $\text{C}=\text{CH}$ ).

**Methyl 2-{3-[2-(3-Ethyl-1,2,5,6-tetrahydro-1-pyridyl)ethyl]-N-methylindol-2-yl}acrylate (15).**\*—Methyl-lithium (1.6M; 0.1 ml; 5% dispersion in diethyl ether) was added to a suspension of methyltriphenylphosphonium bromide (0.3 g, 8.4 mmol) in dry diethyl ether (15 ml). The reaction mixture was stirred for 1 h under nitrogen. The pyruvate (13) (0.1 g, 2.8 mmol) was quickly added to the reaction mixture and the reaction vessel was kept at  $-20^\circ\text{C}$  for 72 h. T.l.c. showed complete conversion of the starting material into a slower moving compound. The mixture was filtered and the filtrate was subjected to preparative t.l.c. to afford pure N-methylsecodine (15) (15 mg, 45%),  $\lambda_{\text{max}}$  (MeOH) 220, 259, 275, and 295,  $\lambda_{\text{min}}$  250, 260, and 280 nm;  $\nu_{\text{max}}$  1 740  $\text{cm}^{-1}$  [Found:  $M^+$ , 352.2153. Calc. for  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_2$ :  $M$ , 352.2150];  $m/z$  276 (10%), 259 (4), 251 (1), 215 (100), 214 (30), 201 (84), 183 (12), 139 (14), 124 (56), 91 (18), and 77 (80);  $\delta(\text{CDCl}_3)$  1.02 (2 H,

\* Methyl 3-[2-(3-ethyl-1,2,5,6-tetrahydro-1-pyridyl)ethyl]-N-methyl- $\alpha$ -methyleneindole-2-acetate, N-methylsecodine.

t,  $J$  7.4 Hz,  $\text{CH}_2\text{CH}_3$ ), 2.09 (3 H, q,  $J$  7.0 Hz,  $\text{CH}_2\text{CH}_3$ ), 5.59 (1 H, d,  $J$  1.7 Hz,  $=\text{CHH}$ ), and 6.99 (1 H, d,  $J$  1.7 Hz,  $\text{CHH}$ ).

# References

- 1 E. Wenkert, *J. Am. Chem. Soc.*, 1962, **84**, 98.
- 2 A. U. Rahman and A. Basha, 'Biosynthesis of Indole Alkaloids,' Oxford University Press, 1983.
- 3 J. P. Kutney, Y. Kartan, N. Kawamura, and B. R. Worth, *Can. J. Chem. Soc.*, 1982, **60**, 1269.
- 4 S. Raucher, J. F. Macdonald, and R. F. Lawrence, *J. Am. Chem. Soc.*, 1981, **103**, 2419.
- 5 J. P. Kutney, R. A. Badger, J. F. Beck, H. Bosshardt, F. S. Mataugh, V. E. Ridaura-Sanz, Y. H. So, R. S. Sood, and B. R. Worth, *Can. J. Chem.*, 1979, **57**, 289.
- 6 C. Marazano, J. L. Fourrey, and B. C. Das, *J. Chem. Soc., Chem. Commun.*, 1977, 742.
- 7 M. E. Kuehne, D. M. Roland, and R. Hafter, *J. Org. Chem.*, 1978, **43**, 3705.
- 8 M. E. Kuehne, T. H. Matsao, J. C. Bohnert, and C. L. Kikemo, *J. Org. Chem.*, 1979, **44**, 1063.

Received 28th January 1983; Paper 3/129