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SYNTHESIS AND ABSOLUTE CONFIGURATION OF THE ENANTIOMERS α-AMINOETHYLCYMANTRENE AND SOME OF ITS DERIVATIVES *

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Summary

Resolution of α-aminoethylcymantrene (I) to its enantiomers has been effected for the first time by means of (+)-*d*-tartaric acid. The molecular structure and absolute configuration of (+)-(*R*)-α-(*N*-acetylamino)ethylcymantrene prepared from (—)-I have been established by an X-ray analysis. On the basis of chemical and chiroptical correlation methods the *R*-configuration of the chiral centre is also assigned to (—)-I, (+)-α-(*N*,*N*-dimethylamino)ethylcymantrene, (+)-II and (+)-α-(*N*,*N*,*N*-trimethylammonium)ethylcymantrene iodide, (+)-III. ORD and CD curves of the prepared optically active compounds have been studied.

Continuing our studies of the properties of chiral monosubstituted compounds of the cymantrene series [1,2], we have carried out the synthesis of optical isomers of aminoethylcymantrene (I) and three of its derivatives (II—IV).

Resolution of (*R*,*S*)-I to its enantiomers was effected by means of (+)-*d*-tartaric acid in 80% ethanol medium. From the less soluble tartrate of amine I $(-)_{578}$-I was isolated. The optically pure (—)-enantiomer was obtained as a result of a triple repetition of the "tartrate formation-tartrate decomposition" operation to a constant value of $[\alpha]_{578}$. In every purification stage the optical purity of (—)-I was controlled by determining the PMR spectrum in the presence of a chiral shifting agent, $Dy(tflc)_3$ (Fig. 1). Pure (—)-I was also prepared by a double crystallization of the less soluble tartrate from ethanol. Crystallization of the tartrate isolated from the mother liquor, followed by treatment with 2 *M* NaOH, gave (+)-I with a 60% optical purity. The PMR and electron spectra of racemic I

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* Dedicated to Prof. G.A. Razuvaev on the occasion of his 85th birthday on August 23rd, 1980.

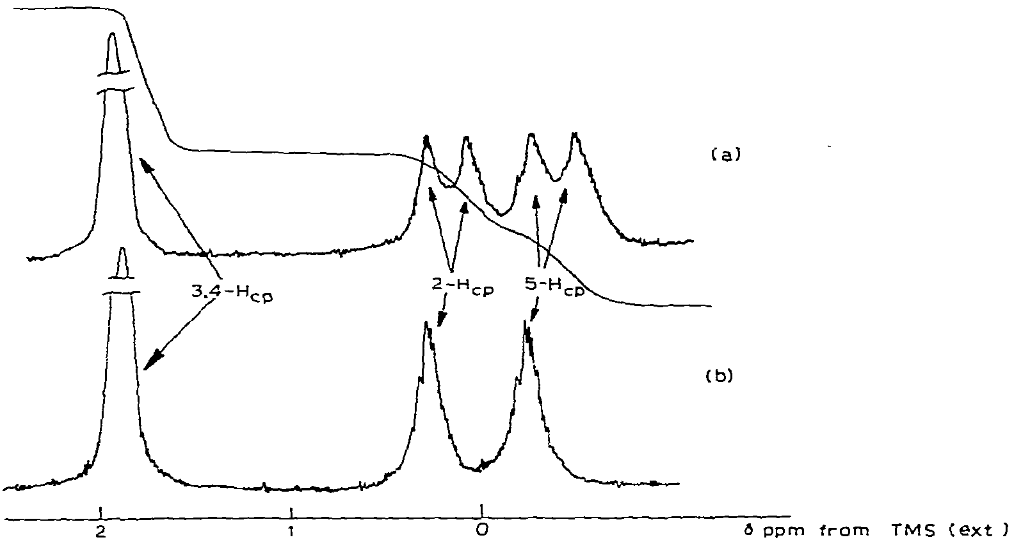
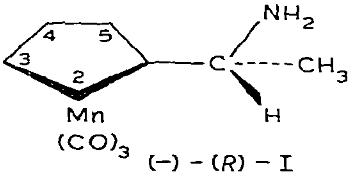
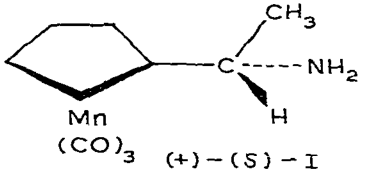


Fig. 1. PMR spectra of the cyclic protons of (*R,S*)-I (a) and of (—)-(*R*)-I (b) in the presence of Dy(tlfc)$_3$; 60 MHz, CHCl$_3$, [amine]/[Dy(tflc)$_3$] ≈ 2.

and (—)- and (+)-I were identical.

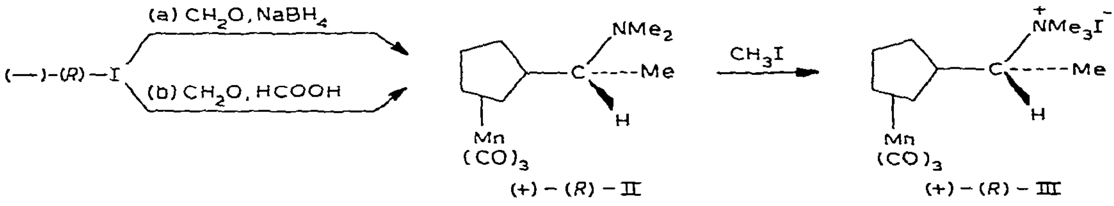


(−) - (*R*) - I



(+) − (*S*) − I

Methylation of (—)-I was effected by two independent methods: (a) treatment with formaldehyde and sodium borohydride in methanol and (b) treatment with formaldehyde in formic acid. Both methods resulted in the preparation of (+)-α-(dimethylamino)ethylcyamantrene, (+)-II, with similar values of $[\alpha]_{578}$, equal to +17.19 and +17.23°, respectively.



The values of $[\alpha]_{578}$ for (—)-II prepared from (+)-I by reactions a and b were also very similar. These data indicated that the transformation of I into II occurred stereoselectively without racemization of the chiral centre in either methods a or method b. The interaction of (+)- or (—)-II with methyl iodide resulted in formation of (+)- or (—)-α-(*N,N,N*-trimethylammonium)ethylcymantrene iodide ((+)- or (—)-III).

TABLE 1

VALUES OF [α] AND THE PARAMETERS OF THE ELECTRONIC AND CD SPECTRAL PARAMETERS FOR OPTICAL PURE (*R*)-$(CO)_3MnC_5H_4CH(CH_3)R$

Compound	R	electronic spectra		CD spectra		$[\alpha]_{578}$	Solvent
		λ_{max}	lg ε	λ_{max}	[θ]		
I	NH_2	330	3.05	335	—190	—10.4	CH_3CH_2OH
II	NMe_2	331	3.13	344	—1584	+17.2	CH_3CH_2OH
III	$\overset{+}{N}Me_3$	333	3.09	342	—1736	+26.9	$CH_3O(CH_2)_2OH$
		332	3.05	344	—1105	—	CH_3CN
IV	$NH(COCH_3)$	330	3.21	333	—1705	+24.5	CH_3CH_2OH

To establish the configurational relationship of the optically active cymantrene derivatives, we studied their ORD and CD spectra (Table 1, Figs. 2 and 3). In the circular dichroism spectra of (—)-I and of its derivatives (+)-II and (+)-III, a negative maximum was observed in the 330—340 nm region, corresponding to the long-wave absorption band of these compounds in the electronic spectrum. The optical rotation dispersion curves of (—)-I, (+)-II, (+)-III have a similar relationship of variation of [*M*] when passing to the short-wave region of the spectrum. The ORD curve of (—)-I in the 600—400 nm region corresponds to a sim-

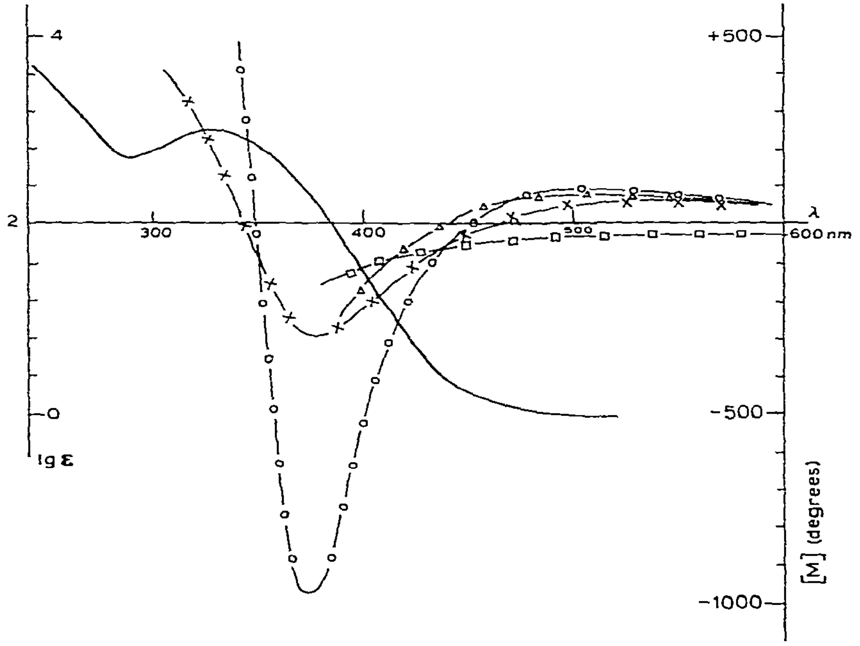


Fig. 2. The ORD curves of (—)-(*R*)-I in EtOH (□———□), (+)-(*R*)-II in EtOH (X———X), (+)-(*R*)-III in MeCN (○———○), (+)-(*R*)-IV in EtOH (△———△) and the electronic spectrum (*R*,*S*)-I in EtOH (———).

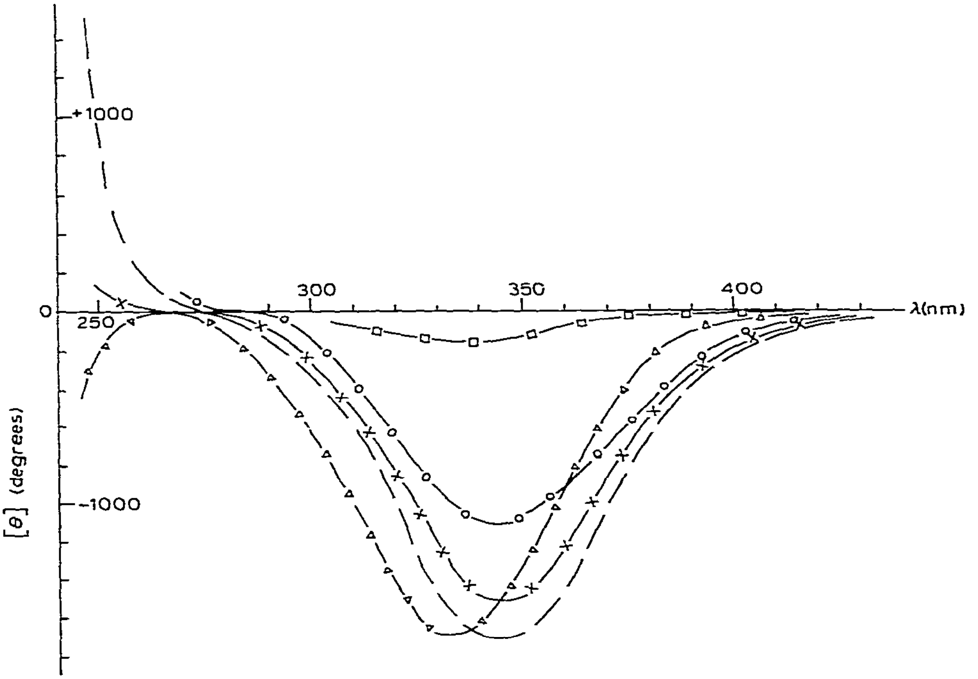


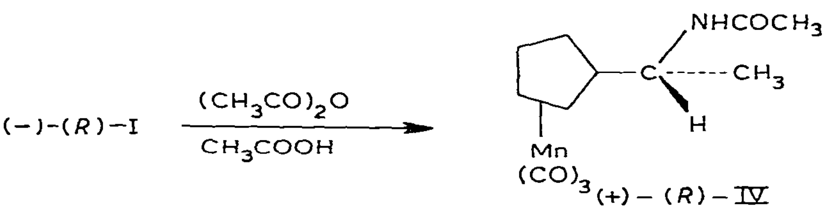
Fig. 3. The CD curves of (—)-(*R*)-I in EtOH (□——□), (+)-(*R*)-II in EtOH (×——×), (+)-(*R*)-III in MeCN (○——○) and in $MeOCH_2CH_2OH$ (— — —), (+)-(*R*)-IV in EtOH (△——△).

ple Drude equation in the form:

$$1/[\alpha]_\lambda = (\lambda^2 - \lambda_c^2)/A$$

with $\lambda_c = 333$ nm and $A = 2.05$ *. In the case of (+)-II and (+)-III the shape of the ORD curves within this region of the spectrum is defined, to a considerable extent, by the background rotation. The ORD and CD spectra of (+)-I, (—)-II and (—)-III are the mirror images of the curves shown in Figs. 2 and 3 for the corresponding enantiomers. Consequently, as one could expect from the method of transformation of I into III, derivatives of (—)-I, (+)-II and (+)-III have the same configuration at the chiral centre. The opposite configuration can be assigned to compounds (+)-I, (—)-II and (—)-III.

In order to establish the absolute configuration of the optically active compounds described in this paper, we carried out an X-ray analysis of (+)-α-(*N*-acetylamino)ethylcymantrene(IV) prepared from the optically pure (—)-I enanmer



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* The value of A corresponds to λ in μ.

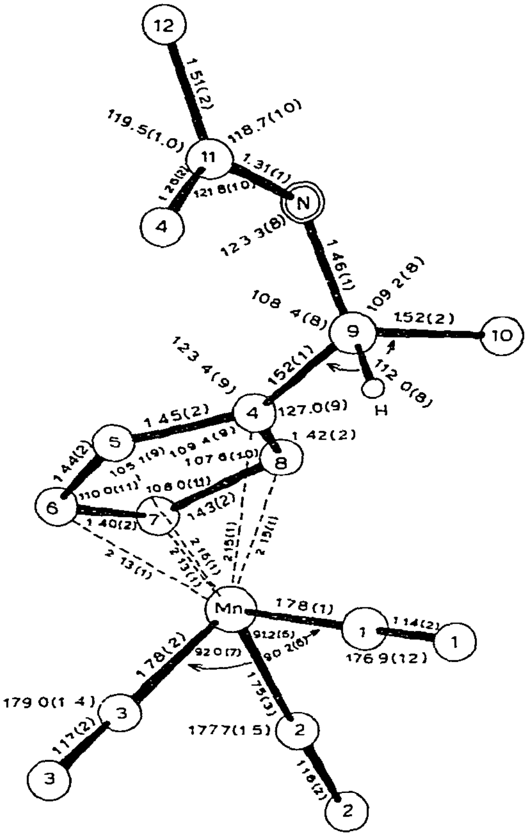

Fig. 4. The molecular structure of (+)-(*R*)-IV.

The molecular structure of (+)-IV with bond lengths and angles is shown in Fig. 4. Atomic coordinates and temperature factors are given in Table 2.

The Mn atom in (+)-IV has a typically octahedral coordination ("piano stool") characteristic for (η^5-C_5H_5)Mn(CO)$_3$ [3] and its derivatives with substantial retention of the ideal C_{3v} symmetry of the Mn(CO)$_3$ fragment, i.e. the (O)C—Mn—C(O) bond angles are close to 90°.

The cyclopentadienyl ligand is planar within ±0.005 Å, with mean C—C distances in the cycle of 1.43(2) Å and Mn—C(Cp) of 2.14(I) Å, differing insignificantly from those found in (η^5-C_5H_5)Mn(CO)$_3$ (1.39 and 2.15 Å, respectively). The C(9) atom is not strictly within the cycle plane, but is displaced outwards from it by 0.10 Å relative to the metal atom.

In the molecule of (+)-IV another substantially planar fragment C(9)NC(11)C(12)O(4) can be defined (the maximum atomic deviation from the root-mean-square plane does not exceed 0.01 Å) which forms a dihedral angle of 76.7° with the cyclopentadienyl ligand. The geometrical parameters of the substituent are quite usual. Thus, a shortening of the N—C(11) distance to 1.31(1) Å, characteristic for an amide bond, is observed along with a corresponding elongation of the ketone bond C(11)=O(4) to a value of 1.26(2) Å comparable with the standard values of this bond length in O=C—N fragments [4].

TABLE 2

ATOMIC COORDINATES ($\times 10^4$) AND THEIR ANISOTROPIC TEMPERATURE FACTORS ($\times 10^2$) IN THE FORM $T = \exp[-1/4(B_{11}H^2a^{*2} + \ldots + 2B_{23}klb^*c^*)$

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Mn	14(2)	2500(0)	2072(2)	266(6)	470(7)	367(6)	−13(7)	37(4)	65(8)
O(1)	−2536(16)	3303(15)	−316(15)	966(68)	837(59)	862(66)	2(58)	−380(61)	287(55)
O(2)	2264(20)	1876(16)	−365(19)	1449(107)	1083(86)	1264(97)	437(8)	1009(93)	335(71)
O(3)	1130(20)	5469(13)	2378(14)	1470(107)	765(69)	804(66)	−609(75)	−126(68)	−9(56)
O(4)	−4763(11)	2695(11)	5348(10)	796(46)	350(44)	638(41)	112(39)	260(35)	1(41)
N	−4261(9)	541(9)	4357(9)	275(32)	391(34)	371(36)	−42(28)	93(29)	−27(31)
C(1)	−1544(15)	3023(13)	639(14)	513(53)	523(58)	499(54)	41(43)	−146(51)	230(44)
C(2)	1383(20)	2145(14)	631(20)	815(83)	558(80)	805(84)	138(55)	408(78)	229(59)
C(3)	703(19)	4290(16)	2255(16)	648(72)	680(79)	525(63)	−174(66)	−153(59)	40(59)
C(4)	−1701(11)	1263(11)	3313(11)	240(35)	434(43)	298(37)	12(34)	30(30)	22(37)
C(5)	−987(13)	2344(15)	4343(12)	374(38)	592(70)	364(38)	−116(49)	−12(32)	−64(48)
C(6)	761(13)	2059(14)	4449(14)	348(44)	680(68)	441(51)	−120(42)	−68(42)	135(47)
C(7)	1104(13)	881(16)	3523(16)	249(39)	727(69)	626(66)	46(44)	−4(45)	269(63)
C(8)	−426(13)	368(13)	2817(13)	308(40)	550(57)	521(51)	88(41)	114(39)	253(46)
C(9)	−3549(11)	1082(11)	2961(11)	266(38)	418(45)	367(41)	−12(33)	22(34)	10(37)
C(10)	−3936(14)	64(16)	1616(13)	430(46)	730(67)	413(46)	−213(50)	60(40)	−148(52)
C(11)	−4813(12)	1360(14)	5446(11)	345(42)	513(57)	358(48)	6(41)	35(37)	11(43)
C(12)	−5497(17)	680(15)	6859(13)	617(64)	651(61)	381(50)	−23(54)	153(46)	12(48)

The metal—carbonyl groups are linear with normal Mn—C (mean 1.77(2) Å) and C—O (mean 1.16(2) Å) bond lengths.

In the crystal the molecules of (+)-IV are linked in chains along screw axes by means of rather weak hydrogen bonds N—H...O(4) of 2.82(1) Å in length.

As shown in Fig. 4, the asymmetric C(9) atom has the (*R*)-configuration. Since (+)-IV, both from the method of its preparation and from the shape of the ORD and CD curves (Figs. 2 and 3), should have the same configuration at the chiral centre as (—)-I, the above data indicate that compounds (—)-I, (+)-II and (+)-III also have the (*R*)-configuration. Consequently, the enantiomers (+)-I, (—)-II and (—)-III also have the (*S*)-configuration. The structural formulae of the optically active compounds shown in the diagrams correspond to their absolute configuration.

The study of chiroptical characteristics of the optically active cymantrene derivatives I—IV discussed here shows that enantiomers of the (*R*)-series have a negative Cotton effect and those of the (*S*)-series a positive one within the metal—carbon bond absorption region (ca. 330 nm).

Experimental

Values of [α] were measured with Polamat-A and Perkin-Elmer 141 polarimeters. The ORD and CD curves were obtained with Jasco ORD/UV-5 and Jasco J-20 spectropolarimeters, respectively. Electron spectra were recorded with a Specord UV-VIS spectrophotometer and PMR spectra with a Perkin-Elmer R-12 spectrometer. The optically active shifting agent Dy(tflc)$_3$ was prepared according to ref. 5 from Dy_2O_3 and 3-(trifluoroacetyl)-*l*-camphor with $[\alpha]^{24}_{578} = -149°$ (c 4, benzene).

(R,S)-α-Aminoethylcymantrene, I

To a solution of 200 g (0.76 mol) of acetylcymantrene oxime [6] in 800 ml of glacial CH_3COOH and 50 ml of water 247 g (3.8 mol) of zinc powder were added in portions over 1.5 hours with stirring under argon atmosphere at 60—80°C. After addition of all the zinc the mixture was heated at reflux for one hour, the hot solution separated from the precipitate, cooled, neutralized with 6 *M* NaOH and extracted with n-hexanol. The extract was vigorously shaken with excess 6 *M* NaOH and rapidly washed with water until the washings were neutral. The organic layer was dried with a mixture of Na_2SO_4 and $MgSO_4$ and the amine was distilled in vacuum. The yield of I was 125 g (66%); b.p. 77—78°C 4×10^{-2} mm Hg, $n_D^{20} = 1.5920$. Analysis: found: C, 48.43, 48.45; H, 4.04, 4.12; $C_{10}H_{10}NO_3Mn$, calcd.: C, 48.64; H, 4.07%. PMR (CCl_4, δ ppm): 1.33 (d, 5 H, $J = 5.3$ Hz, CH_3 and NH_2); 3.83 (q, 1 H, *CH*CH_3); 4.69—4.79 (m, 3 H, C_5H_4) and 4.94 (m, 1 H, C_5H_4).

(—)-R-α-Aminoethylcymantrene, (—)-(R)-I

(a) Solutions of 116 g (0.53 mol) of I in 1450 ml of aqueous ethanol (d = 0.870) and of 79.6 g (0.53 mol) of (+)-*d*-tartaric acid in 1450 ml of aqueous ethanol were mixed at 55°C in a thermostat. The temperature of the resulting solution was then slowly lowered during 10 hours to 17.5°C and maintained at this temperature for 12 hours. After this time 88.2 g of tartrate were precipitated, which after treatment with 2 *M* NaOH, drying of the ethereal extract and distillation gave 41.8 g of the amine with $[\alpha]^{21}_{578}$ = —8.5° (*c* 2, ethanol). Double repetition of the formation of the tartrate and recovery of the amine resulted in (—)-(*R*)-I with $[\alpha]^{24}_{578}$ = —10.4° (*c* 2, ethanol). The yield was 17.6 g (30%), b.p. 80—81°C/6 × 10^{-2} mm Hg; n^{22}_{D} = 1.5910.

(b) 85 g of the tartrate recovered after the first resolution of racemic I were recrystallized directly from ethanol (2 × 650 ml). The yield of tartrate was 52.3 g, isolation of the amine was carried out as described in (a). 25.3 g (43%) of (—)-(*R*)-I were obtained; $[\alpha]^{24}_{578}$ = —10.3° (c 2, ethanol); b.p. 78°C/4 × 10^{-2} mm Hg, n^{20}_{D} = 1.5912.

(+)-(S)-α-Aminoethylcymantrene, (+)-(S)-I

The mother liquor after separation of the first portion of the tartrate (see (a) above) was evaporated to dryness and the residue twice recrystallized from methanol. Decomposition of the salt gives 38 g of (+)-(*S*)-I; $[\alpha]^{28}_{578}$ = +6.2° (c 2, ethanol); b.p. 78—79°C/4 × 10^{-2} mm Hg; n^{20}_{D} = 1.5910.

(+)-(R)-α-(Dimethylamino)ethylcymantrene, (+)-(R)-II

13.3 g (0.05 mol) of (—)-(*R*)-I were slowly added with stirring to 12.5 g (0.27 mol) of HCOOH. The resulting solution mixed with 11 ml of 37% formalin and the temperature gradually (to avoid too vigorous an evolution of CO_2) raised to 95—100°C. The mixture was refluxed for 8 hours, and then poured into water, acidified with 2 *M* HCl and extracted with ether. 4 *M* NaOH was added to the aqueous layer to pH = 9 and the mixture was again extracted with ether. The ethereal extracts were washed with water, dried over $MgSO_4$-Na_2SO_4 and distilled The yield of (+)-(*R*)-II was 11.4 g (76%); b.p. 89—90°C/8 × 10^{-2} mm Hg; m.p. 54—55°C, $[\alpha]^{25}_{578}$ = +17.2° (*c* 2, ethanol). Analysis found: C, 52.33, 52.19; H, 4.96, 4.90; Mn, 20.20, 20.19; $C_{12}H_{14}NO_3Mn$ Calcd.: C, 52.37; H, 5.12; Mn 19.96%. Mol. weight 275 (mass-spectrum). PMR (CCl_4, δ ppm): 1.25 (d, 3 H, *J* = 6.7 Hz, CH_3); 2.12 (s, 6 H, $N(CH_3)_2$); 3.45 (q, 1 H, *J* = 6.7 Hz, C*H*CH_3); 4.56 (m, 1 H, C_5H_4) and 4.73 (m, 3 H, C_5H_4).

(—)-(S)-α-(Dimethylamino)ethylcymantrene, (—)-(S)-II

(a) Following the above described procedure, 23.8 g (62%) of (—)-(*S*)-II were obtained from 35.3 g (0.14 mol) of (+)-(*S*)-I (59.6% oprical purity), 36.1 g HCOOH and 33.4 ml of 37% formalin; b.p. 75°C/3 × 10^{-2} mm Hg, m.p. 28—30°C; n^{22}_{D} = 1.5705, $[\alpha]^{24}_{578}$ = —10.3° (c 2, ethanol).

(b) 10 g (0.04 mol) of (+)-(*S*)-I were dissolved in 247 ml of methanol and to this solution 61 ml of 37% formalin were added. The mixture was cooled to —10°C and 24 g (0.66 mol) of NaBH were added in small portions with stirring under argon atmosphere. After addition of the hydride the reaction mixture was brought up to 40°C and stirring was continued for an additional 1.5 hours. The flask contents were poured into 2 litres of water and the mixture extracted with ether. The extract was shaken with 2 *M* HCl and the aqueous solution alkalified to pH = 9. The ethereal extracts of the aqueous solutions were washed with water, dried over $MgSO_4$ and distilled. According to the PMR spectrum, $(CO)_3MnC_5H_4CH(CH_3)NH(CH_3)$ had been isolated. The yield was 7.1 g; b.p. 87°C/7 × 10^{-2} mm Hg; n^{25}_{D} = 1.5770.

The introduction of the second methyl group was effected in a similar manner using 5.3 g of the monomethyl compound, 31 ml of formalin and 12 g of $NaBH_4$ in 124 ml of methanol. 3.9 g (71%) of (—)-(*S*)-II were obtained, b.p. 83°C/5 × 10^{-2} mm Hg; $n_D^{23} = 1.5720$, $[\alpha]_{578}^{23} = -10.2°$ (c 2, ethanol).

(+)-(R)-α-(N,N,N-Trimethylammonium)ethylcymantrene iodide, (+)-(R)-III

To a solution of 4.95 g (0.018 mol) of (+)-(*R*)-II in 10 ml of dry acetone, 5.4 ml (0.08 mol) of freshly-distilled methyliodide were added dropwise at 0°C under stirring. The reaction mixture was maintained at this temperature for 0.5 hours (a precipitate was formed), diluted with 100 ml of abs. ether and filtered. The precipitate was washed with ether on the filter and dried in a desiccator over P_2O_5. The yield was 7.27 g (99%), m.p. 186—188°C, $[\alpha]_{578}^{25} = +22.6°$ (c 2, ethanol), +26.9° (c 2, methylcellosolve). Analysis found: C, 37.48, 37.36; H, 4.14, 4.31; I, 30.56, 30.08; Mn 13.23, 13.15. $C_{13}H_{17}NO_3MnI$, calcd.: C, 37.41; H, 4.10; I, 30.41; Mn 13.16%.

(R,S)-α-(N-acetylamino)ethylcymantrene, IV

A mixture of 2 g (0.008 mol) of (*R*,*S*)-I, 9.95 g (0.166 mol) of CH_3COOH and 1.72 g (0.017 mol) of $(CH_3CO)_2O$ was heated at reflux for 8 hours. Excess volatile substances were removed in vacuum and the residue was crystallized from heptane-chloroform (1 : 1) by slow evaporation of the solvent. The yield of IV was 1.62 g (70%), m.p. 105—106°C. Analysis found: C, 49.72, 49.50; H, 4.20, 4.28; Mn, 19.24, 19.41; $C_{12}H_{12}NO_4Mn$, calcd.: C, 49.84; H, 4.18; Mn 18.99%.

(+)-(R)-α-(N-acetylamino)ethylcymantrene, (+)-(R)-IV

The enantiomer (+)-(*R*)-IV was prepared by the above procedure from 0.75 g (0.003 mol) of (—)-(*R*)-I. After crystallization, 0.63 g (73%) were isolated; m.p. 77—78°C, $[\alpha]_D^{22} = +24.5°$ (c 1, ethanol). Analysis found: C, 49.94, 49.68; H, 4.43, 4.39; N, 4.60, 4.56; Mn, 18.74, 19.04; $C_{12}H_{12}NO_4Mn$, calcd.: C, 49.84; H, 4.18; N, 4.84; Mn, 18.99%. PMR ($CDCl_3$, δ, ppm): 1.27 (d, 3 H, $J = 5.3$ Hz, $CHCH_3$); 1.93 (s, 3 H, $COCH_3$); 4.67 (m, 2 H) and 4.87 (m, 3 H, C_5H_4 and $CHCH_3$); 5.95 (d, 1 H, NH).

Crystals of (+)-(*R*)-IV are monoclinic, $a = 8.120(1)$, $b = 9.4425(8)$, $c = 8.576(1)$ Å; $\beta = 93.70(1)°$, $V = 656.2(2)$ Å^3 $M = 289.19$, $d_{calc.} = 1.463$ g/cm^3 for $Z = 2$; space group $P2_1$. Intensities of 1017 reflections with $I \geqslant 2\sigma$ were measured on an automatic "Hilger-Watts" diffractometer (λCu, graphite monochromator, $\theta/2\theta$-scanning, $2\theta_{max} = 130°$), absorption neglected. The structure was solved by the heavy atom method and refined by the least-square method in the full-matrix anisotropic approximation to $R = 0.066$. The absolute configuration of (+)-IV was established by the Hamilton test [7]; the *R*-factor for the inverted structure was 0.089.

References

1 D.N. Kursanov, Z.N. Parnes, N.M. Loim, N.E. Kolobova, I.B. Zlotina, P.V. Petrovskii and E.I. Fedin, J. Organometal. Chem., 44 (1972) C15.

2 N.M. Loim, D.N. Kursanov, Z.N. Parnes, N.N. Sul'dina and E.I. Fedin, J. Organometal. Chem., 52 (1973) C33.

3 A.F. Berndt and R.E. Marsh, Acta Crystallogr., 16 (1963) 118.
4 Tables of interatomic distances and configuration in molecules and ions. Special publ. No. 11, London, 1958.
5 H.L. Goering, J.N. Eikenberry and G.S. Koermer, J. Amer. Chem. Soc., 93 (1971) 5913.
6 L.M.C. Shen, G.G. Long and C.C. Moreland, J. Organometal. Chem., 5 (1966) 362.
7 W.C. Hamilton, Acta Crystallogr., 18 (1965) 502.