

Photochemical Studies

II. The Structure of the Photodimers of Carbostyryl and N-Methylcarbostyryl

O. BUCHARDT

*Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen,
The H. C. Ørsted Institute, Copenhagen, Denmark*

On irradiation with ultraviolet light, carbostyryl and some of its derivatives dimerize.¹⁻⁴ Dimers of carbostyryl and N-methylcarbostyryl are shown to have the *trans-head-head-cyclobutane* structures IIa and IIb. The two photodimers are shown to be interrelated.

Photodimerization of α,β -unsaturated lactams have only been observed in a few cases.¹⁻⁷ 2-Pyridone and some of its derivatives were found to form cyclooctadiene rings on irradiation, resulting from 3,6-addition.⁵⁻⁷ The photodimerization of carbostyryl and N-methylcarbostyryl has been described,¹⁻³ but no detailed structural evidence was forwarded. Taylor and Paudler¹ suggested a cyclobutane structure for dimers of both pyridones and N-methylcarbostyryl, but with no definite proof.

The present paper describes the investigation of the structure of the photodimers of carbostyryl and N-methylcarbostyryl. The assignment of a *trans-head-head-cyclobutane* structure to both dimers has been made on the basis of spectroscopic as well as chemical evidence.

SPECTROSCOPIC EVIDENCE

The amide carbonyl absorption band in the infrared spectra (Table 1) showed a shift to higher frequencies on dimerization of the carbostyrils, thus indicating the disappearance of the α,β -double bond.

The absence of the conjugated carbonyl group was confirmed by, (a) the hypsochromic shift in the ultraviolet spectra of the dimers, compared with the spectra of the monomers, and (b) the similarity of the spectra of the dimers with those of the 3,4-dihydrocarbostyrils (Table 2).

The nuclear magnetic resonance spectra of the dimers showed the presence of typical aromatic protons (Table 3). This eliminated the possibility of struc-

Table 1. Observed carbonyl absorption frequencies in the infrared.

	In KBr cm ⁻¹	In dimethylsulfoxide cm ⁻¹
Carbostyryl	1665	1660
Dimer of carbostyryl	1715	1680
N-Methylcarbostyryl	1655	1660
Dimer of N-methylcarbostyryl	1672	1663

It is observed that the unusually high carbonyl frequency of the carbostyryl dimer (compared to the carbonyl frequency of the N-methylcarbostyryl dimer) in the solid state, disappears in solution. The high carbonyl frequency of the compound containing the -CO-NH-group is supposed to be due to intermolecular hydrogen bonding, which may also explain the insolubility in many solvents.²⁻⁴

Table 2. Ultraviolet spectra. Solvent: ethanol

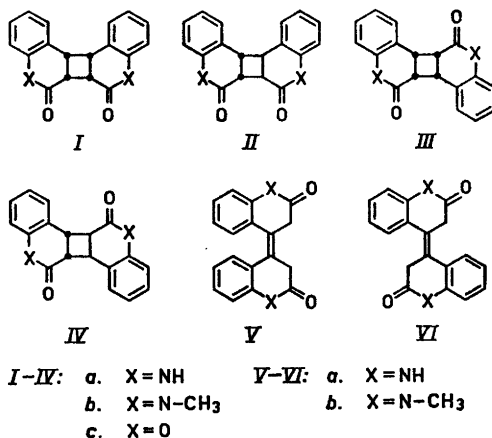
	m μ	log ϵ	m μ	log ϵ	m μ	log ϵ
Carbostyryl	229	4.54	268	3.85	328	3.80
Dimer of carbostyryl						
N-Methylcarbostyryl	229	4.59	270	3.87	329	3.79
Dimer of N-methylcarbostyryl	211	4.62	260	4.26		
3,4-Dihydrocarbostyryl	210	4.33	248	4.14		
N-Methyl-3,4-dihydrocarbostyryl	210	4.32	250	4.01		
	Solvent: dioxane					
	m μ	log ϵ	m μ	log ϵ	m μ	log ϵ
Carbostyryl	232	3.92	276	3.28	331	3.77
Dimer of carbostyryl	224	4.33	259	4.23	290	3.66
N-Methylcarbostyryl	254	4.24	278	3.76	334	3.79
Dimer of N-methylcarbostyryl	259	4.29				
3,4-Dihydrocarbostyryl	252	4.00				
N-Methyl-3,4-dihydrocarbostyryl	253	4.14				

tures analogous to those of the pyridone dimers and others where the aromatic character of the benzene nucleus is affected. The aliphatic protons in the carbostyryl dimer gave rise to a sharp singlet ($\tau = 5.88$) in trifluoroacetic acid. No other suitable solvent could be found for this compound.

The spectrum of the N-methylcarbostyryl dimer could be recorded in both trifluoroacetic acid and deuteriochloroform. In deuteriochloroform the aliphatic protons gave rise to a degenerate doublet ($\tau = 6.27$), (N-CH₃, $\tau = 6.56$). In trifluoroacetic acid this absorption shifted a little downfield and was observed as a narrow pair of doublets ($\tau_1 = 6.00$, $\tau_2 = 5.74$, $j_1 = j_2 = 5$ cps) (N-CH₃, $\tau = 6.33$).

At first, this seemed to exclude a cyclobutane structure, and a search was made for compounds with isolated protons such as V-VI (a and b). However, the ultraviolet spectra ruled out structures of that kind, and interest was

focused on cyclobutane structures like I-IV (a and b). These are very much like the coumarin dimers.⁸ Two such compounds were prepared, and their nuclear magnetic resonance spectra recorded (Table 3). The *trans-head-head*-isomer (IIc) showed the presence of aliphatic protons as a sharp singlet ($\tau = 6.15$) when recorded in deuteriochloroform. This singlet was split into a doublet ($\tau_1 = 5.87$, $\tau_2 = 5.97$) in trifluoroacetic acid. The *cis-head-head*-dimer (Ic), when recorded in trifluoroacetic acid, presented the cyclobutane protons as a singlet ($\tau = 5.69$). The almost identical chemical shifts of the aliphatic protons of the two carbostyryl dimers with the cyclobutane protons of the coumarin dimers strongly suggested structures I-IV (a and b) for the two carbostyryls. The chemical shifts of some other cyclobutane methine protons are also recorded (Table 3).



CHEMICAL EVIDENCE

Many attempts were made to hydrolyze the dimers, but all were unsuccessful.

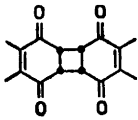
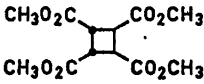
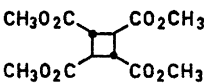
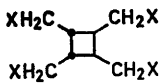
When treated with trifluoroacetic acid for some time, the carbostyryl dimer monomerized. This was shown to be common for dimers containing the NH-group.⁴

In order to examine how substitution affected dimerization, a number of methyl substituted carbostyryls were irradiated, and it was found that while carbostyryls substituted in the benzene nucleus easily dimerized, 3- and 4-substitution seemed to hinder dimerization.⁴

The cyclobutane structure was demonstrated in the following manner:

The carbostyryl dimer was ozonized, oxidized with hydrogen peroxide, and the product hydrolyzed with dilute hydrochloric acid. Without purification the hydrolyzate was methylated with diazomethane. The methylation yielded a crystalline compound. Infrared and nuclear magnetic resonance spectroscopy, and mixed melting point analysis showed the purified sample to be identi-

Table 3. Nuclear magnetic resonance spectra.

Compound	Ref.	Cyclobutane protons τ (p.p.m.)		Aromatic protons τ (p.p.m.)	
	8	CDCl ₃ 6.10	CF ₃ COOH	CDCl ₃	CF ₃ COOH
	9	6.15 6.23	(Found)		
	9	6.67			
 a. X = O ₂ CCH ₃ b. X = O ₂ CC ₆ H ₅	9	a. 7.42 b. 7.10			
Ic			5.69		3.00
IIc		6.15	5.92*	2.82	2.72
Dimer of carbostyryl			5.88		2.75
Dimer of N-methylcarbostyryl		6.27	5.87**	3.00	2.62

* Doublet: $\tau_1 = 5.87$; $\tau_2 = 5.97$

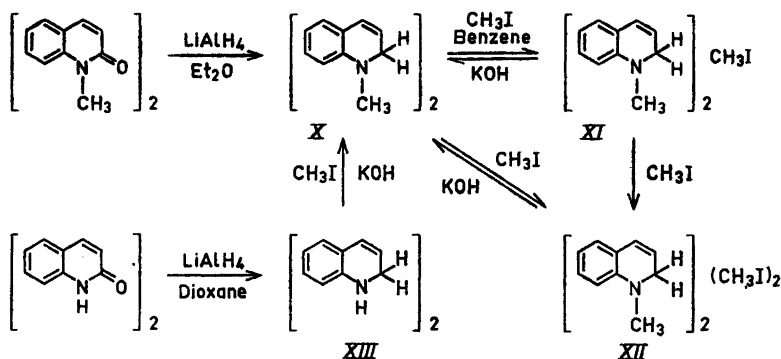
** Narrow doublet of doublets: $\tau_1 = 6.00$; $\tau_2 = 5.74$

cal with a sample of tetramethyl *cis-trans-cis*-cyclobutanetetracarboxylate prepared from *trans-head-head*-coumarin dimer.⁸ By chromatography a further amount of the main product could be obtained together with a small amount of a compound VII, m.p. 152–154°C. This result limits the possible structures for the carbostyryl dimer to IIa or IVa. By treating the N-methylcarbostyryl dimer in a similar manner, the tetramethyl *cis-trans-cis*-cyclobutanetetracarboxylate was obtained, together with small amounts of two other compounds, VIII, m.p. ca. 320°C and IX, m.p. 145–147°C. Thus the N-methylcarbostyryl dimer must have structures IIb or IVb.

Attempts to synthesize the N-methylcarbostyryl dimer from the carbostyryl dimer by methylation with methyl iodide or dimethyl sulfate were unsuccessful. However, it was possible to correlate the dimers in the following manner.

N-Methylcarbostyryl dimer on reduction with lithium aluminium hydride in diethyl ether yielded X. This compound could be converted to its monomethiodide (XI) on treatment with methyl iodide in benzene at room temperature. Both the monomethiodide (XI) and X on treatment with boiling methyl iodide yielded the dimethiodide (XII). On treatment with strong aqueous potassium hydroxide both XI and XII reverted to X.

The carbostyryl dimer was transformed to X in the following manner. Reduction with lithium aluminium hydride in dioxane yielded an oil which crystallized after some time to give XIII. When XIII was treated with methyl iodide followed by strong aqueous potassium hydroxide, it gave a crystalline product which was identified as X by infrared, ultraviolet, and nuclear magnetic resonance spectroscopy, and mixed melting point.



This shows that the two dimers have the same orientation with respect to the cyclobutane ring *i.e.* that they are both either *trans-head-head* IIa-IIb or *trans-head-tail* IVa-IVb compounds. The dipole moment of the *trans-head-tail*-form must be zero, while that of the *trans-head-head*-dimer should be rather large (the dipole moment of the *trans-head-head*-coumarin dimer has been found to be 5.7 D^8). The dipole moment of the carbostyryl dimer could not be measured because of the poor solubility of this compound. However, the dipole moment of the corresponding amine XIII was found to be 2.53 D (in benzene), and the dipole moment of the N-methylcarbostyryl dimer was found to be 5.28 D (in benzene). Lit.¹ gives 4.62 D (in chloroform). This, together with the reported spectroscopic and chemical evidence, establish the two dimers as IIa and IIb.

EXPERIMENTAL

Microanalysis were carried out in the microanalysis department of this laboratory by Preben Hansen.

Melting points (uncorrected) were determined on a Reichert melting point microscope, mixed melting points on a Büchi melting point apparatus.

Infrared spectra were recorded either on a Perkin Elmer "Infracord", or on its model 21 double beam spectrophotometer. Ultraviolet spectra were recorded on a Perkin Elmer model 137 UV spectrophotometer, and nuclear magnetic resonance spectra were recorded on a Varian A60 with tetramethylsilane as internal reference.

Electric dipole moments were determined by measuring the dielectric constants of solutions of the compounds in benzene at 25°C with the apparatus Dipolmeter DM 01 (Wissenschaftlich-Technische Werkstätten, Weilheim). The calculations were made using the equation and method of Hedestrand.¹¹⁻¹²

General procedure for photochemical reactions. Method a. This method has been described elsewhere.³

Method b. The solution to be irradiated was placed in a glass cylinder equipped with a sintered glass inlet for nitrogen.* A low pressure mercury lamp, NK 6/20 (Hanau) was then immersed into the cylinder.

Method c. The irradiations were carried out in a cylinder shaped reaction chamber with outer cooling, which was again equipped with a sintered glass inlet for nitrogen.* In the reaction chamber was placed a Q81 (Hanau) high pressure mercury lamp with a quartz cooling mantle through which was led deionized water during irradiations.

*Carbostyryl dimer.*² *Method a.* See previous paper.³ *Method b.* Carbostyryl (10.00 g 0.069 mole) dissolved in 96 % ethanol (100 ml) was irradiated for 6 days at ca. 35°C. The precipitated crystals were isolated (7.00 g, 70 %) m.p. ca. 300°C, subl. The IR: Table 1, the UV: Table 2, and the NMR: Table 3, spectra were identical with those given for the carbostyryl dimer.

*N-Methylcarbostyryl dimer.*¹ *Method c.* N-Methylcarbostyryl (5.00 g, 0.0315 mole) dissolved in 96 % ethanol (60 ml) was irradiated for 12 h at ca. 10°C. Half an hour before the reaction was started deoxygenized nitrogen was led through the solution, and this was continued during the irradiation. The precipitated white crystals were isolated (4.00 g, 80 %) m.p. 211–213°C. Recrystallization from ethanol raised the melting point to 215–216°C. (Found: C 75.45; H 5.78; N 8.80. Calc. for C₂₀H₁₈N₂O₂: C 75.45; H 5.70; N 8.80). IR: Table 1. UV: Table 2. NMR: Table 3. (N-CH₃, $\tau = 6.56$ in deuteriochloroform; $\tau = 6.33$ in trifluoroacetic acid). Dipole moment 5.28 D (benzene).

Coumarin dimers. These were prepared according to the method described by Schwenk *et al.*⁵

Hydrocarbostyryls. 3,4-Dihydrocarbostyryl was prepared according to the method described by Cavallito *et al.*¹³ The same method was used to prepare N-methyl-3,4-dihydrocarbostyryl.¹⁴ (Found: C 74.37; H 6.91. Calc. for C₁₀H₁₁NO: C 74.51; H 6.88). UV: Table 2.

Attempted hydrolysis of the dimers. The carbostyryl dimer or the N-methylcarbostyryl dimer was boiled with hydrochloric acid in several concentrations, but only the starting material could be isolated. When boiled with 50 % aqueous, 50 % ethanolic, or 80 % ethanolic potassium hydroxide for 24 h only starting material was again isolated.

Monomerization of the carbostyryl dimer in trifluoroacetic acid. The carbostyryl dimer (100 mg) in trifluoroacetic acid (0.5 ml) was kept at room temperature for ca. 60 h. During this time the nuclear magnetic resonance spectrum of the solution changed pattern from that of the carbostyryl dimer to that of the monomer. The solvent was evaporated and it was found that the infrared spectrum and the melting point also corresponded to that of the monomer carbostyryl.

Irradiation of substituted carbostyryls. See Ref.⁴

Tetramethyl cis-trans-cis-cyclobutanetetra-carboxylate. This was prepared from *trans-head-head-coumarin* dimer according to the method described by Schwenk *et al.*⁵ M.p. found: 143–144°C. Lit.⁸ 144.5°C. (Found: C 50.12; H 5.57. Calc. for C₁₂H₁₆O₈: C 50.00; H 5.60). NMR: Table 3. (O-CH₃, $\tau = 6.31$ in deuteriochloroform).

Degradation of carbostyryl dimer. Carbostyryl dimer (1.00 g, 3.45 mmole) was suspended in 80 % aqueous acetic acid (100 ml), and excess ozone passed into the solution for 7 h at room temperature, with constant stirring. 10 % Hydrogen peroxide (36 ml) was then added, and the solution left at room temperature. After 48 h, the solution was diluted to twice its volume with water, and the solvents removed by evaporation *in vacuo*.** Water (50 ml) was added, and the solution again taken to dryness *in vacuo*. The oily residue was dissolved in 0.4 N hydrochloric acid (40 ml), and heated on a steam bath for 2 h. The solution was evaporated to dryness, water was added, and the evaporation

* Only when stated nitrogen was led through the solutions during irradiation.

** Lit.¹⁵ warns that explosion may occur if evaporation is made at temperatures higher than 40°C. However, the author performed more than twenty ozonizations in the described way, followed by evaporations at 100°C, without accidents.

repeated. The residue was dissolved in 96 % ethanol (20 ml), and excess diazomethane in ether added. The solvents were removed by evaporation, and the semicrystalline residue (575 mg) was recrystallized from ethanol (177 mg, 18 %), m.p. 138–141°C. After several recrystallizations from ethanol and benzene the melting point was raised to 143–144°C. (Found: C 50.00; H 5.56. Calc. for $C_{12}H_{16}O_8$: C 50.00; H 5.60). It was identified by infrared and nuclear magnetic resonance spectroscopy, and by mixed melting point as being tetramethyl *cis-trans-cis*-cyclobutanetetracarboxylate.

VII. By chromatography on florisol of the mother liquor from the above methylation, some of the main product (50–50 benzene-petrolether) was isolated as well as a second fraction (2–98 ethyl acetate-benzene, 50 mg), which on recrystallization from ethanol had m.p. 152–154°C. (Found: C 48.50; H 5.51; N 5.30). This was not examined further.

Degradation of the N-methylcarbostyryl dimer. N-Methylcarbostyryl dimer (750 mg, 2.39 mmole) was ozonized and oxidized as described for the carbostyryl dimer. The product was dissolved in 0.4 N hydrochloric acid (40 ml), and the solution left at room temperature for 60 h before heating on a steam bath. The raw product was methylated as described for the carbostyryl dimer. On crystallization from ethanol the product from the methylation gave a crystalline compound (101 mg, 15 %), m.p. 138–140°C, which after several recrystallizations from ethanol and benzene melted at 143–144°C. (Found: C 50.20; H 5.55. Calc. for $C_{12}H_{16}O_8$: C 50.00; H 5.60). It was identified as tetramethyl *cis-trans-cis*-cyclobutanetetracarboxylate by infrared, and nuclear magnetic resonance spectroscopy, and by mixed melting point.

VIII. A small amount of a sparingly soluble compound (5 mg) which after recrystallization from ethyl acetate had m.p. ca. 320°C, subl., was obtained by recrystallization of the tetramethyl ester from N-methylcarbostyryl dimer. (Found: C 54.05; H 4.55).

IX. Chromatography on florisol of the mother liquor from the above methylation gave a compound (30 mg) m.p. 145–147°C. (Found: C 52.00; H 5.25; N 5.86). VIII and IX were not further examined.

X. *Reduction of the N-methylcarbostyryl dimer with lithium aluminium hydride.* N-Methylcarbostyryl dimer (2.98 g, 9.37 mmole) and lithium aluminium hydride (1.0 g) were suspended in anhydrous ether (750 ml). The mixture was stirred under nitrogen for 4 days after which the excess lithium aluminium hydride was decomposed by addition of a solution of acetone (4 ml) in ether (50 ml), followed by water (6 ml). The precipitated inorganic material was removed by filtration, and the solvent evaporated *in vacuo*. This gave an oil which crystallized after a short time. Recrystallization from benzene-ether yielded white cubic crystals (2.39 g, 84 %), m.p. 184–185°C. (Found: C 82.40; H 7.68; N 9.52; Mol.wt. 262 (cryoscopic in dioxane). Calc. for $C_{20}H_{22}N_2$: C 82.72; H 7.64; N 9.65; Mol.wt. 290). $\lambda_{max}^{EtOH} = 209 \text{ m}\mu$, $\log \epsilon = 4.55$; $252 \text{ m}\mu$, $\log \epsilon = 4.27$; $300 \text{ m}\mu$, $\log \epsilon = 3.77$. Nuclear magnetic resonance spectrum in deuteriochloroform: aromatic protons centered at $\tau = 3.16$; aliphatic protons as a strong singlet at $\tau = 7.13$, and a weak singlet at $\tau = 6.97$, in the ratio 4:7. In trifluoroacetic acid: aromatic protons at $\tau = 2.35$, aliphatic protons at $\tau = 5.86$ (triplet), and $\tau = 6.62$ (singlet), in the ratio 4:3:4.

XI. *Monomethiodide of X.* The compound X (260 mg, 0.90 mmole) was dissolved in a mixture of benzene (10 ml) and methyl iodide (3 ml) and left in the dark at room temperature for 8 days. The precipitated crystals were isolated and recrystallized from ethanol-water (325 mg, 86 %), m.p. 185–186°C. (Found: N 6.15; I 31.10. Calc. for $C_{21}H_{25}N_2I$: N 6.69; I 30.34).

XII. *Dimethiodide of X.* Compound X (318 mg, 1.00 mmole) was boiled with methyl iodide (15 ml) for 5 h. The excess methyl iodide was evaporated, and the residue crystallized from water (480 mg, 84 %), m.p. 260–270°C. (Found: C 46.15; H 5.15; I 44.80. Calc. for $C_{22}H_{28}N_2I_2$: C 46.00; H 4.92; I 44.54). The same compound was obtained by boiling XI with methyl iodide, and this was identified by infrared spectroscopy.

Reconversion of monomethiodide (XI) to X. Monomethiodide (XI) (106 mg, 0.25 mmole) and 40 % aqueous potassium hydroxide (10 ml) was heated on a steam bath for 1 h. During this time a precipitate was formed, which was extracted with methylene chloride-ether. The extract was washed with water and then with saturated sodium chloride solution and filtered through anhydrous magnesium sulfate. Evaporation of the solvents left a crystalline residue which after recrystallization was shown to be identical with X, by means of infrared spectroscopy (29 mg, 40 %).

Reconversion of dimethiodide (XII) to X. Dimethiodide (XII) (230 mg, 0.40 mmole) was treated with aqueous potassium hydroxide in the same way as XI to yield X (58 mg, 50 %), which was identified by infrared spectroscopy.

XIII. Reduction of the dimer of carbostyryl with lithium aluminium hydride. The carbostyryl dimer (2.00 g, 7.90 mmole) and lithium aluminium hydride (2.0 g) were suspended in dioxane (250 ml), and the suspension stirred under nitrogen for 19 h at room temperature. The excess lithium aluminium hydride was decomposed with a solution of water (5 ml) in dioxane (35 ml), ether was added, and the inorganic precipitate removed by filtration. The solvents were evaporated, and the resulting yellow oil left for 2 days, after which crystallization had begun. Treatment with ether-petrolether yielded white-yellow crystals (plates), (1.30 g, 63 %), m.p. 120°C. Recrystallization from ethanol raised the melting point to 125–126°C. (Found: C 82.20; H 6.89; N 10.72. Calc. for $C_{18}H_{18}N_2$: C 82.40; H 6.92; N 10.68). $\lambda_{\max}^{EtOH} = 208 \text{ m}\mu$, $\log \epsilon = 4.67$; $243 \text{ m}\mu$, $\log \epsilon = 4.23$; $300 \text{ m}\mu$, $\log \epsilon = 3.78$. Nuclear magnetic resonance spectrum in deuteriochloroform: aromatic protons were centered at $\tau = 3.17$, aliphatic protons as one peak at $\tau = 6.99$, amine protons at $\tau = 6.35$, in the ratio 4:4:1.

Methylation of XIII with methyl iodide. Compound XIII (525 mg, 2.00 mmole) was boiled with methyl iodide (10 ml) for 5 h. The excess methyl iodide was removed by evaporation and the residue was treated with aqueous potassium hydroxide as described for XI. Crystallization from ethanol yielded a compound (70 mg, 12 %), m.p. 184–185°C. (Found: C 82.07; H 7.73; N 9.38. Calc. for $C_{20}H_{22}N_2$: C 82.72; H 7.64; N 9.65). This compound was shown to be identical with X by infrared, ultraviolet, and nuclear magnetic resonance spectroscopy, and by mixed melting point.

Acknowledgements. The author wishes to thank prof. K. A. Jensen for his encouragement and interest in this work. Thanks are also due to Charles Larsen for measuring the dipole moments, and to J. Rastrup Andersen and K. Schaumburg for their help with the nuclear magnetic resonance spectroscopy.

REFERENCES

1. Taylor, E. C. and Paudler, W. W. *Tetrahedron Letters* **1960** 1.
2. Buchardt, O. *Acta Chem. Scand.* **17** (1963) 1461.
3. Elliott, I. W. *J. Org. Chem.* **20** (1964) 305.
4. Buchardt, O. *To be published.*
5. Slomp, G., MacKellar, F. A. and Paquette, L. A. *J. Am. Chem. Soc.* **83** (1961) 4472.
6. Ayer, W. A., Hayatsu, R., de Mayo, P., Reid, S. T. and Stothers, J. B. *Tetrahedron Letters* **1961** 648.
7. Taylor, E. C. and Kan, R. O. *J. Am. Chem. Soc.* **85** (1963) 776.
8. Schwenk, G. O., von Wilucki, I. and Krauch, C. H. *Chem. Ber.* **95** (1962) 1409.
9. Cookson, R. C., Cox, D. A. and Hudec, J. *J. Chem. Soc.* **1962** 1717.
10. Griffin, G. W., Velturo, A. F. and Furukawa, K. *J. Am. Chem. Soc.* **83** (1961) 2725.
11. Hedestrand, G. *Z. physik. Chem. (B)* **2** (1929) 428.
12. Oehme, F. and Wirth, H. *Die Bestimmung des molekularen Dipolmomentes*. Wissenschaftlich-Technische Werkstätten, Weilheim 1960.
13. Cavallito, C. J. and Haskel, T. H. *J. Am. Chem. Soc.* **66** (1944) 1166.
14. Späth, E. *Monatsh.* **40** (1919) 28.
15. Criege, R. and Höver, H. *Chem. Ber.* **93** (1960) 2521.

Received April 13, 1964.