

Sterically Crowded Five-membered Heterocyclic Systems. Part 3.¹ Unexpected Formation of Stable Flexible Pyrrolidinoxyl Biradicals *via* Nitron Aldol Dimers: a Spectroscopic and Mechanistic Study†

Ryszard B. Nazarski* and Romuald Skowroński

Department of Organic Chemistry, Institute of Chemistry, University of Łódź, Narutowicza 68, 90—136 Łódź, Poland

Addition of methylmagnesium iodide to various substituted cyclic nitrones (**1**) and subsequent aerial oxidation gave new pyrrolidinoxyl radicals (**4**) and the corresponding crystalline biradical species, to which the structure (**5**) was assigned unequivocally from spectroscopic (e.s.r., u.v.-visible, mass, and ¹H and ¹³C n.m.r. spectra) and mechanistic considerations. Base-catalysed self-condensation of the nitrones (**1**), to give the nitron hydroxylamines (**18**), is followed by Grignard addition to give the crowded bis-*N*-hydroxy compounds (**3**); these are then oxidised to the biradicals (**5**). The possibility of intramolecular charge transfer interaction between the two aminoxyl groups of the biradicals (**5**) (in order to explain the observed u.v. absorption at *ca.* 328 nm), and also the dimerisation of 1-pyrroline 1-oxides (particularly those that are sterically crowded), are discussed briefly.

Sterically crowded carbo- and hetero-cyclic systems have received considerable attention in recent years, mostly in connection with their usually difficult, multi-step syntheses and often unique properties.² Of such compounds, stable aminoxyl ‡ free radicals⁴ are of particular interest.

In continuation of our previous work on crowded five-membered rings,^{1,5} we focussed our attention on the synthesis of 2,2,5,5-tetramethylpyrrolidin-1-oxyl radicals (**4**) bearing an alkyl or aryl substituent R¹ at C-3. These compounds, with hydroxylamines (**2**) and amines (**6**), served as model compounds in our studies on the oxidation of pyrrolidine derivatives⁶ and in the conformational analysis of saturated five-membered rings.^{6–8} We now report the somewhat surprising results obtained during the synthesis of compounds (**4b, c**) by addition of methylmagnesium iodide to 1-pyrroline 1-oxides (**1b, c**)§ (see Scheme 1). As expected, Grignard reactions in ethereal solution, followed by aqueous work-up in air, afforded a mixture of dia- and para-magnetic compounds. The proportion of the latter increased with time as monitored by ¹H n.m.r. spectroscopy. However, when the crude products were subjected to Cu^{II}-catalysed aerial oxidation, mixtures of two paramagnetic species (separable by column chromatography) were obtained. These were characterised as the desired monoradicals (**4b, c**) and the corresponding solid biradicals (e.s.r., u.v., and mass spectral evidence) C₁₇H₃₂N₂O₂ (**5b**) and C₂₇H₃₆N₂O₂ (**5c**), which had much lower *R_F* values. Biradicals of this type have not previously been prepared in this way.

These results led us to consider the processes affording the title biradicals (**5**) and their air-sensitive *N*-hydroxy precursors (**3**).

Results and Discussion

Synthesis of the Radicals (4).—The 2,2,5,5-tetramethylpyrrolidin-1-oxyl radicals (**4**) may, in principle, be prepared by oxidation of the amine (**6**) or the hydroxylamine (**2**); both methods have been described for the preparation of the parent radical (**4a**).⁹ As the pyrrolidines (**6b, c**) were not available [though they can be obtained¹⁰ from (**2b, c**)], the general nitron method developed by Keana¹¹ was employed to obtain the C-3-substituted radicals (**4b, c**).

The reaction of an organometallic reagent with a nitron to afford the *N*-hydroxy compound can be performed either by addition of a solution of the former reactant to a solution of the nitron (method A) or by the inverse procedure (method B); both methods have been reported in the literature. In the case of sterically crowded nitrones of type (**1**), Lunt reported¹² that the addition of methylmagnesium iodide by method B is the most useful route (52% yield) to the hydroxylamine (**2a**). It was found that addition of methyl-lithium instead of a Grignard reagent, and also use of method A, gave lower yields of the product. It was therefore expected that the desired radicals (**4b, c**) should be formed in respectable yields by addition of methylmagnesium iodide to the nitrones (**1b, c**) by method B, followed by Cu^{II}-catalysed aerial oxidation¹³ of the *N*-hydroxy intermediates (**2b, c**) (not isolated).

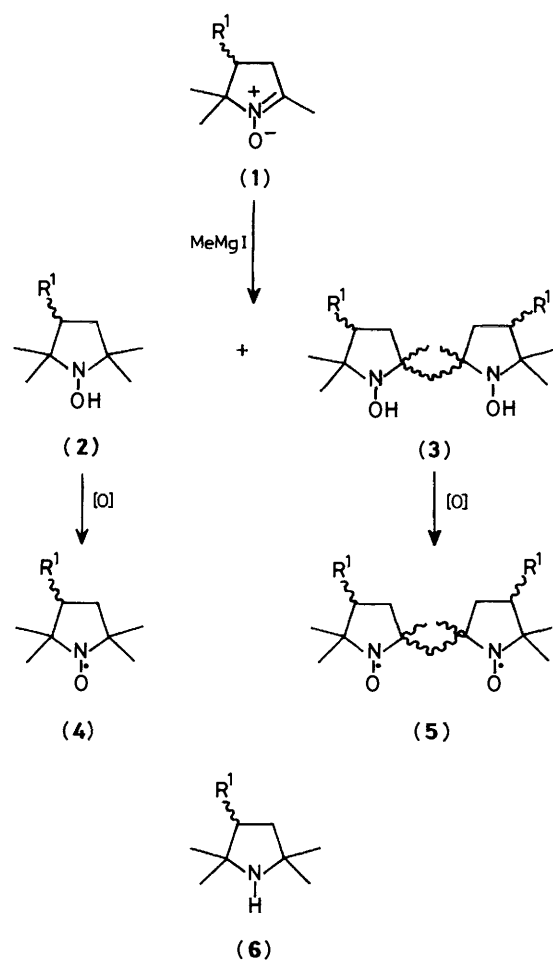
Initially¹⁴ we investigated the synthesis of the pure hydroxylamine (**2a**) by a slight alteration to the literature procedure.¹² Distillation of the crude product afforded, in contrast to Lunt's report, a deep red-orange low-boiling fraction [a mixture of the desired compound (**2a**) and radical (**4a**)] and coloured high-boiling fractions. Aerial oxidation of the former material and subsequent purification of the product gave pure 2,2,5,5-tetramethylpyrrolidin-1-oxyl radical (**4a**) (crystalline below 286–287 K), which was subjected to spectroscopic analysis including a ¹H n.m.r. study at 250 MHz.¹⁴

It was observed that the facile oxidation of the hydroxylamines (**2a–c**) to the corresponding radicals (**4a–c**) in the presence of atmospheric oxygen is particularly rapid in basic media such as the ethereal solutions obtained on work-up after Grignard addition. This explains to some extent the earlier observation¹² that 1-hydroxypyrrolidines are generally rather unstable. Similar facile oxidation of *N*-hydroxy compounds has

† Presented in preliminary form at the Deuxième Colloque Franco-Polonais 'Les Composés Hétérocycliques Azotés', Łódź, Sept. 1–3, 1982, pp. 8–9.

‡ The term 'aminoxyl' was introduced and was deemed more appropriate than 'nitroxyl' or 'nitroxide'.³

§ This name is used for convenience only, since the compounds are systematically named as 3,4-dihydro-2*H*-pyrrole 1-oxides.



a, $R^1 = H$; b, $R^1 = Me$; c, $R^1 = Ph$

Scheme 1.

been reported¹⁵ in the case of the 2,2,4,4-tetramethyl-1,3-imidazolidine system.

Synthesis of the 3-substituted radicals (**4b, c**) by the procedure used to obtain (**4a**) led also to formation of considerable amounts of the stable biradical compounds (**I**) and (**II**) with molecular weights near to double those of the corresponding monoradicals. These biradicals presumably result from oxidation of the corresponding crowded bishydroxylamines, dimeric in comparison with compounds (**2**).

Structure of the Biradicals (I) and (II).—Unambiguous elucidation of the structure of compounds (**I**; $R^1 = Me$) and (**II**; $R^1 = Ph$) appeared to be a complicated problem.

The e.s.r. spectra of the monoradicals (**4b, c**) in dilute pentane solution exhibit a typical 1:1:1 triplet (peak-to-peak line width $\Delta B = 0.15$ and 0.09 mT, respectively) due to the contact hyperfine interaction between an unpaired electron spin ($S = 1/2$) and ^{14}N nuclear spin ($I = 1$). The spectra of compounds (**I**) and (**II**), recorded under similar conditions, are much more complicated ($\Delta B = 2.92$ and 2.95 mT, $g = 2.0071$ and 2.0065 respectively), displaying broad lines with poorly resolved hyperfine structure (see Figure): both compounds can therefore be assigned unequivocally as biradicals.

More detailed analysis demonstrated that the e.s.r. spectra of (**I**) and (**II**) were dissimilar to those of other known stable pyrrolidinoxyl biradicals (**7**);^{16,17} the spectrum of compound

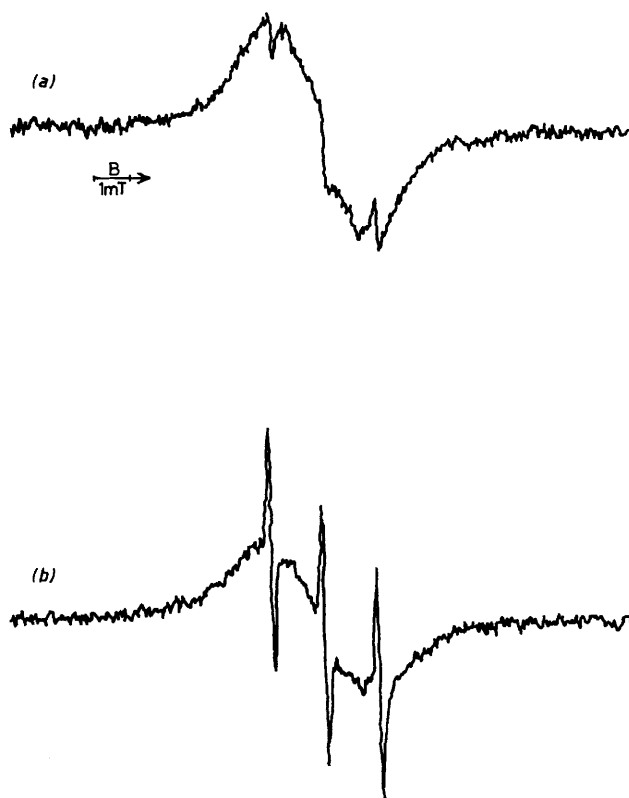
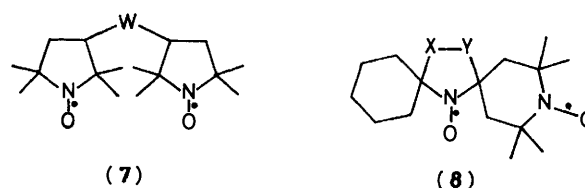
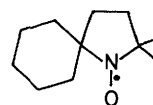


Figure. (a) First derivative e.s.r. spectrum of the biradical (**5b**) in pentane (3.0×10^{-5} mol dm^{-3}). (b) First derivative e.s.r. spectrum of the biradical (**5c**) in pentane (3.4×10^{-5} mol dm^{-3}).



a W = =N=N=
b W = -CO-O-CO-

a X-Y = -O-CH₂-
b X-Y = -NH-CO-



(9)

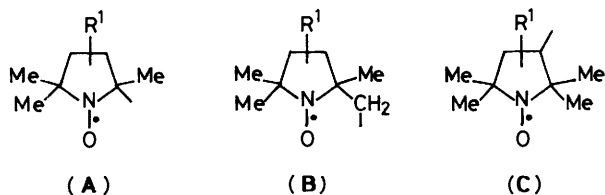
(**7a**)^{16a} showed a well-resolved 1:2:3:2:1 quintet characteristic of systems with a large scalar electron-electron exchange interaction, $|J| \gg |a_N|$. However, the e.s.r. spectrum of compound (**I**) resembled the single broad line spectrum of the biradical (**8a**)¹⁸ ($\Delta B \approx 2.6$ mT in 10^{-3} mol dm^{-3} solution) while the spectrum of compound (**II**) was very similar in appearance to the spectrum of the biradical (**8b**)¹⁹ ($\Delta B \approx 2.8$ mT in 10^{-3} mol dm^{-3} benzene solution).

In biradical aminoxy systems the intramolecular interactions increase with decreasing distance between the radical centres, and this is reflected in their e.s.r. features.^{16b} The spectra of the biradicals (**I**) and (**II**) indicate that the interactions between both radical units are much stronger than in compounds (**7**), and comparable with those in compounds (**8**); this implies that

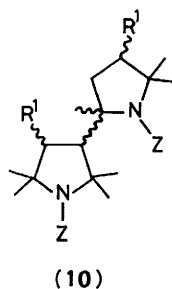
in compounds (I) and (II) the paramagnetic centres are separated by three carbon atoms. Moreover, the Landé g -factor values agree (within experimental error) with the values $g = 2.0068$ observed for the monoradicals (4b, c) and $g = 2.0070$ for radical (9)²⁰ of similar structure; this suggests that compounds (I) and (II) each contain two pyrrolidinoxyl units.

The u.v. spectra confirmed the biradical nature of (I) and (II) [λ_{\max} . 234–235 nm, $\epsilon = 4620$ and $5270 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ respectively; about twice that of the monoradicals (4b, c)], and also indicate that they contain two fragments similar to the monoradical unit [λ_{\max} . 208 nm, $\epsilon = 11950$ and $23900 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for (4c) and (II) respectively].

Electron impact (e.i.) mass spectroscopy showed that the molecular masses M_b of biradicals (I) and (II) obeyed the $M_b = (2 \times M_m - 16)$ relation, where M_m is the molecular weight of the corresponding monoradical (4). A particularly intense peak assigned to the fragment $[M_m + 1 - 15]^+$ was observed in both cases (m/z 142 and 204), with less intense peaks for $[M_m - 15]^+$ and M_m^+ [m/z 141 and 218 for (I) and (II) respectively]. In view of the great stability of the biradicals, these observations indicate the presence of fragments (A) and (B) [or (C)] in the molecules, in agreement with the conclusions which were drawn from the e.s.r. and u.v. spectra.



From the above data, and from mechanistic considerations (see below), two structures for the biradical systems were considered possible; the symmetrical formula (5) and the unsymmetrical formula (10b).



a; Z = OH

b; Z = O[•]

The i.r. spectra (KBr) of compounds (I) and (II) were similar to those of the monoradicals (4b, c), differing only in the presence of appreciable peaks in the region $1360\text{--}1375 \text{ cm}^{-1}$ (ν_{Me} and $\nu_{\text{N}=\text{O}^{21}}$); the number of these bands is greater for biradical species. However, it was not possible to assign structure (5) or (10b) to the biradicals from the i.r. spectra.

Analysis of ¹H and ¹³C n.m.r. spectra of the corresponding bishydroxylamines [derived from biradicals (I) and (II) by *in situ* reduction with an excess of 1,2-diphenylhydrazine²²] indicated that (I) and (II) possessed structure (5). The 80 MHz ¹H n.m.r. spectrum of each compound displayed signals corresponding to three methylene units; compound (3c) displayed two singlets at 7.25 and 7.28 p.p.m. due to two phenyl groups (*throughout, italicized* δ_{H} values refer to the minor peaks).

The structure of the hydroxylamine (3b) was determined unambiguously by ¹³C n.m.r. spectroscopy. The ¹H noise band decoupled (NBD) spectrum was compatible with a mixture of two stereoisomers of this compound; in particular five methylene group singlets [triplets with ¹H single-frequency, off-resonance decoupling (SFORD) procedure] appeared at δ 45.7, 45.9, 48.3, 51.7, and 54.4 p.p.m. The first three signals probably correspond to the ring methylene groups [*cf.* δ 44.6 p.p.m. in the monohydroxylamine (2a)], and the two downfield ones to the methylene bridge groups. The great abundance of the signals in this region ruled out the unsymmetrical formula (10a).

An independent single-crystal X-ray diffraction study²³ on the biradical (I) confirmed the structural analysis given above, and showed the presence of two geometrical isomers of structure (5b). Further details of this study will be given elsewhere.

Spectroscopic Analysis: General Remarks.—With knowledge of the structure of the biradicals, the following points should be noted concerning the spectroscopic investigations:

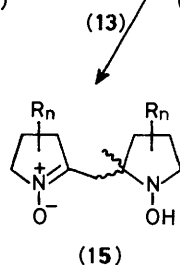
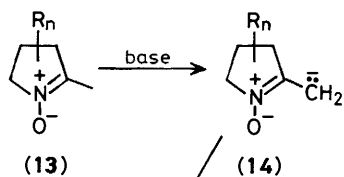
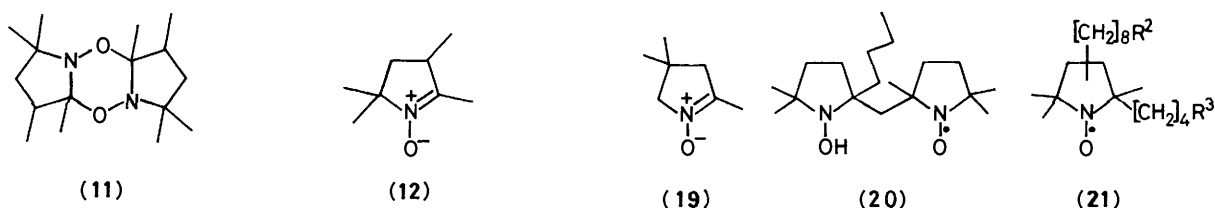
(i) The u.v.-visible spectra of flexible biradicals (5b, c) show an appreciable absorption band at *ca.* 318 nm with $250 < \epsilon_{\max} < 275$ ($\lambda_{\max} \approx 328 \text{ nm}$, $\epsilon_{\max} \approx 110 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$, after graphical separation). As far as we are aware, there is no information about this band in the published work concerning aminoxyl biradicals. This band has a shoulder on the high wavelength side due to overlap with a weak band at *ca.* 424 nm. An interesting feature of this absorption, with a maximum at *ca.* 328 nm, is probably due to the intramolecular contact charge-transfer (c.t.) interaction between the radical centres, but further investigation is necessary to explain this problem.

In the case of the aminoxyl monoradicals, additional absorption in the region 310–450 nm has been attributed to a weak electron donor-acceptor (e.d.a.) complex between the radical and carbon tetrachloride (or iodine).²⁴ It should be emphasised that the weak absorption band in the visible 410–450 nm region ($n \rightarrow \pi^*$ transition) is commonly regarded^{4b} as characteristic of both aminoxyl mono- and bi-radicals: indeed, it is easily observed for the rigid biradical (8a) ($\lambda_{\max} = 420 \text{ nm}$, $\epsilon_{\max} = 15.4 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ in MeOH).¹⁸

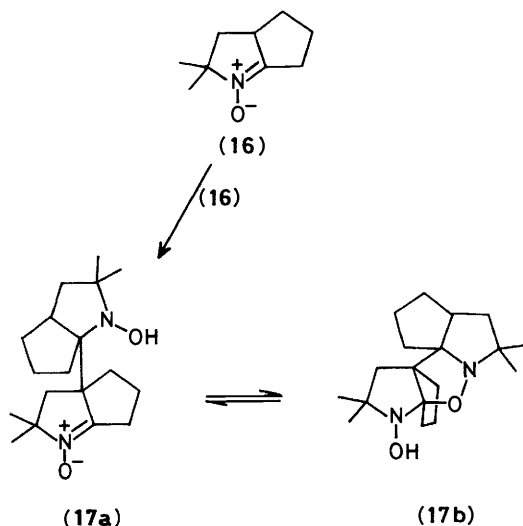
(ii) Peaks corresponding to the cation radicals $[M + 1]^+$ (16 and 58% of the molecular ion) and also of cations $[M + 2]^+$ (5 and 29%), can be readily observed in the e.i. mass spectra of the biradicals (5b and c) respectively, along with the molecular ion peaks M^+ . The peaks at $[M + 2]^+$ confirm the presence of two aminoxyl groups in the compounds discussed. It is interesting to note that some biradicals²⁵ show no $[M + 1]^+$ peak, though this is characteristic of aminoxyl monoradicals.²⁶

(iii) Small differences between the e.s.r. spectra of biradicals (5b) and (5c) (Figure), *i.e.* the presence of three additional narrow lines separated by 1.39 mT in the spectrum of the latter, can be explained by the altered conformational distribution due to the change of the R¹ substituent and the resulting difference of relative motion of the two spin densities.²⁷ In fact, the extra three peaks in the spectrum of (5c) disappeared at lower temperature (*ca.* 245 K) unlike the analogous lines for the triplet of the corresponding monoradical (4c).⁷ Further e.s.r. studies are currently underway in this laboratory.

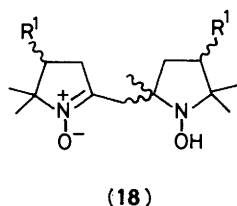
Formation of Pyrrolidinoxyl Biradicals via Dimers of 1-Pyrroline 1-Oxides.—During the 1,3-addition of organometallic reagents to cyclic five-membered nitrones the formation of by-products of unknown structure were sometimes observed.^{11,12,28} It was thought likely that these products were nitrene dimers¹² or higher molecular-weight aminoxyl radicals formed presumably *via* self-condensation of the nitrene.²⁸ For



Scheme 2.



Scheme 3.



example, Lunt¹² tentatively proposed the tricyclic structure (11) for the high-boiling product which had been characterised as a dimer of the nitronium (12).

It is well-documented that under certain conditions (particularly in basic media) some aliphatic nitronium ions dimerise slowly to derivatives of 1,2-oxazolidine. It is thought that this reaction can proceed either by a one-step 1,3-dipolar addition of the nitronium to the corresponding *N*-hydroxy enamine tautomer or by a two-step mechanism through the aldol-dimer intermediate.²⁹ Cyclic five-membered nitronium ions behave specifically,

because they easily condense in an aldol-type process in which the trigonal carbon atom of the nitronium group acts as the electrophilic centre. The self-condensation of 1-pyrroline 1-oxide derivatives containing an activated methyl group at C-2, *i.e.* the so-called 2-methyl nitronium ions [*e.g.* (13)], is thought to occur by nucleophilic attack of the primary carbanion [*e.g.* (14)] to give the nitronium hydroxylamine (aldol dimer) (15) as shown in Scheme 2.^{11,30}

However, Black and Johnstone recently found³¹ that the bicyclic compound (16) dimerises to a crystalline product (17b), which in solution is in equilibrium with the nitronium hydroxylamine (17a) (Scheme 3). If structure (17) and our proposed two-step mechanism for the dimerisation (as in Scheme 3) are correct, it is apparent that the oxide (16) does not behave in a way expected for 2-substituted nitronium ions (*i.e.* with participation of the methylene group of the cyclopentane moiety) but instead employs the 3-position of the pyrroline ring.

In the light of these results we conclude that the course of 1-pyrroline 1-oxide dimerisation is governed by the stability of corresponding carbanions and/or by the steric crowding present in the system, particularly in the environment of the nitronium group.

Returning to the title biradicals (I) and (II), consideration of their spectroscopic data (discussed above) makes it apparent that they were formed by oxidation of the corresponding bis-hydroxylamines (3) or (10a); these latter compounds are formed by simultaneous [with regard to the reaction (1) → (2)] 1,3-addition of methylmagnesium iodide to the corresponding nitronium hydroxylamine, which arises from strong base-catalyzed (MeMgI) self-condensation of the starting nitronium ions (1b, c). As considerable steric crowding characterises the 1-pyrroline 1-oxides (1), it was necessary to consider two possible origins of the dimeric compounds; (i) formation of the nitronium hydroxylamines (18) and then the symmetrical species (3) and (ii) an analogous reaction employing the 3-position of the ring rather than the 2-methyl group, leading to the corresponding unsymmetrical compound (10a).³² The latter process is normally less likely for 2-methyl nitronium ions, though it occurs in the case of the oxide (16).

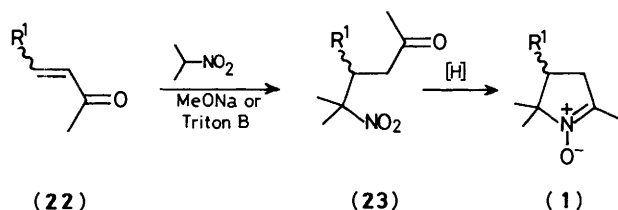
The discriminating n.m.r. study of the bis-*N*-hydroxy compounds derived from biradicals (I) and (II) allows us to assign unambiguously the symmetrical formulae (3) and (5) to the dimeric species; these were present as a mixture of stereoisomers, which is compatible with the former investigations^{30b} concerning the compounds (15). This supports the proposed reaction pathway (1) → (18) → (5) as well as the formation of the nitronium hydroxylamine of type (18) for 2-methyl nitronium ions crowded at C-4 and C-5. Moreover, the present results demonstrate that the indirect structural analysis^{30c} carried out previously [based on ¹H n.m.r. study of the dimer of nitronium (19)] was correct. Conclusions similar to our results were drawn also by Keana;^{*} however, he tentatively assigned to the by-product, obtained from the nitronium (1a) in the presence of butyl-lithium, formula (20), intermediate between structures of type (3) and the more likely (5). This is difficult to accept

* A cautionary note, ref. 11, p. 137.

Table. Selected physical data of compounds (1) and (23)

Compound	Yield (%)	B.p. (K/kPa)	n_D^{20} ³	M.p. (K)	$\nu_{\max.}/\text{cm}^{-1}$	δ gem-Me (p.p.m.) ^a
(1a)	77	330—332/0.020 ^b	1.4893	ca. 294 ^c	1 232 1 611	1.40
(1b)	68	328/0.019 ^b	1.4864	ca. 291 ^d	1 240 1 598	1.19 1.38
(1c) ^e	75			353.5—357 ^{c,f,g}	1 203 ^h 1 617 ^h	0.96 1.52
(23a)	68	389.5—390.5/1.65 ⁱ	1.4450		1 535 1 720	1.57
(23b)	88	342/0.010 ⁱ	1.4518	ca. 288 ^c	1 537 1 718	1.53
(23c)	64			336—336.5 ^{c,j}	1 534 1 722	1.48 1.55

^a ¹H N.m.r. (60 MHz, CDCl₃/SiMe₄). ^b Colourless oil. ^c Needles. ^d Crystals. ^e Hydrate form (water of crystallisation). ^f From Et₂O-Pr₂O. ^g This material was used for the next step without further purification. ^h Additional sharp bands appear at 1 228 (ms) and 1 641 (m) cm⁻¹. ⁱ Pale yellow liquid. ^j From Pr₂O.



a, R¹ = H; b, R¹ = Me; c, R¹ = Ph

Scheme 4.

because of the great instability of the α -tetra-alkyl substituted 1-hydroxypyrrolidines (see above).

Summary and Conclusions.—Experiments described above afforded two members of a new class of stable flexible diaminoxyls (5) in which the paramagnetic centres are separated from each other by only three carbon atoms. These biradicals can be used directly as flexible diaminoxyl spin probes in the structural analysis of macrosystems. Presumably the corresponding nitronium hydroxylamines (18) would be useful starting materials for the synthesis of the title compounds, though the process described here could probably be optimised. Obviously these compounds, like other biradicals, offer the possibility of synthesizing *in situ* monoaminoxyl spin probes through chemical reduction of one of the two radical functions.

The method described here could possibly be used for the synthesis of other biradicals, containing more reactive R¹ groups, which may find future application as bifunctional flexible diaminoxyl spin label molecules. Such double labelling of macromolecular systems is not possible in the case of known pyrrolidine biradicals (7). Biradicals (5), and their easily oxidised bishydroxylamine counterparts (3), are potential starting materials for the synthesis of multisubstituted derivatives of dipyrrolidin-2-ylmethane.

The presence of two paramagnetic centres in (5) suggests new applications in entirely different domains. Indeed, the abnormal absorption in the u.v. spectrum of the biradical (5b) was used with success in photochemical studies³³ as well as in photoacoustics investigations concerning the measurement of heat formed during laser impulse absorption.³⁴

The present work throws some light on the formation of dimers of 1-pyrroline 1-oxides (in particular 2-methylnitrones). In the case of sterically crowded systems (1b, c) the rate of dimerisation in the presence of methylmagnesium is at least equal to the rate of 1,3-addition to the nitronium group. It is likely that the corresponding nitronium dimers are formed during other additions of organometallic reagents to 1-pyrroline 1-oxides, which could explain the poor yields obtained in the syntheses of (2a) (this work) and radicals (21).³⁵ The outcome of the reaction is most probably affected by steric crowding in the starting

components (*i.e.* the nitronium and/or the organometallic reagent), addition sequence of the reagents (method A or B), and the reaction temperature; the great influence of the latter has been encountered previously.³⁶

Experimental

Materials.—1-Pyrroline 1-oxides (1) were prepared as described in the literature^{13,37,38} (Scheme 4). Some physical properties of these compounds and of the intermediates (23) are listed in the Table. Commercial ketones (22b and c) (Aldrich or Fluka) were fractionally distilled or recrystallised, respectively, before use. But-3-en-2-one (22a) and benzyltrimethylammonium hydroxide (Triton B, 40% w/w solution in MeOH) (both Fluka) were used as received. 2-Nitropropane (Fluka) was purified by the method of Shechter *et al.*³⁹

The support for column chromatography was a Woelm neutral alumina. Solvents were purified by drying and distilling in the usual way. Analytical grade MeOH was refluxed for some hours with Mg(OMe)₂, distilled, and stored over Linde-type molecular sieve 3A. Pure diethyl ether, dried over Na wire and separated by decanting, was refluxed for some hours with LiAlH₄ and then distilled off as required immediately before use. All organic solutions (extracts) were dried over anhydrous MgSO₄.

M.p.s were determined in open glass capillaries on an electrically heated block apparatus. All m.p.s and b.p.s are uncorrected. Elemental analyses were performed by the Micro-analytical Laboratory, operating at the Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Łódź.

Spectroscopic Measurements.—The ¹H n.m.r. spectra of diamagnetic compounds were obtained in the FT mode with a Bruker AC 200 spectrometer (200.132 MHz), or in the CW mode with a Bruker WP-80 (80.018 MHz) or Varian EM-360 (60.00 MHz) spectrometer. The ¹³C n.m.r. spectra obtained with ¹H NBD and ¹H SFORD procedures were measured on a Varian XL 100 or CFT-20 spectrometer operating in the pulsed FT mode at 25.16 or 20.00 MHz, using a 5-mm o.d. spinning tube and an internal ²H lock. The samples of all non-diamagnetic compounds examined were dissolved in deuteriochloroform containing tetramethylsilane as internal reference, and excess of 1,2-diphenylhydrazine as reducing agent²² (see text). The ¹H n.m.r. spectrum of radical (4a) was obtained at 250.01 MHz for the neat liquid or deuteriochloroform solution, with benzene or tetramethylsilane as internal standard, in the CW (or FT) mode using a Cameca 250 spectrometer.

The e.s.r. spectra were recorded [for (3.0—6.4) × 10⁻⁵ mol dm⁻³ solutions in pentane or 2-methylbutane] at ambient probe temperature (\approx 275 K) unless otherwise indicated, on an X-band JEOL JES-ME-3X spectrometer ($\nu_0 \approx$ 9.2 GHz, B₀ \approx 0.33 T) employing 100 kHz field modulation, and

equipped with a JEOL JES-VT-3 variable-temperature controller. Samples were made up in quartz tubes (4 mm o.d., 3 mm i.d.), and carefully degassed on a vacuum line (< 1 mPa) by means of repeated freeze (liquid nitrogen)-pump-thaw cycles. Hyperfine splitting constants a_N and g -factors were computed from the measured microwave frequency and line positions. a_N -Values given refer to one-half of the measured splitting of the external lines of the triplet [*i.e.* between the low ($M = 1$) and high field ($M = -1$) nitrogen line, respectively] on a chart calibrated with a pen-coupled proton resonance magnetometer type MJ 100 Aut. Maximum experimental errors in this work are estimated to be ± 0.005 mT for a_N and ± 0.0005 for g -values.

Electronic (u.v.-visible) absorption spectra were taken on a Unicam SP-700 double beam spectrophotometer with methanol as solvent.

The i.r. spectra for neat films of liquids (between NaCl plates) or KBr discs of solids were recorded on a Perkin-Elmer model 325 grating spectrometer. Frequencies are generally accurate to within ± 1 cm^{-1} ; only significant bands are quoted.

The e.i. mass spectra were determined on a LKB type GCMS-2091 instrument (ionisation at 70 eV, ion source temperatures of 480–520 K). Samples were all sufficiently volatile to be introduced into the ion source through a direct insertion probe. The spectrometer output was digitised by an auxiliary DEC PDP-11 data processing system. All peak intensities were calculated in relation to the base peaks.

2,2,5,5-Tetramethylpyrrolidin-1-oxyl (4a).—A solution of freshly distilled nitron (1a) (34.5 g, 0.271 mol) in Et_2O (85 ml) was added dropwise to a stirred solution of methylmagnesium iodide [prepared from freshly distilled methyl iodide (46.9 g, 0.330 mol) and magnesium (7.29 g, 0.300 mol)] in Et_2O (175 ml) at a rate sufficient to maintain gentle reflux (*ca.* 1 h). On completion of addition, the mixture was stirred and refluxed for a further 22 h and then poured into cold saturated aqueous NH_4Cl (200 ml). The ether layer was separated and the aqueous layer extracted with Et_2O . The combined ether extracts were washed with saturated brine, dried, filtered, and then concentrated at atmospheric pressure by evaporation through a 12-cm vacuum-jacketed Vigreux column. Distillation of the residue, a dark red-violet oil, gave a deep red-orange low-boiling fraction {16.6 g, 42.7% with respect to (2a), b.p. 340–341.5 K at 1.95 kPa, n_D^{298} 1.4466; a mixture (t.l.c., e.s.r.) of compounds (2a) and (4a) [lit.,¹³ (2a) b.p. 351–353 K at 2.67 kPa]} and yellow-red high-boiling fractions which were not investigated.

A sample (4.4 g) of the lower-boiling fraction was taken up in MeOH (45 ml) and stirred vigorously with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (0.25 g) in air until a permanent deep blue colouration developed (45 min). The solution was kept overnight after which it was filtered and the solvent removed using a rotatory evaporator at room temperature to afford radical (4a) [4.15 g, 40.6% based on the starting nitron (1a)]. The crude product was purified by column chromatography on activity II alumina, with light petroleum (b.p. 360 ± 5 K) as eluant, to give a red-orange oil which solidified on storage in a refrigerator. Prolonged spontaneous sublimation of this solid at *ca.* 265 K within its container afforded the analytical specimen as golden-yellow crystals, m.p. 286–287 K (lit.,^{9b,40} m.p. 277 K); n_D^{298} 1.4400; e.s.r. (6.0×10^{-5} mol dm^{-3} in 2-methylbutane), triplet, $a_N = 1.375$ mT [lit.,⁴¹ $a_N = 1.35$ mT (cyclohexane); lit.,⁴² $a_N = 1.402$ mT (dodecane)]; δ_H (250 MHz; CDCl_3) –10.55 (12 H, br s, 4 \times Me) and –6.67 (4 H, br s, 2 \times CH_2); δ_H (250 MHz; neat liquid) –12.02 (12 H, br s, 4 \times Me) and –5.27 (4 H, br s, 2 \times CH_2); δ_H (80 MHz; after 1,2-diphenylhydrazine reduction) 1.17 (12 H, s, 4 \times Me) and 1.59 (4 H, s, 2 \times CH_2).

2,2,3,5,5-Pentamethylpyrrolidin-1-oxyl (4b) and 2,2'-Methylenebis(2,4,5,5-tetramethylpyrrolidin-1-oxyl) (5b).—To methylmagnesium iodide in Et_2O (155 ml, *ca.* 1.5 mol dm^{-3}) [from methyl iodide (35.5 g, 0.250 mol) and magnesium (6.0 g, 0.247 mol)] was added with stirring freshly distilled nitron (1b) (32.0 g, 0.227 mol) in Et_2O (100 ml) at a rate sufficient to maintain gentle reflux. The solution was stirred and refluxed for additional 3.5 h then kept at room temperature overnight. Saturated aqueous NH_4Cl was added after which, the orange-brown organic layer was separated, combined with ether washings of the aqueous residue, and dried. Removal of the solvent *in vacuo* afforded a mixture (t.l.c., ^1H n.m.r.) of compounds (2b), (3b), (4b), and (5b) as a red-brown oil (23.5 g).

The mixture was immediately taken up in MeOH (290 ml) and concentrated aqueous NH_4OH (15 ml), stirred vigorously with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (2 g) in air for 5 h, and then left overnight. Evaporation under reduced pressure gave the aqueous residue to which water (100 ml) was added. This solution was thoroughly extracted with Et_2O , and the combined extracts were dried and evaporated under reduced pressure to give a red oil (21.0 g). Column chromatography of this material on activity I alumina gave 16.75 g [48.4% based on the initial nitron (1b)] of paramagnetic species: (i) the monoradical (4b) (9.55 g, 27.0%) [eluted first with light petroleum (b.p. 316 ± 3 K)] as an orange-red oil, n_D^{296} 1.4450–1.4455 (from the two runs) (Found: C, 69.5; H, 11.5; N, 8.8. $\text{C}_9\text{H}_{18}\text{NO}$ requires C, 69.2; H, 11.6; N, 9.0%); e.s.r. (6.1×10^{-5} mol dm^{-3} in pentane) triplet, $a_N = 1.400$ mT, $g = 2.0068$; λ_{max} , 235 (ϵ 2 620 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$) and 411 nm (6.4); δ_H (200 MHz, after reduction) *ca.* 0.85 (3 H, d, J 6.5 Hz, 3-Me), 0.91 and 1.12 (each 3 H, s, Me), 1.17 (6 H, s, 2 \times Me), 1.25–1.5 (1 H, m, 4-H), and 1.6–1.9 (2 H, m, 4-H and 3-H); δ_C (25.2 MHz, after reduction) 14.2, 16.4, 26.0, 26.25, and 29.2 (off res., 5 \times q, 5 \times Me), 37.4 (d, C-3), 44.6 (t, C-4), 62.45 (s, C-5), and 67.7 (s, C-2); m/z 157 [$(M + 1)^+$, 3.45%], 156 (M^+ , 20), 142 [$(M + 1 - 15)^+$, 4.5], 141 [$(M - 15)^+$, 11], 126 [$(M - 30)^+$, 11], 83 (26), 74 (27.5), 70 (100), 69 (27), 55 (61), 42 (30), 41 (60), and 39 (27); and (ii) the biradical (5b) (7.2 g, 21.4%) (eluted second with Et_2O) as a viscous, orange-red oil, n_D^{296} 1.4840–1.4850 (from the two runs), which slowly solidified at room temperature. Three recrystallisations from light petroleum afforded the analytical sample as orange-red crystals m.p. 351–352.5 K (Found: C, 68.7; H, 10.5; N, 9.2. $\text{C}_{17}\text{H}_{32}\text{N}_2\text{O}_2$ requires C, 68.9; H, 10.9; N, 9.45%); e.s.r. (3.0×10^{-5} mol dm^{-3} in pentane) a broad line spectrum [see Figure (a) and text] $g = 2.0071$; λ_{max} , 236 (ϵ 4 610 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$), 319 (250), and *ca.* 423 sh* nm (*ca.* 5*) (see text); δ_H (80 MHz, after reduction) 0.7–0.9 (~9 H, m, Me), 1.03–1.35 (~15 H, 6 \times s, Me), and 1.4–2.2 (8 H, m, 3-H, 4-H, and bridgehead CH_2); δ_C (20.0 MHz, after reduction) 13.7, 14.0, 14.8, 15.5, 15.8, 23.1, 24.5, 24.75, 26.4, 26.7, and 27.9 (off res., 11 \times q, 11 \times Me), 37.9, 38.1, and 39.5 (3 \times d, CHMe), 45.7, 45.9, 48.3, 51.7, and 54.4 (5 \times t, CH_2), and 64.8, 66.5, 66.7, 67.25, 68.0, and 69.3 (6 \times s, C-2 and C-5); m/z 298 [$(M + 2)^+$, 0.35%], 297 [$(M + 1)^+$, 1.1], 296 (M^+ , 6.9), 282 [$(M + 1 - 15)^+$, 0.4], 281 [$(M - 15)^+$, 0.95], 267 [$(M + 1 - 30)^+$, 2.65], 266 [$(M - 30)^+$, 11.5], 142 (64), 141 (18), 126 (27), 124 (26), 83 (37), 70 (39), 69 (40), 55 (96), 43 (34), 42 (33), 41 (100), 39 (24), and 29 (23). An X-ray crystallographic analysis confirmed the structure assigned to compound (5b) (see text).

2,2,5,5-Tetramethyl-3-phenylpyrrolidin-1-oxyl (4c) and 2,2'-Methylenebis(2,5,5-trimethyl-4-phenylpyrrolidin-1-oxyl) (5c).—The procedure given above for (4b) and (5b) was followed. A warm solution of the anhydrous nitron (1c) [48.0 g, 0.236 mol; derived immediately before use from the corresponding nitron hydrate (m.p. 353.5–357 K) by azeotropic dehydration with benzene using a Dean-Stark separator] in anhydrous benzene– Et_2O (13:10, 230 ml), on treatment with methylmagnesium

* From graphical bands separation.

iodide δ in Et₂O (ca. 1.5 mol dm⁻³; 155 ml; gave a mixture (t.l.c., ¹H n.m.r.) of compounds (2c), (3c), (4c), and (5c) as a brown crystalline solid (43.0 g).

This mixture was taken up in MeOH (370 ml) and concentrated aqueous NH₄OH (20 ml) and stirred vigorously with Cu(OAc)₂·H₂O (3 g) in air for 7 h. Work-up as for (4b) and (5b) afforded a brown crystalline residue (40.0 g). Chromatography on activity I alumina gave 31.9 g [62.7% based on the starting nitron (1c)] of paramagnetic species: (i) solid monoradical (4c) (20.5 g, 39.8%) [eluted first with light petroleum (b.p. 316 ± 3 K)–Et₂O, 10:1]. Two recrystallisations from light petroleum afforded the analytical sample as red–orange crystals, m.p. 358–359 K (Found: C, 77.0; H, 9.3; N, 6.15. C₁₄H₂₀NO requires, C, 77.0; H, 9.2; N, 6.4%); e.s.r. (6.4 × 10⁻⁵ mol dm⁻³ in pentane) triplet, $a_N = 1.387$ mT, $g = 2.0068$; λ_{max} , 208 (ε 12 000 dm³ mol⁻¹ cm⁻¹), 236 (3 270), and 413 nm (8.7); ν_{max} , 1 602 m (C=CPh) and 774 s and 709 vs cm⁻¹ (both ArH); δ_H (60 MHz, after reduction) 0.78, 1.18, 1.25, and 1.30 (each 3 H, s, Me), 1.6–2.4 (8 lines, 2 H, AB part of ABX system, CH₂), 2.85–3.2 (4 lines, 1 H, X part of ABX system, CHPh), and 7.25 (5 H, s, Ph); m/z 219 [(M + 1)⁺, 6.1%], 218 (M⁺, 26), 204 [(M + 1) – 15]⁺, 5.1], 203 [(M – 15)⁺, 7.0], 188 [(M – 30)⁺, 2.15], 145 (41), 132 (100), 131 (44), 117 (80), 91 (45), 74 (28), 56 (81), and 41 (25); and (ii) the biradical (5c) (11.4 g, 23.0%) (eluted second with Et₂O) as a yellow–orange microcrystalline powder, m.p. 316.5–318.5 K (decomp.). All attempts to obtain the product in crystalline form were unsuccessful (Found: C, 76.7; H, 8.8; N, 6.25. C₂₇H₃₆N₂O₂ requires C, 77.1; H, 8.6; N, 6.65%); e.s.r. (3.4 × 10⁻⁵ mol dm⁻³ in pentane) a broad line spectrum [see Figure (b) and text], $g = 2.0065$; λ_{max} , 208 (ε 23 900 dm³ mol⁻¹ cm⁻¹), 234 (5 270), 236 (5 270), 317 (275), and ca. 425 sh* nm (ca. 8*) (see text); ν_{max} , 1 602 m (C=CPh), 776 s, and 704 vs cm⁻¹ (both ArH); δ_H (80 MHz, after reduction) 0.7–0.8 (~8 H, m, Me), 1.17–1.53 (~16 H, 6 × s, Me), 1.6–2.6 (6 H, m, CH₂), 2.9–3.4 (2 H, m, CHPh), 7.25, and 7.28 (10 H, s, Ph); m/z 422 [(M + 2)⁺, 2.3%], 421 [(M + 1)⁺, 4.6], 420 (M⁺, 7.7), 406 [(M + 1) – 15]⁺, 0.9], 405 [(M – 15)⁺, 2.9], 391 [(M + 1) – 30]⁺, 16], 390 [(M – 30)⁺, 4.7], 218 (13), 204 (100), 203 (25), 188 (18), 186 (25), 145 (27), 140 (23.5), 132 (68), 131 (62), 129 (20), 117 (54), 105 (30), 91 (56), 56 (21), 43 (27), 42 (24), and 41 (22.5).

Acknowledgements

We thank Mr. A. M. Zakrzewski for his participation in the synthetic part of this research and Mr. M. K. Tasz of this Department for many helpful discussions, critical reading of the manuscript, and some valuable suggestions concerning the presentation of the material. We are indebted to Dr. A. Chodkowska (Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw) and Dr. H. O. Kalinowski (Institut für Organische Chemie, Justus-Liebig-Universität, Giessen) for discussions and for measuring the e.s.r. and ¹³C n.m.r. spectra, respectively. We also thank Prof. A. Rassat (Centre d'Études Nucléaires de Grenoble, Commissariat à l'Énergie Atomique, Grenoble) for the Cameca 250 spectra of radical (4a). This work was supported in part by Research Grants (Nos. MR-I.12 and CPBP 01.13) from the Polish Academy of Sciences.

References

- 1 Part 2, M. Cygler, K. Dobrynin, M. J. Grabowski, R. B. Nazarski, and R. Skowroński, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1495.
- 2 For a review see T. T. Tidwell, *Tetrahedron*, 1978, **34**, 1855.
- 3 A Rassat, presented at the EUCEM Conference on Stable Free

- Nitroxide Radicals: Syntheses and Applications, Hämeenlinna, Finland, Aug. 20–22, 1981, pp. 1–2; see also D. L. Haire, and E. G. Janzen, *Can. J. Chem.*, 1982, **60**, 1514.
- 4 For general reviews see (a) A. R. Forrester, 'Magnetic Properties of Free Radicals,' eds. H. Fischer and K.-H. Hellwege [Landoldt-Börnstein, vol. 9/c1], Springer-Verlag, Berlin, 1979, pp. 192–1066; (b) J. F. W. Keana, *Chem. Rev.*, 1978, **77**, 37.
- 5 R. Skowroński, R. B. Nazarski, and H. Skolimowski, *Pol. P* 102 627/1979 and 108 055/1980; R. B. Nazarski, J. Skolimowski, and R. Skowroński, *Pol. J. Chem.*, 1979, **53**, 821.
- 6 R. B. Nazarski, D.Sc.(Chem.) Thesis, University of Łódź, Łódź, 1983.
- 7 R. B. Nazarski, unpublished results.
- 8 R. B. Nazarski and M. K. Tasz, unpublished work.
- 9 (a) A. M. Feldman and A. K. Hoffmann, U.S.P. 3 334 103/1967; (b) R.-M. Dupeyre, Thèse de Doctorat de 3^{ème} cycle, Université de Grenoble, 1965; Rapport CEA No. R 3176; (c) D. P. Young, B.P. 1 199 351/1970; (d) A. C. Scott, J. M. Tedder, J. C. Walton, and S. Mhatre, *J. Chem. Soc., Perkin Trans. 2*, 1980, 260.
- 10 W. R. Wragg, W. Green, and L. Bretherick, U.S.P. 3 020 288/1962.
- 11 J. F. W. Keana, 'Spin Labelling: Theory and Applications,' ed. L. J. Berliner, Academic Press, New York, 1979, vol. 2, pp. 115–172.
- 12 E. Lunt, Proceedings of the International Symposium on Nitro Compounds, Warsaw, Sept, 18–20, 1963 ['Nitro Compounds,' ed. T. Urbanski; *Tetrahedron*, 1964, **20**, Suppl. 1], Pergamon Press—WNT, Oxford—Warsaw, 1964, pp. 291–315.
- 13 D. H. Johnson, M. A. T. Rogers, and G. Trappe, *J. Chem. Soc.*, 1956, 1903; R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *ibid.*, 1959, 2094; T. D. Lee and J. F. W. Keana, *J. Org. Chem.*, 1975, **40**, 3145.
- 14 R. B. Nazarski, unpublished results, 1978–79.
- 15 G. A. Kutikova and L. B. Volodarskii, *Zh. Org. Khim.*, 1970, **6**, 1505.
- 16 (a) R.-M. Dupeyre, H. Lemaire, and A. Rassat, *J. Am. Chem. Soc.*, 1965, **87**, 3771; (b) R. Brière, R.-M. Dupeyre, H. Lemaire, C. Morat, A. Rassat, and P. Rey, *Bull. Soc. Chim. Fr.*, 1965, 3290.
- 17 L. A. Krintskaya, A. L. Buchachenko, and E. G. Rozantsev, *Zh. Org. Khim.*, 1966, **2**, 1301.
- 18 J. Michon and A. Rassat, *Tetrahedron*, 1980, **36**, 871.
- 19 T. Toda, S. Morimura, E. Mori, H. Horiuchi, and K. Murayama, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 3445.
- 20 W. B. Motherwell and J. S. Roberts, *J. Chem. Soc., Chem. Commun.*, 1972, 328.
- 21 C. Morat and A. Rassat, *Tetrahedron*, 1972, **28**, 735.
- 22 V. V. Gur'yanova, B. M. Kovarskaya, L. A. Krintskaya, M. B. Neiman, and E. G. Rozantsev, *Vysokomol. Soedin.*, 1965, **7**, 1515; A. R. Forrester and R. H. Thomson, *J. Chem. Soc.*, 1965, 1224; *J. Chem. Soc. C*, 1966, 1844; A. Rassat and P. Rey, *Tetrahedron*, 1974, **30**, 3315 and 3597.
- 23 M. Cygler and R. B. Nazarski, unpublished work.
- 24 D. R. Anderson, J. S. Keute, H. L. Chapel, and T. H. Koch, *J. Am. Chem. Soc.*, 1979, **101**, 1904; W. Kołodziejki, *Pol. J. Chem.*, 1979, **53**, 2087.
- 25 T. Toda, E. Mori, and K. Murayama, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 1904.
- 26 A. P. Davies, A. Morrison, and M. D. Barratt, *Org. Mass Spectrom.*, 1974, **8**, 43; E. S. Copeland, M. E. Boykin, J. A. Kelley, and M. P. Kullberg, *Biophys. J.*, 1975, **15**, 1125.
- 27 A. R. Forrester, R. H. Thomson, and G. R. Luckhurst, *J. Chem. Soc. B*, 1968, 1311.
- 28 T. D. Lee and J. F. W. Keana, *J. Org. Chem.*, 1978, **43**, 4226.
- 29 B. Princ and O. Exner, *Collect. Czech. Chem. Commun.*, 1979, **44**, 2221, and references therein.
- 30 (a) R. F. C. Brown, V. M. Clark, and A. Todd, *Proc. Chem. Soc.*, 1957, 97; (b) R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *J. Chem. Soc.*, 1959, 2109; (c) J. F. Elsworth and M. Lamchen, *J. Chem. Soc. C*, 1966, 1477; (d) J. F. Elsworth and M. Lamchen, *J. S. African Chem. Inst.*, 1971, **24**, 196; *ibid.*, 1972, **25**, 1; (e) D. St. C. Black, V. M. Clark, B. G. Odell, I. O. Sutherland, and Lord Todd, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1942.
- 31 D. St. C. Black and L. M. Johnstone, *Aust. J. Chem.*, 1984, **37**, 117.
- 32 R. F. C. Brown, V. M. Clark, M. Lamchen, and A. Todd, *J. Chem. Soc.*, 1959, 2116.
- 33 A. Chodkowska, personal communication, 1983.
- 34 S. J. Komorowski, D.Sc. Thesis, Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, 1985; S. J. Komorowski, personal communication, 1984.

* From graphical bands separation.

- 35 K. Hideg and L. Lex, *J. Chem. Soc., Chem. Commun.*, 1984, 1263.
36 M. W. Tse-Tang, B. J. Gaffney, and R. E. Kelly, *Heterocycles*, 1981, **15**, 965.
37 G. R. Delpierre and M. Lamchen, *J. Chem. Soc.*, 1963, 4693.
38 J. B. Bapat and D. St. C. Black, *Aust. J. Chem.*, 1968, **21**, 2483.
39 H. Shechter, D. E. Ley, and L. Zeldin, *J. Am. Chem. Soc.*, 1952, **74**, 3664.
40 R.-M. Dupeyre, H. Lemaire, and A. Rassat, *Tetrahedron Lett.*, 1964, 1781.
41 F. D. Greene and K. E. Gilbert, *J. Org. Chem.*, 1975, **40**, 1409.
42 J. F. W. Keana, T. D. Lee, and E. M. Bernard, *J. Am. Chem. Soc.*, 1976, **98**, 3052.

Received 21st November 1988; Paper 8/04608E