

Intramolecular Meerwein Reactions of the Anthraquinone System. Synthesis, X-Ray Structural Analysis and Spectroscopic Properties of Anthra[9,1-*bc*:10,5-*b'**c'*]tetrahydrodipyrans Derivatives

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Received May 21, 1981

Meerwein reactions of 1,5-anthraquinone bis(diazonium hydrogen sulfate) with sufficiently activated olefins, such as acrylonitrile, acrylic esters, methacrylonitrile and its esters, styrene and α -methylstyrene yielded derivatives of the new heterocyclic system anthra[9,1-*bc*:10,5-*b'**c'*]2,3,7,8-tetrahydrodipyrans. Isolation of derivatives was realized and yields enhanced by using dimethyl methylphosphonate as reaction medium. Compounds **5-18** were isolated as mixtures of diastereomers, some of which were separated by crystallization. Proof of structure and stereochemistry was obtained for some of the compounds by X-ray crystallographic analysis. The ^1H - and ^{13}C -nmr data provided further support. Surprisingly large chemical shift differences between some of the proton signals of isomers were observed although the two asymmetric centers are far apart through bonds and through space. The mechanism of formation is explained on the basis of redox modulation of a charge transfer complex in which the aliphatic radical attacks the oxygen atom of the anthraquinone. It is proposed to classify this new type of reaction as an intramolecular Meerwein reaction.

J. Heterocyclic Chem., **18**, 1571 (1981).

Introduction.

This paper reports Meerwein reactions of 1,5-anthraquinone bis(diazonium hydrogensulfate) with substituted olefins involving the ketone moiety of the anthraquinone and subsequent formation of two pyran rings attached to the anthracene system. This method provided a simple and direct approach to derivatives of anthra[9,1-*bc*:10,5-*b'**c'*]2,3,7,8-tetrahydrodipyrans, whereby two new heterocyclic rings are formed in a single step under mild reaction conditions.

Such intramolecular Meerwein reactions have apparently not been observed previously.

A number of antibiotics have been established which possess a substituted anthra[1,2-*b*]pyran nucleus (1).

The important biological activity of this family of antibiotics enhanced the interest in these substances as a subject for further synthetic investigation. Our interest stemmed from the structural relationship of such antibiotics with the new type of anthradipyrans which we have synthesized. The synthetic scheme outlined below proffers a serendipitous and facile synthetic entrance into these new structures of anthradipyrans.

The unique properties of dimethyl methylphosphonate (2a,b) to promote many reactions which fail to proceed in other solvents, supposedly because of the solvating effects of the phosphonate have now produced a further example in which strong evidence for a radical mechanism of the Meerwein reaction is put forward.

This in its consequence opened the way for the preparation of the new class of compounds, and provided further proof for the redox modulated type of mechanism of Meer-

wein reactions (3).

The Meerwein arylation reaction is only one type of reaction of the general group of redox modulated radical addition reactions to olefins (3,4). The cationic mechanism strongly favored at one time is no longer accepted in the general sense in which it was supposed to explain the overall reaction.

The conditions for initiating the reaction have been greatly varied. Most authors ascribe the first step to a one electron reduction of the diazonium salt by cuprous chloride. Although this may be correct in many cases, it has already been recognized that it may not be so acceptable in solvents such as acetonitril, sulfolane (4) and *N*-methylpyrrolidone (5). Consideration of the most advantageous solvents suggests that their effect may be traced to their possessing easily polarized electrons which may assist the transfer of an electron from the olefin to the diazonium salt. When the anion of the diazonium salt is a halogen atom one always isolated either halogenated reaction products or halogenated derivatives of the solvent in which the reaction had been conducted (3,4).

Almost all studies of the Meerwein reaction have been performed with diazonium halides (4) and only some experiments have been reported using the hydrogensulfates or nitrates (6). In most cases such experiments either failed, or gave low yields of products. This situation was briefly discussed and the explanation was proffered that large anions such as bisulfate, sulfate or nitrate do not readily form covalent bonds, in contrast to the halogen anions (4).

Although the yields of arylated olefins are generally higher when diazonium chlorides have been employed for

the arylation instead of the sulfates (3,4), this apparently does not hold true for the arylation of olefins using anthraquinone-diazonium hydrogensulfate. These reactions have been catalyzed by copper(I) chloride yielding *C*-substituted anthraquinones in high yields. Well known examples are represented a) by the reaction of 1-anthraquinone diazonium hydrogensulfate with methacrylonitrile, yielding 1-(2-oxopropyl)anthraquinone, which was subsequently cyclized to 2-hydroxybenzanthrone (7), and b) by the arylations of 1,1-dichloro- and 1,1,2-trichloroethylene, respectively, with the same diazonium salt again catalyzed by copper(I) chloride yielding 1-anthraquinone acetic acid (8).

Also some earlier work seemed to provide indications that some 1,5-disubstituted anthraquinone derivatives may undergo a double cyclization involving reduction of the ketone moieties of the anthraquinone system (9,10).

The reaction of 1,5-anthraquinone bis(diazonium hydrogensulfate) with olefins was investigated because consideration of the electronic structure of the intermediate fragments formed during the decomposition of the bis-diazonium salt implied that there existed a possibility of a synthetic route to derivatives of the hitherto inaccessible ring system of tetrahydroanthradipyran. The aim of our experiments was to produce evidence in support of the possible intermediate formation of transient 1,5-disubstituted anthraquinoyl fragments, whereby the quinone system partakes in the reaction due to its inherent redox character in the anthraquinone molecule. It soon became obvious, however, that special experimental requirements had to be met to achieve this synthetic goal.

Synthesis of Anthradipyrans.

The diazotation of 1,5-diaminoanthraquinone (**1**) in concentrated sulfuric acid by the addition of solid sodium nitrite had been reported earlier by Scholl (11). This method, including the tedious purification of crude pro-

duct gave the bis-diazonium salt (**2**) in a yield of about 50%. The yield could be considerably improved by adding two moles of nitrosyl sulfuric acid in concentrated sulfuric acid to a solution of 1,5-diaminoanthraquinone in sulfuric acid. The analytical investigation of the crystalline bis-diazonium salt showed that, generally, it was sufficiently pure to be used for Meerwein reactions, although it was repeatedly observed that using a bis-diazonium salt which failed to meet these specifications (*e.g.*, preparation of the crude product according to the method described by Scholl) drastically lowered the yields.

Although the state of art generally does not permit a reliable prediction as to the best solvent for any given type of Meerwein reaction, it soon became obvious that solvents commonly employed such as acetone, methanol, *N*-methylpyrrolidone or aliphatic ethers were unsatisfactory in the anthraquinone series, since large amounts of mixtures of anthraquinone and small quantities of substituted products thereof were isolated.

However, when the reaction was performed in freshly distilled dimethyl methylphosphonate as solvent, preferably in the presence of a small quantity of water, the amounts of anthraquinone by-products formed were reduced significantly.

When an excess of olefin was added to the suspension of **2** in dimethyl methylphosphonate (Scheme I) containing 10-15% of water, followed by a catalytic amount of copper(I) chloride immediately nitrogen evolution commenced.

Only a very limited number of olefins (Table I) could be induced to undergo this intramolecular Meerwein cyclization reaction, and for the most part only when the ethylenic double bond was attached to a strongly electron attracting group. These olefins included the nitriles and esters of acrylic acid and the acid itself, methacrylonitrile, methacrylic acid esters, styrene and derivatives thereof. Acrylonitrile and methacrylonitrile were among the most

SCHEME I

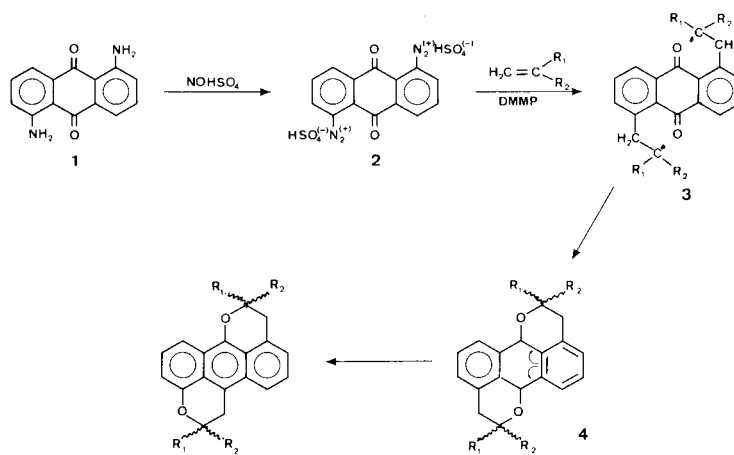


Table I
Substituted Tetrahydroanthradipyrans

Compound	Olefin	R'	R ²	Yield %	Mp, °C	Recrystallized from	Ratio of Diastereomers (HPLC) <i>trans/cis</i>	Molecular Formula	Analyses
5	CH ₂ =CH-CN	H	CN	64.5	287-288	Cyclohexanone (1:13)	1:1	C ₂₀ H ₁₃ N ₂ O ₂	Calcd. C, 76.92 H, 3.88 N, 8.97 Found C, 76.74 H, 3.95 N, 9.20
6	CH ₂ =C(CH ₃) ₂ CN	CH ₃	CN	60.0	> 300 dec	Cyclohexanone (1:50)	2.4:1	C ₂₂ H ₁₆ N ₂ O ₂	Calcd. C, 77.63 H, 4.74 N, 8.23 Found C, 77.66 H, 4.88 N, 8.33
7	CH ₂ =C(CN)CH ₂ CH ₂ CN	CN	CH ₂ -CH ₂ CN	64.0	302 dec	Cyclohexanone (1:20)	1:1	C ₂₆ H ₁₈ N ₄ O ₂	Calcd. C, 74.63 H, 4.34 N, 13.39 Found C, 74.48 H, 4.31 N, 13.50
8	CH ₂ =CH-COOCH ₃	H	COOCH ₃	37.2	223-227	1,3-Xylene (1:10)	1:1	C ₂₂ H ₁₈ O ₆	Calcd. C, 69.84 H, 4.80 Found C, 69.50 H, 4.85
9	CH ₂ =CH-COOC ₂ H ₅	H	COOC ₂ H ₅	42.5	195.5-197	1,3-Xylene (1:10)	1:1	C ₂₄ H ₂₂ O ₆	Calcd. C, 70.93 H, 5.46 Found C, 71.25 H, 5.61
10	CH ₂ =CH-COOC ₄ H ₉	H	COOC ₄ H ₉	13.0	124-127	Ethanol	1:1.03	C ₂₈ H ₃₀ O ₆	Calcd. C, 72.71 H, 6.54 Found C, 72.60 H, 6.43
11	CH ₂ =CH-COOC ₄ H ₉ (<i>iso</i>)	H	COOC ₄ H ₉ (<i>iso</i>)	11.0	137-138	Benzene	1:1	C ₂₈ H ₃₀ O ₆	Calcd. C, 72.71 H, 6.54 Found C, 72.50 H, 6.48
12	CH ₂ =C(CH ₃) ₂ COOCH ₃	H	COOCH ₃	53.5	221-224	1,3-Xylene	1.04:1	C ₂₄ H ₂₂ O ₆	Calcd. C, 70.93 H, 5.46 Found C, 70.69 H, 5.45
13a	CH ₂ =C(CH ₃) ₂ COOC ₂ H ₅ (<i>trans</i>)	CH ₃	COOC ₂ H ₅	41.6	207-208.5	Methylethylketone	1:1.1	C ₂₆ H ₂₆ O ₆	Calcd. C, 71.87 H, 6.03 Found C, 71.63 H, 5.88
13b	CH ₂ =C(CH ₃) ₂ COOC ₂ H ₅ (<i>cis</i>)	CH ₃	COOC ₂ H ₅	166-167.5		Benzene		C ₂₆ H ₂₆ O ₆	Found C, 71.79 H, 5.98
14	CH ₂ =C(CH ₃) ₂ COOC ₆ H ₁₁	CH ₃	COOC ₆ H ₁₁	13.0	210-212	Benzene	1:1	C ₃₄ H ₃₈ O ₆	Calcd. C, 75.25 H, 7.06 Found C, 75.38 H, 7.29
15	CH ₂ =CH-C ₆ H ₅	H	C ₆ H ₅	88.0	279-281	Cyclohexanone (1:15)	1:1.2	C ₃₀ H ₂₂ O ₂	Calcd. C, 86.93 H, 5.35 Found C, 87.21 H, 5.25
16	CH ₂ =C(CH ₃) ₂ C ₆ H ₅	CH ₃	C ₆ H ₅	47.0	244-247	Cyclohexanone (1:15)	1:1.04	C ₃₂ H ₂₆ O ₂	Calcd. C, 86.85 H, 5.92 Found C, 86.96 H, 5.69
17	CH ₂ =CH-C ₆ H ₄ CH ₃ - <i>p</i>	H	C ₆ H ₄ CH ₃ - <i>p</i>	49.1	260-262	Toluene (1:20)	1:1.12	C ₃₂ H ₂₆ O ₂	Calcd. C, 86.85 H, 5.92 Found C, 86.78 H, 5.96
18	CH ₂ =CH-C ₆ H ₄ Cl- <i>p</i>	H	C ₆ H ₄ Cl- <i>p</i>	68.3	293-297	Cyclohexanone (1:17)	1.12:1	C ₃₀ H ₂₀ Cl ₂ O ₂	Calcd. C, 74.54 H, 4.17 Cl, 14.67 Found C, 74.35 H, 4.00 Cl, 14.61
19		H	COOH (b)	73.7	> 300		1:1	C ₂₀ H ₁₄ O ₆	Calcd. C, 68.57 H, 4.03 Found C, 68.64 H, 3.99
20		CH ₃	COOH (c)	90	> 300		1:1	C ₂₂ H ₁₈ O ₆	Calcd. C, 69.84 H, 4.80 Found C, 69.60 H, 4.73

(a) Ratio of diastereomers in the crude mixture. (b) Prepared from 9. (c) Prepared from 12.

reactive olefins and gave consistently yields of 60-65% while the acrylic acid esters gave lower yields.

There was an impressive array of olefins which were notably unreactive, although they are known to participate readily in conventional Meerwein reactions.

Vinyl ethers in general, although they underwent a violent reaction on adding cuprous chloride, yielded only anthraquinone, and tri- or tetrachloroethylenes failed to furnish any dipyrans derivatives. Other compounds which also failed to react, included maleic anhydride, fumaric acid esters, acrolein, ethylene and also dimethyl acetylenedicarboxylate.

The reaction temperatures varied between 25-50° in general, and reaction times were judged by termination of the nitrogen evolution. Yields have not been optimized in all cases, and lower yields were often a result of isolation difficulties of products rather than due to side reactions. Dilution of reaction mixture with water furnished compounds **5-18** (Table I), generally in crystalline form, and small amounts of tars could be removed by washing the crystalline compounds with methanol. These formed light yellow crystals, sparingly soluble in organic solvents. Several esters could be recrystallized from ethanol, in particular those having large alkyl groups. The yields compiled in Table I were realized only with distilled dimethyl methylphosphonate and diazonium salts prepared according to the above mentioned procedure.

Ease of isolation of the dipyrans decreased as the ester chain is lengthened from methyl to butyl or cyclohexyl ester. The reaction products formed with styrenes yielded crystals which were easily purified, since no resinous by-products were formed.

The addition of water to dimethyl methylphosphonate promoted strongly the evolution of nitrogen at lower temperatures, since when conducting the reaction in anhydrous dimethyl methylphosphonate the temperature had to be increased to about 50-60° before nitrogen evolu-

tion started, but this favored the formation of darkly colored by-products.

A study of a variety of catalysts revealed that copper(I) chloride was one of the most effective with respect to yields and purity of the products obtained.

Other catalysts also promote this type of reaction (Table II). The use of copper(II) chloride resulted in significantly lower yields, and likewise the addition of metals such as copper or iron initiated nitrogen evolution but yields were also lower. A combination of iron filings and iron(III) chloride gave yields comparable to those obtained with copper(I) chloride, but either one of those reagents alone gave unsatisfactory results.

The compounds isolated consisted of a mixture of two diastereomers with the two chiral centers at C-2 and C-8 of the dihydropyran rings. Most of these compounds could be separated by thin layer chromatography on silica gel plates in a solvent mixture of toluene-heptane-acetone. A quantitative determination of the relative ratios of the two isomers was achieved by high performance liquid chromatography (hplc) of the crude mixtures.

The isomeric ratio of products formed was in almost all cases 1:1. The crude mixtures of products were heated with methanol to remove dark colored by-products and anthraquinone. Different catalysts were employed and although yields of products varied there was no remarkable deviation from the 1:1 composition of diastereomers (Table II).

Repeated crystallizations of some of the isomeric mixtures permitted in a few cases the isolation of pure crystalline diastereomeric forms. The dinitrile **5** was recrystallized from cyclohexanone and subsequent X-ray structural analysis showed it to be the compound having the two nitrile groups in *trans* position to each other. Compound **7** behaved similarly, and it may be tentatively concluded in analogy to **5** that it is also the isomer having the two nitrile groups in *trans* position to each other.

Crystallization of the isomeric mixture of the diethyl esters of **13a**, **13b** from methyl ethyl ketone gave the *trans*-diastereomer (**13a**) with a melting point of 207-208°, while crystallization from benzene furnished exclusively the *cis*-isomer (**13b**) having a melting point of 166-167°.

The addition of methacrylonitrile to 1,5-bis-diazonium salt (**2**) gave rise to the formation of two diastereomers (**6**) in a ratio of approximately 2.5:1. Recrystallization of this mixture from cyclohexanone furnished the pure *trans* isomer, as the predominant constituent of the mixture. The *trans*-configuration of the cyano- and the methyl substituents, respectively, relative to each other was again established from the crystallographic data.

Alkaline hydrolysis of the esters **9** and **12**, respectively, furnished the corresponding acids **19** and **20**, largely insoluble in organic solvents.

Table II
The Influence of Different Catalysts on Yield and Ratio of Mixtures of Diastereomers

Olefin	Catalyst	Yield %	Ratio of Diastereomers of Compounds
Acrylonitril	Cu ₂ Cl ₂	65.4	1:1 5
Acrylonitril	CuCl ₂	40.0	1:1 5
Acrylonitril	Fe/FeCl ₃	63.0	1:1 5
Methacrylonitril	Cu ₂ Cl ₂	60.0	2.4:1 6
Methyl methacrylate	Cu ₂ Cl ₂	53.5	1.04:1 12
Methyl methacrylate	CuCl ₂	50.0	1.15:1 12
Methyl methacrylate	Fe/FeCl ₃	57.4	1.13:1 12
Styrene	Cu	68.0	1.1:1 15
Styrene	Cu ₂ Cl ₂	88.0	1.1:1 15
Styrene	CuCl ₂	52.3	1:1.1 15
Styrene	Fe/FeCl ₃	73.8	1:1.6 15
α-Methylstyrene	Cu ₂ Cl ₂	47.0	1:1.04 16
α-Methylstyrene	Fe/FeCl ₃	50.5	1:1.04 16

Experiments designed to obtain the dicarboxylic acids directly by reaction of the corresponding acrylic acids with the diazonium salt yielded the acid **19** in a yield of only 24%.

Solutions of the anthradipyran derivatives in organic solvents exhibit a strong fluorescence in daylight or on irradiation with ultraviolet light. However, only the aqueous solutions of the sodium salts of the dicarboxylic acid retained their fluorescence over a period of several weeks.

A mechanism which explains the formation of substituted tetrahydroanthradipyrans has been outlined in Scheme I. It is suggested that in a charge transfer complex formed from olefin-metal salt-diazonium cation an electron is transferred to the diazonium cation to form a radical which then loses nitrogen. The resulting aryl radical attacks the olefin to yield an aliphatic radical (**3**) which attacks the oxygen atom of the built-in quinone system. In this formulation (**3**), the electron required for the reduction of the quinone system is supplied by the reaction system itself (**4-6**) and does not have to be generated by an outside source, as it has been shown, for example, in the arylation of benzoquinones (**3**). This is reminiscent of the generation of a semiquinone radical from a quinone by the addition of a small amount of hydroquinone which then reduces the diazonium cation to a radical (**3**), although attempts to initiate reaction in our system by the addition of hydroquinone failed.

X-Ray Analysis.

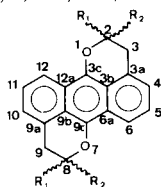
Crystal data for compounds **5**, **6**, **13a** and **13b** are given in Table III. Intensity measurements were made on a Philips PW 1100 diffractometer with monochromated $\text{MoK}\alpha$ radiation. Lorentz- and Polarisation- but no absorption-corrections were applied. The structures were solved by direct methods using the computer program MULTAN 77 (13). All hydrogen atoms could be located in different Fourier maps. Least squares refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms and isotropic ones for hydrogen atoms. Final R-factors and number of reflections used in the refinements are listed in Table III also.

Table III
Crystal Data of Compounds **5**, **6**, **13a**, **13b**

Crystal System	5	6	13a	13b
	monoclinic	monoclinic	monoclinic	monoclinic
Space group	P2 ₁ /c	P2 ₁ /c	P2 ₁ /n	P2 ₁ /c
a (Å)	5.822	8.804	9.957	10.276
b (Å)	15.939	5.613	10.205	13.733
c (Å)	7.706	16.913	11.219	16.005
β (°)	91.28	96.79	104.88	94.99
z	2	2	2	4
Molecular symmetry	C _i	C _i	C _i	C _i
Number of reflections	1219	1468	1839	2346
Number of parameters	133	150	197	393
Final R-value	0.042	0.051	0.083	0.049

Table IV

Schematic Drawings of the Molecules **5**, **6**, **13a**, **13b**, Bond Distances and Molecular Symmetries



Compounds	5	6	13a	13b
R ¹ (axial substituent)	-CN	-CN	-COOC ₂ H ₅	-COOC ₂ H ₅
R ² (equatorial substituent)	-H	-CH ₃	-CH ₃	-CH ₃
Configuration	<i>trans</i>	<i>trans</i>	<i>trans</i>	<i>cis</i>
Molecular Symmetry	C _i	C _i	C _i	C _i
Angle between the planes O(1) C(3c) C(3b) C(3a) C(3) and O(1) C(2) C(3)	47°	46°	45°	47/51°
Distances:				
O(1)-C(2)	1.432(3)	1.443(5)	1.443(3)	1.443(5)
C(2)-C(3)	1.517(4)	1.524(6)	1.534(4)	1.527(6)
C(3)-C(3a)	1.507(4)	1.507(6)	1.500(4)	1.503(6)
C(3a)-C(3b)	1.429(4)	1.434(6)	1.437(4)	1.429(6)
C(3b)-C(3c)	1.392(4)	1.395(6)	1.405(4)	1.393(6)
O(1)-C(3c)	1.385(3)	1.383(6)	1.378(3)	1.384(5)
C(3a)-C(4)	1.355(4)	1.363(6)	1.381(4)	1.358(6)
C(4)-C(5)	1.420(4)	1.423(6)	1.415(4)	1.419(6)
C(5)-C(6)	1.366(4)	1.363(6)	1.377(4)	1.366(6)
C(6)-C(6a)	1.423(4)	1.432(6)	1.435(4)	1.425(6)
C(3b)-C(6a)	1.432(4)	1.432(6)	1.427(4)	1.429(6)
C(6a)-C(9c)	1.399(4)	1.407(6)	1.388(4)	1.392(6)

In Table IV some selected conformational parameters and bond lengths are listed. The *trans* compounds possess C_2 -symmetry. All the molecules exhibit a very similar ring system, the heterocyclic six membered ring adopts a sofa (14a,b) conformation with the atoms O(1), C(3c), C(3b), C(3a) and C(3) all lying in one plane. The distances of C(1) to these planes were found to be between 0.61 and 0.67 Å. The methyl groups of compounds **6**, **13a** and **13b** are situated in a quasi equatorial position. It is noteworthy that in compound **5** with R = H and R² = CN, the hydrogen is located in a quasi equatorial position, and torsion angles with the two hydrogen atoms at C-3 of 51° and 66°, respectively, are observed.

The bond lengths and angles are within the range of normally expected values. The distances C(3a)-C(4) and C(5)-C(6) each belong to the shortest, C(3a)-C(3b), C(3b)-C(6a) and C(6)-C(6a) to the longest distances of the aromatic part of the molecule.

Corresponding differences have been found earlier in the anthracene molecule (15,16).

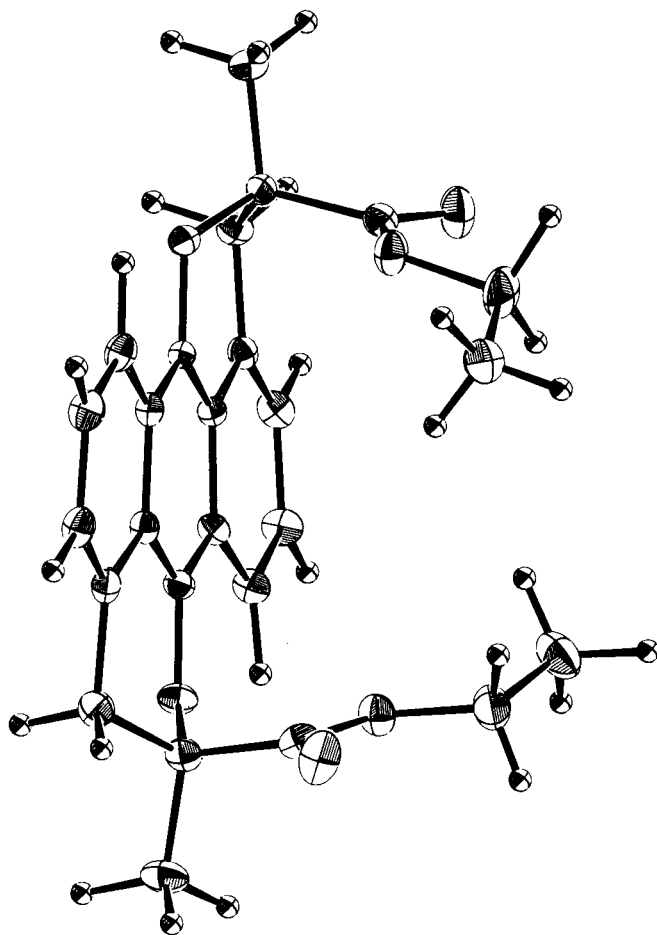


Figure 2. ORTEP drawing of the Molecule **13b** showing 20% Ellipsoids.

Perspectivic views of the two isomers **13a** and **13b** are shown in Figures 1 and 2 which were drawn with the aid of the ORTEP program (17). In the *cis* compound **13b** the conformations of the two ester side chains are slightly different from each other. In one case the methyl group is twisted out of the plane of the carboxylic group by an angle of 11°, while in the other case the angle is 23°. In the *trans* compound **13a** the corresponding angle is 28°.

Spectroscopic Properties.

Ultraviolet spectroscopic parameters of compounds **5-20** are compiled in Table V. As expected, they show little dependence on the nature and stereochemistry of the substituents on C-2(8). The infrared spectra of the compounds show a band varying little in frequency between 1620 and 1623 cm^{-1} , and a strong absorption between 1080 and 1105 cm^{-1} , attributable to a C-O stretching frequency. Bands at similar frequencies, 1622 and 1079 cm^{-1} appear in the infrared spectrum of 9,10-dimethoxyanthracene. The ¹H chemical shifts of compounds **5-20** are given in Table VI. ¹³C chemical shifts for **5** and **8**, together with

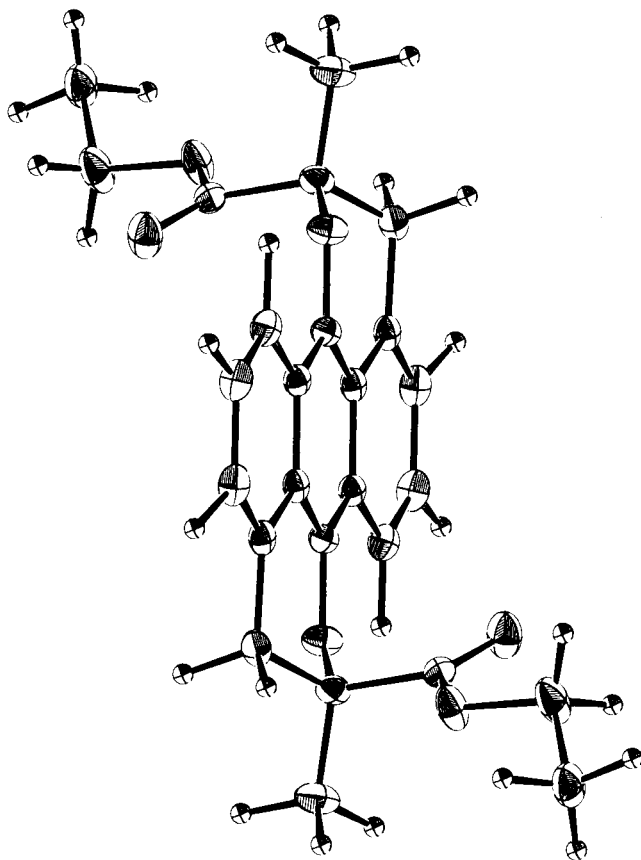


Figure 1. ORTEP drawing of the Molecule **13a** showing 20% Ellipsoids.

^1H and ^{13}C chemical shifts for the comparison compound 9,10-dimethoxyanthracene, are shown in Table VII. (The ^{13}C spectra of the other compounds were not recorded because of their low solubility.)

Most of the compounds were examined as mixtures of the two diastereoisomers. This can be inferred from the spectra, which show two signals for some of the protons or ^{13}C nuclei. [In these cases, two values are given in the tables; where only one value is given, the signals of the two isomers overlap.] Where only one set of signals is observed for all of the protons, we conclude, that only one isomer is present. The stereochemistry can, however, not be deduced from the nmr spectra. It is therefore only known for the compounds examined by X-ray diffraction, *e.g.*, **5**, **6**, and the two isomers of **13**.

The aromatic protons give rise to AMX spectra which $J(4,5) = 6.5$ Hz and $J(5,6) = 8.5$ Hz for all the compounds. The signals for H-4 and H-6 show additional broadening because of unresolved meta coupling $J(4,6)$ and benzylic couplings to the protons at C-3. In isomeric mixtures, the signals for the two isomers perfectly overlap. The assignment of the signals rests on comparison with corresponding chemical shifts and coupling constants of 9,10-dimethoxyanthracene. The corresponding ^{13}C chemical shifts in compounds **5** and **8** were connected with the ^1H shifts by off resonance decoupling experiments. As is seen in Table VII, the ^{13}C chemical shifts of these carbons are also independent of stereochemistry. For compounds with $\text{R}_1 = \text{H}$ the signals for the protons at C-2 and C-3 give rise to ABX spectra. In mixtures, the two isomers have different chemical shifts for H-2 and one of the protons at C-3. The coupling constants, on the other hand, are the same for the two isomers, indicating the same average con-

formation of the hetero rings. The vicinal coupling constants $J(2,3)$ and $J(2,3')$ strongly depend on the nature of the substituent R_2 . For **5** ($\text{R}_2 = \text{CN}$) they are 4.5 and 4.5 Hz, compatible with a sofa conformation of the rings with quasi axial CN groups, as has been observed for the crystalline state. For compounds **15**, **17**, and **18** on the other hand, the corresponding values are 9.5 and 4.5 Hz, strongly suggesting that in these compounds the substituents R_2 adopt quasi equatorial positions. Intermediate values of 7 and 5 Hz are observed for the esters **8-11** and the acid **19**, indicating a conformational equilibrium between sofa conformers with quasi axial and quasi equatorial R_2 substituents in approximately equal proportions.

Compounds having two substituents at C-2(8) exhibit AB spectra with $J(3,3') = 17$ Hz for the protons at C-3(9). The high field signals, which we tentatively assign to axial protons, are additionally broadened because of benzylic couplings. These signals also show a small shift difference for the two isomers, as do the C-2 methyl signals. We assume, that the compounds with $\text{R}_2 = \text{CN}$ and COOR adopt sofa conformations with quasi axial R_2 substituents. Compound **16** with $\text{R}_2 = \text{phenyl}$ appears to have the phenyl ring equatorially disposed.

In view of the fact that the two asymmetric centers are far apart through bonds and through space as well, surprisingly large chemical shift differences are exhibited for some of the proton signals of the R_2 substituents. For instance, in the isomer mixture of the *n*-butyl esters **10** even the CH_3 signals differ by 0.01 ppm. In compounds **15**, **17**, and **18**, the protons in the phenyl rings and for **17** even the protons of the para methyl groups show appreciable shift differences for the two isomers. The largest effect however, is exhibited by the ester methyl signals of the two

Table V
Ultraviolet Spectral Data of Anthradipyrans **5-20**

Compound	UV λ Max (log ϵ) (a)						
5	255 (sh)	263 (108400)	340 (sh)	358 (4200)	377 (8600)	400 (7200)	425 (5800)
6	256 (14400)	264 (26800)		358 (1200)	376 (2100)	400 (1900)	426 (1600)
7	256 (8200)	264 (15200)		358 (600)	376 (1200)	400 (1200)	424 (1000)
8	256 (sh)	264 (38800)	345 (sh)	360 (1600)	378 (3200)	406 (2400)	430 (2000)
9	256 (sh)	264 (40000)		360 (1600)	378 (3200)	406 (2400)	430 (2000)
10		264 (107200)	342 (sh)	361 (4800)	380 (10200)	407 (7800)	431 (6200)
11		265 (103200)	343 (sh)	361 (4600)	380 (9800)	408 (7400)	432 (6000)
12		265 (87200)	342 (sh)	361 (4600)	380 (9400)	409 (7000)	433 (5600)
13a (b)		266 (94400)	344 (sh)	362 (5000)	381 (10400)	410 (7800)	434 (6200)
13b (c)		266 (93600)	344 (sh)	362 (5000)	381 (10600)	410 (7800)	434 (6320)
14		266 (76000)	344 (sh)	362 (4200)	381 (8480)	410 (6400)	435 (5120)
15	258 (sh)	266 (4100)			380 (800)	410 (600)	435 (500)
16	255 (sh)	268 (42800)	345 (1200)	363 (2800)	382 (5200)	416 (4400)	441 (3600)
17	257 (sh)	266 (7600)		360 (sh)	380 (800)	410 (800)	440 (600)
18	256 (sh)	266 (2400)			380 (200)	410 (200)	435 (100)
19	258 (sh)	266 (94800)	345 (sh)	362 (4800)	382 (9600)	412 (7000)	437 (5600)
20		268 (94000)	346 (sh)	365 (4600)	384 (9800)	418 (6600)	442 (5280)

(a) Measured in methanol solution. (b) *trans* configuration. (c) *cis* configuration.

Table VI
¹H Chemical Shifts for Compounds **5-20** in DMSO-d₆ Solution (a)

Compound No.	R ₁	R ₂	T °K (b)	Composition (c)	H-4	H-5	H-6	H-R ₁	H-3,3'	H(R ₂)	
5	H	CN	313	90:10	7.42	7.54	8.15	6.08	3.79; 3.63		
6	CH ₃	CN	320	100 60:40	7.41	7.55	8.19	2.11 2.12	3.78; 3.65 3.62		
7	CH ₂ CH ₂ CN	CN	310	100	7.44	7.57	8.39	3.10; 2.76	3.77; 3.77		
8	H	COOCH ₃	313	65:35	7.28	7.43	8.12	5.36 5.32	3.63; 3.50 3.61	3.66 3.68	
9	H	COOC ₂ H ₅	330	50:50	7.27	7.42	8.14	5.31 5.29	3.62; 3.50 3.63	4.12; 1.15 1.13	
10	H	COO- <i>n</i> -Butyl	320	60:40	7.26	7.41	8.12	5.37 5.36	3.26; 3.50	4.01; 1.39 4.02	1.09; 0.72 0.71
11	H	COO- <i>iso</i> -Butyl	320	100	7.27	7.41	8.12	5.39	3.63; 3.52	3.81; 1.71	0.69 0.68
12	CH ₃	COOCH ₃	320	50:50	7.23	7.40	8.13	1.77 1.78	3.68; 3.41 3.39	3.48 3.44	
13b (cis)	CH ₃	COOC ₂ H ₅	310	100	7.22	7.39	8.13	1.80	3.67; 3.39	3.82; 0.70	
13a (trans)	CH ₃	COOC ₂ H ₅	310	100	7.22	7.40	8.13	1.78	3.67; 3.41	3.85; 0.79	
14	CH ₃	COO-C ₆ H ₁₁	330	100	7.20	7.37	8.14	1.77	3.66; 3.38	4.46; 1.42-0.84	
15	H	C ₆ H ₅	313	50:50	7.27	(7.5-7.38)	8.13	5.49 5.46	3.56; 3.55	7.68; 7.50-7.38 7.66	
16	CH ₃	C ₆ H ₅	313	100	7.26	7.40	8.20	1.73	3.89; 3.52	7.50; 7.16; 7.08	
17	H	C ₆ H ₄ CH ₃ - <i>p</i>	360	50:50	7.26	7.39	8.13	5.44 5.42	3.56; 3.55	7.54; 7.24; 2.36 7.52 2.35	
18	H	C ₆ H ₄ Cl- <i>p</i>	320	50:50	7.28	7.42	8.14	5.51 5.48	3.60; 3.49 3.58	7.71; 7.51 7.68; 7.49	
19	H	COOH	330	50:50	7.26	7.41	8.15	5.22 5.20	3.61; 3.49 3.60		
20	CH ₃	COOH	310	50:50	7.20	7.37	8.13	1.79 1.78	3.61; 3.34 3.33		

(a) δ -Values in ppm (± 0.01 ppm) at 360 MHz; internal standard tetramethylsilane (δ (TMS) = 0), concentration approximately 5 mg/ml solvent; numbering system of hydrogens see Table VII. (b) Measuring temperature in K. (c) The composition of mixtures was estimated from a comparison of peak heights in the ¹H nmr spectra, except for **5** where composition was estimated from ¹³C nmr spectra.

isomers of the ethyl ester **13**. Not only are these signals at abnormally high field as compared to the corresponding signals in **9**, they also are almost 0.1 ppm apart in the two isomers.

We assume, that in **13b (cis)** and **13a (trans)** the ethyl groups reside mainly above the plane of the aromatic rings and thus are shielded by the ring current effect. In **13 cis** the two ethyl groups are on the same side of the aromatic plane and can come close to each other in space. This spatial proximity exerts a through space effect on their chemical shifts. In the *trans* compound the two ethyl

groups are on different sides of the aromatic plane and thus show no through space interaction.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. The ¹H- and ¹³C nmr spectra were recorded on a Bruker HX-360 nmr spectrometer in the fourier transform mode.

Samples for infrared spectra were prepared in potassium bromide pellets.

Dimethyl methylphosphonate was of commercial quality and was distilled before use. It contained 92% of dimethyl methylphosphonate,

Table VII
¹³C Chemical Shifts of Compounds **5**, **8** and of 9,10-Dimethoxyanthracene (a)



Compound No.	T °K	C-2(8)	C-3(9)	C-3a(9a)	C-3b(9b)	C-3c(9c)	C-4(10)	C-5(11)	C-6(12)	C-6a(12a)	C of R
5	313	63.61	31.96	126.22	118.66	139.15	123.53	125.51	119.87	116.06	117.98
		63.55	31.80	126.12							
8	333	73.08	30.91	127.61	118.21	140.07	122.10	124.46	119.83	116.11	170.06
		73.13		127.66							170.02

(a) δ -values in ppm (± 0.02 ppm) at 90.53 MHz, internal standard TMS (δ (TMS) = 0), solvent DMSO-*d*₆ for **5** and **8**, deuteriochloroform for 9,10-dimethoxyanthracene, ¹³C chemical shifts for 9,10-dimethoxyanthracene are given directly in the formula, values in parenthesis are ¹H chemical shifts in DMSO-*d*₆.

2.3% of trimethylphosphate and 5.7% of dimethylphosphate (by gas chromatography).

The high performance liquid chromatography (hplc) was performed with a Perkin Elmer model series III B, and injection port permitting direct syringe injection on top of the column and at a wave length of 264 nm with an ultraviolet detector LC-75 from Perkin Elmer. A commercially available ion-pair reversed-phase column was used with a packing material prepared from LICHROSORB RP-17 from E. Merck, Darmstadt, Germany. The column length was 250 mm with an inner diameter of 4 mm, the size of the particles being 5 μ and 10 μ , respectively. The mobile phase was a solvent pair consisting of methanol-water varying in the required methanol ratio from 80-93% at a flow rate of 1 ml/minute.

The acids were separated with the same column and a particle size of 10 μ . The solvent ion-pair consisted of 45-55% of methanol and an aqueous solution of 0.005 molar tetrabutylammonium phosphate.

The separation of nitriles was achieved with a ZORBAX CN column with a particle size of 10 μ and a flow rate of 1 ml/minute at 264 nm.

Thin layer chromatography (tlc) was run on silica gel 60 plates, and detection of components was by ultraviolet light.

The olefins were distilled before use. The procedures described below for the preparations of the different anthratetrahydrodipyrans are typical.

Suitable single crystals for the X-ray diffraction analysis were obtained as follows.

Crystals of **6** (0.2 g) were dissolved in 20 ml of boiling cyclohexanone and the solution kept at 110° for 24 hours, then the temperature slowly lowered to 95° and kept there for another 24 hours. The solvent was decanted from the crystals which were then dried at 130°/1 torr.

Single crystals of **13b** (*cis*) were obtained from a saturated solution of the compound in benzene which was allowed to stand at room temperature for 2 days. Slow crystallization occurred.

Crystals of **13a** (*trans*) were obtained by slow crystallization from methylethylketone.

Single crystals of **5** were obtained from a solution of cyclohexanone in a manner analogous to the one described above.

1,5-Anthraquinone Bis(diazonium hydrogensulfate) (**2**).

1,5-Diaminoanthraquinone (23.9 g, 0.1 mole) was added over a period of 3 minutes to 100 ml of concentrated sulfuric acid and the slurry stirred at 60° for 30 minutes. The red solution was then cooled to 20° and 18

ml of water were added, whereupon a fine suspension of crystals precipitated. To these were added 66.7 g of a solution of 40% nitrosyl sulfuric acid over a period of 40 minutes. After the addition was complete, stirring was continued for 1 hour, and occasional cooling was required during the entire operation to ensure that the temperature did not exceed 25°. Then, 400 ml of ice water were added over 20 minutes and stirring continued for a further 15 minutes at 10°. The crystalline suspension was filtered, and the crystals washed on the filter with 50 ml of ice water followed by 300 ml of a mixture of ethanol-ether (1:1) and dried at 25°/12 torr, yielding 44.1 g (96.7%) of product, mp 155° dec; ir (potassium bromide): 3080 (m), 2870 (m), 2500 (m), 2322 (m), N₂⁺, 1700 (s) carbonyl, 1610 (m), 1535 (s), 1512 (s), 1230 (s), 1170 (s), 1030 (s), 863 (s).

Anal. Calcd. for C₁₄H₈N₄O₁₀S₂: C, 36.85; H, 1.77; N, 12.28; S, 14.05. Found: C, 36.38; H, 1.85; N, 12.23; S, 14.14.

The decomposition temperature of the dry crystals varies somewhat with the method of determination. In capillary tubes the crystals decomposed at about 150° while dropping them in a fine dispersion on hot metal plates with a temperature gradient results in a violent decomposition at 130°. The bis-diazonium salt retained its original light yellow color on storing in dark brown bottles for several months, however, it became strongly discolored after exposure to bright daylight for only several hours.

Anthra[9,1-*bc*:10,5-*b'**c'*]-2,3,7,8-tetrahydrodipyrans-2,8-dicarbonitrile (**5**).

To a stirred suspension of 9.6 g (0.02 mole) of **2** (95%) in 100 ml of dimethyl methylphosphonate, 15 ml of water and 20.13 g (0.38 mole) of acrylonitrile was added 2 g of copper(I) chloride in small portions over a period of 30 minutes. Nitrogen evolution commenced and the temperature rose gradually from 25° to 60°. After nitrogen evolution had subsided stirring was continued for an additional 30 minutes. Then the suspension was added to 500 ml of water. The product precipitated usually first in a viscous form which became crystalline after stirring for several minutes. Crystals were filtered, washed with 50 ml of water and dried at 80°/12 torr, yielding 6.9 g of crude product. Further purification was achieved by refluxing in 60 ml of methanol for about 5 minutes, then the crystals were filtered and washed with methanol until the washings were colorless, yielding 4.0 g (64.5%). A sample of 1 g was recrystallized from 13 ml of cyclohexanone and afforded light yellow crystals, mp 287-288°; ir cm⁻¹: 2250 (CN), 1622, 1410, 1367, 1092, 800.

2,8-Dimethylanthra[9,1-*bc*:10,5-*b'**c'*]-2,3,7,8-tetrahydrodipyrans-2,8-dicarbonitrile (**6**).

To a stirred suspension of 9.6 g (0.02 mole) of **2** (95%) in 100 ml of dimethyl methylphosphonate, 15 ml of water and 20 g (0.2 mole) of methylacrylonitrile were added 1.5 g of iron filings and 2.0 g of ferric(III) chloride. When nitrogen evolution subsided the temperature was increased to 60° for 3 hours. Then the suspension was decanted from metallic particles and added to 500 ml of water. The aqueous phase was decanted and the resinous precipitate refluxed in 100 ml of methanol, whereupon crystallization occurred. The insoluble crystals were filtered from the solution, washed on the filter with 40 ml of hot methanol and dried, yielding 4.6 g (57%) of product.

Anthra[9,1-*bc*:10,5-*b'c'*]2,3,7,8-tetrahydrodipyrans-2,8-dicarboxylic Acid Dimethyl Ester (**8**).

To a suspension of 48 g (0.1 mole) of **2** (95%) in 500 ml of dimethyl methylphosphonate, 86 g (1 mole) of methyl acrylate and 75 ml of water were added 7.5 g of copper(I) chloride over a period of 2 hours. The temperature rose gradually to 55° during the addition of the catalyst. After nitrogen evolution had subsided, the solution was added to 2.5 l of water. The resinous precipitate formed was stirred for 20 minutes, the aqueous phase decanted and the resinous material heated to reflux in 350 ml of methanol. Filtration at 45° gave crystals which were washed on the filter with 200 ml of cold methanol, followed by 50 ml of ether yielding 14.05 g of product.

2,8-Bis(4-methylphenyl)anthra[9,1-*bc*:10,5-*b'c'*]2,3,7,8-tetrahydrodipyrans (**17**).

To a stirred suspension of 4.8 g (0.01 mole) of **2**, 14.6 g (0.1 mole) of 4-methylstyrene in 50 ml of dimethyl methylphosphonate and 7.5 ml of water were added 0.9 g of copper(I) chloride. When nitrogen evolution had ceased the suspension was heated to 60° for one hour. Then it was added to 250 ml of water and stirred until crystallization occurred. Crystals were filtered from the solution and refluxed in 60 ml of methanol, filtered hot and washed on the filter with 20 ml of methanol, yielding 2.2 g of product.

Anthra[9,1-*bc*:10,5-*b'c'*]2,3,7,8-tetrahydrodipyrans-2,8-dicarboxylic Acid (**19**).

A. To a solution of 1.5 g of potassium hydroxide (85%) in 40 ml of ethanol were added 2.03 g (0.006 mole) of **9** and heated to reflux for 15 minutes. Then the suspension was added to 200 ml of water and 0.5 g of decolorizing carbon added. The solution was filtered and 6 ml of 4*N* hydrochloric acid added to the filtrate. Crystals were filtered and washed with water, yielding 1.3 g (63.8%) of acid, mp >300° dec.

B. To a stirred suspension of 9.6 g (0.02 mole) of **2** in 100 ml of dimethyl methylphosphonate, 15 ml of water and 14.4 g (0.2 moles) of acrylic acid were added 1.1 g of copper(I) chloride in small portions over one hour. After nitrogen evolution had subsided stirring was continued for an additional 2 hours at 50°. Then the solution was added to 500 ml of water and the resinous precipitate stirred for several hours until it became crystalline. Crystals were filtered, washed with water, and dissolved in 200 ml of aqueous sodium hydroxide solution. Addition of decolorizing carbon and filtration followed by acidification with 150 ml of 4*N* hydrochloric acid gave a brown colored precipitate. This was filtered, and repeatedly extracted with boiling methanol, yielding 1.8 g (25.7%) of dicarboxylic acid which was identified by comparison of its infrared spectra with that of the sample prepared under A.

2,8-Dimethylanthra[9,1-*bc*:10,5-*b'c'*]2,3,7,8-tetrahydrodipyrans-2,8-dicarboxylic Acid (**20**).

To a solution of 2 g of potassium hydroxide (85%) in 30 ml of methyl cellosolve was added 4.06 g (0.01 mole) of **12** and the suspension heated at 100° for 10 minutes. Then the heavy suspension of crystals was added to 350 ml of water and 0.5 g of decolorizing carbon added. Filtration and subsequent acidification of the filtrate with 4 ml of concentrated hydrochloric acid precipitated crystals which were collected by filtration, washed with water and dried at 80°/12 torr, yielding 3.6 g (95%) of dicarboxylic acid.

9,10-Dimethoxyanthracene (**21**).

The compound was prepared according to the literature (12), mp 198°.

Acknowledgement.

The authors wish to acknowledge the skillful performance of Mr. F. Gaspar on the hplc analysis.

REFERENCES AND NOTES

- (1) F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, **45**, 3061 (1980).
- (2a) H. Fuhrer, P. Sutter and C. D. Weis, *J. Heterocyclic Chem.*, **16**, 1121 (1979); (b) P. Sutter and C. D. Weis, *ibid.*, **17**, 493 (1979); (c) P. Sutter and C. D. Weis, *Phosphorus Sulfur*, **4**, 335 (1978).
- (3) C. S. Rondestvedt, Jr., in "Organic Reactions", Vol. 24, W. G. Dauben, ed., John Wiley and Sons, Inc., New York, N. Y., 1976, p. 225.
- (4) C. S. Rondestvedt, Jr., in "Organic Reactions", Vol. **11**, 189 (1960).
- (5) R. Filler, L. Gorely and B. Taqui-Khan, *Proc. Chem. Soc.*, 117 (1962).
- (6) N. I. Ganushchak, B. D. Grishchuk and A. V. Dombrovskii, *Zh. Org. Khim.*, **9**, 1004 (1973), (Engl. Transl. p. 1030).
- (7) German Offenlegungsschrift 2,627,867 (1977), Montedison Corp., *Chem. Abstr.*, **86**, 91746n (1977).
- (8) German Offenlegungsschrift 2,323,543 (1972), Montedison Corp., *Chem. Abstr.*, **80**, 61068b (1974).
- (9a) "Methoden der Organischen Chemie (Houben Weyl)", Vol. 7, Part 3C, O. Bayer, ed., Georg Thieme Verlag, Stuttgart 1979, p. 109; (b) *ibid.*, p. 115.
- (10) German Patent 238,488 (1910).
- (11) R. Scholl, *Monatsh. Chem.*, **32**, 1051 (1911).
- (12) J. S. Meek, P. A. Monroe and C. J. Bouboulis, *J. Org. Chem.*, **28**, 2572 (1963).
- (13) A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data (1977), (a) P. Main, L. Lessinger and M. M. Woolfson, Department of Physics, University of York, York, England; (b) G. Germain and J. P. Declercq, Laboratoire de Chimie Physique et de Crystallographie, Batiment Lavoisier, 1 Place Louis Pasteur, 1348 Louvain-La-Neuve, Belgique.
- (14a) R. Bucourt and D. Hainaut, *C. R. Acad. Sci. Paris*, **258**, 3305 (1964); (b) R. Bucourt and D. Hainaut, *Bull. Soc. Chim. France*, 4562 (1967).
- (15) R. Mason, *Acta Cryst.*, **17**, 547 (1964).
- (16) D. W. J. Cruickshank and A. Sparks, *Proc. Royal Soc.*, **A 258**, 270 (1960).
- (17) C. K. Johnson, ORTEP Report ORNL-3794, (1965), Oak Ridge National Laboratory, Tennessee, USA.