Stable nitroxyl radicals with a hydrogen atom at α-carbon atom of nitroxyl group

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Nitroxyl radicals containing the diphenylmethyl group as one of the substituents at the nitroxyl group are stable compounds that can be isolated in an individual state. *N*-(2-Hydroxy-3-methyl-2-phenylcyclohexyl)-*N*-diphenylmethylnitroxyl was characterized by X-ray diffraction analysis for the first time.

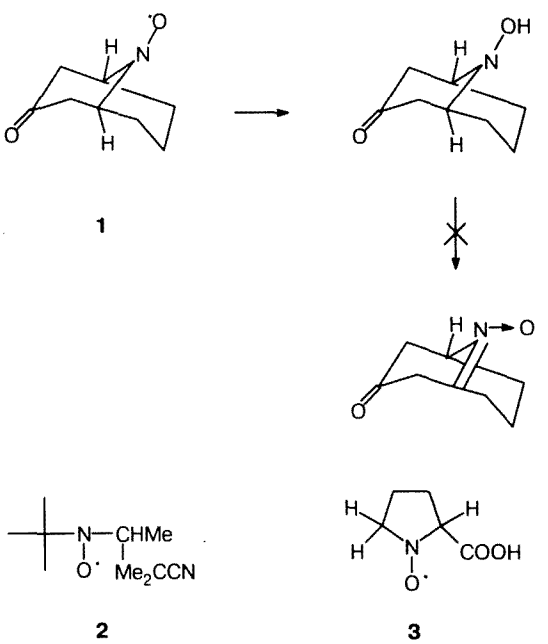
Key words: nitroxyl radicals, nitrones.

Spin trapping of short-lived radicals by aldonitrones is widely used in studies of transformations involving these radicals.[1] Nitroxyl radicals (NR) thus formed, which contain an H atom in the α-position, are unstable, though they are easily detected by ESR and, therefore, have been studied in detail. The low stability of these radicals is due to the fact that they readily disproportionate, giving nitrone and hydroxylamine.[2] An exception is provided by bicylic NR of type **1**, whose stability is due to the fact that formation of a bridgehead double bond is forbidden (the Bredt rule).[3] Another factor that may increase the stability of NR containing an α-H atom is steric shielding of the nitroxyl group with bulky substituents. This apparently accounts for the stability of NR **2**, which has been isolated in an individual state.[4] However, NR **3** exists in the individual state,[5] though its acyclic analogs, even those containing no α-H atoms, exist only as salts (Scheme 1).[6]

Previously we have shown that acyclic NR containing one diphenylmethyl substituent at the nitroxyl group are stable.[7] This fact is also rather unusual. The purpose of the present work is to find out whether the existence of stable NR containing an α-H atom is a general phenomenon.

One of the methods for the synthesis of sterically hindered *N*,*N*-disubstituted hydroxylamines, which are potential precursors of NR, is the addition of organometallic compounds to nitrones. We used this reaction to prepare sterically hindered hydroxylamines. It was found that oxidation of hydroxylamines **4a,b** formed in the reaction of aldonitrones **5a,b** with PhMgBr yields stable NR **6a,b** containing α-H atoms, which were isolated in the individual state. Similarly, stable radical **6d** was obtained by oxidation of hydroxylamine **4d**. It should be noted that radicals **6d,b** are less stable than the previously synthesized[7] radical **6e**, and they rapidly decompose on attempted crystallization from hexane. Unlike this, NR **6c** is so unstable that it even cannot be detected by chromatography. Its formation is indicated only by

Scheme 1



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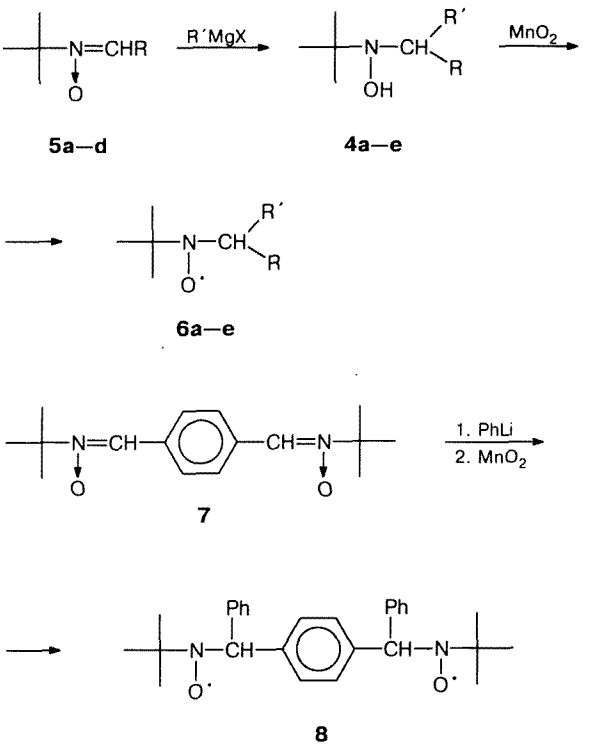
Scheme 2



R = 4-pyridyl (**a**), 2-pyridyl (**b**), 2-furyl (**c**), Ph (**d**, **e**)
R' = Ph (**a**–**c**, **e**), Bu^t (**d**)

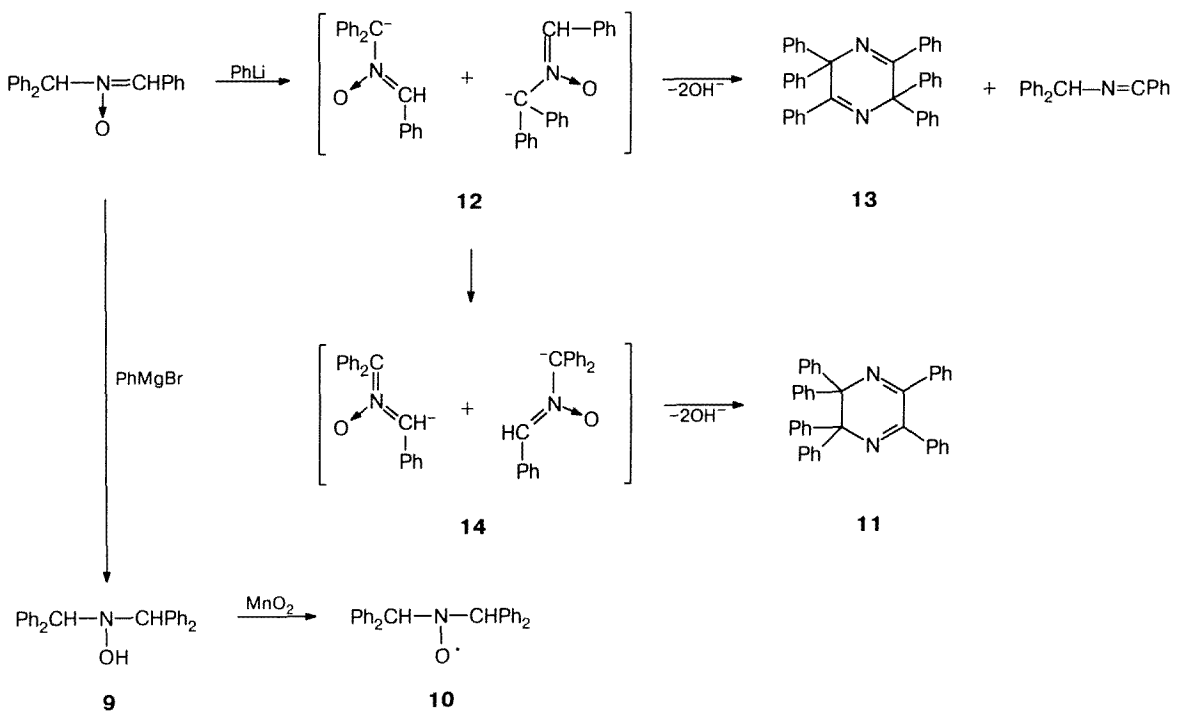
the appearance of the characteristic color (yellow), which disappears several seconds after the beginning of oxidation, and by the ESR spectrum of the reaction mixture, which exhibits a triplet of doublets. The oxidation probably yields the corresponding nitrone.

The reaction of dinitrone **7** with PhLi followed by oxidation affords stable nitroxyl biradical **8** (Scheme 2).

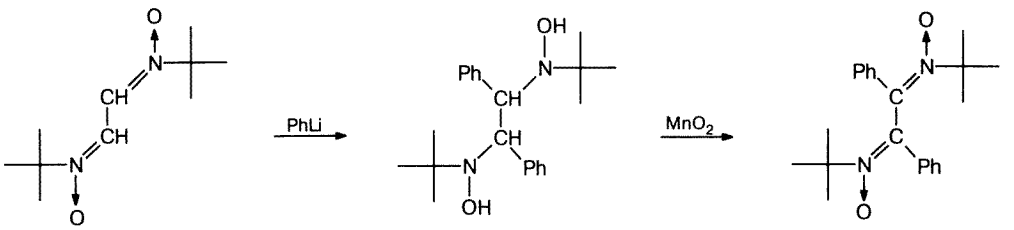
In order to obtain hydroxylamine **9**, the precursor of the symmetrically substituted bis-diphenylmethylnitroxyl radical **10**, we studied the reaction of diphenylmethylphenylnitrone with PhLi. However, the reaction unexpectedly gave dihydropyrazine **11** and benzophenone diphenylmethylimine. One might expect that dimerization of metallated derivative **12** would more likely yield isomeric 3,6-dihydropyrazine **13**. The UV spectrum of compound **11** exhibits a band at λ_{max} = 408 nm, which is in agreement with the presence of conjugated C=N bonds, but does not correspond to the separate phenylimino groups present in compound **13**. The formation of compound **11** can be explained by the interaction of metallated anions **12** and **14** followed by elimination of two equivalents of LiOH (Scheme 3).

The metallation of *N*-diphenylmethylphenylnitrone can be avoided by using PhMgBr instead of PhLi. PhMgBr adds to nitrone to give hydroxylamine **9** in an almost quantitative yield. Nitroxyl radical **10** cannot be isolated in an individual state, though it is stable in

Scheme 3

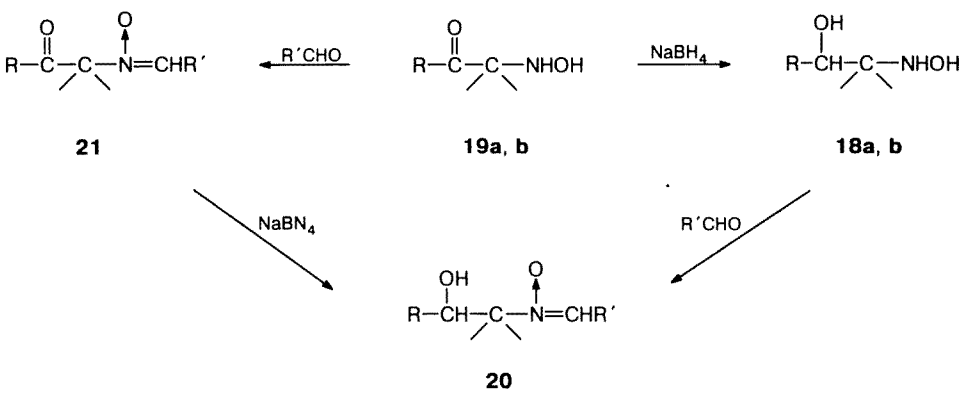


Scheme 4



15 **16a, b** **17**

Scheme 5



21 **19a, b** **18a, b**

20

18a, 19a, 20c, 20d, 21c, 21d: R = Ph
18b, 19b, 20a, 20b, 21a, 21b: R = Me
20a, 20c, 21a, 21c: R′ = Ph
20b, 20d, 21b, 21d: R′ = 2-furyl

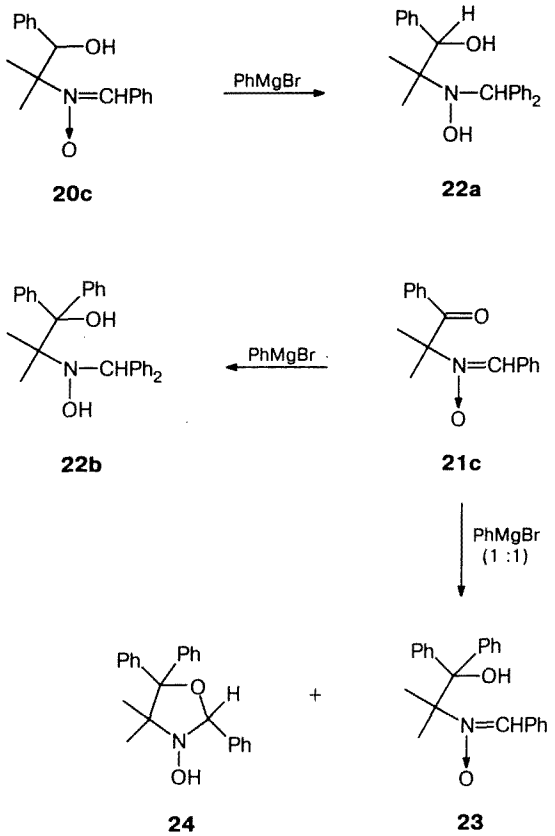
solution under ambient conditions for several days. The ESR spectrum of radical **10** is a triplet with constants a_N = 14.0 G and a_H = 5.7 G, and the ratio between the intensities of lines in the triplet with the smaller constant (1 : 2 : 1) points to splitting on two H atoms.

The reaction of **15** with excess PhLi gives diastereomeric bis-hydroxylamines **16a,b**, whose oxidation affords dinitrone **17** rather than NR (Scheme 4).

By the condensation of functionally substituted hydroxylamines with aldehydes we synthesized some aldonitrono ketones and aldonitrono alcohols that can be converted into stable NR, containing an α-H atom and an additional functional group, by reaction with organometallic compounds followed by oxidation. Unlike hydroxylamino alcohol **18a**, compound **18b** cannot be isolated from the products of the reduction of hydroxylamino alcohol **19b**. Therefore, compound **18b** was subjected to condensation with aldehydes without preliminary isolation. An alternative method for the synthesis of nitrono alcohols **20a,b** is selective reduction of nitrono ketones **21a,b** with $NaBH_4$, in which the nitrone group remains unaffected (Scheme 5).

The reactions of nitrono alcohol **20c** and nitrono ketone **21c** with excess PhMgBr yield hydroxylamino alcohols **22a,b**, respectively. The reaction of nitrono ketone **21c** with PhMgBr in a ratio of 1 : 1 gives isomeric compounds **23** and **24**, whose molecular formulas correspond to the addition of one mole of PhMgBr. The UV spectrum of compound **23** exhibits a band at λ_{max} = 302 nm, typical of a phenylnitrone group, and its IR spectrum exhibits no band associated with the carbonyl group; therefore a nitrono alcohol structure was attributed to this compound. The UV spectrum of isomer **24** exhibits no absorption above 220 nm, and the IR spectrum contains no band corresponding to the carbonyl group. Therefore, compound **24** is also a product of

Scheme 6

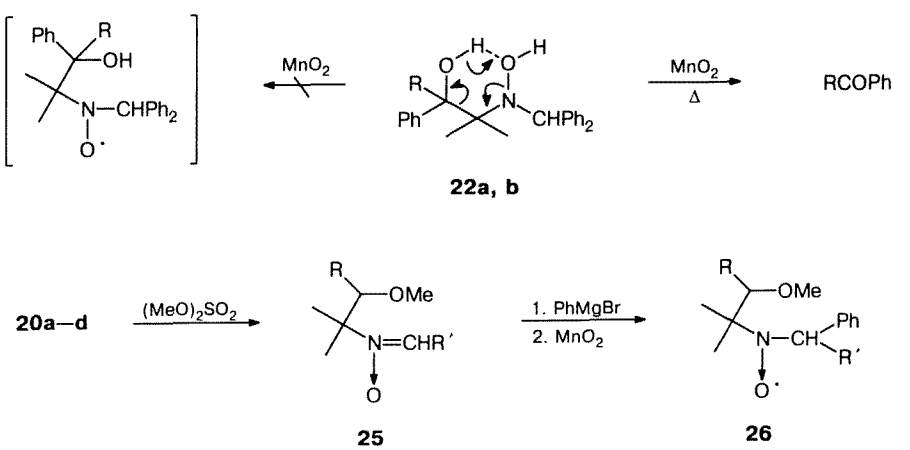


addition at the carbonyl group, and an oxazolidine structure was attributed to it. We were not able to confirm the structure of compound **24** by NMR spectra, because of its extremely low solubility. It should be noted that type **23** nitrono alcohols can exist in a tautomeric equilibrium with the corresponding oxazolidines **24** (see Ref. 8); however, we were not able to carry out interconversion of compounds **23** and **24** (Scheme 6).

Compounds **22a,b** proved to be quite unstable; they decompose when stored at ~20 °C or on attempted recrystallization to yield a complex mixture of products, from which benzaldehyde and benzophenone, respectively, were isolated. Oxidation of these compounds affords mixtures of similar compositions rather than NR. This behavior of compounds **22a,b** can be explained by the presence of an intramolecular hydrogen bond (IMHB), favorable for the cleavage of the C—C bond in the planar six-membered transition state. In order to rule out the possibility of this cleavage, we converted nitrono alcohols **20a—d** into nitrono ethers **25a—d** by alkylation; the reaction of the latter with PhMgBr followed by oxidation leads to stable NR **26a,c**, which were isolated in the individual state. Radicals **26b,d** containing a phenylfurylmethyl substituent at the nitroxyl group are unstable (*cf.* compound **6c**) (Scheme 7).

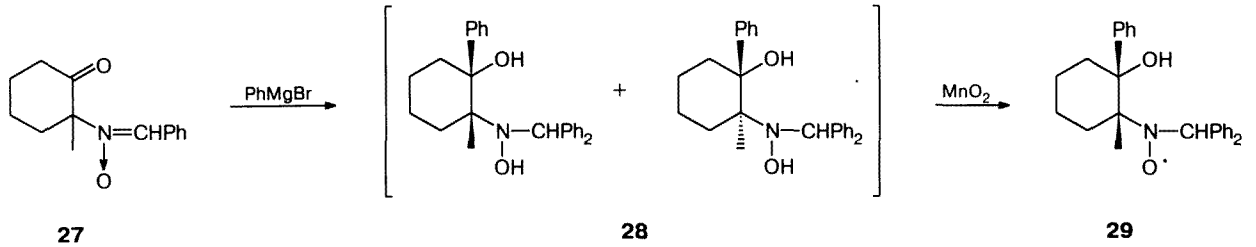
One could expect that interaction of nitrono ketone **27** with an excess of PhMgBr would yield diastereomers **28a,b**. It is obvious that the formation of IMHB is possible in both isomers, though in the case of *trans*-isomer it is somewhat less likely. According to TLC, this reaction actually affords a mixture of two isomers that cannot be separated by chromatography because of the

Scheme 7



25, 26: R = Me (**a,b**), Ph (**c,d**);
R′ = Ph (**a,c**), 2-furyl (**b,d**)

Scheme 8



27 **28** **29**

low stability of α-hydroxylamino alcohols **28**. Oxidation of this mixture gives stable individual NR **29**, in which, as shown by X-ray diffraction analysis, the hydroxy and nitroxyl groups are *cis*-arranged and linked by an IMHB. This implies that the presence of an IMHB is insufficient to make α-hydroxylamino alcohols and the corresponding nitroxyl radicals unstable. A possible reason for the instability of these compounds is oxidation by air oxygen accompanied either by cleavage of the C—C bond or by disproportionation, similarly to what has been observed for geminal bishydroxylamines (Scheme 8).[9]

Molecular structure of radical **29** is presented in Fig. 1. The C(2)—N(8)—O(28)—C(9) nitroxyl fragment is planar, the root-mean-square deviation of the above-mentioned atoms from the plane being 0.066 Å. The length of the N(8)—O(28) bond, equal to 1.287 Å, is larger than the corresponding bond length in 2,2,5,5-tetramethyl-4-phenyl-3-imidazolin-1-oxyl 3-oxide, equal to 1.268 Å,[10] and than the lengths of these bonds in the series of 3-imidazoline nitroxyl radicals with gem-dialkoxy groups at the α-carbon atom of the nitroxyl group, which are 1.26(1)—1.265(5) Å.[11] The orientation of the nitroxyl fragment with respect to the cyclohexane ring is apparently determined by the relatively strong IMHB with the following parameters: O(29)—H(29) 0.80(3), H(29)...O(28) 1.92(4), O(29)...O(28) 2.616 Å, the O(29)—H(29)...O(28) angle 145(3)°. This hydrogen bond may affect the length of the N(8)—O(28) bond. The benzene rings are planar, and the maximum root-mean-square deviation in the C(10)—C(15) ring is 0.010 Å. The dihedral angles between the pairs of planes, C(2)—N(8)(—O(28))—C(9) and C(10)—C(15), C(2)—N(8)(—O(28))—C(9) and C(16)—C(21), and C(10)—C(15) and C(16—C(21) are 77.7 (1)°, 77.5 (1)°, and 75.9 (1)°, respectively.

Nitroxyl radicals containing α-H atoms are unstable, because they easily disproportionate giving nitrone and a radical. The conformation in which the C—H bond of the leaving atom is parallel to the π-orbital of the unpaired electron of the nitroxyl group is the most favorable for this process.[12] The value of the a_H constant is related to the dihedral angle ϕ between the C—H bond and the π-orbital by the simple relationship (1). The average value of this angle for all the stable nitroxyl radicals synthesized may be estimated as being ~80°, and this indicates that the predominant conformation of these molecules in solution is unfavorable for elimination.

$$a_H = \rho^N(B_0 + B_2\cos\phi), \quad (1)$$

where $B_0 \simeq 0$, $B_2 \simeq 59$ G, $\rho \simeq 0.45$.

According to X-ray diffraction data, the ϕ angle in the molecule of compound **29** is ≃77°. Thus, the kinetic stability of these radicals is likely to be due to the rather high energy barrier to the rotation around the C—N bond, which may be caused by specific steric features of the diphenylmethyl group.

Experimental

IR spectra were recorded on a Specord M-80 instrument in KBr pellets (at a concentration of 0.25 %) or in CCl_4 (at a concentration of 1 %). UV spectra were obtained on a Specord

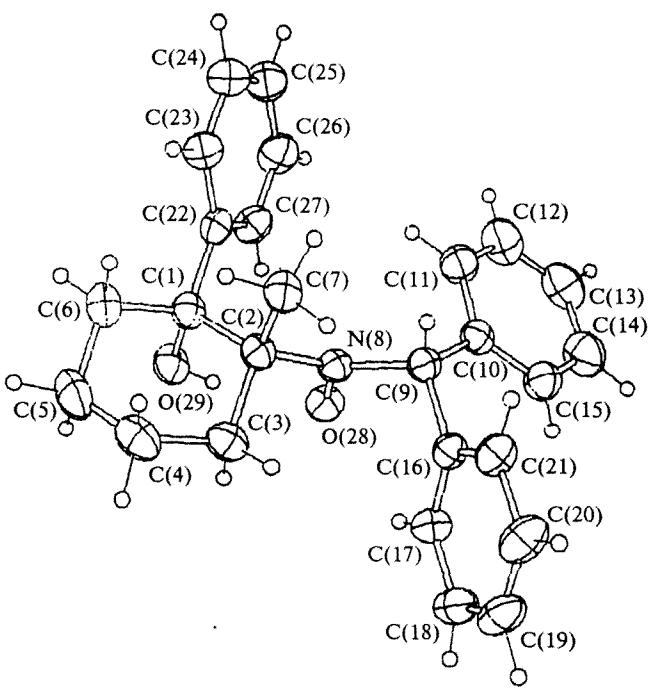


Fig. 1. Molecular structure of *N*-(2-hydroxy-1-methyl-2-phenylcyclohex-1-yl)-*N*-diphenylmethylnitroxyl (**29**).

UV-VIS spectrophotometer in EtOH. The ^1H NMR spectra were run on a Bruker WP-200SY instrument with 5 % solutions in $CDCl_3$; the solvent served as the internal standard. Mass spectra were recorded on a Finnigan MAT-8200 mass spectrometer, and ESR spectra were obtained on a Bruker ER-SRC spectrometer.

***N-tert*-Butyl-R-phenylmethylnitroxyls (6). General procedure.** A solution of nitrone **5a—c** (3 mmol) was added dropwise to a stirred solution of PhMgBr prepared from Mg (0.22 g, 9 mmol) and PhBr (0.94 mL, 9 mmol) in 20 mL of ether. The mixture was stirred at 20 °C for an additional 15 min, excess PhMgBr was decomposed by adding 10 mL of saturated aqueous solution of NH_4Cl, the ethereal layer was separated, and the aqueous layer was extracted with ether (2×20 mL). The extract was dried with $MgSO_4$, and the solvent was evaporated. The residue was washed with 3 mL of hexane, and the precipitated hydroxylamines **4a,b** were filtered off. Hydroxylamine **4c** was oxidized without isolation in an individual state. Treatment of nitrone **5d** with Bu^+MgCl under similar conditions gave hydroxylamine **4d**, which was also used for oxidation without purification.

To prepare radicals **6**, hydroxylamine **4** (0.2 g) and MnO_2 (1 g) in ether (10 mL) were stirred for 2 min at 20 °C. The solution was filtered through a silica gel layer (2 cm), using ether as the eluent, and concentrated.

The treatment of *N*-diphenylmethyl-α-phenylnitrone with PhMgBr under similar conditions gave hydroxylamine **9**, which was purified by chromatography on a column packed with silica gel using a $CHCl_3$—hexane mixture (2 : 3) as the eluent.

Nitroxyl radicals **26** were obtained from nitrones **25** under similar conditions.

Bis(3,3-dimethyl-2-oxyl-1-phenyl-2-azabutyl-1)benzene (8). Dinitrone **7** (0.5 g, 1.8 mmol) was added portionwise to a stirred solution of PhLi prepared from PhBr (0.94 mL, 9 mmol) and Li (0.13 g, 18 mmol) in 20 mL of dry ether. The reaction was carried out in an argon atmosphere. The mixture was stirred for 3 h at 20 °C, H_2O (10 mL) was added, the ethereal layer was separated, and the aqueous layer was extracted with ether (2×20 mL). The extract was dried with $MgSO_4$, the solvent was evaporated, and the residue was dissolved in 10 mL of $CHCl_3$. MnO_2 (1 g) was added, the mixture was stirred for 5 min at 20 °C, excess oxidant was filtered off, the solvent was evaporated, the residue was washed with hexane, and the precipitated biradical **8** was filtered off.

2,3-Dihydro-2,2,3,3,5,6-hexaphenylpyrazine (11). *N*-Diphenylmethyl-α-phenylnitrone (0.5 g, 1.74 mmol) was added portionwise to a stirred solution of PhLi prepared from PhBr (0.9 mL, 8.7 mmol) and Li (0.12 g, 17.4 mmol) in 20 mL of ether. The reaction was carried out in an argon atmosphere. The mixture was stirred for 10 min at 20 °C, H_2O (10 mL) was added, the ethereal layer was separated, and the aqueous layer was extracted with $CHCl_3$ (4×20 mL). The extract was dried with $MgSO_4$, the solvent was evaporated, and the residue was chromatographed on a column packed with silica gel using a $CHCl_3$—hexane mixture (1 : 1) as the eluent. Benzophenone diphenylmethylimine was eluted first, yield 0.2 g (30 %), m.p. 154—155 °C (EtOH, *cf.* Ref. 13), and then the colored area containing pyrazine **11** was collected.

3,6-Dihydroxy-2,2,7,7-tetramethyl-4,5-diphenyl-3,6-diazaoctanes (16a,b). This compound was obtained by the reaction of dinitrone **15** with PhLi under the conditions described above. After the addition of H_2O, the ethereal solution was separated, and the aqueous layer was extracted with ether. The extract was dried with $MgSO_4$, the solvent was evaporated, the residue was diluted with hexane, and the precipitated bishydroxylamine **16a** was filtered off. The filtrate was concen-

Table 1. Atomic coordinates (×10⁴, in cell fractions) and heat factors (U×10³) for nonhydrogen atoms of compound **29**

Atom	*x*	*y*	*z*	U_{eq}/Å²
C(1)	393(3)	7368(2)	2913(2)	54(1)
C(2)	1255(2)	8261(2)	2594(2)	50(1)
C(3)	2625(3)	8001(3)	2785(2)	69(1)
C(4)	2845(4)	7720(3)	3800(3)	86(1)
C(5)	2013(4)	6882(3)	4098(3)	89(1)
C(6)	657(3)	7131(3)	3931(2)	71(1)
C(7)	908(3)	9237(2)	3065(2)	59(1)
N(8)	1101(2)	8395(1)	1569(1)	49(1)
C(9)	1246(2)	9368(2)	1088(2)	50(1)
C(10)	436(2)	9367(2)	221(2)	54(1)
C(11)	−819(3)	9167(3)	313(3)	76(1)
C(12)	−1576(4)	9139(3)	−459(3)	92(1)
C(13)	−1107(4)	9336(3)	−1321(3)	89(1)
C(14)	116(4)	9563(3)	−1410(3)	89(1)
C(15)	883(3)	9581(3)	−641(2)	69(1)
C(16)	2603(2)	9607(2)	923(2)	51(1)
C(17)	3415(3)	8909(2)	547(2)	62(1)
C(18)	4648(3)	9153(3)	404(2)	74(1)
C(19)	5077(3)	10083(3)	633(2)	80(1)
C(20)	4289(3)	10775(3)	1003(3)	82(1)
C(21)	3046(3)	10539(2)	1149(2)	64(1)
C(22)	−976(2)	7595(2)	2734(2)	56(1)
C(23)	−1705(3)	8104(2)	3363(2)	70(1)
C(24)	−2942(3)	8291(3)	3188(3)	87(1)
C(25)	−3473(3)	7994(3)	2380(3)	87(1)
C(26)	−2771(3)	7482(3)	1739(2)	80(1)
C(27)	−1535(3)	7272(2)	1926(2)	66(1)
C(28)	1225(2)	7626(1)	1047(1)	60(1)
C(29)	730(2)	6467(1)	2452(2)	67(1)

Table 2. Selected bond lengths (*d*) and angles (ω) in molecule **29**

Bond	*d*/Å	Angle	ω/deg
C(1)—O(29)	1.428(3)	C(29)—C(1)—C(22)	109.6(2)
C(1)—C(22)	1.530(4)	C(29)—C(1)—C(6)	103.1(2)
C(1)—C(6)	1.535(4)	C(22)—C(1)—C(6)	112.5(2)
C(1)—C(2)	1.585(3)	C(29)—C(1)—C(2)	110.8(2)
C(2)—N(8)	1.504(3)	C(22)—C(1)—C(2)	111.5(2)
C(2)—C(7)	1.523(4)	C(6)—C(1)—C(2)	109.1(2)
C(2)—C(3)	1.542(4)	N(8)—C(2)—C(7)	108.2(2)
C(3)—C(4)	1.535(5)	N(8)—C(2)—C(3)	108.1(2)
C(4)—C(5)	1.503(6)	C(7)—C(2)—C(3)	110.4(2)
C(5)—C(6)	1.519(5)	N(8)—C(2)—C(1)	108.2(2)
N(8)—O(28)	1.287(2)	C(7)—C(2)—C(1)	112.1(2)
N(8)—C(9)	1.487(3)	C(3)—C(2)—C(1)	109.8(2)
C(9)—C(16)	1.516(3)	C(4)—C(3)—C(2)	112.1(3)
C(9)—C(10)	1.530(4)	C(5)—C(4)—C(3)	111.5(3)
		C(4)—C(5)—C(6)	111.4(3)
		C(5)—C(6)—C(1)	112.1(3)
		O(28)—N(8)—C(9)	114.7(2)
		O(28)—N(8)—C(2)	118.2(2)
		C(9)—N(8)—C(2)	123.7(2)
		N(8)—C(9)—C(16)	111.2(2)
		N(8)—C(9)—C(10)	108.8(2)
		C(16)—C(9)—C(10)	114.9(2)

Table 3. Characterisctics of the compounds synthesized

Compound	Yield (%)	M.p.[a] /°C	IR spectrum (KBr), ν/cm^{-1}	UV spectrum, λ_{max} /nm (lg ε)	Found / Calculated (%) C	H	N	Molecular formula
4a	90	149—150	1600 (C=N, C=C), 3100—3300 (OH)	—	74.9 75.0	7.7 7.8	10.9 11.0	$C_{16}H_{20}N_2O$
4b	70	93—95	1570, 1600 (C=N, C=C), 3150 (OH, KBr)	—	75.3 75.0	8.1 7.8	10.8 11.0	$C_{16}H_{20}N_2O$
4d	100	Oil	3600 (OH)	—	76.4 76.6	10.6 10.6	5.8 6.0	$C_{15}H_{25}NO$
6a	100	79—81	1590 (C=C, C=N)	—	75.0 75.3	7.5 7.4	10.8 11.0	$C_{16}H_{19}N_2O$
6b	100	63—65	1560, 1590 (C=C, C=N),	—	75.3 75.3	7.6 7.4	10.8 11.0	$C_{16}H_{19}N_2O$
6d	100	Oil		—	77.1 76.9	10.4 10.3	5.8 6.0	$C_{15}H_{24}NO$
8	65[b]	141—142		—	77.9 78.2	8.0 7.9	6.3 6.5	$C_{28}H_{34}N_2O_2$
9	80	Oil	3590 (OH)	—	85.9 85.6	6.1 6.3	3.6 3.8	$C_{26}H_{23}NO$
11	30	215—217	1580, 1595, 1615 (C=C, C=N)	252 (4.26) 312 (3.85) 408 (3.48)	89.1 89.4	5.6 5.6	4.9 5.2	$C_{40}H_{30}N_2$[c]
16a	40	146—148	3550 (OH)	—	73.9 74.1	9.1 9.0	7.7 7.7	$C_{22}H_{32}N_2O_2$
16b	40	108—110	3150—3450 (OH, KBr)	—	73.9 74.1	9.3 9.0	8.1 7.7	$C_{22}H_{32}N_2O_2$
17	100	70—71	1560, 1580 (C=C, C=N)	224 (4.20) 295 (4.51) 308 sh (3.80)	74.6 74.8	8.2 8.0	7.9 8.0	$C_{22}H_{28}N_2O_2$
20a	65	69—71	1590 (C=N), 3100—3300 (OH)	300 (4.24)	69.8 69.6	8.2 8.2	6.9 6.8	$C_{12}H_{17}NO_2$
20b	75	81—82	1550, 1580 (C=N), 3200—3400 (OH)	310 (4.38)	61.1 60.9	7.8 7.6	6.9 7.1	$C_{10}H_{15}NO_3$
21a	90	81—82	1720 (C=O), 1555, 1575 (C=N)	232 (3.85) 300 (4.24)	70.5 70.2	7.5 7.3	7.0 6.8	$C_{12}H_{15}NO_2$
21b	95	104—106	1725 (C=O), 1570, 1600 (C=N)	238 (3.34) 312 (4.39)	61.7 61.5	6.8 6.7	7.3 7.2	$C_{10}H_{13}NO_3$
21d	70	112—114	1675 (C=O), 1550, 1580, 1595 (C=C, C=N)	246 (4.09) 312 (4.42)	70.2 70.0	6.0 5.8	5.6 5.5	$C_{15}H_{15}NO_3$
22a	75	149—150	3380 (OH)	—	79.7 79.6	7.3 7.2	4.1 4.0	$C_{23}H_{25}NO_2$
23	25	150—151	1590 (C=N)	300 (4.25)	80.0 80.1	7.0 6.7	3.9 4.1	$C_{23}H_{23}NO_2$
24	50	226—227	3100—3400 (OH)	—	79.9 80.1	6.7 6.7	3.8 4.1	$C_{23}H_{23}NO_2$
25a	80	Oil	1555, 1565 (C=N)	297 (4.07)	70.4 70.6	8.3 8.5	6.3 6.3	$C_{13}H_{29}NO_2$
25b	60	Oil	1570, 1580 (C=N)	310 (4.34)	62.5 62.5	7.9 7.6	6.3 6.6	$C_{11}H_{16}NO_3$
25c	70	112—113	1555, 1570 (C=N)	300 (4.30)	76.5 76.3	7.4 7.4	5.2 5.0	$C_{18}H_{17}NO_2$
25d	80	130—131	1545, 1585 (C=N)	310 (4.01)	70.5 70.3	7.2 7.0	5.0 5.1	$C_{16}H_{19}NO_3$
26a	65	51—52		—	76.2 76.5	8.1 8.1	4.5 4.7	$C_{19}H_{24}NO_2$
26c	80	118—119		—	79.7 80.0	7.5 7.2	4.0 3.9	$C_{24}H_{26}NO_2$
27	85	112—114	1725 (C=O), 1510, 1580 (C=N)	302 (4.31)	72.6 72.8	7.3 7.4	5.8 6.1	$C_{14}H_{17}NO_2$
29	30	128—130		—	80.9 81.0	7.3 7.2	3.6 3.6	$C_{26}H_{28}NO_2$

[a] Compounds **4a**, **20b**, **21a**,**b**,**d**, **23**, and **29** were purified by recrystallization from a hexane—ethyl acetate mixture, **4b**, **16a**, **20a**, **25c**,**d**, and **26a**,**c** were recrystallized from hexane, **8**, **16b**, and **22a** were recrystallized from ethanol, and **17** and **27** were recrystallized from heptane. Compounds **4d**, **6a**,**b**,**d**, **9**, and **25a**,**b** were purified by chromatography, and compound **11** had satisfactory elemental analysis data without further purification. [b] The yield is based on dinitrone **7**. [c] MS, M^+: found 538.2407, calculated 538.2409.

Table 4. Parameters of the ^1H NMR spectra ($CDCl_3$) of the compounds synthesized

Compound	^1H NMR, δ (*J*/Hz)
4a	1.07 (s, 9 H, Me_3C); 5.17 (s, 1 H, C<u>H</u>—Ph); 7.4 (m, 7 H, Ph, *m*-Py); 8.39 (m, 2 H, *o*-Py)
9	4.45 (br.s, 1 H, OH); 4.99 (s, 1 H, C<u>H</u>Ph_2); 7.2—7.5 (m, 20 H, Ph_4)
16a	0.73 (s, 18 H, Me_3C); 4.66 (s, 2 H, C<u>H</u>—Ph); 7.2—7.5 (m, 10 H, Ph_2)
17	1.58 (s, 18 H, Me_3S); 7.4 (m, 6 H, Ph); 8.25 (m, 4 H, Ph); 7.51 (s, 2 H, C<u>H</u>=N)
20a	1.16 (d, 3 <u>H</u>, <u>Me</u>CH, J = 6); 1.52 (s, 3 H, Me); 1.60 (s, 3 H, Me); 3.92 (dq, 1 H, CHOH, $J = J_1$ = 6); 5.10 (d, 1 H, OH, OH, J = 6); 7.4 (m, 3 H, Ph); 8.24 (m, 2 H, Ph); 7.46 (s, 1 H, CH=N)
20b	1.15 (d, 3 H, Me, J = 6); 1.51 (s, 3 H, Me); 1.58 (s, 3 H, Me); 3.92 (q, 1 H, C<u>H</u>—OH, J = 6); 4.87 (br.s, 1 H, OH); 6.56 (m, 1 H, furyl); 7.51 (m, 1 H, furyl); 7.76 (m, 1 H, furyl); 7.66 (s, 1 H, CH=N)
20d	1.41 (s, 3 H, Me); 1.57 (s, 3 H, Me); 4.85 (d, 1 H, S<u>H</u>—OH, J = 6); 5.92 (d, 1 H, OH, J = 6); 6.56 (m, 1 H, furyl); 7.78 (m, 1 H, furyl); 7.24 (m, 6 H, Ph, furyl); 7.45 (s, 1 H, CH=N)
21a	1.67 (s, 6 H, Me_2); 2.18 (s, 3 H, MeCO); 7.4 (m, 3 H, Ph); 8.25 (m, 2 H, Ph); 7.53 (s, 1 H, CH=N)
21b	1.66 (s, 6 H, Me_2); 2.17 (s, 3 H, Me); 6.56 (m, 1 H, furyl); 7.51 (m, 1 H, furyl); 7.79 (m, 1 H, furyl); 7.74 (s, 1 H, C<u>H</u>=N)
21d	1.83 (s, 6 H, Me_2); 6.5 (m, 1 H, furyl); 7.67 (s, 1 H, SH=N); 7.3—7.9 (m, 7 H, Ph, furyl)
22a	0.72 (s, 3 H, Me); 0.98 (s, 3 H, Me); 4.88 (br.s, 1 H, OH); 4.97 (br.s, 1 H, OH); 5.28 (s, 1 H, C<u>H</u>Ph_2); 7.29 and 7.51 (both m, 15 H, Ph_3)
22b	1.20 (s, 6 H, Me_2); 4.01 (br.s, 1 H, OH); 5.40 (s, 1 H, C<u>H</u>Ph_2), 6.54 (br.s, 1 H, OH); 7.2—7.7 (m, 20 H, Ph_4)
23	1.80 (s, 6 H, Me_2); 7.81 (s, 1 H, CH=N); 7.2—8.1 (m, 15 H, Ph_3)
25a	1.07 (d, 3 H, Me—CH, J = 6.5); 1.43 (s, 3 H, Me); 1.52 (s, 3 H, Me); 3.94 (q, 1 H, C<u>H</u>—Me, J = 6.5); 7.3 (m, 3 H, Ph); 8.24 (m, 2 H, Ph); 7.49 (s, 1 H, CH=N)
25b	1.04 (d, 3 H, Me, J = 6); 1.40 (s, 3 H, Me); 1.48 (s, 3 H, Me); 3.25 (s, 3 H, MeO); 3.84 (q, 1 H, S<u>H</u>—Me, J = 6); 6.48 (m, 1 H, furyl); 7.43 (m, 1 H, furyl); 7.72 (m, 1 H, furyl); 7.67 (s, 1 H, CH=N)
25c	1.32 (s, 3 H, Me); 1.60 (s, 3 H, Me); 3.22 (s, 3 H, MeO); 4.94 (s, 1 H, C<u>H</u>—OMe); 7.3 (m, 3 H, Ph); 8.2 (m, 2 H, Ph); 7.34 (s, 1 H, CH=N)
25d	1.25 (s, 3 H, Me); 1.53 (s, 3 H, Me); 3.17 (s, 3 H, MeO); 4.84 (s, 1 H, <u>S</u>H—Me); 6.49 (m, 1 H, furyl); 7.39 (m, 1 H, furyl); 7.79 (m, 1 H, furyl); 7.24 (m, 5 H, Ph); 7.50 (s, 1 H, CH=N)
27	1.72 (s, 3 H, Me); 1.9 (m, 2 H); 3.0 (m, 4 H, $(CH_2)_4$); 7.37 (m, 3 H, Ph); 8.24 (m, 2 H, Ph); 7.68 (s, 1 H, CH=N)

trated, and the residue was chromatographed on a column packed with silica gel using an ether—hexane mixture (1 : 3) as the eluent; isomer **16a** was eluted first. Oxidation of bishydroxylamines **16a,b** under the conditions described for hydroxylamines **4** affords dinitrone **17** in a quantitative yield.

3,3-Dimethyl-4-oxo-1-furyl-2-azapent-1-ene 2-oxide (21b). A solution of MeONa in MeOH was added to a solution of 2-hydroxyamino-2-methyl-3-oxobutane hydrochloride (2 g, 13 mmol) in 50 mL of MeOH, until the medium became alkaline according to phenolphthaleine. Then furfural (1.26 g, 13 mmol) was added, the solution was kept for 6 h at 20 °C and concentrated, and the residue was diluted with 20 mL of H_2O and extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solvent was evaporated, the residue was washed with hexane, and the precipitated nitrone **21b** was filtered off.

Nitrone **21a** was obtained by the reaction of 2-hydroxyamino-2-methyl-3-oxobutane hydrochloride with benzaldehyde under similar conditions, and nitrone **27** was prepared by the reaction of 1-hydroxyamino-1-methylcyclohexan-2-one hydrochloride with benzaldehyde. Nitrono ketone **21c** was synthesized by a known procedure.[4]

3-Methyl-4-oxo-4-phenyl-1-furyl-2-azabut-2-ene 1-oxide (21d). A solution of 2-hydroxyamino-2-methyl-3-oxo-3-phenylpropane (2 g, 11.2 mmol) and furfural (1.09 g, 11.3 mmol) in 20 mL of MeOH was kept for 20 h at 20 °C and concentrated. The residue was washed with hexane, and the precipitate of nitrone **21d** was filtered off.

4-Hydroxy-3,3-dimethyl-1-phenyl-2-azapent-1-ene 2-oxide (20a). Method 1. A solution of MeONa in EtOH was added to a solution of 2-hydroxyamino-2-methyl-3-oxobutane hydrochloride (1 g, 6.6 mmol) in 30 mL of EtOH, until the medium became alkaline according to phenolphthalein. $NaBH_4$ (0.26 g, 6.6 mmol) was added in portions to the resulting solution with stirring and cooling to 0 °C. Stirring was continued for 1 h at 0 °C, and the solvent was evaporated. The residue was diluted with 15 mL of MeOH and concentrated; this procedure was

Table 5. Parameters of the ESR spectra of the nitroxyl radicals synthesized

Compound	a_N	a_H	Solvent
6a	16.1	3.6	H_2O
6b	16.1	4.2	H_2O
6d	16.7	3.5	H_2O
8*	16.3	4.1	H_2O
8**	14.8	—	Ethyl acetate
10	14.0	5.7	Benzene
26a	14.5	3.04	Hexane
26c	14.7	3.8	Hexane
29	15.9	3.9	$CHCl_3$

* Triplet of doublets. ** Quintet.

repeated. The residue was dissolved in 50 mL of EtOH, benzaldehyde (1.4 g, 13.2 mmol) was added, and the solution was kept for 3 days at 20 °C and concentrated. The residue was diluted with 50 mL of $CHCl_3$ and washed with 20 mL of H_2O, and the aqueous layer was extracted with 20 mL of $CHCl_3$. The extract was dried with $MgSO_4$, the solvent was evaporated, and nitrone **20a** was isolated by chromatography on a column with silica gel using an ethyl acetate—hexane mixture (1 : 2) as the eluent. Nitrone **20b** was obtained under similar conditions.

Method 2. A solution of nitrone **21a** (1 g, 4.9 mmol) and $NaBH_4$ (0.19 g, 4.9 mmol) in 25 mL of EtOH was stirred for 15 min at 0 °C and concentrated. Nitrone **20a** (yield 60 %) was isolated as described above. Nitrone **20b** was synthesized by the reduction of **21b** under similar conditions (yield 75 %). Nitrones **20c,d** were prepared by a previously reported procedure.[8]

2,4-Dihydroxy-3,3-dimethyl-1,1,4-triphenyl-2-azabutane (22a) and 2,4-dihydroxy-3,3-dimethyl-1,1,4,4-tetraphenyl-2-azabutane (22b). These compounds were prepared by treatment of nitrones **20c** and **21c**, respectively, with PhMgBr under the conditions described for hydroxylamines **4**; oxidation of **21a,b** was carried out as described above.

4-Hydroxy-3,3-dimethyl-1,4,4-triphenyl-2-azabut-1-ene 2-oxide (23) and 3-hydroxy-4,4-dimethyl-2,5,5-triphenyloxazolidine (24). A solution of PhMgBr prepared from PhBr (0.63 mL, 1.2 mmol) and Mg (0.16 g, 6.2 mmol) in 10 mL of ether was added dropwise to a stirred solution of nitrone **21c** (1 g, 3.7 mmol) in 10 mL of anhydrous THF until the starting nitrono ketone disappeared according to TLC (Silufol UV-254, $CHCl_3$ as the eluent). A saturated aqueous solution of NH_4Cl (10 mL) and 10 mL of hexane were added to the resulting solution. The precipitated oxazolidine **24** was filtered off and washed with H_2O, hexane, and ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer and the extract were concentrated to a volume of ≈5 mL and diluted with 10 mL of a mixture of ether and hexane (1 : 1), and the precipitated nitrone **23** was filtered off and washed with hexane.

3,3-Dimethyl-4-methoxy-1-phenyl-2-azapent-1-ene 2-oxide (25a). NaH (80 % in silicone oil) (0.3 g, 9.5 mmol) was added to a solution of nitrone **20a** (0.5 g, 1.9 mmol) in 10 mL of anhydrous THF, the suspension was stirred for 10 min at 20 °C, and a solution of dimethyl sulfate (0.28 mL, 2.9 mmol) in 2 mL of THF was added dropwise with stirring. Stirring was continued for 1 h at 20 °C, 1 mL of MeOH and 10 mL of H_2O were added, the solution was extracted with $CHCl_3$ (3×20 mL), the extract was dried with $MgSO_4$, and the solvent was evaporated. Hexane (2 mL) was added to the residue, and the precipitated methoxy derivative **25a** was filtered off.

Methoxy derivatives **25b—d** were prepared under similar conditions.

***N*-(2-Hydroxy-1-methyl-2-phenylcyclohex-1-yl)-*N*-diphenylmethylnitroxyl (29).** Thoroughly powdered nitrone **27** was added in portions to a stirred solution of PhMgBr prepared from Mg (0.52 g, 21.7 mmol) and PhBr (2.3 mL, 21.7 mmol). The mixture was stirred for an additional 1 h at 20 °C, 10 mL of a saturated aqueous solution of NH_4Cl was added, the ethereal layer was separated, and the aqueous layer was extracted with ether (2×20 mL). The combined ethereal layer and the extract was dried with $MgSO_4$, the solvent was evaporated, the residue was dissolved in 20 mL of $CHCl_3$, and the solution was stirred for 5 min with MnO_2 (2 g) at 20 °C. Excess oxidant was filtered off, and the solvent was evaporated. The residue was washed with hexane, and the precipitated radical **29** was filtered off and washed with hexane and 5 mL of ether.

The X-ray structural study of radical **29** was carried out on a SYNTEX-$P2_1$ diffractometer with a graphite monochromator using Cu-Kα-radiation. The crystals of compound **29** are rhombic: a = 10.780(2) Å, b = 13.417(2) Å, c = 14.480(2) Å, V = 2094.3(6) Å^3, space group $P2_12_12_1$, $C_{26}H_{28}NO_2$, Z = 4, d_{calc} = 1.226 g cm^{-3}, $F(000)$ = 828, μ = 0.60 mm^{-1}. The independent set of 2038 reflections from a crystal 0.3×0.7×0.8 mm^3 in size was measured by θ/2θ-scanning in the region of 2θ < 130°. Corrections for absorption were introduced by the semiempirical method using ψ-curves (transmission 0.82—0.96). The structure was solved by the direct method using the SHELXS-86 program and refined by the least-squares method in the full-matrix anisotropic or isotropic (for H atoms) approximation using the SHELXL-93 program to R_w = 0.0924 (R = 0.0336 for 1804 $F_0 > 4\sigma(F)$), S = 1.07. The positions of the H atoms were found from the differential synthesis. The coordinates of the atoms are presented in Table 1, the bond lengths and angles are listed in Table 2, characteristics of the compounds synthesized are given in Table 3, the data of ^{1}H NMR spectra are in Table 4, and the data of ESR spectra are in Table 5.

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