The deuterium NMR experiments were run with a spectral width of 500 Hz and an 8K block size giving an acquisition time of 8.19 s. The spectra were broad-band decoupled. The tip angle was set at 10°. On multipulse experiments, a delay of 5 s was sufficient to let the nuclei relax completely. This was shown by comparing the integration with the corresponding single-pulse experiment.

Metalation of Phenylcyclopropane. In a typical metalation reaction, potassium *tert*-butoxide (1.25 g, 11.2 mmol), phenylcyclopropane (1.25 g, 10.6 mmol), *n*-butyllithium (6.9 mL of 1.6 M *n*-butyllithium, 11.0 mmol), and 20 mL of dry hexane were combined under nitrogen in a Schlenk flask equipped with a magnetic stirring bar. The heterogeneous reaction was stirred at room temperature under nitrogen before quenching with D_2O or H_2O. If the reaction mixture was heated, the stopper was replaced by a reflux condenser and gas tube. The flask was placed in an oil bath, and the solvent was allowed to reflux with stirring.

Preparation of 1-Phenylchlorocyclopropane (7). In a 250-mL three-neck round-bottom flask equipped with a reflux condenser and magnetic stirring bar, 100 mL of dry benzene, 1-phenylcyclopropanecarboxylic acid (5 g, 30.9 mmol; mp 80–81 °C),[27] and LiCl (1.3 g, 30.6 mmol) were combined and degassed. $Pb(OAc)_4$[28] (14 g, 31.6 mmol) was added, and then the mixture was stirred until it became nearly homogeneous. The flask was then placed in an oil bath at 100 °C and the mixture stirred until gas evolution ceased. The reaction mixture was filtered, the solids were washed with ether, and the combined organic phase was then washed three times with saturated aqueous $NaHCO_3$ and then dried over $MgSO_4$. After removal of the drying agent, the benzene and ether were then removed by rotary evaporation. The residue was then bulb-to-bulb distilled to give 2.8 g of 1-phenylchlorocyclopropane (7), pure by GLC analysis:[29] NMR ($CDCl_3$) δ 1.28 (m, 2 H), 1.49 (m, 2 H), 7.25 (m, 3 H), 7.48 (m, 2 H). Anal. Calcd for C_9H_9Cl: C, 70.83; H, 5.94. Found: C, 70.78; H, 5.96.

Preparation of Bis(1-phenylcyclopropyl)mercury (8). In a three-neck 100-mL round-bottom flask equipped with a reflux condenser, magnetic stirring bar, and dropping funnel, Mg (0.40 g, 17 mmol), 20 mL of the THF, and a crystal of iodine were combined under nitrogen. 1-Phenylchlorocyclopropane (2.5 g, 16 mmol) in 5 mL of THF was added dropwise with stirring. Upon completion of the addition, the mixture was heated at reflux for 1 h under nitrogen. After cooling to room temperature, the Grignard reagent was taken up by syringe and added slowly to $HgCl_2$ (1.7 g, 6.3 mmol) in 20 mL of THF under nitrogen. The reaction mixture was then heated at reflux for 1 h and then worked up as follows: saturated aqueous ammonium chloride (50 mL) and ether (50 mL) were added; the organic layer was separated, and the aqueous layer was washed twice with 25 mL of ether. The combined organic layers were dried over $MgSO_4$ and filtered, and the solvents were removed by rotary evaporation. The residue was recrystallized from acetone/water, giving 2.1 g of bis(1-phenylcyclopropyl)mercury (8) as clear colorless needles, mp 109–111 °C: ^1H NMR ($CDCl_3$) δ 0.98 (m, 4 H), 1.11 (m, 4 H), 7.00 (m, 4 H), 7.17 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 10.08 (t), 49.11 (s, $^1J_{^{13}C-^{199}Hg}$ = 532 Hz), 124.37 (d), 128.12 (d), 128.93 (d, $^3J_{^{13}C-^{199}Hg}$ = 19 Hz), 150.63 (s); MS (EI), *m/e* (relative intensity) 436 (9), 206 (15), 117 (100), 91 (53). Anal. Calcd for $C_{18}H_{18}Hg$: C, 49.71; H, 4.17. Found: C, 49.66; H, 4.17.

Preparation of (1-Phenylcyclopropyl)potassium (5). In a Schlenk flask under nitrogen were combined Na/K alloy (0.10 mL), 8 (0.11 g, 0.25 mmol), and 10 mL of hexane. The flask was stoppered and the mixture stirred at room temperature for 1 h. The stopper was removed and replaced by a refulx condenser and gas tube. The reaction mixture was then heated to reflux in an oil bath. After heating for 4 h, the heterogeneous mixture was allowed to cool to room temperature and 2 mL of water was added. The sole product detected by GLC analysis was phenylcyclopropane (96% yield by the internal standard method).

Acknowledgment. We thank the Research Corporation (Grant 10693) and the UNCC Foundation for their partial support of this work. C.A.O. would also like to thank Dan Deadwyler for obtaining the ESR spectra and Tony Aldridge for obtaining the GC/MS data.

(27) Sychkova, L. D.; Shabarov, Y. S. *Zh. Org. Khim.* **1980**, *16*, 2086–91; *Chem. Abstr.* **1981**, *94*, 156437z. Attempts to prepare 1-phenylbromocyclopropane by the procedure suggested here failed in our hands.

(28) When old $Pb(OAc)_4$ was used or the reaction was not thoroughly degassed, the major product was 1-phenylcyclopropyl acetate: ^1H NMR ($CDCl_3$) δ 1.24 (m, 2 H), 1.31 (m, 2 H), 2.06 (s, 3 H), 7.18–7.37 (m, 5 H); IR neat 1742 cm^{-1}.

(29) If the temperature of the injector port was greater than 150 °C or the injector port was dirty, 7 was observed to rearrange to give 2-phenylallyl chloride: ^1H NMR ($CDCl_3$) δ 4.51 (s, 2 H), 5.56 (s, 1 H), 5.74 (s, 1 H), 7.30–7.60 (m, 5 H).

Synthesis of Substituted Cyclopentenones via Boron Trifluoride Mediated Ring Cleavage in Polycyclic Ketones

Alan P. Marchand* and V. Vidyasagar

Department of Chemistry, University of North Texas, Denton, Texas 76203-5068

Received October 30, 1987

The use of the retrograde Diels–Alder reaction as a strategy in the synthesis of natural products is well documented.[1,2] Currently, there is intense interest in the use of substituted tricyclo[5.2.1.$0^{2,6}$]decenones and -decadienones as intermediates in the synthesis of cyclopentanoid natural products. These compounds have been found to undergo [4 + 2] cycloreversion under flash vacuum pyrolysis (FVP) conditions to afford substituted cyclopentenones.[3-5] We now report a procedure for effecting ring cleavage in these systems that employs a Lewis acid catalyst (i.e., boron trifluoride etherate) at low temperatures (−10 °C to room temperature).

Thus, *exo*-2-carbomethoxy-*exo*-3-methyltricyclo[5.2.1.$0^{2,6}$]dec-8-en-5-one (**1**)[6] was reacted with a slight molar excess of boron trifluoride etherate at room temperature. Workup of the reaction mixture afforded 3-carbomethoxy-4-methylcyclopent-2-en-1-one (**2**) in 95% yield along with dicyclopentadiene. Compound **2** could also be obtained in similar yield via reaction of $F_3B{\cdot}OEt_2$ with *exo*-2-carbomethoxy-*exo*-3,7-dimethyltricyclo[5.2.1.$0^{2,6}$]dec-8-en-5-one (**3**[6]) at −10 °C. In another set of experiments, the reaction of either **1** or **3** with $F_3B{\cdot}OEt_2$ was initiated at −78 °C and then allowed to warm slowly to 0 °C. In each case, the reaction mixture was stirred for 3 h at 0 °C, at which time ethanedithiol (1 equiv) was added. Workup of each reaction mixture afforded **4** (i.e., the dithioketal of keto ester **2**) in essentially quantitative yield. These results along with the results of other closely related reactions are summarized in Table I.

Other results that appear in Table I merit comment. First, the corresponding reaction of dimer ketone **5** (synthesized via $Fe(CO)_5$-promoted coupling of norbornadiene to carbon monoxide)[7] with boron trifluoride etherate at ambient temperature affords *exo*-tricyclo[5.2.1.$0^{2,6}$]deca-

(1) For reviews, see: (a) Ripoll, J.-L.; Rouessac, A.; Rouessac, F. *Tetrahedron* **1978**, *34*, 19. (b) Lasne, M.-C.; Ripoll, J.-L. *Synthesis* **1985**, 121. (c) Ichihara, A. *Synthesis* **1987**, 207.

(2) Klunder, A. J. H.; Huizinga, W. B.; Sessink, P. J. M.; Zwanenburg, B. *Tetrahedron Lett.* **1987**, *28*, 357 and references cited therein.

(3) Verlaak, J. M. J.; Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron Lett.* **1982**, 5463.

(4) Klunder, A. J. H.; Bos, W.; Zwanenburg, B. *Tetrahedron Lett.* **1981**, 4557.

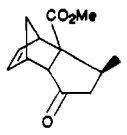
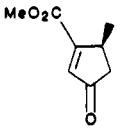
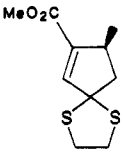
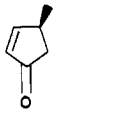
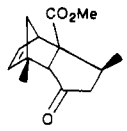
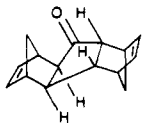
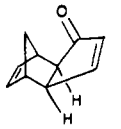
(5) Klunder, A. J. H.; Houwen-Claassen, A. A. M.; Kooy, M. G.; Zwanenburg, B. *Tetrahedron Lett.* **1987**, *28*, 1329.

(6) Smith, W. B.; Marchand, A. P.; Suri, S. C.; Jin, P.-w. *J. Org. Chem.* **1986**, *51*, 3052.

(7) (a) Pettit, R. *J. Am. Chem. Soc.* **1959**, *81*, 1266. (b) Green, M. L. H.; Pratt, L.; Wilkinson, G. *J. Chem. Soc.* **1960**, 989. (c) Green, M.; Lucken, E. A. C. *Helv. Chim. Acta* **1962**, *45*, 1870. (d) Cookson, R. C.; Henstock, J.; Hudec, J. *J. Am. Chem. Soc.* **1966**, *88*, 1059.

0022-3263/88/1953-4412$01.50/0

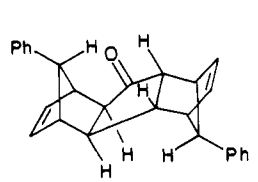
Table I

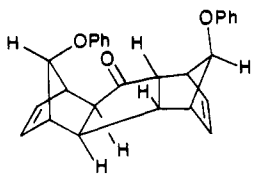
entry	substrate	reaction conditions	product (% yield)	ref
1	 1	$F_3B{\cdot}OEt_2$, 25 °C, 6 h	 2 (95)[a]	2
2	1	$F_3B{\cdot}OEt_2$, 25 °C, 6 h, $HSCH_2CH_2SH$ (1 equiv)	 4 (95)[a]	
3		$F_3B{\cdot}OEt_2$, 25 °C, 6 h	 (70)[a]	2
4	 3	$F_3B{\cdot}OEt_2$, −10 °C, 6 h	2 (95)[a]	7
5	 5	$F_3B{\cdot}OEt_2$, 25 °C, 4 h	 6 (80)[b]	8

[a] Yield of isolated material. [b] Yield based upon recovered starting material.

4,8-dien-3-one (**6**) in 80% yield (entry 5, Table I). Further fragmentation of **6** (which would afford cyclopentadiene and cyclopentadienone) does not occur. Thus, Lewis acid promoted fragmentation of **5** provides a useful method for synthesizing **6** (in which the cyclopentenone ring is fused to the exo face of the norbornenyl moiety).[8]

Finally, it should be noted that two additional dimer ketones, **7**[9] and **8**,[10] which are closely related to **5**, both fail to cleave when treated with boron trifluoride etherate at room temperature. The reasons for this are not clear, particularly in view of the fact that both **5** and **8** possess identical exo,trans,exo geometries.


7


8

It is likely that these boron trifluoride promoted fragmentation processes occur with initial 5-exo-trig ring opening (a favorable process, according to Baldwin's rules[11]). Driving force for the reaction is provided by the cleavage of a relatively strained σ-bond in the substrate–Lewis acid complex with concomitant formation of an allylic carbonium ion. Further fragmentation can then occur, thereby affording the observed reaction products. The intermediacy of a carbocation is suggested by the fact that the presence of the 1-methyl group in **3** appears to facilitate reaction with boron trifluoride etherate (cf. entries 1 and 4 in Table I). Interestingly, there appears to be no configurational bias in the ring opening; both exo- and endo-fused systems appear to suffer Lewis acid promoted cycloreversion with comparable facility (cf. entries 3 and 5 in Table I).

Experimental Section

Melting points are uncorrected. Chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. High-resolution mass spectra were obtained by the Midwest Center for Mass Spectrometry at the University of Nebraska, Lincoln, NE 68588-0362.

General Procedure for Boron Trifluoride Mediated Ring Cleavage. Synthesis of 3-Carbomethoxy-4-methylcyclopent-2-en-1-one (2). To a stirred solution of **1** (440 mg, 2.00 mmol) in methylene chloride (5 mL) under argon at 25 °C was added boron trifluoride etherate (250 mg, 2.20 mmol). The progress of the reaction was monitored periodically via thin-layer chromatography. After the reaction was judged to be complete (6 h), solid sodium bicarbonate (500 mg, excess) was added. The resulting mixture was stirred for 30 min, water (10 mL) was added, and the aqueous suspension was extracted with methylene chloride (3 × 10 mL). The combined organic layers were dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The crude product was purified via column chromatography (silica gel). The column was eluted initially with hexane (100 mL) to remove dicyclopentadiene and then with 1:9 ethyl acetate–hexane mixture (300 mL). Compound **2** (292 mg, 95%) was obtained: the infrared, ^1H NMR, and ^{13}C NMR spectra agreed with values reported previously for **2**.[2]

3-Carbomethoxy-4-methylcyclopent-2-en-1-one Dithioethylene Ketal (4). A solution of **1** (220 mg, 1.00 mmol) in methylene chloride (5 mL) was cooled to −70 °C via an external dry ice–acetone bath. To this cold solution was added boron trifluoride etherate (130 mg, 1.20 mmol). The resulting solution was stirred at −70 °C for 6 h, the cold bath was then removed, and the reaction mixture was allowed to warm gradually to ambient temperature. Ethanedithiol (188 mg, 2.00 mmol) was added to the reaction mixture, and the resulting solution was stirred at room temperature for 2 h. The reaction was quenched via addition of 10% aqueous sodium bicarbonate solution (15 mL). The organic layer was washed sequentially with water (5 mL) and with brine (5 mL). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography (silica gel). The column was eluted initially with hexane (75 mL) to remove dicyclopentadiene. Further elution with 1:9 ethyl acetate–hexane mixture (200 mL) afforded dithioketal **4** (218 mg, 95%): IR ($CHCl_3$) 1700 (s), 1600 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, J = 7.0 Hz, 3 H), 2.20 (dd, J_1 = 11.0 Hz, J_2 = 2.0 Hz, 1 H), 2.80 (dd, J_1 = 11.0 Hz, J_2 = 2.0 Hz, 1 H), 3.07 (m, 1 H), 3.35 (m, 4 H), 3.75 (s, 3 H), 6.60 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.0 (q), 38.0 (d), 40.0 (t), 41.0 (t), 50.5 (t), 51.8 (q), 70.5 (s), 137.0 (s), 145.8 (d), 165.0 (s); mass spectrum (70 eV), m/e (relative intensity) 230 (molecular ion, 100.0), 170 (92.0), 138 (57.8), 111 (41.9), 110 (41.7), 59 (43.6); exact mass calcd for $C_{10}H_{14}O_2S_2$: M_r 230.0434, found (high-resolution mass spectroscopy) M_r 230.0436.

Reaction of 5 with Boron Trifluoride Etherate. To a stirred solution of **5** (212 mg, 1.00 mmol) in dry methylene chloride (3 mL) was added boron trifluoride etherate (120 mg, 1.10 mmol) at ambient temperature. Stirring was continued for 4 h, and the reaction then was quenched with 10% aqueous sodium bicarbonate solution (15 mL). The organic layer was washed with water (20 mL), dried (anhydrous magnesium sulfate), and filtered, and the filtrate was concentrated in vacuo. The residue was

(8) Compound **6** has been prepared previously via reaction of (acetylene)hexacarbonyldicobalt with norbornadiene. See: (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 1* **1973**, 973. (b) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 977.

(9) Marchand, A. P.; Goodin, D. B.; Hossain, M. B.; van der Helm, D. *J. Org. Chem.* **1983**, *48*, 5392.

(10) Watson, W. H.; Marchand, A. P.; Dave, P. R. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1988**, *C44*, 940.

(11) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

purified via column chromatography (silica gel, eluted with 1:19 ethyl acetate–hexane mixture), to recover **5** (126 mg) and pure **6** (30 mg, 80% yield based upon recovered starting material); exact mass calcd for $C_{10}H_{10}O$: M_r 146.0732, found (high-resolution mass spectroscopy) M_r 146.0732. The infrared, ^1H NMR, and ^{13}C NMR spectra of this material were in agreement with values reported previously for **6**.[8]

Acknowledgment. We thank the Air Force Office of Scientific Research (Grant AFOSR-88-0132), the Robert A. Welch Foundation (Grant B-963), the National Institutes of Health (Biomedical Research Support Grant), and the University of North Texas Faculty Research Committee for financial support of this study.

Registry No. 1, 115514-30-2; 2, 115514-31-3; 3, 102830-58-0; 4, 115514-32-4; 5, 7427-90-9; 6, 699-82-1; 7, 90991-05-2; 8, 115514-33-5; dicyclopentadiene, 77-73-6; *exo*-3-methyltricyclo-[5.2.1.$0^{2,6}$]dec-8-en-5-one, 19305-54-5; 4-methylcyclopent-2-en-1-one, 23033-96-7.

Microwave-Induced Hydrolysis of Phospho Anhydride Bonds in Nucleotide Triphosphates

Wei-Che Sun,† Pamela M. Guy,† Jessica H. Jahngen,‡ Edward F. Rossomando,‡ and Edwin G. E. Jahngen*,†

Department of Chemistry, University of Lowell, Lowell, Massachusetts 01854, and Department of Oral Biology, University of Connecticut Health Center, Farmington, Connecticut 06032

Received March 21, 1988

A large body of literature exists on the effect of microwave radiation on biosystems which debates whether the observed aberations are due to general heating of the biosystem (hyperthermia) or are a consequence of the specific absorption of microwave energy.[1-7] Except for the precipitation of proteins such as in the formation of microwave-induced cataracts due to hypothermia,[3] very few reports address molecular changes due to the absorption of microwave energy on a chemical reaction or discrete compound. In contrast to microwave irradiation, recent reports indicate that ultrasound has been successfully employed in organic synthesis. Ultrasound has been used to effect the hydrolysis of carboxylic esters,[8] induce the cleavage of carbon–halogen bonds in the presence of zinc,[9] increase the rate of formation of lithium organometallic reagents,[10] and accelerate the synthesis of thioamides.[11] In one report ultrasound and/or microwave excitation of alkali-metal vapors was found to dehalogenate organic dihalides.[12]

Due to the reported changes of ATP levels in vivo following microwave radiation of an organ or oragnism,[13-15] we subjected purine and pyrimidine nucleotide 5′-triphosphates (NTP) to continuous wave microwave radiation at 2.54 GHz with a power density of 0.16 W/cm^2. Since the temperature of the samples became elevated during the period of irradiation, controls were externally heated by convection. The rate of heating and final temperature were shown to be similar for both controls and samples exposed to microwave radiation.

In the initial experiments, ATP was exposed to microwave radiation. A rapid, time-dependent loss of ATP was observed followed initially by a concomitant rise in the level of ADP and subsequently AMP. In a radiation period of 4 min, 90.9% of the ATP was hydrolyzed, while controls heated in a dry block demonstrated only 6.9% hydrolysis over the same time period. After a total of 15 min of heating in the dry block, hydrolysis of the controls rose

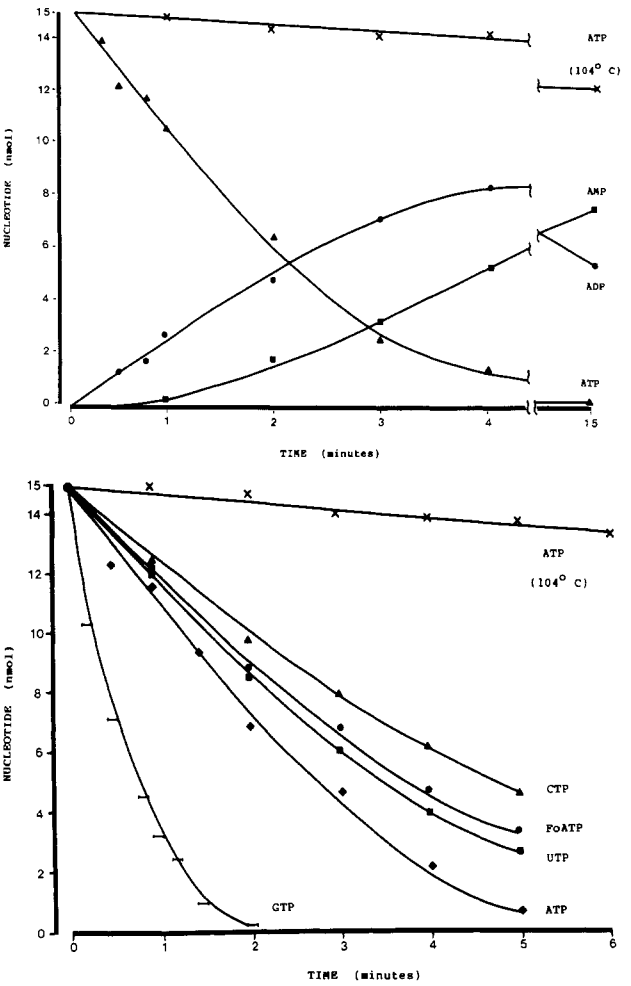


Figure 1. (a) Kinetics of the hydrolysis of ATP initiated by convection heating (X–X) and by microwave irradiation (▲–▲). ADP (●–●) and AMP (■–■) formation are from the microwave experiments. (b) Kinetics of microwave-induced hydrolysis of purine and pyrimidine nucleotide triphosphates. The control reaction is ATP (X–X) heated in a dry block.

* To whom correspondence should be addressed at Department of Chemistry, University of Lowell, Lowell, MA 01854.
† Department of Chemistry.
‡ Department of Oral Biology.

(1) Daily, L.; Wakim, K.S.; Herrich, J. F.; Parkhill, E. M. *Am. J. Physiol.* **1948**, *155*, 432.
(2) Richardson, A. W.; Duane, T. D.; Hines, H. M. *AMA Arch. Opthamol.* **1951**, *45*, 382–386.
(3) Glavin, M. J.; Parks, D. L.; McRee, D. I. *Radiat. Environ. Biophys.* **1981**, *19*, 149–156.
(4) Aragon, J. J.; Tornheim, K.; Goodman, M. N.; Lowenstein, J. *Curr. Top. Cell. Regul.* **1981**, *18*, 131–158.
(5) Swicord, M. L.; Edwards, G. S.; Sagripanti, J. L.; Davis, C. *Biopolymers* **1983**, *22*, 2513–2516.
(6) van Zandt, L. L.; Kohli, M.; Prohofsky, E. W. *Biopolymers*, **1982**, *21*, 1465–1468.
(7) Jensh, P. R. *Radiat. Res.* **1984**, *97*, 272–281.
(8) Moon, S.; Duchin, L.; Cooney, J. V. *Tetrahedron Lett.* **1979**, 3717–3921.
(9) Han, B. H.; Boudjouk, P. *J. Org. Chem.* **1982**, *47*, 751–752.
(10) Luche, J. L.; Petrier, C.; Gemal, A. L.; Zirkra, N. *J. Org. Chem.* **1982**, *47*, 3805–3808.
(11) Otteson, D.; Michl, J. *J. Org. Chem.* **1984**, *49*, 866–873.
(12) Raucher, S.; Klein, P. *J. Org. Chem.* **1981**, *46*, 3558–3559.
(13) Sanders, A. P.; Joines, W. T.; Allis, J. W. *Bioelectromagnetics (N.Y.)* **1984**, *5*, 419–433.
(14) Sanders, A. P.; Joines, W. T.; Allis, J. W. *Bioelectromagnetics (N.Y.)* **1985**, *6*, 89–97.
(15) Jahngen, E. G. E.; Rossomando, E. F.; Sun, W.-C. *Abstracts of Papers*, 13th International Congress of Biochemistry, 1985, Abstract 665, p 125.

0022-3263/88/1953-4414$01.50/0