23 °C, the mixture was partitioned between 1 mL of saturated Na_2CO_3 and 15 mL of CH_2Cl_2. The organic phase was washed with 10% aqueous NaOH and worked up to give a 1:1 mixture of epoxides (151 mg, 96%) as a colorless oil: IR 1070, 1200, 1310, 1460, 1745, 2965, 3000, 3040, 3600 cm^{-1}; ^1H NMR δ 1.25 (s, 1.5), 1.26 (s, 1.5), 1.55 (s, 1.5), 1.56 (s, 1.5), 1.4–2.1 (m, 8), 2.4 (m, 1), 3.22 (t, 1, J = 5.9), 3.75 (s, 3), 4.06 (t, 1, J = 8.3), 4.98 (t, 1, J = 8.55), 7.2–7.4 (m, 5). Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 67.89; H, 7.87.

Acknowledgment. We thank the Fonds National Suisse de la Recherche for a fellowship to C.C. and the National Institutes of Health (Grant no. GM-30141) for support of this work. We are also indebted to Dr. P. C. Ting and Prof. J. P. Michael for initial work on the project and to Prof. J. Rebek for insightful suggestions.

Supplementary Material Available: Experimental details and characterization of the synthetic intermediates not described above (12 pages). Ordering information is given on any current masthead page.

Notes

Evidence for Hydrogen Transfer in the Photochemistry of 2,2,6,6-Tetramethylpiperidine-*N*-oxyl[1]

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There have been several reports on the photochemistry of stable nitroxide free radicals.[3-9] Two types of reactivity have been observed: (i) cleavage of one of the C–N bonds and (ii) hydrogen abstraction by an excited nitroxide. The former is the mechanism in the case of di-*tert*-butyl nitroxide[7] which yields 2-methyl-2-nitrosopropane and *tert*-butyl radical which is then scavenged by a second nitroxide molecule. In the case of cyclic nitroxide, 3-carbamoyl-2,2,5,5-tetramethylpyrroline-1-oxyl, α-cleavage is followed by loss of nitric oxide to yield a diene as product.[3] The abstraction mechanism (ii) has been observed in systems such as 4-hydroxy-2,2,6,6-tetramethylpiperidine-*N*-oxyl[6] and a steroid nitroxide.[4]

Recent work from this laboratory[10] on the reaction of nitroxides such as 2,2,6,6-tetramethylpiperidine-*N*-oxyl (Tempo) with diphenylcarbene showed that some nitroxide decomposition occurred on direct photolysis of Tempo in both acetonitrile and isooctane. The products (GC–MS) indicated the addition of a solvent moiety (e.g., $-CH_2CN$ from acetonitrile) to the nitroxide; mechanisms i and ii were suggested as possible reaction paths, with the former followed by addition of the radical resulting from α-cleavage to the solvent being favored. This reaction has now been examined in detail by product studies and quantum yield measurements. The results, which indicate that excited Tempo is an efficient hydrogen abstractor, may be compared with recent data for hydrogen abstraction by excited states of transient radicals.

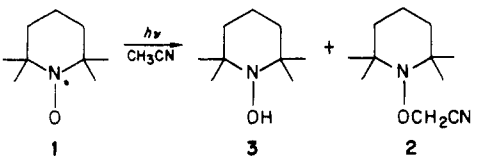
Table I. Quantum Yields for Product Formation for the Photolysis of Tempo in Various Solvents at 310 K

solvent	product	quantum yield[a]
acetonitrile	2	0.14
acetonitrile-d_3	2-d_2	0.16
toluene	4	0.022
toluene-d_8	4-d_7	0.021

[a] Average of two measurements.

Results and Discussion

Prolonged irradiation of a deaerated acetonitrile solution of Tempo (1) led almost exclusively to a single product, which GC–MS showed to correspond to the addition of $-CH_2CN$ to Tempo. The material was isolated and identified as **2** on the basis of its IR, NMR, MS, and elemental analysis. Examination of the photolysis mixture by capillary GC after short irradiation times (i.e., conversions $\leq$20%) indicated the formation, in addition to **2**, of a second primary photoproduct and that the two were formed in equal yields at low conversion. However, the second product readily reverted to starting material upon standing. This material was identified as **3** on the basis of its GC–MS spectrum and its ready oxidation to **1** and by analogy with earlier work.[9] These results indicate that excited Tempo abstracts hydrogen from the solvent to produce **3** plus a $\dot{C}H_2CN$ radical which then couples with a second Tempo molecule to produce **2**. This is a somewhat surprising result as hydrogen abstraction from acetonitrile is not normally a facile process. For example, the combined data from competitive reactions indicate that even at 408 K hydrogen abstraction from acetonitrile by *tert*-butoxyl radicals is ~20 times slower than that from cyclohexane.[11]



1 3 2 (1)

Photolysis of Tempo in toluene resulted in a similar hydrogen abstraction reaction to yield the expected

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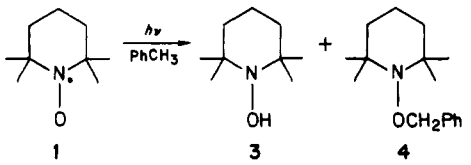
products, 3 and 4 (2), as previously observed for 4-



(2)

1 3 4

hydroxy-Tempo.[4] Quantum yields for the production of 2 and 3 in acetonitrile and toluene, respectively, were measured by using the production of acetophenone from valerophenone in benzene ($\Phi = 0.3$) as an actinometer.[12] The values obtained in these two solvents and in their deuterated analogues are given in Table I. The quantum yield in acetonitrile was ~6 times higher than that in toluene, even though toluene is normally considered the better hydrogen donor. The quantum yields in both cases changed very little upon deuteration of the solvent. However, photolysis of Tempo in a 1:1 acetonitrile/acetonitrile-d_3 mixture gave a 1.0:1.1 mixture of 2 and 2-d_2, which indicates a small inverse isotope effect on the hydrogen abstraction reaction.

A possible explanation for the low quantum yield in toluene relative to that in acetonitrile is that excited Tempo undergoes efficient nonreactive quenching by toluene. A reduction in the excited state lifetime would tend to decrease the quantum yield for product formation even though the rate of hydrogen abstraction in toluene could be similar to or greater than that in acetonitrile. To test for this possibility Tempo was photolyzed in a 1:1 molar mixture of toluene and acetonitrile. The ratio of 2/4 was ~5.5, which agrees well with the ratio of quantum yields in acetonitrile and toluene. Therefore, the differences in quantum yields cannot be due to a reduced lifetime for excited Tempo in toluene.

A number of attempts to detect transient signals from Tempo in toluene and a variety of other solvents by laser flash photolysis were carried out by using 308-nm laser pulses for excitation. However, no signals which could be assigned to radicals formed by hydrogen abstraction from solvent were observed.[13] We attribute this to the small radical yield in these systems and the rapid scavenging of the solvent-derived radical by Tempo (e.g., $k_q = 6.3 \times 10^7$ M^{-1} s^{-1} for reaction of benzyl radical in toluene from ESR measurements).[14] Attempts to observe fluorescence from Tempo were similarly unsuccessful.

The high reactivity of acetonitrile remains a puzzling question. Comparison of the UV–vis spectra in acetonitrile and toluene does not show evidence of complexation of the type reported in carbon tetrachloride;[8] only a small blue shift of the visible band in acetonitrile was observed. It is, however, likely that charge transfer plays a role in the reaction; quite simply, homolytic cleavage of the C–H bond cannot lead to higher reactivity for acetonitrile than toluene given the higher bond dissociation energy for the former.[15] The small isotope effects would also be consistent with this idea, although low or negligible isotope effects are not unexpected in fast reactions, particularly when their rates approach diffusion control.

The excited state of Tempo must be very short-lived since it could not be detected by either fluorescence or absorption measurements. Hydrogen abstraction must be competitive with the other deactivation pathways and is, thus, estimated to be $\geq 10^9$ M^{-1} s^{-1}; this is several orders of magnitude larger than the rate constants observed for excited diphenylmethyl[16] and 1-naphthylmethyl radicals.[17] For example, the reaction of the excited 1-naphthylmethyl radical with the excellent hydrogen donor tri-*n*-butylstannane occurs with only $k \sim 1 \times 10^7$ M^{-1} s^{-1} at room temperature.[17] It should also be noted that excited Tempo may also undergo reversible α-cleavage in competition with hydrogen abstraction and radiationless deactivation pathways. Finally, irradiation of Tempo in acetonitrile at $\lambda > 390$ nm did not lead to any detectable chemical change. In more quantitative terms, the quantum yield in this region is at least 10 times lower than that in the UV ($300 < \lambda < 350$ nm) region. This seems to indicate that the reaction occurs from an upper excited state. Quantum yields somewhat higher than ours have been reported in cyclohexane[18,19] at irradiation wavelengths as short as 250 nm; this might reflect some wavelength dependence even in the UV region.

Experimental Section

Tempo (Aldrich) was sublimed before use. Toluene was purified by washing with cold H_2SO_4 and water and then distilling from calcium hydride. Acetonitrile (spectro grade) and benzene (Aldrich, gold label) were used as received. Valerophenone was distilled before use. Acetonitrile-d_3 and toluene-d_8 (Merck, Sharp and Dohme; 99.7 and 99.6 atom % D, respectively) were used as received.

GC analyses were done on a Perkin-Elmer 8320 gas chromatograph equipped with a 12-m BP1 on vitreous silica capillary column. GC–MS spectra were recorded on a Hewlett-Packard 5995 instrument with a 10-m Ultra 1 (OV-101) capillary column. ^{13}C NMR and 500-MHz ^1H NMR spectra were measured on a Bruker AM-500 spectrometer. The 60-MHz NMR spectra were recorded on a Varian EM-360 spectrometer. Liquid chromatographic separations were done on a Perkin-Elmer instrument with a Lobar silica gel 60 prepacked column (Merck, 1 cm × 24 cm). All except the visible irradiations were done with RPR 3000 lamps. The visible irradiations were done with a 150-W xenon lamp and a 400-nm cutoff filter.

Quantum Yields. Quantum yields were measured for Tempo in acetonitrile-d_0 and acetonitrile-d_3 (0.138 M) and toluene-d_0 and toluene-d_8 (0.110 M) by using valerophenone in benzene as an actinometer (Φ(acetophenone) = 0.3[12]). The solutions were deaerated with bubbling nitrogen and irradiated (RPR 3000 lamps) in a merry-go-round reactor to ≤10% conversion. Substrate concentrations were chosen to ensure >99% light absorption at 310 nm. Product analyses were done by GC using 1-methylnaphthalene (added after the irradiation) as an internal standard.

Product Studies. (a) A degassed solution of 0.05 M Tempo in acetonitrile was irradiated to ~20% conversion. GC–MS analysis showed approximately equal amounts of 2 and 3. However, 3 was not particularly stable in solution at room temperature and was readily reoxidized to Tempo. Prolonged photolysis led to nearly quantitative conversion of Tempo to 2; a small amount (~5%) of a minor unidentified material was also formed: mass spectrum, *m/e* (relative intensity) 214 (2.6), 156 (10.6), 126 (32.1), 42 (100); ^1H NMR ($CDCl_3$) δ 6.4 (br s, 1 H), 5.6 (br s 1 H), 4.35 (s, 3 H), 1.6–1.3 (m, 6 H), 1.16 (s), 1.13 (s).

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(13) Typical concentrations of Tempo in these experiments were 0.005–0.012 M. Attempts to detect $PhCH_2$ in toluene were unsuccessful even when the expected lifetimes (controlled by nitroxide trapping) would be approximately 1 μs.[14] The details of the experimental set-up have been reported elsewhere: Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747–7754.

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(18) For adequate comparison the reported yields[19] need to be divided by 2; since they correspond to nitroxide consumption, rather than product formation.

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Photolysis of 200 mg of Tempo in 20 mL of acetonitrile to >95% conversion followed by liquid chromatography (1:9 CH_3CN/CH_2Cl_2) gave a pure sample of **2** as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 4.51 (s, 2 H), 1.6–1.3 (m, 6 H), 1.20 (s, 6 H), 1.10 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 115.89, 62.59, 60.20, 39.46, 32.89, 19.61, 16.80; mass spectrum, *m/e* (relative intensity) M^+ 196 (2.5), 181 (26.5), 156 (47.1), 41 (100); IR 2060 (w), 1740, 1690 cm^{-1}.[20] Anal. Calcd for $C_{11}H_{20}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 66.92; H, 10.18; N, 14.10.

(b) Irradiation of a degassed solution of 0.05 M Tempo in toluene to ~20% conversion gave approximately equal amounts of two compounds which GC–MS indicated to be **3** and **4**. The photolysis mixture contained a large number of components if the photolysis was continued to >40% conversion. Therefore, the structure of **4** was confirmed by comparison with an authentic sample prepared by photolysis of 0.2 M dibenzyl ketone plus 0.04 M Tempo in benzene. The photolysis mixture contained ~60% **4** and ~40% of a second material probably formed by Tempo trapping of the phenylacetyl radical before decarbonylation. Flash chromatography on silica gel using 5% EtOAc/hexane as eluent gave a pure sample of **4** as a colorless oil: NMR (60 MHz, $CDCl_3$) δ 7.3 (s, 5 H), 4.8 (s, 2 H), 1.5 (s, 6 H), 1.3–1.1 (m, 12 H); mass spectrum, *m/e* (relative intensity) M^+ 247 (2.3), 156 (100).

Registry No. **1**, 2564-83-2; **2**, 102261-91-6; **3**, 7031-93-8; **4**, 102261-92-7; CH_3CN, 75-05-8; $PhCH_3$, 108-88-3.

(20) The weak band at 2060 cm^{-1} is assigned to the C≡N group and agrees well with the reported spectrum for methoxyacetonitrile,[21] although it is much weaker and somewhat shifted from the usual C≡N bands.

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Structure Elucidation of a New Neutral Macrolide Antibiotic

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The macrolide antibiotics are a class of complex natural products which may be broadly divided into two general classes, namely, basic macrolides and neutral macrolides. Although the basic macrolides comprise all of the antibacterials that are of commercial interest in the human health area, the neutral members of this family are of considerable interest as lead structures in semisynthetic programs. This report details the structure elucidation of a new, neutral, 16-membered macrolide antibacterial, which has been isolated from *Streptomyces hirsutus*.[1]

Results and Discussion

I. Molecular Formula. The antibacterial class of the natural product was readily established, since it proved to have a narrow, gram-positive in vitro spectrum with no microbiologial activity against a typical macrolide resistance marker.

The structure elucidation was initiated by assigning a molecular formula to compound **1**. This was expeditiously accomplished by ^{13}C NMR spectroscopic techniques, since electrophoresis revealed that **1** was neutral and combustion analysis established the presence of only C, H, and O. (Anal. Found: C, 61.27; H, 8.19). The standard ^{13}C NMR spectrum as well as a polarization transfer (DEPT)[2] experiment (illustrated in Figure 1) of **1** supported a carbon number of 35 with 54 nonexchangeable protons bonded directly to carbon. Furthermore, the number of exchangeable protons, and their corresponding vicinally attached carbons was ascertained by the direct observation of vicinal deuterium isotope shifts of –0.06 ppm[3] for two carbon resonances absorbing at 75.11 ppm and 72.74 ppm, respectively; thus, the total number of protons must be 56. Therefore, the ^{13}C NMR observations in conjunction with the combustion analysis support a molecular formula of $C_{35}H_{56}O_{13}$.

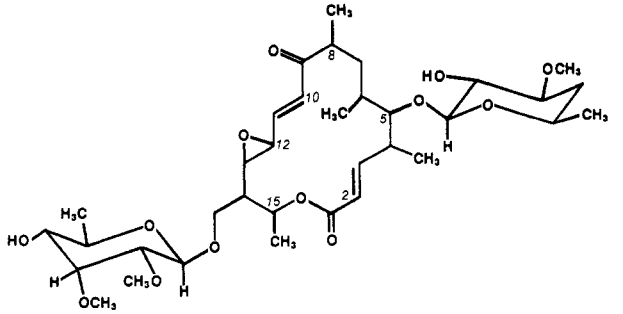
Table I. ^{13}C NMR Summary

carbohydrate carbon assignment	^1H NMR band	mycinose		^1H NMR band	chalcose	
1	IIb	100.93[a]	101.3[b]	IIc_1	103.44[a]	104.0[b]
2	IIg_1	81.92	82.1	IIf_2	75.11	74.7
3	IId	79.69	79.0	IIf_4	80.52	80.2
4	IIf_5	72.74	72.9	$IIIb/IVb_1$	36.85	37.4
5	IIe_4	70.71	70.8	IIe_5	67.82	68.0
5′	IVb_2	17.78	17.7	IVb_3	20.91	21.0
3′	IIe_2	61.69	61.4		56.81	56.9
2′	IIe_3	59.65	58.9			

[a] ^{13}C NMR chemical shifts for natural product. [b] ^{13}C NMR chemical shifts for β-methyl acetals.

Table II. ^{13}C NMR Summary

δC	proton attachments	^1H NMR band	aglycon carbon assignment
200.95	0		9
165.39	0		1
151.21	1	Ia_1	3
143.96	1	Ia_3	11
125.60	1	Ia_2	10
120.55	1	Ib	2
86.96	1	IIf_1	5
68.70	1	IIa	15
67.04	2	IIc_2,IIe_1	14′
59.04	1	IIf_3	12
58.91	1	IIg_2	13
49.48	1	IVa_1	14
44.68	1	$IIIa_2$	8
41.78	1	$IIIa_1$	4
34.14	1	IVb_5	6
32.02	2	IIIc	7
18.75	3	IVb_4	4′
18.41	3	IVa_2	15′
17.58	3	IVc	8′
17.01	3	IVd	6′



1

II. Carbohydrate Fragments. The ^{13}C NMR spectrum (Figure 1) indicates two carbon resonances with

(1) The fermentation and isolation of **1**, as well as the characterization of the producing organism, will appear elsewhere.

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