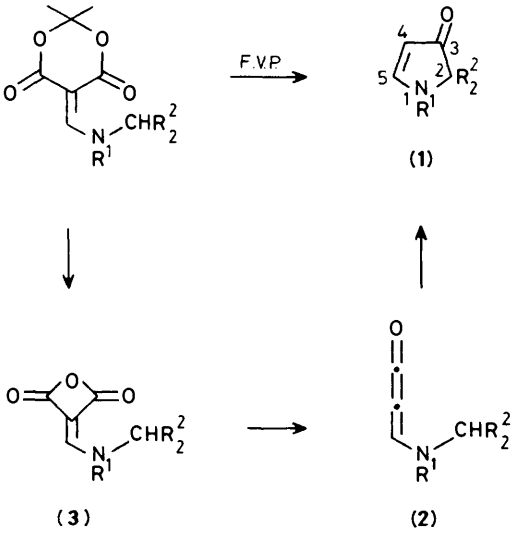
3-Hydroxypyrroles and 1*H*-Pyrrol-3(2*H*)-ones. Part 3.[1,2] Pyrrolones from Pyrolyses of Aminomethylene Meldrum's Acid Derivatives: Loss of Chirality at the Site of Hydrogen Transfer

Hamish McNab * and Lilian C. Monahan
Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

Pyrolysis of the diastereoisomeric Meldrum's acid derivatives (**4**) and (**5**), or of the chiral derivatives (**6**), (**7**), and (**9**), gives 2,2-disubstituted 1*H*-pyrrol-3(2*H*)-ones in which there is loss of configuration at the reaction site [*e.g.* (**15**) obtained from (**9**)]. The extent of configuration loss is greater if the reaction site is part of a ring. These results are explained by a two-step, hydrogen-transfer–cyclisation mechanism, following initial generation of a methyleneketene.

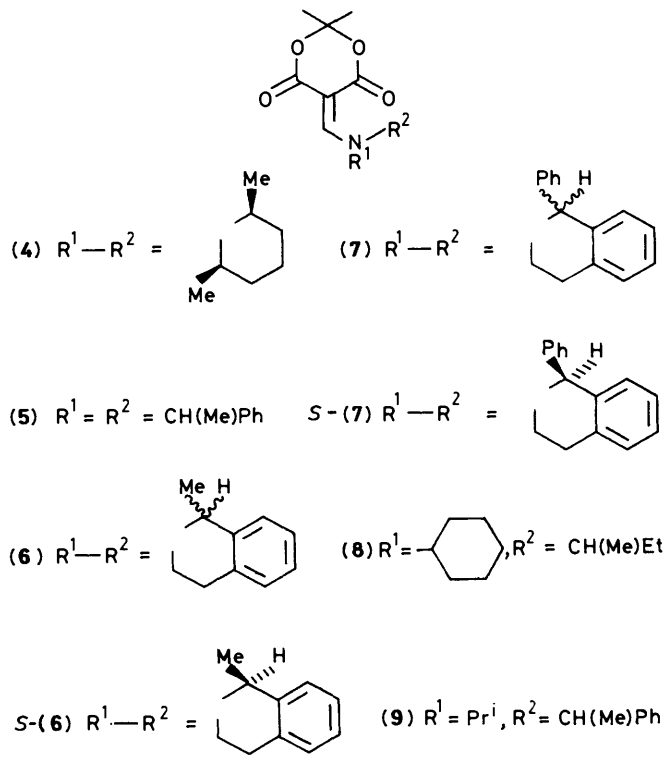
The pyrolytic formation of the 1*H*-pyrrol-3(2*H*)-one (**1**) nucleus from aminomethylene Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) derivatives (Scheme 1) is of both mechanistic and synthetic[1] interest. The course of the reaction has been well studied as far as the methyleneketene (**2**) stage. Wentrup *et al.* have obtained spectroscopic data for an intermediate anhydride (**3**), as well as for the methyleneketene



Scheme 1.

(**2**) itself:[3] these results follow the expected pattern of Meldrum's acid pyrolyses.[4,5] However, much less is known of the key hydrogen-transfer–cyclisation steps, although we have shown by deuterium-labelling experiments that the hydrogen transfer is specific, intramolecular, and probably rate-determining.[6] The results of competitive experiments suggest that radical intermediates are probably not involved,[1] although the situation was less clear cut with some related thermal hydrogen-transfer–cyclisation processes.[7,8] In this paper, we employ chiral centres at the site of hydrogen transfer, as a detailed probe of the stereochemical changes during the course of the reaction.

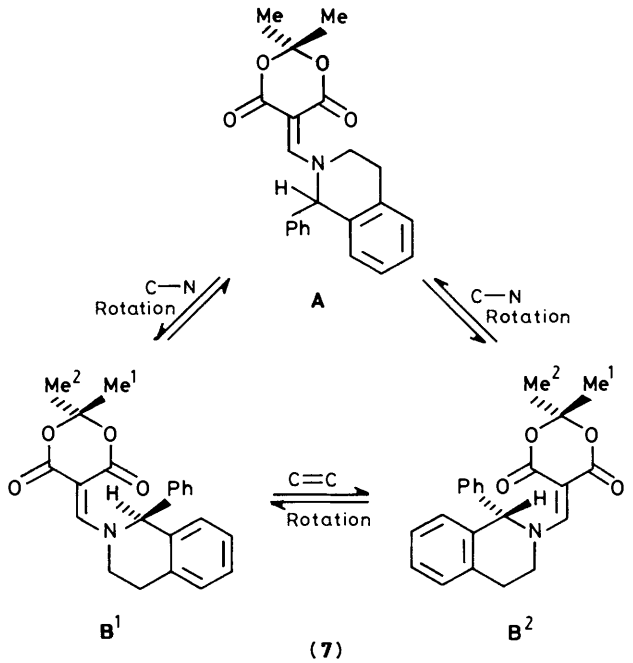
The Meldrum's acid derivatives (**4**)—(**9**) were prepared and characterised by standard methods.[1] Those with two chiral centres [(**4**) and (**5**)] were shown to be single diastereoisomers by ^{13}C n.m.r. spectroscopy. The *Z*-configuration of the 2,6-dimethylpiperidino example (**4**) was established by literature comparison of the melting point of the hydrochloride salt of the free secondary amine.[9] The bis(α-methylbenzyl) isomer (**5**) was



obtained pure, although in low yield, by fortuitous crystallisation: its configuration was not determined. The chiral tetrahydroisoquinoline derivatives[10] *S*-(**6**) and *S*-(**7**) were prepared from the corresponding chiral amine, which was resolved by the traditional method,[10] whereas the α-methylbenzyl examples *R*- and *S*-(**9**) were obtained, in two steps, from *R*- and *S*-α-methylbenzylamine, respectively. In these latter cases, n.m.r. analysis of chiral (**9**) in the presence of the chiral shift reagent[11] tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) failed to reveal any of the opposite enantiomer, although these spectra were complicated by poor separation of the enantiomers, and by overlapping peaks, and so are probably accurate to only ±10%.

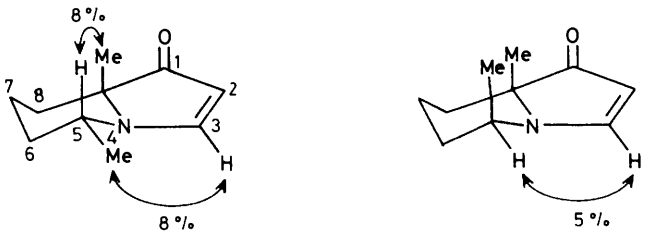
The n.m.r. spectra of the unsymmetrical derivatives (**6**)—(**8**) showed the expected[1] presence of two rotamers due to restricted rotation around the C–N bond. However, the ^1H n.m.r. spectrum of compound (**7**) showed evidence of *two* independent exchange processes. First, the coalescence of the

two unequal singlets corresponding to the methine proton of rotamers *A* and *B* gives a measure of the rate of C–N rotation [T_c([$^2H_6$]DMSO) 420 ± 2 K, $\Delta G^{\ddagger}$ 86.5 ± 0.5 kJ mol^{-1}]. The two rotamers also give rise to different signals corresponding to the 2-methyl groups, those of the major rotamer occurring as a sharp singlet at room temperature, shifted slightly to higher frequency of the broad signal due to those of the minor rotamer. At lower temperatures, this latter signal separates into two peaks, which coalesce at 301 K ($CDCl_3$) corresponding to a $\Delta G^{\ddagger}$ of 62.6 ± 0.4 kJ mol^{-1}. These results may be explained by interconversion of the rotamers **B**^{1} and **B**^{2} (Scheme 2) by C–C rotation. The boat shape of Meldrum's acid is such that in rotamer **B**^{1}, the methyl group Me^1 is in the shielding zone of the phenyl substituent and is shifted to relatively low frequency. C–C Rotation produces a similar effect on Me^2 in rotamer **B**^{2}, imposed by the inflexibility of the configuration of the tetrahydroisoquinoline ring.* It is surprising that rotation around the formal double bond is more facile than around the C–N single bond, but this conclusion is supported by *X*-ray crystallographic studies of other Meldrum's acid derivatives,[12] and by n.m.r. investigations of related systems.[13]



Scheme 2.

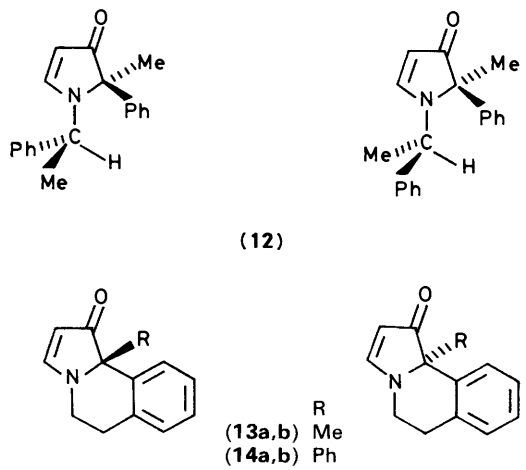
Flash vacuum pyrolysis of the precursors (**4**)—(**9**) at 600 °C gave 1,2,2-trisubstituted 1*H*-pyrrol-3(2*H*)-ones (or their fused derivatives) as the only significant products in all cases. However, *two* isomeric pyrrolones were obtained from both of the single diastereoisomers (**4**) and (**5**), which could be separated by chromatography. Thus the cyclic precursor (**4**) yielded a 52:48 (*ca.* 1:1) mixture of diastereoisomers, whose configurations were established by n.O.e. experiments. The more polar component was the *E*-isomer (**10**), in which irradiation of the bridgehead (singlet) methyl resonance gives an 8% enhancement at the proton α to the nitrogen atom, whereas irradiation of the doublet methyl signal affects the 3-proton by a similar amount (Scheme 3). The other isomer (**11**), was present in slightly greater amount, and was characterised by n.O.e. effects at the two protons α to the nitrogen atom (Scheme 3): the small effect may be due to a low concentration of the conformer in which the two methyl groups adopt the diaxial configuration. These results suggest that reaction at the bridgehead centre may have taken place with inversion to give the *E*-orientation of methyl groups in compound (**10**), whereas the *Z*-configuration of the starting piperidine is maintained in compound (**11**), although adventitious loss of configuration at the other chiral centre cannot be excluded.



(**10**) (**11**)

Scheme 3. N.O.e. results for indolizinones (**10**) and (**11**)

Pyrolysis of the acyclic precursor (**5**) resulted in a separable mixture of diastereoisomers (**12**) in 68:32 ratio, although in this case the relative configurations were not established. It is also not clear as to why the ratio of diastereoisomers is not *ca.* 1:1 as for the piperidino derivative (**4**). Since it is possible that either the presence of the ring, or the presence of the aryl substituent at the reaction site, may be responsible, a variety of other



R
(**13a,b**) Me
(**14a,b**) Ph

derivatives (**6**)—(**9**) were synthesized in which these structural features are systematically changed. In addition, these contain only one chiral centre, and were prepared enantiomerically pure, so that any loss of configuration found must be unambiguously at the reaction site. In all cases, trial pyrolyses were carried out on the racemic materials, so that analysis by ^{1}H n.m.r. spectroscopy using chiral shift reagents could be optimised (see Experimental section). The enantiomeric pyrrolones from the dialkylamino derivative (**8**) could not be analysed in this way, and this substrate was not studied further.

The pyrolysis of the α-methylbenzyl derivatives (**9**) were studied in particular detail, and a number of control experiments were carried out. First, reaction took place exclusively at the benzylic site, as expected.[1] Second, a quantitative study of the effect of the shift reagent on the pyrrolones (**15**) established that the largest effect is at the 4-

* An alternative explanation, that the methyl groups are non-equivalent due to interconversion of Meldrum's acid boat conformers, is excluded, since the corresponding signals of Meldrum's acid itself are equivalent, even at −80 °C.

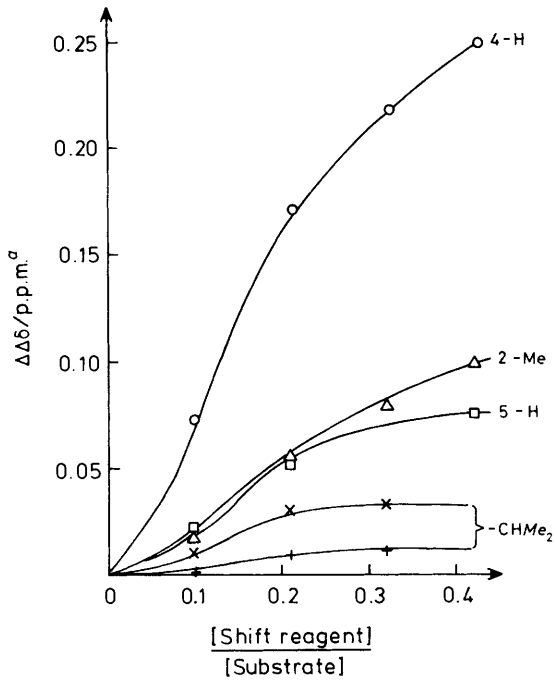
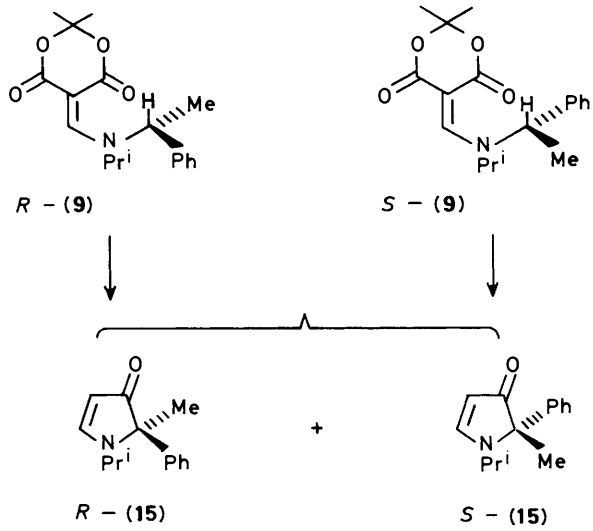


Figure. Effect of chiral shift reagent on ^{1}H n.m.r. spectra of the pyrrolones (**15**). [a] $\Delta\Delta\delta$ Represents the difference in chemical shift between the *R* and *S* enantiomer signals

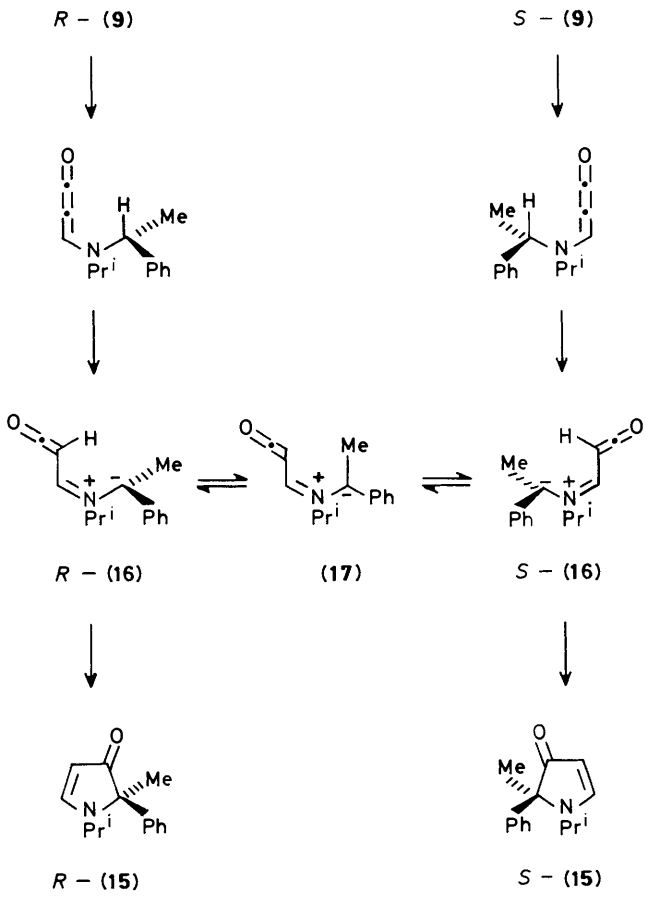
position (Figure), consistent with complex formation at the carbonyl group, which is the normal site of protonation of such systems.[14] Third, we have shown by examination of recovered starting material after pyrolysis at 400 °C, that there is no fortuitous equilibration of *R*-(**9**) and *S*-(**9**), and also that the products (**15**) are not racemised on re-pyrolysis at 600 °C. This is in accord with the results of Meier and Rüchardt, who observed complete retention of configuration in the rearrangement of isonitriles to nitriles under flash vacuum pyrolysis conditions.[15] We believe, therefore, that any loss of configuration at the chiral centre takes place as a consequence of the hydrogen-transfer–cyclisation sequence at that site.*

The following results were obtained. Pyrolysis of one enantiomer of the α-methylbenzyl derivative (**9**) gave a 75:25 mixture of the enantiomeric pyrrolones (**15**), whereas the alternative configuration gave the reverse ratio (Scheme 4). These data are in accord with the results for the related acyclic diastereoisomeric example (**5**). On the other hand, pyrolysis of the cyclic derivatives *S*-(**6**) or *S*-(**7**) gave a 50:50 mixture of fused pyrrolone enantiomers (**13**) and (**14**). These results correspond to those for the cyclic diastereoisomeric example (**4**): the ratio of enantiomers formed is clearly controlled by the presence of the ring, rather than the manner of substitution at the reaction site.

The formation of the 1*H*-pyrrol-3(2*H*)-one nucleus from the methyleneketene (Scheme 1) requires hydrogen transfer from, and ring closure to, a site adjacent to the nitrogen atom. These processes may, in principle, be stepwise or concerted. Since there is (at least partial) loss of chirality in all of the examples studied, the ring formation from the methyleneketene cannot be concerted, and must involve an intermediate with sufficient



Scheme 4. From *R*-(**9**), enantiomeric ratio 75:25 and from *S*-(**9**), enantiomeric ratio 25:75



Scheme 5.

lifetime for racemisation after the hydrogen-transfer step. Since a diradical intermediate is unlikely,[1] the most reasonable alternative[16] involves a 1,4-hydrogen shift *via* a 6-electron transition state to give a dipolar intermediate *e.g.* (**16**), and the results of the pyrolyses of the chiral precursors support this structure. Thus the initially formed dipole (**16**) (Scheme 5) has a spiral geometry and the ketene portion of the intermediate can

* We cannot exclude fortuitous equilibration at the malonic anhydride (**3**) or methyleneketene (**2**) intermediates, but any such reaction must be reversible and intramolecular,[6] and would generate species at least as likely to lie on the reaction co-ordinate to pyrrolone, as to revert to starting materials.

undergo electrocyclic ring closure to the same face of the dipole (and therefore give retention of configuration), regardless of the direction of rotation about the newly formed single bond. However, the dipole will be most stable in its planar form (**17**), and rotation about the new single bond to give ring closure will now generate both enantiomers, depending on the direction of the rotation. The observed, partial, retention of configuration in the acyclic case (Scheme 5) suggests that rotation to give ring closure occurs faster than the dipole can achieve planarity. However, in the cyclic examples from compounds (**6**) and (**7**) where complete racemisation is found, the initially formed dipole has a much less pronounced spiral due to the geometric constraints of the ring. The completely planar dipole [*cf.* (**17**)] is therefore more readily formed, prior to ring closure, and hence results in complete racemisation. It should also be noted that the 1,3-dipolar mechanism is consistent with the marked preference for reaction at benzylic sites,[1] since the dipole [*e.g.* (**17**)] is clearly stabilised by delocalisation into the aromatic ring.

Experimental

^{1}H N.m.r. spectra were recorded at 200 or 80 MHz, and ^{13}C n.m.r. spectra were recorded at 50 or 20 MHz, for solutions in [^{2}H]chloroform. Quaternary signals in the ^{13}C n.m.r. spectra are designated '(q)'.

Preparation of Secondary Amines.—The following amines were prepared either by alkylation of a primary amine (Method 1), or by imine formation followed by reduction (Method 2), as described in Part 2:[1] di-α-methylbenzylamine (Method 1, 52%), b.p. 125 °C (0.4 Torr) [lit.,[17] 169—171 °C (18 Torr)]; 1-methyltetrahydroisoquinoline (Method 2, 64%), b.p. 228 °C [lit.,[10] 233 °C (745 Torr)]; 1-phenyltetrahydroisoquinoline (Method 2, 95%), m.p. 94—96 °C (lit.,[10] 97 °C); *N*-s-butylcyclohexylamine (Method 2, 75%), b.p. 109—111 °C (lit.,[18] 110.6 °C); *N*-isopropyl-α-methylbenzylamine (Method 2, 61%), b.p. 95 °C (28 Torr) [lit.,[19] 92 °C (20 Torr)]. Both enantiomers of the latter compound were prepared from (+)- and (−)-α-methylbenzylamine, respectively (Method 1, 60 and 65%). Resolution of the tetrahydroisoquinolines was effected by the literature method[10] involving recrystallisation of the tartrate salt from water, to constant m.p. The free base of the 1-phenyl derivative had $[\alpha]_D^{25}$ −47.5 (*c* 2.8 in CCl_4) (lit.,[10] −47.6) and that of the 1-methyl derivative had $[\alpha]_D^{25}$ −83.1 (*c* 0.9 in CCl_4) (lit.,[10] −79.9) [in our hands, the m.p. of the latter tartrate was 124 °C (lit.,[10] 92 °C)]. 2,6-Dimethylpiperidine was characterised as the *Z*-isomer by the m.p. of its hydrochloride salt [m.p. 284—286 °C (lit.,[9] 289—291 °C)]. The hydrochloride of the *E*-isomer has m.p. 240—242 °C.[9]

5-*Methylene*-2,2-*dimethyl*-1,3-*dioxane*-4,6-*diones.*—The following new compounds were prepared by Methods A—D outlined in the previous paper.[1]

5-[1-(2,6-*Dimethylpiperidino*)] *derivative* (**4**) (Method A, 11%), m.p. 101 °C (from cyclohexane) (Found: C, 63.1; H, 8.15; N, 5.25. $C_{14}H_{21}NO_4$ requires C, 62.9; H, 7.85; N, 5.25%); δ_H 7.99 (1 H, s), 4.80 (1 H, m), 3.86 (1 H, m), 1.10—1.81 (6 H, m), 1.55 (6 H, s), 1.35 (3 H, d), and 1.31 (3 H, d) (singlet and doublets clearly superimposed on methylene signals); δ_C 163.74(q), 159.13, 102.29(q), 83.34(q), 62.41, 53.96, 30.44, 29.81, 26.42, 22.14, 20.88, and 12.72; *m/z* 267 (M^+, 4%), 210(22), 209(56), 165(10), 150(20), 137(24), 136(100), and 122(22).

5-N,N-*Bis*(α-*methylbenzyl*)*amino derivative* (**5**) (Method A, 29%), m.p. 206 °C (from ethanol) (Found: C, 72.9; H, 6.5; N, 3.85. $C_{23}H_{25}NO_4$ requires C, 72.8; H, 6.6; N, 3.7%); δ_H 8.36 (1 H, s), 7.32 (6 H, m), 7.15 (2 H, m), 6.5 (2 H, m), 6.42 (1 H, q), 4.67 (1 H, q), 1.86 (3 H, d), 1.70 (3 H, d), and 1.69 (6 H, s); δ_C 163.34(q), 156.93, 138.28(q), 137.34(q), 128.42 (2 peaks superimposed), 128.26 (2 peaks superimposed), 127.94, 126.68, 102.21(q), 84.44(q), 61.43, 57.97, 26.40, 23.06, and 16.45; *m/z* 379 (M^+, <1%), 321(55), 216(100), 172(90), and 105(90).

5-[2-(1-*Methyl*)*tetrahydroisoquinolyl*] *derivative* (**6**) (Method C, 85%) (chiral derivative was prepared by Method C, 88%), m.p. 134—135 °C (from methanol) (Found: C, 67.7; H, 6.3; N, 4.65. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.3; N, 4.65%); δ_H (peaks of minor rotamer given in brackets) 8.35 (8.20) (1 H, s), 7.0—7.35 (7.0—7.35) (4 H, m), 4.88 (6.16) (1 H, q), 4.5—4.6 (3.9—4.0) (2 H, m), 2.9—4.0 (2.9—4.0) (2 H, m), 1.71 (1.71) (6 H, s), and 1.68 (1.70) (3 H, d); δ_C (peaks of minor rotamer given in brackets; quaternary signal missing) 157.84 (157.57), 135.60 (136.59) (q), 132.30 (131.04) (q), 127.27 (128.59), 128.42 (2 peaks superimposed), 126.73 (126.54), 125.77 (126.41), 102.38 (102.45) (q), 83.74 (84.23) (q), 63.85 (56.64), 45.23 (51.41), 28.60 (29.40), 26.37 (2 peaks superimposed), and 23.70 (22.79); *m/z* 301 (M^+, <1%), 275(14), 243(58), 228(25), 184(22), 170(100), and 126(88).

5-[2-(1-*Phenyl*)*tetrahydroisoquinolyl*] *derivative* (**7**) (Method C, 77%), m.p. 221—222 °C (from acetonitrile) (chiral derivative was prepared by Method C, 91%) (Found: C, 73.1; H, 5.85; N, 4.10. $C_{22}H_{21}NO_4$ requires C, 72.7; H, 5.8; N, 3.85%); δ_H (peaks for minor rotamer given in brackets) 8.56 (8.22) (1 H, s), 5.90 (7.69) (1 H, s), 7.0—7.4 (9 H, m), 3.7—4.4 (2 H, m), 2.8—3.3 (2 H, m), and 1.69 (1.58) (6 H, s); δ_C (peaks for minor rotamer given in brackets, some aromatic peaks superimposed and not assigned) 172.88 (q) (second resonance not observed), 158.33 (157.27), 138.65 (140.40) (q), 133.78 (132.35) (q), 133.43 (133.94) (q), 128.83, 128.60, 128.52, 128.44, 128.14, 128.07, 127.64, 127.54, 127.31, 126.89, 126.60, 102.69 (102.74) (q), 84.40, (85.55) (q), 71.70 (63.08), 46.07 (53.18), 29.63 (28.42), and 26.55 (second resonance superimposed); *m/z* 363 (M^+, <1%), 305(36), 277(100), 232(43), and 219(50).

5-(N-*Cyclohexyl*-N-*s-butyl*)*amino derivative* (**8**) (Method A, 34%), m.p. 113—115 °C (from cyclohexane) (Found: C, 65.85; H, 8.7; N, 4.3. $C_{17}H_{27}NO_4$ requires C, 66.0; H, 8.75; N, 4.55%); δ_H (peaks for second rotamer given in brackets) 8.26 (8.13) (1 H, s), 4.60 (3.50) (1 H, m), 4.4 (3.3) (1 H, m), 1.69 (1.68) (6 H, s) (clearly superimposed on methylene signals), and 0.75—2.0 (18 H, m); δ_C (peaks for second rotamer given in brackets) 163.56 (163.28) (q), 157.01 (156.13), 102.14 (second resonance superimposed) (q), 82.94 (83.09) (q), 61.79 (63.70), 58.01 (56.07) (the following 11 CH_2 resonances were not assigned to individual rotamers) 35.61, 33.31, 31.26, 30.90, 30.68, 27.44, 25.70 (two peaks superimposed), 25.40, 25.26, 25.06, 24.64, 26.53 (two peaks superimposed), 17.91 (21.70), and 11.17 (10.87); *m/z* 309 (M^+, 16%), 252(47), 251(100), 222(60), 205(84), and 178(60).

5-[N-*Isopropyl*-N-(α-*methylbenzyl*)]*amino derivative* (**9**) (Method A, 44%) (chiral derivatives were prepared by Method B, 80 and 88%), m.p. 90—91 °C (from cyclohexane) (Found: C, 68.3; H, 7.25; N, 4.3. $C_{18}H_{23}NO_4$ requires C, 68.15; H, 7.25; N, 4.4%); δ_H 8.30 (1 H, s), 7.2—7.4 (5 H, m), 6.23 (1 H, q), 3.57 (1 H, m), 1.77 (3 H, d), 1.74 (6 H, s), 1.33 (3 H, d), and 0.91 (3 H, d); δ_C 163.84(q), 155.91, 137.70(q), 128.56, 128.33, 127.51, 102.49(q), 83.96(q), 61.56, 51.37, 26.57, 24.96, 22.47, and 16.07; *m/z* 317 (M^+, <1%), 259(100), 216(35), 172(47), 154(29), and 148(59).

Preparation of 1H-*Pyrrol*-3(2H)-*ones and Related Fused Derivatives.*—Pyrolyses were carried out as described in Part 2.[1] Diastereoisomers were separated by chromatography on alumina using ethyl acetate–light petroleum (b.p. 40—60 °C) (60:40) as eluant. The Meldrum's acid derivative pyrolysed, together with furnace temperature and inlet temperature are quoted in parentheses. The following derivatives were made.

5,8a-*Dimethyl*-5,6,7,8-*tetrahydroindolizin*-1(8aH)-*ones* (**10**) and (**11**) {5-[1-(2,6-dimethylpiperidino)]methylene, 600 °C, 155 °C}. (Two diastereoisomers were obtained in 52:48 ratio. They were separated by column chromatography and the relative stereochemistry of each determined by n.O.e.

experiments), 5,8a-*cis*-dimethyl (**11**) (23%), m.p. 72—73 °C (from hexane) (Found: C, 72.5; H, 9.3; N, 8.65. $C_{10}H_{15}NO$ requires C, 72.75; H, 9.1; N, 8.5%); δ_H 7.64 (1 H, d), 4.82 (1 H, d), 3.75—4.0 (1 H, m), 1.3—2.0 (6 H, m), 1.19 (3 H, d), and 1.20 (3 H, s); δ_C 206.89(q), 162.70, 93.99, 65.28(q), 53.77, 32.36, 31.80, 21.16, 20.42, and 15.19; *m/z* 165 (M^+, 100%), 150(14), 136(71), and 122(77); 5,8a-*trans*-dimethyl (**10**) (9%), b.p. 136 °C (0.5 Torr) (Found: C, 72.5; H, 9.25; N, 8.55. $C_{10}H_{15}NO$ requires C, 72.75; H, 9.1; N, 8.5%); δ_H 7.76 (1 H, d), 4.99 (1 H, d), 3.3—3.6 (1 H, m), 1.4—2.0 (6 H, m), 1.32 (3 H, d), and 1.20 (3 H, s); δ_C 206.87(q), 156.90, 94.18, 66.35(q), 50.07, 36.59, 32.36, 20.06, 17.84, and 17.60; *m/z* 165 (M^+, 100%), 150(14), 136(71), and 122(77).

1-(α-*Methylbenzyl*)-2-*methyl*-2-*phenyl derivatives* (**12**) {5-[*N*,*N*-(α-methylbenzyl)]aminomethylene, 600 °C, 175—190 °C} (two diastereoisomers were present in 68:32 ratio, and were isolated by column chromatography; available data for the minor isomer is given in brackets [9% (3.5%)], m.p. 114—115 °C (from hexane) (Found: C, 82.25; H, 6.8; N, 5.15. $C_{19}H_{19}NO$ requires C, 82.3; H, 6.85; N, 5.05%); δ_H 8.03 (8.32) (1 H, d), 6.8—7.6 (10 H, m), 5.14 (5.19) (1 H, d), 4.43 (4.35) (1 H, q), 1.79 (1.35) (3 H, s), and 1.61 (1.50) (3 H, d); δ_C (certain aromatic signals superimposed) 204.04 (203.64) (q), 161.82 (161.33), 140.57 (142.71) (q), 136.70 (137.24) (q), 128.35 (128.75), 127.89 (127.87), 127.61 (127.61), 126.63 (125.89), and 126.63 (125.72), 95.53 (94.80), 72.85 (73.31) (q), 54.54 (55.18), 22.07 (23.26), and 20.03 (22.92); *m/z* 277 (M^+, 23%), 174(59), 173(100), 146(41), and 144(59).

10b-*Methyl*-5,6-*dihydropyrrolo*[2,1-a]*isoquinolin*-1(10bH)-*one* (**13**) {5-[2-(1-methyl)tetrahydroisoquinolyl]methylene, 600 °C, 200 °C} (82%), b.p. 164 °C (0.2 Torr) (Found: M^+, 199.0997 $C_{13}H_{13}NO$ requires M^+, 199.0997); δ_H 7.89 (1 H, d), 7.88 (1 H, d), 7.0—7.3 (3 H, m), 5.25 (1 H, d), 3.5—3.8 (2 H, m), 2.8—3.0 (2 H, m), and 1.59 (3 H, s); δ_C 203.11(q), 163.96, 135.67(q), 131.67(q), 128.17, 127.00, 126.63, 126.51, 100.15, 66.92(q), 43.62, 31.18, and 25.42; *m/z* 199 (M^+, 100%), 144(72), 128(33), 115(52), 103(29), and 77(37).

10b-*Phenyl*-5,6-*dihydropyrrolo*[2,1-a]*isoquinolin*-1(10bH)-*one* (**14**) {5-[2-(1-phenyl)tetrahydroisoquinolyl]methylene, 600 °C, 210 °C} (86%), m.p. 162—163 °C (from methanol) (Found: C, 82.4; H, 5.65; N, 5.4. $C_{18}H_{15}NO$ requires C, 82.75; H, 5.75; N, 5.35%); δ_H 8.04 (1 H, d), 7.89—7.95 (1 H, m), 7.0—7.3 (8 H, m), 5.32 (1 H, d), 3.5—3.7 (2 H, m), and 2.85—3.0 (2 H, m); δ_C 202.38(q), 164.93, 140.27(q), 133.45(q), 133.10(q), 128.33, 128.25, 127.96, 127.69, 127.47, 127.28, 126.49, 99.98, 72.66(q), 43.32, and 30.18; *m/z* 261 (M^+, 45%) and 232(100).

1-*s*-*Butyl*-2,2-*pentamethylene derivative* [5-(*N*-cyclohexyl-*N*-s-butyl)aminomethylene, 600 °C, 140 °C] δ_H 7.76 (1 H, d), 4.98 (1 H, d), 3.33 (1 H, m), 1.5—2.5 (15 H, m) (doublet centred at 1.20 clearly superimposed on methylene signals), and 0.88 (3 H, t); 1-*cyclohexyl*-2-*ethyl*-2-*methyl derivative* [5-(*N*-cyclohexyl-*N*-s-butyl)aminomethylene, 600 °C, 140 °C] δ_H 7.94 (1 H, d), 5.06 (1 H, d), 2.75—3.25 (1 H, m), 1.0—2.0 (15 H, m) (singlet at 1.21 clearly superimposed on methylene signals), and 0.63 (3 H, t) (60:40) (products not isolated; assignments by analogy).

1-*Isopropyl*-2-*methyl*-2-*phenyl derivative* (**15**) {5-[*N*-isopropyl-*N*-(α-methylbenzyl]aminomethylene, 600 °C, 170 °C} (55%), m.p. 65—67 °C (from hexane) (Found: C, 78.0; H, 7.65; N, 6.25. $C_{14}H_{17}NO$ requires C, 78.1; H, 7.9; N, 6.5%); δ_H 8.08 (1 H, d), 7.0—7.5 (5 H, m), 5.11 (1 H, d), 3.39 (1 H, m), 1.67 (3 H, s), 1.25 (3 H, d), and 1.10 (3 H, d); δ_C 203.50(q), 160.73, 137.03(q), 128.41, 127.67, 125.98, 94.34, 72.69(q), 46.47, 23.95, 22.92, and 19.78; *m/z* 215 (M^+, 100%), 200(33), 186(33), 172(95), 171(60), 144(50), 130(23), 105(40), 104(53), and 103(80).

Use of Chiral Shift Reagents.—Chiral lanthanide shift reagents[11] were used to determine the enantiomeric excess of 1-isopropyl-2-methyl-2-phenyl-1*H*-pyrrol-3(2*H*)-ones and 10b-substituted 5,6-dihydropyrrolo[2,1-*a*]isoquinolin-1(10b*H*)-ones by ^{1}H n.m.r. spectroscopy. The tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) derivative was found most suitable for the analysis because of the shift of signals to more deshielded positions. The equivalent praseodymium derivative shifted signals to more shielded positions which made the spectra more complex.

All attempts to separate enantiomers of the 2-ethyl-2-methyl pyrrolone derived from compound (**8**) were unsuccessful. The methyl and ethyl groups are apparently not sufficiently different for the signals of the diastereoisomeric complexes to be resolved.

Samples were prepared satisfactorily without the use of a dry box. Best results were obtained using only small quantities of substrate (5—10 mg) since these required less shift reagent to fully resolve the enantiomeric signals. Samples were filtered through Celite to remove insoluble impurities, and to improve the resolution of the spectra. The quantity of reagent required to give base-line separation of peaks varied from sample to sample, possibly because of the presence of insoluble material. Hence, increments of shift reagent (*ca.* 0.10 mol equiv.) were added until the required separation was achieved.

Acknowledgements

We are grateful to the S.E.R.C. for a Research Studentship (to L. C. M.), and to Mr. J. R. A. Millar and Dr. D. Reed for the variable temperature n.m.r. and n.O.e. measurements, respectively.

References

1 Part 2, H. McNab and L. C. Monahan, *J. Chem. Soc., Perkin Trans. 1*, 1988, preceding paper.
2 Preliminary communication, H. McNab and L. C. Monahan, *J. Chem. Soc., Chem. Commun.*, 1987, 138.
3 P. Lorenčak, J. C. Pommelet, J. Chuche, and C. Wentrup, *J. Chem. Soc., Chem. Commun.*, 1986, 369.
4 J. Besida and R. F. C. Brown, *Aust. J. Chem.*, 1982, **35**, 1385, and earlier papers in the series.
5 C. Wentrup, G. Gross, H.-M. Berstermann, and P. Lorenčak, *J. Org. Chem.*, 1985, **50**, 2877.
6 C. L. Hickson, E. M. Keith, J. C. Martin, H. McNab, L. C. Monahan, and M. D. Walkinshaw, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1465.
7 H. McNab and M. E.-A. Murray, *J. Chem. Soc., Perkin Trans. 1*, 1988, 333.
8 C. L. Hickson and H. McNab, *J. Chem. Soc., Perkin Trans. 1*, 1988, 339.
9 R. K. Hill, T. H. Chan, and J. A. Joule, *Tetrahedron*, 1965, **21**, 147.
10 W. M. Whaley and W. H. Hartung, *J. Org. Chem.*, 1949, **14**, 650; W. Leithe, *Monatsh. Chem.*, 1929, **53—54**, 956.
11 G. R. Sullivan, *Top. Stereochem.*, 1978, **10**, 287.
12 A. J. Blake, H. McNab, and L. C. Monahan, unpublished work.
13 For example, U. Kölle, B. Kolb, and A. Mannschreck, *Chem. Ber.*, 1980, **113**, 2545.
14 H. McNab and L. C. Monahan, *J. Chem. Soc., Chem. Commun.*, 1985, 213, and unpublished results.
15 M. Meier and C. Rüchardt, *Tetrahedron Lett.*, 1984, **25**, 3441.
16 *Cf.* H. Dhimane, J. C. Pommelet, J. Chuche, G. Lhommet, M. G. Richaud, and M. Haddad, *Tetrahedron Lett.*, 1985, **26**, 833.
17 M. Busch and L. Leefhelm, *J. Prakt. Chem.*, 1907, **77**, 1.
18 D. G. Norton, V. E. Haury, F. C. Davis, L. J. Mitchell, and S. A. Ballard, *J. Org. Chem.*, 1954, **19**, 1054.
19 M. C. De Leeuw, *Recl. Trav. Chim. Pays-Bas*, 1911, **30**, 239.

Received 23*rd March* 1987; *Paper* 7/516