Table I. Physical Properties of Polyisocyanides Prepared via α-Metalation Reactions

compd	mp, °C	^{1}H NMR ($CDCl_3$)	ν(CN), cm^{-1}	anal.:	calc (found)	yield,[a] %
1	78–80	7.35 (m, 10 H), 3.34 (t, 2 H), 2.54 (t, 2 H), 1.98 (m, 2 H)	2135	C:	64.97 (65.00)	72
				H:	5.14 (5.16)	
				N:	4.46 (4.57)	
2	117	7.36 (m, 20 H), 2.47 (t, 4 H), 1.65 (p, 2 H)	2136	C:	87.29 (87.35)	67
				H:	6.14 (6.50)	
				N:	6.57 (6.50)	
3	*b*	7.32 (m, 15 H), 4.61 (t, 1 H), 2.41 (t, 2 H), 1.88 (m, 2 H), 1.63 (p, 2 H)	2136		*c*	63
4	50–56	7.26 (m, 25 H), 2.23 (m, 4 H), 1.89 (m, 4 H), 1.51 (m, 2 H), 1.29 (m, 2 H)	2136	C:	86.40 (86.44)	61
				H:	6.40 (6.60)	
				N:	7.19 (6.96)	
5	50 dec	7.25 (m, 30 H), 2.15, 1.86, 1.48, 1.27, 1.15, 0.93 (m, 18 H)	2135	C:	85.90 (85.96)	10
				H:	6.54 (6.41)	
				N:	7.56 (7.60)	
6	120	7.32 (m, 20 H), 2.52 (t, 2 H), 2.06 (m, 2 H), 1.60 (m, 2 H)	2140	C:	83.03 (82.97)	70
				H:	6.25 (6.17)	
				N:	3.34 (3.14)	

[a] Corresponds to final step in reaction sequence. [b] Compound was isolated as a nondistillable oil. [c] We were unable to obtain a sample of this compound pure enough for an elemental analysis. However, it was used successfully in all subsequent reactions in slightly impure form.

chains of metals, as well as to heterobimetallic compounds, we have used α-metalated isocyanides to build potential ligands with two, three, and four isocyanide groups in a linear array (Figure 1). These compounds include 1,5-diisocyano-1,1,5,5-tetraphenylpentane; 1,5-diisocyano-1,1,5-triphenylpentane; 1,5,9-triisocyano-1,1,5,9,9-pentaphenylnonane; and 1,5,9,13-tetraisocyano-1,1,5,9,13,13-hexaphenyltridecane. Additionally, we were able to use this route to synthesize the first example of a bifunctional isocyanide–phosphine ligand ((4-isocyano-4,4-diphenylbutyl)diphenylphosphine).

Experimental Section

All reactions were carried out under a nitrogen atmosphere at −78 °C in THF freshly distilled from sodium benzophenone ketyl. Diphenylmethyl[7] and benzyl[8] isocyanides were prepared according to literature procedures; 2.5 M *n*-BuLi in hexane and 1,3-dibromopropane were purchased from Aldrich Chemical Co. Diphenylphosphine was obtained from Strem Chemicals. ^{1}H NMR spectra were recorded on an IBM Bruker 200-MHz spectrometer. IR spectra (CH_2Cl_2 solution) were taken on a Perkin-Elmer 1710 FT spectrophotometer. As a typical experimental procedure:

Synthesis of 1. Ten grams (0.052 mmol) of benzhydryl isocyanide in 75 mL of THF were cooled to −78 °C in a dry ice/acetone bath. With vigorous stirring, 20.8 mL of 2.5 M *n*-BuLi in hexane were slowly added, causing the solution to turn deep red. The red solution was transferred dropwise by means of an insulated cannula to a cold (−78 °C) solution of 20 mL (0.196 mol) of 1,3-dibromopropane in 40 mL of THF.[9] The mixture was allowed to warm to room temperature overnight, at which time the solvent was stripped off under vacuum. Once dry, the isocyanide was dissolved in a small amount of CH_2Cl_2 and chromatographed down a short column of alumina to remove solid LiBr. The product, which initially appeared as a pale yellow oil, precipitated after several hours under high vacuum (10^{-6} Torr). The resulting solid was washed with cold pentane and then recrystallized from hot ethanol to yield 11 g of a white crystalline solid.

Results and Discussion

The general synthetic route to these compounds is outlined in Figure 1. With the exception of **2**, the first step involves reacting lithiodiphenylmethyl isocyanide with an excess of 1,3-dibromopropane to yield compound **1**. Once isolated, **1** is treated with the lithium salt of benzylisocyanide to give **3**. Compound **3** can then be deprotonated and reacted with either 1 equiv of **1** to yield **4**, or 0.5 equiv of 1,3-dibropropane to give **5**. Ligand **2** is formed directly by the reaction of lithiodiphenylmethyl isocyanide with half an equivalent of 1,3-dibromopropane. Finally, the mixed isocyanide–phosphine compound, **6**, is prepared by treating diphenylphosphine with *n*-BuLi followed by slow addition of **1**.

All of the compounds, with the exception of **3**, are white, crystalline solids and can be purified by recrystallization from ethanol; compound **3** was obtained as a nondistillable, sticky, pale yellow oil. Table I includes physical data for the compounds **1–6**. With the exception of **6**, all were air stable materials but were stored in the refrigerator to prevent polymerization. Our initial attempts to prepare the Rh(I) complexes of several of these compounds have been successful and will be reported elsewhere.[10]

Acknowledgment. We thank Johnson-Matthey, Inc. for a generous loan of rhodium trichloride.

(7) Isenring, H. P.; Hofheing, W.; *Synthesis* **1981**, *1*, 385.
(8) Malatesta, L. *Gazz. Chim. Ital.* **1947**, *77*, 238.
(9) The slow rate of addition of lithiodiphenylmethyl isocyanide and large excess of 1,3-dibromopropane were found necessary to prevent the formation of substantial amounts of compound **2**.

(10) The formation of polynuclear complexes is indicated for the compounds based on characteristic color reactions with [Rh(1,5-cyclooctadiene)(μ-Cl)]$_2$.[11] This reagent is a very useful developer for thin-layer chromatographic separations of isocyanides because it produces colors which are characteristic of the formation of oligomeric Rh(I) compounds.[12] The wavelength of absorption of the Rh(I) complex is often indicative of the number of isocyanide groups in the ligand.
(11) Chatt, J.; Venanzi, L. M. *J. Chem. Soc.* **1957**, 4735.
(12) Di Pierro, M. J. Ph.D. Thesis, University of Minnesota, 1984.

An Improved Synthesis of 2-Oxathianyl Ketones

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The bicyclic oxathiane **1** (Scheme I)[1] has been found to be a useful chiral auxiliary both by us[2,3] and by others.[4]

(1) Eliel, E. L.; Lynch, J. E.; Kume, F.; Frye, S. V. *Org. Synth.* **1987**, *65*, 215.

0022-3263/90/1955-4951$02.50/0

Scheme I

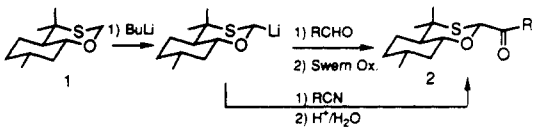

Table I

R	t, h	T, °C	2,[a] %	1,[b] %
^{i}Pr	1	0	63	–
^{i}Pr	1.5	0	67	13
^{i}Pr	5	0	67	13
^{i}Pr[c]	1.5	0	58	18
^{i}Pr	17	0	*d*	*d*
^{i}Pr	1.5	rt	58	8
^{i}Pr	1.5	−78	48	33
Et	1	0	60	17
Me	1	0	7	44
^{t}Bu	1.5	−20	78	–
Ph	1	0	82	–
p-ClC_6H_4	1.5	0	62	–
2-C_4H_3O	1.5	0	*e*	–

[a] Isolated yield of 2. [b] Recovered 1. [c] A solution of nitrile in THF was added slowly to the 2-lithiooxathiane solution in THF. [d] Low yield of product and recovery of starting material. [e] Complicated reaction produces, only 5 mg of desired ketone 2 was isolated.

The first step in the asymmetric synthesis shown in Scheme I (top) is the reaction of the chiral oxathiane, as the 2-lithium derivative, with an aldehyde followed by Swern oxidation to the ketone. This leads exclusively to the equatorial isomer, which, in a subsequent highly stereoselective[5] reaction with a Grignard reagent, R'MgX, followed by oxathiane cleavage, yields the chiral synthon RR'C(OH)CHO.

The conversion of oxathiane 1 to ketone 2 requires two steps of which the second, a Swern oxidation,[6] proceeds in good yield only if experimental conditions (such as dryness of solvent) are very carefully controlled.

We have now found that fair to good yields of ketones 2 (R = aryl or alkyl larger than methyl) can be obtained in a one-pot reaction by treating the lithio derivative of 1 with the appropriate nitrile followed by hydrolysis (Scheme I, bottom). While in initial experiments the reaction seemed to be confined to nitriles devoid of α-hydrogens, such as ArCN and $(CH_3)_3CCN$, we subsequently found that nitriles of type RCH_2CN or R_2CHCN (but not CH_3CN) could be used under appropriate conditions. The results are shown in Table I; a reaction time (*t*) of 1.5 h at 0 °C appears optimal.

While the reaction is not general (it failed with 3-cyanopyridine and with α,β-unsaturated nitriles such as acrylonitrile, crotononitrile, cinnamonitrile, which tended to polymerize under the conditions of the reaction; also, the yield of the product from 2-cyanofuran was very poor), it is a convenient method to produce alkyl ketones (except methyl ketone) which are useful intermediates. Evidently, nucleophilic addition competes favorably with α-proton abstraction from these nitriles, except in the case of acetonitrile, the most acidic of the aliphatic nitriles.

Experimental Section

General Procedures. Proton and carbon-13 NMR spectra were recorded in $CDCl_3$ at 200 and 50.3 MHz, respectively. Melting points are uncorrected. The ratio of ketone and unreacted oxathiane in the crude products was calculated using the integration of the proton signal at C (2) position of the oxathianyl ketone and the unreacted oxathiane.

Phenyl Oxathianyl Ketone 2 (R = Ph). To bicyclic oxathiane 1 (510 mg, 2.54 mmol) in dry THF (10 mL) under nitrogen at −78 °C was added 2.0 mL (3.30 mmol) of 1.6 M *n*-butyllithium in hexanes dropwise by syringe pump over 10 min. Stirring was continued for another 3 min. The solution was allowed to warm to 0 °C, and then benzonitrile (0.34 mL, 3.30 mmol) was added dropwise under nitrogen over 20 min by syringe pump. The reaction mixture darkened during the addition. Stirring was continued for 40 min at 0 °C, 2 N hydrochloric acid (5 mL) was added, and the mixture was stirred briefly at room temperature until two clear phases appeared. The organic layer was separated, and the aqueous layer was extracted four times with diethyl ether (5 mL each). The combined organic solution was washed with water (10 mL) and saturated aqueous sodium chloride (10 mL), dried over sodium sulfate, and concentrated to yield 0.87 g of a dark brown oil. Purification by flash chromatography on silica gel 60 (230–400 mesh) with 5% of ethyl acetate in hexanes gave 633 mg (82%) of the desired ketone, mp 93–94.5 °C (lit.[2] mp 94.5–95.5 °C). ^{1}H NMR and ^{13}C NMR spectra were identical to those reported.[2] ^{1}H NMR: δ 8.09–8.04 (m, 2 H), 7.59–7.38 (m, 3 H), 6.22 (s, 1 H), 3.57 (dt, *J* = 4.3, 10.4 Hz), 1 H), 1.56 (s, 3 H), 1.30 (s, 3 H), 0.92 (d, *J* = 6.4 Hz, 3 H), and others. ^{13}C NMR: δ 192.5 (C), 134.0 (C), 133.4 (CH), 129.3 (CH), 128.2 (CH), 80.7 (CH), 77.4 (CH), 50.3 (CH), 44.4 (C), 41.4 (CH_2), 34.4 (CH_2), 31.3 (CH), 29.1 (CH_3), 24.2 (CH_2), 22.3 (CH_3), 21.9 (CH_3).

Methyl Oxathianyl Ketone 2 (R = Me). By the same procedure above, 17 mg (7%) of the desired ketone was obtained from 200 mg of oxathiane 1 and 0.16 mL of acetonitrile; 87 mg of oxathiane 1 was recovered in this reaction. The proton NMR spectrum of ketone 2 was identical with that reported.[3b] ^{1}H NMR: δ 5.41 (s, 1 H), 3.41 (dt, *J* = 4.3, 10.4 Hz, 1 H), 2.24 (s, 3 H), 1.43 (s, 3 H), 1.26 (s, 3 H), 0.91 (d, *J* = 6.4 Hz, 3 H), and others.

Ethyl Oxathianyl Ketone 2 (R = Et). By the procedure described above, 153 mg (60%) of the desired ketone was prepared from 200 mg of starting oxathiane 1 and 0.22 mL of propionitrile; 33 mg of oxathiane 1 was recovered. ^{1}H NMR and ^{13}C NMR spectra of 2 were identical with those in the literature.[2] ^{1}H NMR: δ 5.44 (s, 1 H), 3.41 (dt, *J* = 4.3, 10.4 Hz, 1 H), 2.65 (q, *J* = 7.3 Hz, 2 H), 1.43 (s, 3 H), 1.26 (s, 3 H), 1.03 (t, *J* = 7.3 Hz, 3 H), 0.91 (d, *J* = 6.4 Hz, 3 H), and others. ^{13}C NMR: δ 208.1 (C), 82.5 (CH), 77.0 (CH), 50.3 (CH), 43.9 (C), 41.5 (CH_2), 34.6 (CH_2), 31.4 (CH), 31.3 (CH_2), 29.3 (CH_3), 24.3 (CH_2), 22.5 (CH_3), 22.0 (CH_3), 7.2 (CH_3).

Isopropyl Oxathianyl Ketone 2 (R = ^{i}Pr). By the reaction procedure described above 180 mg of pure product was obtained from 200 mg (1.0 mmol) of 1 and 0.27 mL of isobutyronitrile; 26 mg of oxathiane 1 was recovered. Recrystallization from pentane provided an analytical sample: mp 52–52.5 °C. Anal. Calcd for $C_{15}H_{26}O_2S$: C, 66.64; H, 9.69. Found: C, 66.29, 66.24; H, 9.83, 9.70. ^{1}H NMR: δ 5.52 (s, 1 H), 3.40 (dt, *J* = 4.3, 10.4 Hz, 1 H), 3.08 (h, *J* = 6.9 Hz, 1 H), 1.42 (s, 3 H), 1.24 (s, 3 H), 1.07 (d, *J* = 6.9 Hz, 3 H), 1.05 (d, *J* = 6.9 Hz, 3 H), 0.89 (d, *J* = 6.4 Hz, 3 H), and others. ^{13}C NMR: δ 208.9 (C), 81.8 (CH), 77.1 (CH), 50.3 (CH), 43.8 (C), 41.5 (CH_2), 36.1 (CH), 34.6 (CH_2), 31.3 (CH), 29.3 (CH_3), 24.2 (CH_2), 22.4 (CH_3), 22.0 (CH_3), 18.6 (CH_3), 18.2 (CH_3).

Oxathianyl *tert*-Butyl Ketone 2 (R = ^{t}Bu). When the above described reaction was performed at −20 °C, 1.080 g (78%) of product, mp 94.5–96.5 °C (lit.[7] mp 99–100 °C), was obtained from 0.981 g of oxathiane 1 and 1.18 g of trimethylacetonitrile. The proton NMR spectrum was identical with that of the compound

(2) Lynch, J. E.; Eliel, E. L. *J. Am. Chem. Soc.* **1984**, *106*, 2943. For a review, see: Eliel, E. L. *Phosphorus Sulfur* **1985**, *24*, 73.

(3) (a) Frye, S. V.; Eliel, E. L. *Tetrahedron Lett.* **1985**, *26*, 3907. (b) Frye, S. V.; Eliel, E. L. *J. Org. Chem.* **1985**, *50*, 3402. (c) Frye, S. V.; Eliel, E. L. *Croat. Chim. Acta* **1985**, *58*, 647. (d) Ohwa, M.; Kogure, T.; Eliel, E. L. *J. Org. Chem.* **1986**, *51*, 2599. (e) Ko, K.-Y.; Eliel, E. L. *J. Org. Chem.* **1986**, *51*, 5353. (f) Ohwa, M.; Eliel, E. L. *Chem. Lett.* **1987**, *41*. (g) Eliel, E. L.; Alvarez, M. T.; Lynch, J. E. *Nouv. J. Chim.* **1986**, *10*, 749. (h) Eliel, E. L.; Lynch, J. E. *Tetrahedron Lett.* **1987**, *41*, 4813. (i) Frye, S. V.; Eliel, E. L. *J. Am. Chem. Soc.* **1988**, *110*, 484.

(4) Kaulen, J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 462. Cervantes-Cuevas, H.; Joseph-Nathan, P. *Tetrahedron Lett.* **1988**, *29*, 5535.

(5) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748. See also: Eliel, E. L. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, p 125.

(6) Omura, K.; Sharma, A. K.; Swern, D. *J. Org. Chem.* **1976**, *41*, 957.

(7) Lynch, J. E. Ph.D. Dissertation, University of North Carolina, Chapel Hill, NC, 1982, p 56: Anal. Calcd for $C_{16}H_{28}O_2S$: C, 67.57; H, 9.92. Found: C, 67.18; H, 10.32. See also ref 3 h.

prepared previously.[7] ^{1}H NMR: δ 5.78 (s, 1 H), 3.43 (dt, J = 4.3, 10.4 Hz, 1 H), 1.44 (s, 3 H), 1.26 (s, 3 H), 1.21 (s, 9 H), 0.90 (d, J = 6.4 Hz, 3 H), and others.

p-Chlorophenyl Oxathianyl Ketone 2 (R = p-ClC$_6$H$_4$). To 50 mg (0.25 mmol) of oxathiane 1 in 1 mL of dry THF was added dropwise 0.36 mL of 1.39 M n-butyllithium in hexanes under N_2 at −78 °C. The solution was stirred for 0.5 h and then allowed to warm to 0 °C; p-chlorobenzonitrile (103 mg, 0.75 mmol) was added. Stirring was continued for 1.5 h at 0 °C, and then 1 mL of 2 N hydrochloric acid was added. After a few minutes the solution was neutralized with saturated aqueous sodium carbonate and extracted twice with ether (10 mL each). The extract was washed with saturated aqueous sodium chloride (5 mL), dried with magnesium sulfate, and concentrated to yield 133 mg of crude products. The ^{1}H NMR spectrum indicated over 90% conversion of starting oxathiane 1. The unreacted p-chlorobenzonitrile was removed by codistillation with 40 mL of water, and the residue was chromatographed using silica gel and 0–2% ethyl acetate in hexanes to give 53 mg (62%) of a light purple crystalline product: mp 95–95.5 °C. Anal. Calcd for $C_{18}H_{23}ClO_2S$: C, 63.79; H, 6.84. Found: C, 63.84; H, 6.87. ^{1}H NMR: δ 8.03 (td, J = 2.2, 8.6 Hz, 2 H), 7.40 (td, J = 2.2, 8.6 Hz, 2 H), 6.12 (s, 1 H), 3.56 (dt, J = 4.3, 10.4 Hz, 1 H), 1.55 (s, 3 H), 1.30 (s, 3 H), 0.92 (d, J = 6.4 Hz, 3 H), and others. ^{13}C NMR: δ 191.8 (C), 174.3 (C), 132.4 (C), 131.0 (CH), 128.6 (CH), 81.2 (CH), 77.6 (CH), 50.5 (CH), 44.7 (C), 41.5 (CH_2), 34.5 (CH_2), 31.4 (CH), 29.3 (CH_3), 24.3 (CH_2), 22.4 (CH_3), 22.0 (CH_3).

Oxathianyl Furyl Ketone 2 (R = 2-C$_4$H$_3$O). By the procedure described above, only 5 mg of the desired ketone was isolated from the reaction of 50 mg of oxathiane 1 and 70 mg of 2-furonitrile: (MH^+) calcd for $C_{16}H_{23}O_3S$ 295.1367, found 295.1364. ^{1}H NMR : δ 7.64 (dd, J = 0.6, 1.6 Hz, 1 H), 7.52 (dd, J = 0.6, 3.6 Hz, 1 H), 6.52 (dd, J = 1.6, 3.6 Hz, 1 H), 5.98 (s, 1 H), 3.53 (dt, J = 4.3, 10.5 Hz, 1 H), 1.51 (s, 3 H), 1.29 (s, 3 H), 0.92 (d, J = 6.3 Hz, 3 H), and others. ^{13}C NMR: δ 181.7, 149.8, 147.3, 121.5, 112.2, 81.2, 77.6, 50.6, 44.5, 41.6, 34.6, 31.5, 29.3, 24.4, 22.5, 22.0.

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Registry No. 1, 79618-03-4; 2 (R = iPr), 92572-77-5; 2 (R = Et), 79563-61-4; 2 (R = Me), 79563-75-0; 2 (R = t-Bu), 92572-79-7; 2 (R = Ph), 89556-31-0; 2 (R = p-ClC$_6$H$_5$), 127645-44-7; i-PrCN, 78-82-0; H_3CCH_2CN, 107-12-0; MeCN, 75-05-8; t-BuCN, 630-18-2; PhCN, 100-47-0; p-ClC$_6$H$_5$CN, 623-03-0; 2-furanonitrile, 617-90-3.

Synthesis of a New Photoactivatable Analogue of 11-*cis*-Retinal

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Introduction

Rhodopsin, an integral membrane protein, functions as a photoreceptor in vertebrate retina. Bovine rhodopsin consists of a single polypeptide chain of 348 amino acids whose sequence is known.[1-3] Hydropathy analysis[1,2] of the protein sequence and proteolysis and monoclonal antibody studies[4,5] suggest that the protein traverses the lipid bilayer seven times as α-helical segments. One model for the secondary structure of the protein is shown in Figure 1. The chromophore, 11-*cis*-retinal, is linked to Lys-296 in helix G as a Schiff base.[6,7] It is important to understand the nature of the chromophore–protein interactions which give rise to characteristic visible absorbance of rhodopsin with the absorption maximum at 500 nm. For this purpose it would be desirable to determine the orientation of retinal within the protein. One approach to this problem is the use of a retinal analogue that carries a photoactivatable group. The use of photoactivatable ligands to study their three-dimensional interactions with the proteins was introduced by Westheimer and his co-workers.[8] Previously, in this laboratory, the photosensitive analogue of retinal, *all-trans*-(*m*-diazirinylphenyl)retinal, has been used to study the orientation of retinal in bacteriorhodopsin, a seven-helical transmembrane protein.[9] On photoactivation, the analogue crosslinked efficiently to specific sites in bacterio-opsin. The crosslinking sites were identified by fragmentation of the labeled protein and sequence analysis of the appropriate fragments.[9]

We have now developed a similar approach to investigate the orientation of retinal in the visual pigment, bovine rhodopsin. Nakanishi and his co-workers have reported the synthesis of the photosensitive analogue, 3-(diazoacetoxy)-9-*cis*-retinal,[10] and used it in the crosslinking

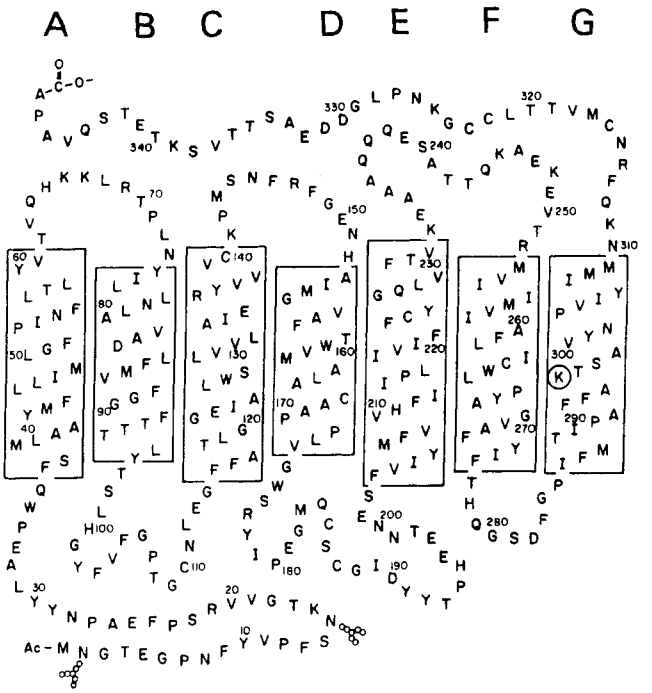

Figure 1. Secondary structure model of bovine rhodopsin (from ref 2). Seven transmembrane helices were designated as A–G. Lysine-296, the attachment site of retinal, is circled. Oligosaccharides (three molecules of each mannose and *N*-acetylglucoseamine) attached to two sites at Asparagine 2 and 15 are indicated by small circles. Amino acids are shown by one-letter codes.

(1) Ovchinnikov, Y. A.; Abdulaev, N. G.; Feigina, M. Y.; Artamonov, I. D.; Zolotarev, A. S.; Kostina, M. B.; Bogachuk, A. S.; Moroshnikov, A. I.; Martinov, V. I.; Kudelin, A. B. *Bioorg. Khim.* **1982**, *8*, 1011.
(2) Hargrave, P. A.; McDowell, J. H.; Curtis, D. R.; Wang, J. K.; Juszczak, E.; Fong, S.-L.; Rao, J. K. M.; Argos, P. *Biophys. Struct. Mech.* **1983**, *9*, 235.
(3) Nathans, J.; Hogness, D. S. *Cell* **1983**, *34*, 807.
(4) Dratz, E. A.; Hargrave, P. A. *Trends Biol. Sci.* **1983**, *8*, 128.
(5) Ovchinnikov, Y. A. *Trends Biol. Sci.* **1987**, *12*, 454.
(6) Bownds, D. *Nature (London)* **1967**, *216*, 1178.
(7) Wang, J. K.; McDowell, J. H.; Hargrave, P. A. *Biochemistry* **1980**, *19*, 5111.
(8) Chowdhry, V.; Westheimer, F. H. *Ann. Rev. Biochem.* **1979**, *48*, 293.
(9) Huang, K.-S.; Radhakrishnan, R.; Bayley, H.; Khorana, H. G. *J. Biol. Chem.* **1982**, *257*, 13616.
(10) (a) Sen, R.; Carriker, J. D.; Balogh-Nair, V.; Nakanishi, K. *J. Am. Chem. Soc.* **1982**, *104*, 3214. (b) Ok, H.; Caldwell, C.; Schroeder, D. R.; Singh, A. K.; Nakanishi, K. *Tetrahedron Lett.* **1988**, *29*, 2275.

0022-3263/90/1955-4953$02.50/0