

Azo Compounds. Investigation of Optically Active Azonitriles¹C. G. OVERBERGER AND D. A. LABIANCA²*Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48104**Received July 18, 1969*

The resolution of (\pm)-4,4'-azobis(4-cyanopentanoic acid) and the syntheses of (\pm)- and (-)-dimethyl 4,4'-azobis(4-cyanopentanoate) are reported. Photochemical decomposition of the (+) acid gives (-)-4-cyanopentanoic acid, whereas similar decomposition of the (+) ester results in no significant optical activity in the reaction products. Mechanistic interpretations of these results are discussed. The kinetics of thermal decomposition of the enantiomers and diastereomers of the azonitriles have been investigated and the ORD and CD data of the corresponding (-) isomers are presented.

For several years, the chemistry of azo compounds has been the subject of intensive study in our laboratories.^{1b} Of particular significance has been our interest in the question of whether or not the decomposition of an asymmetric dialkylazonitrile would result in the formation of asymmetric products. In order to explore these possibilities, the syntheses and properties of the first optically active aliphatic azonitriles were investigated. This paper describes the preparation of both enantiomers of 4,4'-azobis(4-cyanopentanoic acid) and of the corresponding dimethyl esters. Photochemical decomposition of (+)-4,4'-azobis(4-cyanopentanoic acid) led to the formation of an optically active disproportionation product, while the decomposition of the (+) ester gave rise to essentially no optical activity in the decomposition products. The difference in decomposition behavior between the (+) acid and the (+) ester is rationalized in terms of a mechanistic pathway involving either of two prestructured intermediates. The rates of thermal decomposition and the activation energies of the various azonitriles have been determined, and their ORD and CD properties are also discussed.

Results and Discussion

***meso*- and (\pm)-4,4'-Azobis(4-cyanopentanoic acid).**—The procedure of Haines and Waters,³ with some modification, was used to prepare the two diastereomers of 4,4'-azobis(4-cyanopentanoic acid). The two isomers were separated from each other by virtue of the fact that the *meso* isomer, unlike the racemic compound, is insoluble in 10% aqueous methanol. The procedural modifications involved stirring the mixed acids [*meso* and (\pm) isomers] in 10% aqueous methanol for 24 hr instead of shaking for 1 hr. This would presumably ensure a more complete separation. The (\pm) isomer was obtained by refrigeration of the filtrate remaining after isolation of the *meso* isomer. Evaporation of the filtrate under reduced pressure, the method previously employed to obtain the racemic isomer,³ was avoided to prevent possible contamination of the (\pm) isomer by concomitant precipitation of any *meso* isomer which may have been in solution. These changes were initiated to guarantee maximum purity of the (\pm) isomer, because Haines and Waters³ were unsuccessful

in their attempts to resolve this compound with brucine and with strychnine in acetone.

The determination of the amount of *meso* and (\pm) isomers comprising 4,4'-azobis(4-cyanopentanoic acid) was accomplished by nuclear magnetic resonance spectroscopy. The C-methyl hydrogens and the methylene hydrogens of either of the diastereomers of 4,4'-azobis(4-cyanopentanoic acid) exhibit singlets in their respective nmr spectra, whereas the commercially available acid, which consists of a mixture of two diastereomers, shows a pair of doublets in its nmr spectrum. This phenomenon is attributed to the fact that the methyl and methylene hydrogens of the *meso* isomer and those of the (\pm) isomers are diastereotopic by external comparison,⁴ and are classified as anisochronous⁴ because of their chemical-shift nonequivalence.

From the ratio of the average peak areas (integrals were determined by at least three scans in each direction) of the methyl doublet appearing in the nmr spectrum of the mixed acids, the mixture was found to contain $51.6 \pm 0.5\%$ *meso* isomer. Haines and Waters,³ who prepared the mixed acids from a Strecker-type synthesis involving the reaction of levulinic acid with hydrazine sulfate and sodium cyanide, followed by bromine oxidation of the intermediate hydrazine, found by titration analysis that the acid consists of 52% *meso* isomer. The commercially available acid is prepared *via* the same route.⁵

Preparation of the Optically Active Azonitriles.—The resolution of (\pm)-4,4'-azobis(4-cyanopentanoic acid) was accomplished by fractional crystallization of the diastereomeric salts, employing quinine to separate the enantiomeric pair and acetone as solvent. The (+) and (-) acids were obtained from the corresponding salts by treatment with hydrochloric acid, and the maximum specific rotations ($[\alpha]^{25D}$) were +45.3 and -44.8°, respectively.

Other solvent systems, namely ethyl acetate and ether-methanol (*ca.* 20:1, v/v), were also utilized for the resolution of the (\pm) isomer.⁶ However, with both solvent systems, the yields of the quinine salt of the (+) isomer and the specific rotations of the (+) isomer isolated were not so high as those obtained when acetone was used as solvent.

Resolution of the racemic acid could also be effected by preferential fractional crystallization of the (+)

(1) (a) This is the 48th in a series of papers concerned with the preparation and decomposition of azo compounds; (b) for the previous paper, see C. G. Overberger, J. Reichenenthal, and J.-P. Anselme, *J. Org. Chem.*, **35**, 138 (1970).

(2) This paper comprises a portion of the dissertation submitted by D. A. Labianca in partial fulfillment of the requirements for the degree of Doctor of Philosophy at The University of Michigan, 1969.

(3) R. M. Haines and W. A. Waters, *J. Chem. Soc.*, 4256 (1955).

(4) K. Mislow and M. Raban in "Topics in Stereochemistry," Vol. 1, N. Allinger and E. L. Eliel, Ed., Interscience Publishers, Inc., New York, N. Y., 1967, pp 1-38.

(5) Aldrich Chemical Co., Inc., Milwaukee, Wis., personal communication, 1968.

(6) D. A. Labianca, B. S. Thesis, Polytechnic Institute of Brooklyn, 1965.

isomer, a procedure which is quite rare.⁷ The impure (+) isomer crystallized from a slowly cooled water solution of (±) isomer, and, after two careful recrystallizations of this material from water, (+) isomer of 90% optical purity (based on $[\alpha]^{25D} + 45.3^\circ$) was obtained. The resolution could be facilitated by seeding the initial water solution of racemic compound with a crystal of (+) isomer. However, the reproducibility of this experiment was found to be dependent on careful control of temperature and on volume of solvent used. Furthermore, the yields of (+) isomer isolated were low, and the procedure was quite tedious. Consequently, the classical resolution with quinine was preferred.

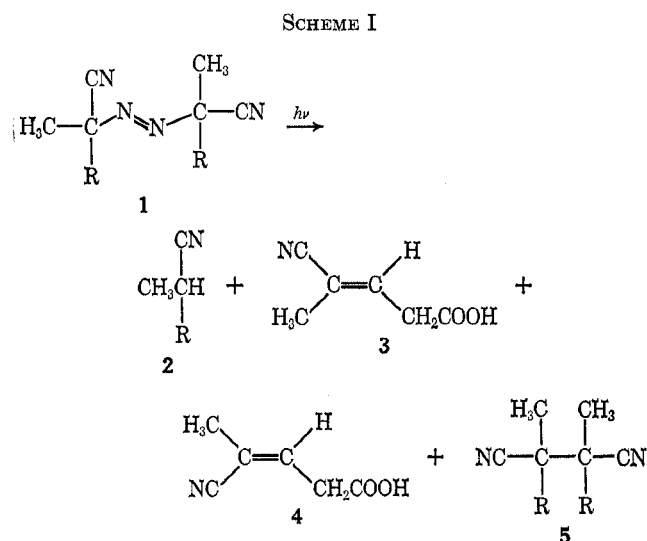
The syntheses of (+)- and (-)-dimethyl 4,4'-azobis(4-cyanopentanoate) were accomplished by esterification of the corresponding (+) and (-) acids with diazomethane. Maximum optical purity was attained in each case after one recrystallization ($[\alpha]^{25D} + 51.0$ and -50.6° , respectively).

The determination of the composition of mixtures of *meso*- and (-)-^{8a} dimethyl 4,4'-azobis(4-cyanopentanoate) could also be facilitated by nmr analysis. For these isomeric esters, the methylene hydrogens, in contrast to those of the parent acids, possess nearly identical chemical shifts and are, therefore, not perceptibly anisochronous. However, the C-methyl hydrogens are separated by 2.5 cps, a difference of 1.5 cps from the separation observed (4 cps) for the C-methyl hydrogens of the diastereomeric acids.

Decomposition Studies. A. Photochemical Decomposition of (+)-4,4'-Azobis(4-cyanopentanoic acid).—The photolyses of (+)-4,4'-azobis(4-cyanopentanoic acid) in methanol were conducted at 10, -8, and -20°. For each of the decompositions, the product mixtures exhibited observed rotations whose signs were negative. The results of these experiments are summarized in Table I. It is interesting to note that the amount of

investigated. Similar behavior characterized the photolyzed methanol solutions of the (-) isomer,⁶ and, in these cases, the observed rotations were positive.

B. Photolysis Products.—The products resulting from photochemical decomposition of (+)-4,4'-azobis(4-cyanopentanoic acid) at -20° were shown to be those summarized in Scheme I (R = CH₂CH₂COOH).



The predominant isolation procedure involved column chromatography of the photolysis products over silica gel. The isolation of the higher melting isomer (HMDA) of coupled diacid 4,5-dicyano-4,5-dimethyloctane-1,8-dioic acid (5) was accomplished by taking advantage of the fact that HMDA precipitates when water is added to the extremely viscous photolysis mixture. Subsequent refrigeration of the filtrate allowed the partial precipitation of the corresponding lower melting isomer (LMDA), the remainder of which was accounted for by chromatographic analysis of a portion of the mixture remaining after removal of the water by lyophilization. In addition, no additional HMDA was isolated by column chromatography. Attempts to distil the liquid disproportionation products (2-4) from these mixtures under reduced pressure or to isolate them by preparative vapor phase chromatographic analysis were unsuccessful. In both approaches, extensive decomposition occurred and no separations could be effected.

The product distributions in the parent photolysis mixture are summarized in Table II. Both HMDA

TABLE I
VARIATION OF OBSERVED ROTATION WITH CONCENTRATION
FOR THE PHOTOCHEMICAL DECOMPOSITION OF
(+)-4,4'-AZOBIS(4-CYANOPENTANOIC ACID)

Wt of azo compound, g	Solvent	Concn, M	Temp, °C	Obsd rotation, deg
7.0	MeOH	0.250	10	-0.040
9.6	MeOH	0.342	-8	-0.050
17.2	MeOH	0.614	-20	-0.096

optical activity in the product mixtures varies directly with the concentration of azo compound subjected to photolysis. Consideration of the reactions undertaken at 10 and -20°, for example, indicates that the molar concentrations of (+) isomer in each instance differ by ca. 41% and that the corresponding observed rotations differ by nearly the same quantity (ca. 42%). Furthermore, the data show that temperature does not affect the amount of optical activity exhibited by the product mixtures, at least in the range of temperatures in-

TABLE II
PRODUCTS OF PHOTOLYSIS OF
(+)-4,4'-AZOBIS(4-CYANOPENTANOIC ACID) AT -20°

Compd	Yield, %
LMDA	11.7
HMDA	13.1
2	29.8
3 and 4	33.5

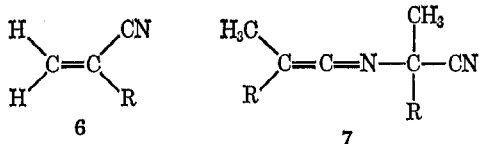
and LMDA, which are known compounds,⁸ were optically inactive and possessed melting points identical with those reported in the literature.⁸ (-)-4-Cyanopentanoic acid (2, $[\alpha]^{25D} - 13.1^\circ$) and olefins 3 and 4, which were isolated as a mixture, were the major products. These results are nearly identical with those

(7) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 78-79.

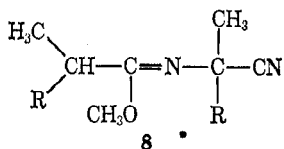
(8) (a) Since enantiomeric conditions are indistinguishable by nmr,^{8b} the spectra of the (-) and (+) esters would be identical with that of the (±) ester in achiral solvents; (b) M. Raban and K. Mislow in "Topics in Stereochemistry," Vol. II, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, Inc., New York, N. Y., 1967, pp 217-226.

obtained by Haines and Waters,³ who reported that the coupled products (HMDA and LMDA) constitute the minor fractions of the product mixtures resulting from the thermolyses of *meso*- and (\pm)-4,4'-azobis(4-cyanopentanoic acid).

It is, of course, also possible that terminal olefin 6 formed during photolysis of the (+)-azo acid, but no evidence was found to indicate the presence of this compound. Ketenimine 7 was not detected. Its



apparent lack of formation was not entirely unexpected, because ketenimines derived from dialkylazonitriles isomerize photochemically (and thermally)⁹ to the more stable coupled products similar to LMDA and HMDA. Moreover, these compounds exhibit a characteristic ultraviolet absorption maximum centered at 290 $m\mu$ (ϵ_{max} ca. 165),^{9,10} and the parent photolysis mixture did not show any absorption in this region. The possibility that ketenimine 7 reacted with methanol to give imidate 8 was also considered, but this



compound was not detected, nor was there any indication of its presence in the ultraviolet spectrum of the photolysis mixture. Alkyl imidates absorb at ca. 255 $m\mu$ (ϵ_{max} ca. 100).¹¹

C. Identification of the Photolysis Products.—The microanalyses and the infrared and nmr spectra of each of the isolated products were consistent with their assigned structures. Both HMDA and LMDA and (-)-4-cyanopentanoic acid (2) exhibited the expected absorption in their respective infrared spectra for nonconjugated nitrile groups at ca. 2240 cm^{-1} ¹² (exact assignments are given in the Experimental Section). The infrared spectrum of the mixture of 4-cyano-*cis*-3-pentenoic acid (3) and 4-cyano-*trans*-3-pentenoic acid (4) showed a nitrile absorption band at 2225 cm^{-1} , which is characteristic of α,β -unsaturated alkylnitriles.¹² Moreover, the carbon-carbon double-bond-stretching frequency of this mixture appeared at 1635 cm^{-1} , in agreement with the expected range of absorption for trisubstituted alkenes, one substituent of which is a nitrile group.¹³

Certain salient features of the nmr assignments for each of the compounds under consideration are also worthy of note. The nmr spectra (CF_3COOH) of HMDA and LMDA exhibited the expected singlets for the C-methyl hydrogens of these isomers at τ 8.33 and

8.35, respectively, and the methyl absorption [$(\text{CD}_3)_2\text{CO}$] at τ 8.90 of (-)-4-cyanopentanoic acid (2) was split into the anticipated doublet ($J = 6.5$ cps) by the corresponding methine hydrogen. The difference in chemical shifts for the diastereotopic C-methyl groups in HMDA and LMDA were quite negligible, so that the nmr spectrum of the mixed isomers was nearly identical with those of the individual isomers. It is also interesting that, in contrast to the *meso*- and (\pm)-azo compounds, the methylene hydrogens of HMDA and LMDA were characterized by multiplets rather than by singlets in their respective nmr spectra, thereby indicating that the absence of the azo linkage gives rise to a significant difference in chemical environment between both pairs of methylene hydrogens in each of the coupled products. Furthermore, the methylene hydrogens of the two isomers of the coupled diacid failed to exhibit any perceptible chemical-shift nonequivalence.

The components of the olefinic mixture were also readily identified by nmr [$(\text{CD}_3)_2\text{CO}$]. Of particular significance in the spectrum of this mixture was the observation that the coupling constant ($J = 3$ cps) of the doublet at τ 8.05 assigned to the C-methyl hydrogens of *cis* olefin 3 was, as expected, larger than that ($J = 1$ cps) of the doublet at τ 7.94 assigned to the methyl group of *trans* olefin 4. Both the absolute and relative magnitudes of these coupling constants are consistent with the fact that in *cis* olefin 3 the methyl group is *trans* to the vinyl hydrogen (larger coupling constant¹⁴) and in *trans* olefin 4 the methyl group and the vinyl hydrogen are *cis* to each other (smaller coupling constant¹⁴). Integration of both doublets indicated that the *cis* and *trans* olefins were present in the mixture in equal amounts.

The ORD spectrum of (-)-4-cyanopentanoic acid (2) in methanol was also of some assistance in the identification of this compound. The ORD curve of the photolyzed mixture of (+)-4,4'-azobis(4-cyanopentanoic acid) exhibited a negative Cotton effect, with the first extremum at 225 $m\mu$, which was assigned to the asymmetrically perturbed carboxyl group of the optically active product. Compound 2 gave a similar curve ($[\text{M}] - 352^\circ$), thereby confirming the source of optical activity in the parent product mixture.

D. Photochemical Decomposition of (+)-Dimethyl 4,4'-Azobis(4-cyanopentanoate).—The photochemical decompositions of the (+) ester were undertaken at -20 and -50° in tetrahydrofuran. The reactions were not conducted in methanol because of the insolubility of the ester in this solvent at the indicated temperatures. Both photolyses gave about a 70% yield of an optically inactive (at the sodium D line and in the 450¹⁵-200- $m\mu$ range) mixture of two isomers (LMDE and HMDE) of coupled diester dimethyl 4,5-dicyano-4,5-dimethyloctane-1,8-dioate. Furthermore, the photolyzed solutions showed no optical activity at the sodium D line and the ORD spectra of these solutions in the 450¹⁵-290- $m\mu$ range and of the liquid products resulting from both decompositions in the 300-208- $m\mu$ range gave no indication of significant activity. The ORD spectra of the tetrahydrofuran solutions could not be determined at lower wavelengths because of the lack of transparency of the solvent below 290 $m\mu$.

(9) J. R. Fox and G. S. Hammond, *J. Amer. Chem. Soc.*, **86**, 4031 (1964).
 (10) G. S. Hammond, O. D. Trapp, R. T. Keyes, and D. L. Neff, *ibid.*, **81**, 4878 (1959).

(11) "Handbook of Organic Structural Analysis," Y. Yukawa, Ed., W. A. Benjamin, Inc., New York, N. Y., 1965, p 22.

(12) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 37.

(13) D. G. I. Felton and S. F. D. Orr, *J. Chem. Soc.*, 2170 (1955).

(14) Reference 12, p 99.

(15) Preliminary experiments indicated the absence of optical activity above 450 $m\mu$.

The mixture of LMDE and HMDE was separated from the unidentified liquid disproportionation products by preparative glpc analysis and by distillation of the liquid products from the reaction mixtures. The latter procedure was considerably less time consuming. A partial separation of the mixture of coupled diesters into both diastereomers was effected by vacuum sublimation. The infrared and nmr spectra of the impure isomers and of the isomeric mixture were essentially indistinguishable from the corresponding spectra of analytically pure LMDE and HMDE prepared by esterification of LMDA and HMDA, respectively, with diazomethane.

E. Mechanism of Decomposition.—In recent years, several investigations concerned with studies of the stereochemical course of the decomposition of azo compounds have been conducted. Bartlett and McBride¹⁶ have reported that the photolysis of *meso*- and of predominantly (\pm)-azobis(2-phenyl-3-methyl-2-butane) in methylcyclohexane glass at -196° gave only *meso*-3,4-diphenyl-2,3,4,5-tetramethylhexane (TMDPH) and mostly (\pm)-TMDPH, respectively. From these experiments, it was concluded that the two radicals produced in a frozen medium under photochemical conditions have the properties anticipated for a radical pair in a cage in which the process of recombination or disproportionation becomes faster than random orientation of the radicals.

In contrast to these results, Greene^{17a-c} found, quite recently, that, of the 28% yield of *meso*- and non-*meso*-2,3-diphenylbutanes obtained from the thermal decomposition of optically pure azobis- α -phenylethane in benzene at 105° in the presence of 2-methyl-2-nitroso-propane as scavenger, only a small amount of the non-*meso* coupled product was optically active. These observations were considered to be indicative of significant progress toward complete randomization of the thermally generated radicals within the solvent cage prior to recombination. The results of this work are in excellent agreement with those of Kopecky and Gillan,^{17d} who studied the decomposition of racemic and optically active 1,1'-diphenyl-1-methylazomethane.

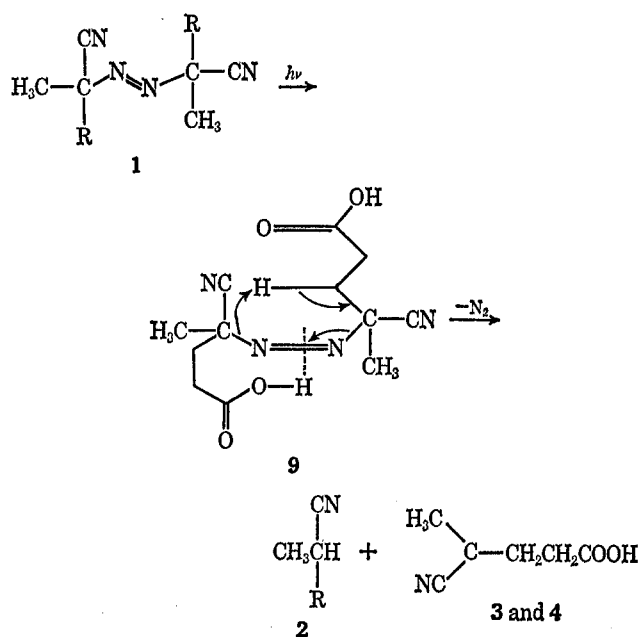
The decomposition of an optically active six-membered cyclic azo compound has been reported by Bartlett and Porter¹⁸ to give an optically active coupled product. However, in this report, which was concerned primarily with the thermolyses and with the direct and sensitized photolyses of the *meso* and (\pm) cyclic azo compounds, the details of the optically active work were not given.

The formation of optically active decomposition products derived from optically active peroxides has also received considerable attention.¹⁹ In these cases, some of the interpretations presented were similar to those previously mentioned.

The foregoing, brief mechanistic discussions facilitate the consideration of somewhat related arguments to

explain the formation of ($-$)-4-cyanopentanoic acid (2) during the photochemical decomposition of (+)-4,4'-azobis(4-cyanopentanoic acid). The formation of optically inactive coupled products (LMDA and HMDA) and an optically active disproportionation product (2) might be rationalized in terms of a pre-structured intermediate (9, Scheme II), the formation of which would depend on the photochemically induced isomerization of the *trans*-azo bond of the optically active acid to the corresponding *cis*-azo linkage,^{20a,b} which would be stabilized by hydrogen bonding^{20c} with the proton of one of the carboxyl groups. Models indicate that structure 9 is feasible. Subsequent elimination of nitrogen followed by rapid abstraction of a hydrogen atom by the intermediate radical within the solvent cage would give ($-$)-2 and the two isomers of 4-cyano-3-pentenoic acid (3 and 4). Since the distance between the two radicals generated from intermediate 9 is greater than that separating one of the radicals from the hydrogen atom to be abstracted, the coupling of these radicals would be expected to require more time than the disproportionation process. As a consequence of this time factor, the intermediate radicals could achieve complete random orientation prior to their recombination and, accordingly, optically inactive coupled products would form. The elimination of nitrogen might also occur to some extent *via* a concerted process, as depicted in Scheme II.

SCHEME II



This mechanism would also explain the insignificant amount of optical activity exhibited by product mixtures resulting from the thermal decomposition of optically active azo acid,⁶ since isomerization of alkyl-azo compounds has not been detected during thermolysis. Furthermore, the thermally generated radicals would be expected to become randomly oriented at a considerably faster rate^{17a-c} than the corresponding

(16) P. D. Bartlett and J. M. McBride, *Pure Appl. Chem.*, **15**, 89 (1967).

(17) (a) F. D. Greene, Massachusetts Institute of Technology, personal communication, 1968; (b) F. D. Greene and M. A. Berwick, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, No. 0112; (c) F. D. Greene, M. A. Berwick, and J. C. Stowell, *J. Amer. Chem. Soc.*, **92**, 867 (1970); (d) K. R. Kopecky and T. Gillan, *Can. J. Chem.*, **47**, 2371 (1969).

(18) P. D. Bartlett and N. A. Porter, *J. Amer. Chem. Soc.*, **90**, 5317 (1968).

(19) (a) S. Oae, T. Kashiwagi, and S. Kozuka, *Chem. Ind. (London)*, 1694 (1965), and references cited therein; (b) H. M. Walborsky and C. J. Chen, *J. Amer. Chem. Soc.*, **89**, 5499 (1967).

(20) (a) R. F. Hutton and C. Steel, *ibid.*, **86**, 745 (1964), and references cited therein; (b) I. I. Abram, G. S. Milne, B. S. Solomon, and C. Steel, *ibid.*, **91**, 1220 (1969); (c) H. Zollinger, "Azo and Diazo Chemistry," Interscience Publishers Inc., New York, N. Y., 1961, pp 328-337.

TABLE III
 ORD, CD, AND UV DATA FOR (–)-4,4'-AZOBIS(4-CYANOPENTANOIC ACID) AND
 (–)-DIMETHYL 4,4'-AZOBIS(4-CYANOPENTANOATE)

Compd	Solvent	Concn, <i>M</i>		ORD		CD		UV	
		ORD, CD	UV	λ_{extr} , $m\mu$	[<i>M</i>], deg	λ_{max} , $m\mu$	$\Delta\epsilon_{\text{max}}$	λ_{max} , $m\mu$	ϵ_{max}
(–)-4,4'-Azobis-(4-cyanopentanoic acid) ^a	Methanol	0.0178	0.0177	375	–1682	349	–0.84	348	20
				353	0				
				327	+2298				
				227	+1289				
(–)-Dimethyl 4,4'-azobis(4-cyanopentanoate) ^b	Methanol	0.0170	0.0161	375	–2173	347	–0.97	348	19
				352	0				
				328	+2760				
				225	+1468				
(–)-4,4'-Azobis-(4-cyanopentanoic acid) ^a	Dioxane	0.0185	0.0167	374	–1840	350	–0.73	347	18
				348	0				
				325	+1515				
				230	+758				
(–)-Dimethyl 4,4'-azobis(4-cyanopentanoate) ^b	Dioxane	0.0173	0.0155	373	–1793	347	–0.87	347	18
				351	0				
				326	+2430				
				225	+1620				

^a $[\alpha]^{25D} - 44.8^\circ$ (*c* 2.463, methanol), 98.9% optically pure based on $[\alpha]^{25D} + 45.3^\circ$ for the (+) isomer. ^b $[\alpha]^{25D} - 49.9^\circ$ (*c* 3.802, methanol), 97.8% optically pure based on $[\alpha]^{25D} + 51.0^\circ$ for the (+) isomer.

radicals generated at low temperatures under photochemical conditions.¹⁶

The question as to why the photochemical decomposition of optically active dimethyl 4,4'-azobis(4-cyanopentanoate) gives rise to larger amounts of coupled products (LMDE and HMDE) than the photolysis of the optically active azo acid and to no significant optical activity in the resulting product mixtures must also be considered. Perhaps an intermediate similar to **9** could not be generated in this case because the ester functions would be incapable of stabilizing the *cis*-azo linkage by hydrogen bonding.

An alternate explanation for these results would depend upon the formation of an intermediate involving hydrogen bonding between the carboxyl substituents of the optically active acid.²¹ Models indicate that within such a 13-membered cyclic structure in which the configuration of the azo linkage is *cis*, a six-membered cyclic transition state similar to that depicted in **9** is possible. Accordingly, hydrogen abstraction by the intermediate radical is again more favorable than the corresponding coupling process because of the closer proximity of the hydrogen atom to the abstracting radical. However, on the basis of the available data, no definite choice can yet be made between this structure and structure **9**.

ORD and CD Properties of the Optically Active Azonitriles.—The first optically active azo alkane for which ORD and CD data have been reported in 2,2'-azobis(2-phenylbutane).²² The ORD curve of the (+) isomer of this compound was determined in isoctane; the positive Cotton effect curve exhibited a peak at 412 $m\mu$ ($[M] + 1420^\circ$) and a trough at 355 $m\mu$ ($[M] - 2250^\circ$). Bartlett and McBride¹⁶ found that the optical rotatory dispersion of (+)-azobis(2-phenyl-3-methyl-2-butane) is quite similar to that of (+)-2,2'-azobis(2-phenylbutane),²² although the rotation in the latter case is stronger.

The optical rotatory dispersions of (–)-4,4'-azobis(4-cyanopentanoic acid) and of (–)-dimethyl 4,4'-

azobis(4-cyanopentanoate) in dioxane and in methanol were investigated. Both compounds gave the expected negative Cotton effect curve owing to the asymmetrically perturbed azo group. Another salient feature of both sets of spectra is a second Cotton effect, with the first extremum appearing in the region 225–230 $m\mu$. This second effect is due to the asymmetrically perturbed carbonyl function of the carboxyl and carboxylate groups, respectively. The magnitude of this Cotton effect is significantly smaller than that attributed to the azo group because the carboxyl and carboxylate moieties are further removed from the asymmetric carbon atoms of the respective azo compounds. These data as well as the corresponding ultraviolet absorption data are summarized in Table III.

The CD spectrum of (+)-2,2'-azobis(2-phenylbutane)²² was found to be quite interesting. Kosower and Severn²² observed that the circular dichroism of this compound changes sign in the region of the $n \rightarrow \pi^*$ absorption.^{23a} The same result, with opposite sign, was exhibited by the corresponding (–) isomer. The possibility that this apparent splitting is due to two separate transitions, $n_+ \rightarrow \pi^*$ and $n_- \rightarrow \pi^*$,^{23a} with the latter having a small rotational strength and a sign opposite to that of the main $n_+ \rightarrow \pi^*$ bond, was postulated. However, on the basis of theoretical calculations by Robin, Hart, and Kuebler,^{23b} Huang and Kosower^{24a} recently narrowed the assignment to that of a single electronic transition, $n_+ \rightarrow \pi^*$, with the observed change of sign being attributed to the presence of two vibronic states, each with some $n_+ \rightarrow \pi^*$ electronic state but having accompanying vibrations of different symmetries. It is interesting to note that Robin and coworkers^{23b} indicate that Kosower informed them that the circular dichroism spectrum of a derivative of

(23) (a) The originating orbital, n_+ , is the antibonding combination of the two nonbonding orbitals on the azo nitrogens, and n_- is the corresponding bonding combination;^{23b} (b) M. B. Robin, R. R. Hart, and N. A. Kuebler, *J. Amer. Chem. Soc.*, **89**, 1564 (1967).

(24) (a) P. C. Huang and E. M. Kosower, *ibid.*, **90**, 2367 (1968). (b) The derivative is probably optically active 2,2'-azobis(2-cyclohexylbutane); see D. J. Severn and E. M. Kosower, *ibid.*, **91**, 1710 (1969).

(21) R. G. Lawton, The University of Michigan, personal communication, 1969.

(22) E. M. Kosower and D. J. Severn, *Tetrahedron Lett.*, 3125 (1966).

TABLE IV
RATE CONSTANTS AND ACTIVATION ENERGIES FOR THE THERMAL DECOMPOSITION OF
AZONITRILES IN N,N-DIMETHYLACETAMIDE

Compd	$[\alpha]^{25D}$, deg (c, solvent)	Optical purity, %	k , min ⁻¹	Decompn temp, °C	E_a , kcal/mol
<i>meso</i> -4,4'-Azobis- (4-cyanopentanoic acid)	8.02×10^{-3}	77.6	31.9
			2.23×10^{-2}	85.3	
			4.32×10^{-2}	90.9	
			1.22×10^{-1}	99.8	
(±)-4,4'-Azobis- (4-cyanopentanoic acid)	9.20×10^{-3}	77.9	32.1
			2.48×10^{-2}	85.8	
			4.22×10^{-2}	90.1	
			1.26×10^{-1}	99.1	
(+)4,4'-Azobis- (4-cyanopentanoic acid)	+44.5 (4.768, methanol)	98.2 ^a	9.36×10^{-3}	78.0	32.1
			2.44×10^{-2}	85.4	
			4.21×10^{-2}	90.0	
			1.21×10^{-1}	99.0	
(-)4,4'-Azobis- (4-cyanopentanoic acid)	-43.1 (4.602, methanol)	95.1 ^a	9.10×10^{-3}	77.7	32.1
			2.62×10^{-2}	86.0	
			4.42×10^{-2}	90.5	
			1.35×10^{-1}	99.7	
<i>meso</i> -Dimethyl 4,4'-azobis(4- cyanopentanoate)	8.60×10^{-3}	77.9	32.0
			2.27×10^{-2}	85.0	
			4.10×10^{-2}	90.2	
			1.24×10^{-1}	99.7	
(+)Dimethyl 4,4'-azobis(4- cyanopentanoate)	+49.7 (3.880, methanol)	97.5 ^b	8.83×10^{-3}	77.6	31.9
			2.43×10^{-2}	85.9	
			4.16×10^{-2}	90.0	
			1.23×10^{-1}	99.2	
(-)Dimethyl 4,4'-azobis(4- cyanopentanoate)	-49.9 (3.802, methanol)	97.8 ^b	8.99×10^{-3}	77.9	31.9
			2.35×10^{-2}	85.4	
			4.19×10^{-2}	90.2	
			1.19×10^{-1}	99.0	

^a Based on $[\alpha]^{25D} + 45.3^\circ$ for the (+) isomer. ^b Based on $[\alpha]^{25D} + 51.0^\circ$ for the (+) isomer.

optically active 2,2'-azobis(2-phenylbutane)²² shows only one band in the $n \rightarrow \pi^*$ region. However, the structure of this derivative was not specified.^{24b}

To determine whether similar behavior is exhibited by optically active 4,4'-azobis(4-cyanopentanoic acid) and by the corresponding dimethyl ester, the circular dichroisms of the (-) isomers of both compounds were determined in dioxane and in methanol. The CD curves possessed a single absorption in the $n \rightarrow \pi^*$ region (Table II), and, on the basis of the conclusions arrived at by Robin and coworkers²³ and by Huang and Kosower,^{24a} this band can be assigned to the $n_+ \rightarrow \pi^*$ transition.

Kinetics.—The rates of thermal decomposition of the various isomers of 4,4'-azobis(4-cyanopentanoic acid) and of dimethyl 4,4'-azobis(4-cyanopentanoate) were determined at four temperatures. The volume of nitrogen evolved during specified time intervals was determined from the displacement of mercury in a gas buret, and the rate constant, k , was calculated

from the product of 2.303 and the slope of a plot of $\log [v_\infty / (v_\infty - v_t)]$ vs. time. Activation energies were obtained from the slopes of plots of $\ln k$ vs. $1/T \times 10^3$. Each reaction investigated was found to exhibit first-order kinetics. The rate data are summarized in Table IV.

Small differences in rate constants for optical isomers of the same compound can be attributed to slight differences in decomposition temperature for corresponding runs. The activation energies are quite similar to those reported for related azonitriles.²⁵

Experimental Section

Melting points are uncorrected. Microanalyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Mülheim (Ruhr), West Germany, and by Spang Microanalytical Laboratory, Ann Arbor, Mich. Nuclear magnetic resonance

(25) "Polymer Handbook," J. Brandrup and E. H. Immergut, Ed., John Wiley & Sons, Inc., New York, N. Y., 1966, pp 113-118.

spectra were obtained on a Varian Associates Model A-60 spectrometer using tetramethylsilane as internal standard, except where noted otherwise. Infrared spectra were recorded on a Perkin-Elmer Model 521 spectrophotometer and on a Perkin-Elmer Model 257 spectrophotometer. Ultraviolet absorption data were obtained with a Beckman Model DU spectrophotometer, and the ORD and CD measurements were made with a Jasco ORD/CD/UV-5 spectropolarimeter at room temperature. All observed rotations at the sodium D line were determined with a Bendix-Ericsson Type 143A polarimeter (0.1-dm cell) at 25°, and, in those instances where specific rotations are listed without reference to sample concentration, the reader should assume that the concentration for the specific rotation in question was given in an earlier experiment. Refractive indices were measured with an Abbe (Spencer 1747) refractometer. All preparative and analytical glpc was performed on a Varian Aerograph Model A-700 with a 20 ft × 0.375 in. aluminum column packed with 20% SE-30 silicone gum rubber on 60–80 mesh Chromosorb W. Petroleum ether refers to the fraction boiling at 30–60°.

Separation of meso- and (±) Isomers of 4,4'-Azobis(4-cyanopentanoic acid).—The procedure of Haines and Waters,³ somewhat modified, was utilized. A slurry of 360 g (1.28 mol) of 4,4'-azobis(4-cyanopentanoic acid) (Aldrich) in 21,600 ml of 10% aqueous methanol (60 ml per gram of mixed acids), distributed between two 6000-ml erlenmeyer flasks, was stirred for 24 hr, after which time it was filtered to give crude meso isomer. This isomer was dissolved at 75–80° in ca. 12,000 ml of water, and cooling of the solution to room temperature afforded 114.5 g (ca. 60% yield)²⁶ of colorless needles: mp 134.5–135° dec (lit.³ mp 128° dec); $\nu_{\max}^{\text{Nujol}}$ 2255 (C≡N) and 1715 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 350 m μ (ϵ 18); nmr (CF₃COOH) τ 8.17 (singlet, 6 H, CCH₃) and 7.37 (singlet, 6 H, CH₂CH₂COOH).

Anal. Calcd for C₁₂H₁₆N₄O₄: C, 51.43; H, 5.75; N, 19.99. Found: C, 51.75; H, 5.92; N, 19.96.

Upon cooling the filtrate at -3° for 24 hr, crude (±) isomer precipitated. Recrystallization from ca. 4000 ml of water maintained at 60–65° gave 86.5 g (ca. 50% yield)²⁶ of colorless solid: mp 117–118° dec (lit.³ mp 110–111° dec); ν_{\max}^{KBr} 2245 (C≡N) and 1715 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 349 m μ (ϵ 19); nmr (CF₃COOH) τ 8.24 (singlet, 6 H, CCH₃) and 7.32 (singlet, 8 H, CH₂CH₂COOH).

Anal. Calcd for C₁₂H₁₆N₄O₄: C, 51.43; H, 5.75; N, 19.99. Found: C, 51.56; H, 5.80; N, 19.87.

Resolution of (±)-4,4'-Azobis(4-cyanopentanoic acid) with Quinine.—A mixture of 83 g (0.296 mol) of (±)-4,4'-azobis(4-cyanopentanoic acid) and 192.2 g (0.592 mol) of quinine was added portionwise and with stirring to ca. 6000 ml of acetone maintained at room temperature. Stirring was continued for 2 hr after the addition of the mixture to ensure complete precipitation of the quinine salt of the (+) isomer. Subsequent filtration followed by several washings of the salt with 2000-ml portions of acetone gave 180.9 g (61% yield, theoretical yield 50%) of impure quinine salt of (+) isomer, mp 120–123° dec. This salt was added portionwise and with stirring to an excess of 4 N hydrochloric acid (275–300 ml) kept at 0–5°. The resulting suspension was cooled at -3° for 7 hr and then filtered to give 47.5 g (0.169 mol) of impure (+) isomer, mp 119–122° dec. A further resolution of this isomer, conducted in the same manner as the first, utilizing 110 g (0.339 mol) of quinine and ca. 5000 ml of acetone, gave 110 g (40% yield based on the first resolution) of analytically pure quinine salt of the (+) isomer, $[\alpha]_{\text{D}}^{25}$ -131° (c 3.056, methanol), mp 129–130° dec. Recrystallization of this salt from large volumes of acetone did not change its melting point or specific rotation.

Anal. Calcd for C₆₂H₈₄N₈O₈: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.35; H, 7.03; N, 12.19.

Generation of the (+) isomer by treatment of this salt with 4 N hydrochloric acid in the same fashion as previously described and subsequent recrystallization of this isomer from water maintained at 60–65° gave 23 g (55.4% overall yield) of colorless platelets, $[\alpha]_{\text{D}}^{25}$ +45.3° (c 3.037, methanol), mp 130–131° dec. Further recrystallization of the (+) isomer from water did not alter its melting point or specific rotation: $\nu_{\max}^{\text{Nujol}}$ 2255 (C≡N) and 1715 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 348 m μ (ϵ 20); nmr (CF₃COOH) τ 8.24 (singlet, 6 H, CCH₃) and 7.32 (singlet, 8 H, CH₂CH₂COOH).

Anal. Calcd for C₁₂H₁₆N₄O₄: C, 51.43; H, 5.75; N, 19.99. Found: C, 51.60; H, 5.81; N, 19.85.

The combined acetone filtrate was evaporated under reduced pressure at room temperature, and to the remaining quinine salt of (-) isomer kept at 0–5° was added, with stirring, excess 4 N hydrochloric acid (275–300 ml). The resulting suspension was cooled at -3° for 10 hr, after which time filtration and subsequent recrystallization of the (-) isomer from water at 60–65° gave 20 g (48.2% overall yield) of colorless platelets, $[\alpha]_{\text{D}}^{25}$ -44.8° (c 2.463, methanol), mp 130–131° dec. No change in the melting point or specific rotation could be effected by further recrystallization. The ORD and CD data for the (-) isomer are summarized in Table III; $\nu_{\max}^{\text{Nujol}}$ 2255 (C≡N) and 1715 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 348 m μ (ϵ 20); nmr (CF₃COOH) τ 8.24 (singlet, 6 H, CCH₃) and 7.32 (singlet, 8 H, CH₂CH₂COOH).

Anal. Calcd for C₁₂H₁₆N₄O₄: C, 51.43; H, 5.75; N, 19.99. Found: C, 51.61; H, 5.89; N, 19.84.

Resolution of (±)-4,4'-Azobis(4-cyanopentanoic acid) by Fractional Crystallization.—(±)-4,4'-Azobis(4-cyanopentanoic acid) (33 g) was dissolved in ca. 1000 ml of water at 60–65°, and slow cooling of the resulting solution to room temperature afforded 25 g of a mixture of racemic isomer (colorless solid) and impure (+) isomer (colorless platelets), $[\alpha]_{\text{D}}^{25}$ +1.36° (c 2.980, methanol), mp 120–122° dec. The platelets (5.5 g) were separated from the racemic isomer with tweezers and subjected to slow recrystallization from ca. 400 ml of water as previously described; after 4 hr, 1.5 g of colorless platelets formed, $[\alpha]_{\text{D}}^{25}$ +8.53° (c 2.355, methanol), mp 125–127° dec. A third recrystallization of this material from ca. 250 ml of water gave 0.65 g of colorless platelets, $[\alpha]_{\text{D}}^{25}$ +40.8° (c 2.875, methanol), 90% optically pure based on $[\alpha]_{\text{D}}^{25}$ +45.3°, mp 129–130° dec.

Syntheses of (+) and (-) Dimethyl 4,4'-Azobis(4-cyanopentanoate).—A solution of diazomethane in ether was prepared from 35 g (0.340 mol) of N-nitroso-N-methylurea according to the method of Eistert^{27a} and distilled as described by Arndt.^{27b} This solution was added slowly to a stirred slurry of 8.35 g (29.8 mmol) of (+)-4,4'-azobis(4-cyanopentanoic acid), $[\alpha]_{\text{D}}^{25}$ +45.3°, in ether maintained at 0–5°. The resulting yellow solution was stirred for 1 hr, after which time the ether was removed under vacuum and the residual colorless solid was dissolved in ethanol. Refrigeration of the solution at -20° for 10 hr allowed the precipitation of 7.8 g (85% yield) of colorless needles, $[\alpha]_{\text{D}}^{25}$ +51.0° (c 2.970, methanol), mp 72–73°. Further recrystallization from ethanol failed to increase the specific rotation and the melting point: $\nu_{\max}^{\text{Nujol}}$ 2240 (C≡N) and 1735 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 348 m μ (ϵ 19); nmr (DMSO-*d*₆) τ 8.37 (singlet, 6 H, CCH₃), 7.61 (singlet, 8 H, CH₂CH₂COOCH₃), and 6.42 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₄O₄: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.53; H, 6.48; N, 18.07.

The (-) isomer was prepared in a similar fashion from 1 g (3.57 mmol) of (-)-4,4'-azobis(4-cyanopentanoic acid), $[\alpha]_{\text{D}}^{25}$ -44.8°, utilizing a solution of diazomethane prepared from 17 g (0.165 mol) of N-nitroso-N-methylurea. Recrystallization from ethanol at -20° gave 0.91 g (83% yield) of colorless needles, $[\alpha]_{\text{D}}^{25}$ -50.6° (c 3.104, MeOH), mp 72–73°, and no change in these data could be effected by further recrystallization. The ORD and CD data for the (-) isomer are listed in Table III; $\nu_{\max}^{\text{Nujol}}$ 2240 (C≡N) and 1735 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 348 m μ (ϵ 19); nmr (DMSO-*d*₆) τ 8.37 (singlet, 6 H, CCH₃), 7.61 (singlet, 8 H, CH₂CH₂COOCH₃), and 6.42 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₄O₄: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.63; H, 6.52; N, 18.26.

Synthesis of meso-Dimethyl 4,4'-Azobis(4-cyanopentanoate).—The esterification of 7.5 g (26.8 mmol) of meso-4,4'-azobis(4-cyanopentanoic acid) was conducted in the manner described in the preceding experiment, utilizing a solution of diazomethane in ether prepared from 35 g (0.340 mol) of N-nitroso-N-methylurea. The crude ester was dissolved in ethanol and refrigeration of the solution at -20° gave 6.21 g (75.3% yield) of colorless platelets: mp 98–99°; $\nu_{\max}^{\text{Nujol}}$ 2250 (C≡N) and 1735 cm⁻¹ (C=O); $\lambda_{\max}^{\text{MeOH}}$ 349 m μ (ϵ 19); nmr (DMSO-*d*₆) τ 8.32 (singlet, 6 H, CCH₃), 7.62 (singlet, 8 H, CH₂CH₂COOCH₃), and 6.43 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₄O₄: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.52; H, 6.35; N, 18.05.

(26) The indicated yield was calculated on the basis of the approximate theoretical composition of the mixed acids as determined by nmr analysis.

(27) (a) B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, New York, N. Y., 1948, p 564; (b) F. Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, pp 165, 166.

Synthesis of the Isomers (LMDE, HMDE) of Dimethyl 4,5-Dicyano-4,5-dimethyloctane-1,8-dioate.—The procedure employed was identical with that described for the esterification of (+) and (–)-4,4'-azobis(4-cyanopentanoic acid). The solutions of diazomethane in ether were prepared from 17 g (0.165 mol) of N-nitroso-N-methylurea. Esterification of 3 g (11.9 mmol) of HMDA³ and recrystallization of the resulting HMDE from ethanol at –15° gave 2.4 g (72% yield) of colorless needles: mp 136.5–138°; $\nu_{\max}^{\text{Nujol}}$ 2240 (C≡N) and 1740 cm⁻¹ (C=O); nmr (internal standard, DSS, DMSO-*d*₆) τ 8.57 (singlet, 6 H, CCH₃), 7.95 (multiplet, 4 H, CH₂CH₂COOCH₃), 7.45 (multiplet, 4 H, CH₂CH₂COOCH₃), and 6.38 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₂O₄: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.82; H, 7.10; N, 9.98.

Similar treatment of 2.7 g (10.7 mmol) of LMDA³ gave 2.6 g (86.7% yield) of LMDE as a colorless solid: mp 105.5–107°; $\nu_{\max}^{\text{Nujol}}$ 2240 (C≡N) and 1740 cm⁻¹ (C=O); nmr (DSS internal standard, DMSO-*d*₆) τ 8.57 (singlet, 6 H, CCH₃), 7.95 (multiplet, 4 H, CH₂CH₂COOCH₃), 7.47 (multiplet, 4 H, CH₂CH₂COOCH₃), and 6.38 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₂O₄: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.73; H, 7.15; N, 10.03.

Photochemical Decompositions of (+)-4,4'-Azobis(4-cyanopentanoic acid).—The results of these experiments are summarized in Table I. The samples of (+) acid were dissolved in 100 ml of Spectrograde methanol (Matheson Coleman and Bell) in a Pyrex photolysis cell (ca. 240-ml capacity) fitted with a ground-glass joint. The cell was connected to a copper coil surrounded by a Pyrex glass jacket through which circulating water flowed. The coil, in turn, was connected by means of Tygon tubing to the mouth of a Pyrex bottle containing water (ca. 2000 ml). An opening at the bottom of the bottle was connected by means of a rubber tubing to a manometer (upper half of a polyethylene wash bottle). The progress of each reaction was followed by the volume of water displaced by the evolved nitrogen, the water being collected in a graduated cylinder. This technique proved to be considerably accurate.

The cell containing the solution of azo compound was placed in a dewar flask (6-in. i.d., 4300-ml capacity) adjacent to a quartz jacket containing a Hanovia 450-W medium-pressure mercury lamp. This dewar flask, containing a thermometer, was filled with ethanol and lined with a copper coil which was connected by means of tygon tubing to the quartz jacket and to another copper coil lining the sides of a second dewar flask (6-in. i.d., 4300-ml capacity). For the reaction at 10°, the second dewar flask was filled with an acetone-ice mixture (replenished ca. every 50 min) and the solution of azo compound, 7 g (25.0 mmol), [α]_D²⁰ +43.7° (c 3.531, methanol), 96.7% optically pure based on [α]_D²⁰ +45.3°, was cooled by circulating ethanol through the entire system. Irradiation of the solution of azo compound was conducted intermittently for 21 hr, during which time quantitative nitrogen evolution occurred. The resulting solution exhibited an observed rotation of –0.040°.

A mixture of methanol–water (ca. 50:50 v/v) and Dry Ice was used to cool the circulating ethanol for the reaction at –8°. Quantitative nitrogen evolution occurred after intermittent irradiation of the solution of azo compound, 9.6 g (34.2 mmol), [α]_D²⁰ +43.7°, for 20 hr and the resulting solution possessed an observed rotation of –0.050°. Similarly, a Dry Ice–methanol mixture was used to cool the circulating ethanol for the photolysis conducted at –20°. The solution of (+) acid, 17.2 g (61.4 mmol), [α]_D²⁰ +45.3° (c 3.107, methanol), was irradiated intermittently for 24 hr, after which time quantitative nitrogen evolution occurred. An observed rotation of –0.096° was exhibited by the photolyzed solution.

Decomposition Products.—The solution photolyzed at –20° was subjected to thin layer chromatography, utilizing a precoated silica gel (polyethylene terephthalate) sheet (Eastman Chromogram Sheet 6060) and methanol as developing solvent. Two nearly overlapping spots, detected by exposing the dried sheet to iodine vapor, appeared in close proximity to the point of initial spotting. These spots were attributed to HMDA and LMMA, respectively, by comparison with authentic samples.³

Methanol was removed by rotary evaporation (40°) from the photolyzed solution, and upon addition of 100 ml of water to the product mixture (15.3 g), 2 g (13.1% yield) of HMDA precipitated. Recrystallization of this isomer from dioxane gave colorless needles, mp 207–208° (lit.³ mp 207–208°). Subsequent cooling of the aqueous filtrate at –3° afforded 0.8 g (5.2% yield) of LMMA, which was recrystallized from water to give a colorless

solid, mp 182–183° (lit.³ mp 182–183°). Samples of LMMA (c 3.472, methanol) and of HMDA (c 3.768, methanol) exhibited no optical activity at the sodium D line or in the range of 600–210 m μ (ORD):²⁸ ν_{\max}^{KBr} HMDA, 2240 (C≡N) and 1710 cm⁻¹ (C=O); LMMA 2240 (C≡N) and 1710 cm⁻¹ (C=O); nmr (CF₃COOH) HMDA τ 8.33 (singlet, 6 H, CCH₃), 7.75 (multiplet, 4 H, CH₂CH₂COOH), and 7.15 (multiplet, 4 H, CH₂CH₂COOH); LMMA, τ 8.35 (singlet, 6 H, CCH₃), 7.77 (multiplet, 4 H, CH₂CH₂COOH), and 7.17 (multiplet, 4 H, CH₂CH₂COOH).

Anal. Calcd for C₁₂H₁₆N₂O₄: C, 57.13; H, 6.39; N, 11.11. Found: HMDA C, 57.18; H, 6.38; N, 11.10. LMMA C, 57.00; H, 6.26; N, 11.07.

The remaining aqueous solution was lyophilized (0.025 mm) for 24 hr, and column chromatography (65 × 2.2 cm column) of a 4-g portion of the remaining product mixture (12.4 g) over 160 g of silica gel adsorbent (Grace–Davison Chemical, Grade 923) using ether as eluent gave, in the order in which they came off the column, 0.32 g (8% yield) of LMMA [optically inactive at the sodium D line and in the 600–210-m μ range (ORD) (c 3.312, methanol)], mp 182–183°, 1.75 g (43.8% yield) of analytically impure (–) acid 2, [α]_D²⁵ –9.94° (c 3.116, methanol), and 1.65 g (41.3% yield) of a mixture of *cis* and *trans* olefins 3 and 4, n_D^{25} 1.4575. Impure acid 2 was rechromatographed (48 × 2.2 cm column) over 80 g of silica gel and elution with an 80% ether–petroleum ether (v/v) solvent mixture gave 1.47 g (36.8% yield) based on the mixture added to the first column)²⁹ of 2: [α]_D²⁵ –13.1° (c 3.112, methanol); [M]₂₂₅ –352° (c 0.3107, methanol); n_D^{25} 1.4476; ν_{\max}^{neat} 2 2245 (C=N) and 1715 cm⁻¹ (C=O); 3 and 4, 2225 (C≡N), 1710 (C=O), and 1635 cm⁻¹ (C=C); nmr [(CD₃)₂C=O], 2, τ 8.90 (doublet, 3 H, *J* = 6.5 cps, CCH₃), 8.22 (multiplet, 2 H, CH₂CH₂COOH), 7.51 (multiplet, 2 H, CH₂CH₂COOH), 5.39 (multiplet, 1 H, CH), and –1.48 (singlet, 1 H, COOH); 3 and 4, τ 8.05 and 7.94 (two doublets, 6 H, *J* = 3 and 1 cps, respectively, CCH₃), 6.09 and 5.97 (two doublets, 4 H, *J* = 9.5 and 10 cps, respectively, CH₂COOH), 3.95 (multiplet, 2 H, C=CH), and –1.62 and –1.73 (two singlets, 2 H, COOH).

Anal. Calcd for C₆H₉NO₂ (2): C, 56.68; H, 7.13; N, 11.02. Found: C, 56.89; H, 6.98; N, 11.06. Calcd for C₆H₇NO₂ (3 and 4): C, 57.59; H, 5.64; N, 11.19. Found: C, 57.36; H, 5.39; N, 10.97.

Photochemical Decomposition of (+)-Dimethyl 4,4'-Azobis(4-cyanopentanoate) at –20°.—A solution of 6.7 g (21.7 mmol) of (+)-dimethyl 4,4'-azobis(4-cyanopentanoate), [α]_D²⁵ +50.8° (c 1.000, methanol), in 100 ml of tetrahydrofuran (freshly distilled from LiAlH₄) was intermittently irradiated, as described for the (+) acid, for 38 hr, after which time quantitative nitrogen evolution occurred. A Dry Ice–acetone mixture was used to maintain the reaction temperature at –20°. In this case, ethanol was not circulated through the quartz jacket. Instead, that area of the jacket through which coolant would normally flow was filled with ethanol. The photolyzed solution exhibited no optical activity at the sodium D line and its ORD spectrum gave no indication of significant activity in the range 450–290 m μ .

A portion (25 ml) of the photolyzed solution was analyzed by preparative glpc at 285°. An analytical run indicated the presence of three components with retention times of 1.5, 1.9, and 10 min, respectively. The two components with the shortest retention times were collected with the solvent and the major component with the longest retention time was a slightly yellow solid, 0.98 g (65.3% based on the fraction analyzed). Two recrystallizations of this material from methanol gave a colorless, crystalline solid, mp 100–133°. Solutions of this compound exhibited no optical activity at the sodium D line (c 3.758, 2,2,2-trifluoroethanol) or in the region of 450–200 m μ (ORD, c 0.6484, 2,2,2-trifluoroethanol).²⁸ The broad melting point range indicated that the compound was a mixture of two isomers of coupled diester, and the corresponding infrared and nmr data were essentially identical with those of LMDE and HMDE.

Tetrahydrofuran was removed by rotary evaporation (40°) from the remaining photolyzed solution (75 ml), and, after distillation of the photolysis mixture at 80° (0.25 mm), a mixture of colorless solid and a minimum of yellow liquid remained. The

(28) The coupled products exhibited no optical activity at the sodium D line or in the indicated ORD range prior to their purification by recrystallization.

(29) The overall yields summarized in Table I were calculated on the basis of the fact that the original photolysis mixture weighed 15.3 g and that, after nearly complete separation of the coupled products, a 4-g portion of the remaining mixture which weighed 12.4 g was analyzed by column chromatography.

ORD spectrum of the distilled liquid products (*c* 2.500, methanol) showed no optical activity in the range 300–208 $m\mu$. The residue was washed with 50 ml of ether and subsequent filtration gave 3.1 g (67.4% based on the fraction distilled) of colorless solid. Two recrystallizations of this compound from methanol afforded a colorless, crystalline solid, mp 100–133°, whose infrared and nmr spectra were identical with those of the material obtained by preparative glpc. Samples of the compound (*c* 3.216, 2,2,2-trifluoroethanol) and of the ether filtrate failed to exhibit optical activity at the sodium *D* line and in the 450–200- $m\mu$ range (ORD) (*c* 0.6132, 2,2,2-trifluoroethanol):²⁸ $\nu_{\max}^{\text{Nujol}}$ 2240 (C≡N) and 1740 cm^{-1} (C=O); nmr (internal standard DSS, DMSO-*d*₆) τ 8.58 (singlet, 6 H, CCH₃), 7.95 (multiplet, 4 H, CH₂CH₂COOCH₃), 7.45 (multiplet, 4 H, CH₂CH₂COOCH₃), and 6.38 (singlet, 6 H, COOCH₃).

Anal. Calcd for C₁₄H₂₀N₂O₄: C, 59.99; H, 7.19; N, 9.99. Found: C, 60.07; H, 7.12; N, 10.01.

Photochemical Decomposition of (+)-Dimethyl 4,4'-Azobis(4-cyanopentanoate) at -50°.—A solution of 7.3 g (23.7 mmol) of (+)-dimethyl 4,4'-azobis(4-cyanopentanoate), [α]_D²⁵ +51.0°, in 100 ml of tetrahydrofuran (freshly distilled from LiAlH₄) was irradiated in the usual manner. A Dry Ice-acetone mixture was used to maintain the reaction temperature at -50°, and in this case ethanol was circulated through the quartz jacket. Quantitative nitrogen evolution occurred after intermittent irradiation for 46 hr. The photolyzed solution exhibited no significant optical activity in the range of 450–290 $m\mu$ (ORD).

Distillation of the photolysis mixture, employing the conditions described in the preceding experiment, ultimately gave 4.5 g (68% yield) of coupled products. Two recrystallizations of this isomeric mixture from methanol afforded a colorless, crystalline solid, mp 100–133°, whose infrared and nmr spectra were identical with those of the mixture obtained in the preceding experiment. Samples of this mixture exhibited no optical activity at the sodium *D* line (*c* 3.518, 2,2,2-trifluoroethanol) and in the range of 450–200 $m\mu$ (ORD) (*c* 0.5984, 2,2,2-trifluoroethanol).²⁸ An ORD spectrum of the distilled products (*c* 2.430, methanol) failed to show any activity in the range of 300–208 $m\mu$.

Vacuum Sublimation of the Mixture of LMDE and HMDE.—A sample of the isomeric mixture of coupled diesters (1.5 g) was sublimed at 50° (0.025 mm) for 48 hr, after which time 0.68 g of colorless solid, mp 103–120°, was collected. This material was resublimed at 45° (0.025 mm) for 24 hr to give 0.51 g of solid, mp 104.5–118°. The melting point range could not be significantly altered (mp 105–117.5°) after a third sublimation at 40° (0.025 mm). Recrystallization of the latter sublimate and residue afforded a colorless, crystalline solid, mp 105.5–114°. A second recrystallization from methanol failed to narrow the melting-point range.

The residue from the first sublimation, 0.78 g, mp 122–134°, and that from the second, 0.24 g, mp 124–135°, were combined and recrystallized from methanol to give a colorless, crystalline solid, mp 126–137°. Subsequent recrystallization from methanol did not change the melting-point range. The infrared and nmr spectra of both impure isomers were essentially identical with those of the parent mixture and of pure LMDE and HMDE.

Kinetics of the Thermal Decompositions.—The apparatus employed was similar to that used by Overberger and Gainer.³⁰ It consisted of an inner chamber into which the sample was introduced and an outer chamber in which a suitable liquid was refluxed. A 10-mm-diameter tube allowed the nitrogen evolved to pass from the inner chamber, through a cooling coil at 27°, into a 100-ml gas buret (graduated in 0.1 ml) surrounded by a glass jacket through which water maintained at 27° flowed. The course of each decomposition was followed by measuring the rate of evolution of nitrogen, which displaced a volume of mercury.

For a typical run, 15 ml of *N,N*-dimethylacetamide was placed in the inner chamber. A suitable liquid, chosen according to the temperature desired (ethanol at *ca.* 100°), was refluxed in the outer chamber. When the temperature had reached equilibrium and the levels of mercury in both sides of the manometer were brought to the same level, the initial volume reading (*v*₁) from the buret was recorded. The sample (*ca.* 300 mg) was quickly introduced into the inner chamber, which was stoppered with a Reducing-Bushing-type adapter containing a thermometer immersed in the solution of azo compound. Stirring of the solution was effected continuously with a Teflon-coated stirring bar, and no variation in reaction temperature was observed during each of the decompositions. At specific time intervals (based on the rate of nitrogen evolution), the volume of nitrogen evolved (*v*_{*t*}) was recorded. This procedure was followed until *ca.* 75–80% of the theoretical volume of nitrogen had been evolved. When the evolution of nitrogen ceased, that volume reading was taken as *v*_{*t*}; these final readings agreed well with the stoichiometric values. All *v*_{*t*} readings were recorded after 10–12 half-times had elapsed and *v*_∞ was determined from the relationship $v_{\infty} = v_t - v_t$.

Registry No.—(-)-4,4'-Azobis(4-cyanopentanoic acid), 23886-45-5; *meso*-4,4'-azobis(4-cyanopentanoic acid), 23886-46-6; (±)-4,4'-azobis(4-cyanopentanoic acid), 23886-47-7; (+)-4,4'-azobis(4-cyanopentanoic acid), 23942-62-3; (+)-4,4'-azobis(4-cyanopentanoic acid) (quinine salt), 23886-48-8; (-)-dimethyl 4,4'-azobis(4-cyanopentanoate), 23886-49-9; *meso*-dimethyl 4,4'-azobis(4-cyanopentanoate), 23886-50-2; (+)-dimethyl 4,4'-azobis(4-cyanopentanoate), 23886-51-3; dimethyl 4,5-dicyano-4,5-dimethyloctane-1,8-dioate, 23886-55-7; 4,5-dicyano-4,5-dimethyloctan-1,8-oic acid, 23886-56-8; 2, 23886-52-4; 3, 23886-53-5; 4, 23886-54-6.

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(30) C. G. Overberger and H. Gainer, *J. Amer. Chem. Soc.*, **80**, 4561 (1958).