[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY, THE OHIO STATE UNIVERSITY]

α-(2,4,5,7-Tetranitro-9-fluorenylideneaminoöxy)-propionic Acid, a New Reagent for Resolution by Complex Formation[1]

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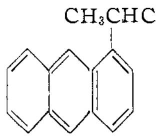
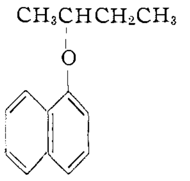
The preparation of (+)- and (−)-α-(2,4,5,7-tetranitro-9-fluorenylideneaminoöxy)-propionic acid (III) by reaction of (−)- and (+)-α-(isopropylideneaminoöxy)-propionic acid (I) with 2,4,5,7-tetranitro-9-fluorenone (II) is described as well as the use of (+)- and (−)-III for partial resolution of 1-naphthyl 2-butyl ether and methyl α-(1-anthryl)-propionate. Several complexes of II with polycyclic aromatic hydrocarbons are described. The melting points of these complexes are in general about 50° higher than the corresponding derivatives with 2,4,7-trinitro-9-fluorenone.

Many methods have been used for the resolution of compounds which do not possess a functional group capable of salt formation with an optically active acid or base.[3] However, these methods did not appear promising for the resolution of polycyclic aromatic hydrocarbons which depend on intramolecular overcrowding to produce molecular asymmetry.[4] The use of optically active polynitro biphenyl derivatives for resolution has proved unsuitable because of the poor complexing ability of these reagents.[5]

In this paper we report on the synthesis of (+)- and (−)-α-(2,4,5,7-tetranitro-9-fluorenylideneaminoöxy)-propionic acid (III) and the use of these reagents in the partial resolution of methyl α-(1-anthryl)-propionate (VI) and 1-naphthyl 2-butyl ether (VII). No attempt was made to achieve maximum resolution of VI and VII. The synthesis and resolution of phenanthro[3,4-c]phenanthrene (hexahelicene) as reported[6] will be described later.



VI



VII

At the beginning of our attempts to prepare a new resolving agent we thought to prepare a derivative of 2,4,7-trinitrofluorenone[7] modified to include an optically active carbon[8] at position 9. During the course of this work we obtained a quantity of 2,4,5,7-tetranitrofluorenone,[9] TENF, II, and noted the excellent complexing ability. In general the complexes formed between the tetranitro derivative II and hydrocarbons are higher melting and more easily crystallized from solvents than are the corresponding complexes with 2,4,7-trinitrofluorenone, TNF. A few complexes of II are described in Table I,[10] together with three new complexes of TNF, the melting points of which are appreciably lower than those of the corresponding TENF complexes.

Interestingly hexaethylbenzene[11] failed to form a complex with TENF whereas hexamethylbenzene formed a deep red complex (see Table I). This result may be ascribed to steric hindrance as the adjacent ethyl groups are partly forced above and below the plane of the ring. This prevents the acceptor polynitro compound from approaching the ring closely enough to interact with the π-electrons.[12]

Because of the difficulty of preparing suitable 9-substituted 2,4,7-trinitrofluorene derivatives and of the strong complexing ability of the tetranitrofluorenone nucleus we thought of introducing an optically active center by oximation of the ketone function followed by replacement of the oxime hydrogen by some group containing an asymmetric carbon atom. The oxime and oxime acetate[13] of II were prepared and found to complex readily with acenaphthene.

Several possibilities for the introduction of a group containing an asymmetric carbon were considered. For several reasons the preparation of III was chosen. Accordingly acetoxime was converted into α-(isopropylideneaminoöxy)-propionic acid (I)

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(1) The work herein reported is largely taken from the Ph.D. thesis of Wilson B. Lutz, The Ohio State University, 1955.

(2) This work was supported in part by the Newman Fund for Fundamental Research.

(3) A short summary of reagents or devices that have been used for such purposes is given: (a) digitonin, A. Windaus, F. Klanhardt and R. Weinhold, *Z. physiol Chem.*, **126**, 308 (1923); (b) desoxycholic acid, H. Sobotka, *Naturwiss.*, **19**, 595 (1931), H. Sobotka and A. Goldberg, *Biochem. J.*, **26**, 905 (1932); (c) brucine, F. Eisenlohr and G. Meier, *Ber.*, **71**, 1005 (1938); (d) tri-*o*-thymotide, H. M. Powell, *Nature*, **170**, 155 (1952), and A. C. D. Newman and H. M. Powell, *J. Chem. Soc.*, 3747 (1952); (e) thiourea, W. Schlenk, Jr., *Experientia*, **8**, 337 (1952); (f) crystallization from optically active solvent, C. Buchanan and S. Graham, *J. Chem. Soc.*, 500 (1950); (g) chromatography over optically active adsorbents, G. Henderson and H. Rule, *Nature*, **141**, 917 (1938), *J. Chem. Soc.*, 1568 (1939), V. Prelog and H. Wieland, *Helv. Chim. Acta*, **27**, 1129 (1944), and G. DiModica and E. Angeletti, *Ricerca sci.*, **22**, 715 (1952), *C. A.*, **47**, 6918d (1953).

(4) See M. S. Newman and R. M. Wise, THIS JOURNAL, **78**, 450 (1956), for a review of this field.

(5) B. Brown and D. Hammick, *J. Chem. Soc.*, 1396 (1948), found dimethyl 4,4',6,6'-tetranitrodiphenate unsatisfactory, and B. Bennett, M.S. thesis, The Ohio State University, 1948, found 2,2',4,4',6-pentanitro-3-methylbiphenyl and the corresponding 3-carboxy compound unsuitable.

(6) M. S. Newman, W. B. Lutz and D. Lednicer, THIS JOURNAL, **77**, 3420 (1955).

(7) (a) M. Orchin and E. O. Woolfolk, *ibid.*, **68**, 1727 (1946); (b) M. Orchin, L. Reggel and E. O. Woolfolk, *ibid.*, **69**, 1225 (1947).

(8) F. E. Ray and E. Kreiser, *ibid.*, **67**, 504, 3068 (1945), have successfully resolved 9-substituted fluorene derivatives.

(9) F. E. Ray and W. Francis, *J. Org. Chem.*, **8**, 52 (1943), proved structure and mentioned complex formation with tetralin. E. Hertel and H. Kurth, *Ber.*, **61**, 1650 (1928), reported that 2,3,6,7-tetranitrofluorenone (really the 2,4,5,7-isomer) formed complexes with anthracene and stilbene.

(10) Presented before the division of Organic Chemistry at the Cincinnati Meeting of the American Chemical Society, April, 1955.

(11) We are indebted to the Continental Oil Co., Ponca City, Oklahoma, for a sample of hexaethylbenzene, m.p. 129.5–130.0°.

(12) Note the low values for the equilibrium constants for the complexes of iodine and iodine chloride with hexaethylbenzene, L. J. Andrews and R. M. Keefer, THIS JOURNAL, **74**, 4500 (1952); see also N. Ogimachi, L. J. Andrews and R. M. Keefer, *ibid.*, **77**, 4202 (1955).

(13) J. Schmidt, F. Retzlaff and A. Haid, *Ann.*, **390**, 210 (1912), reported melting points of 249° dec. and 223° dec., respectively, for the oxime and oxime acetate of II.

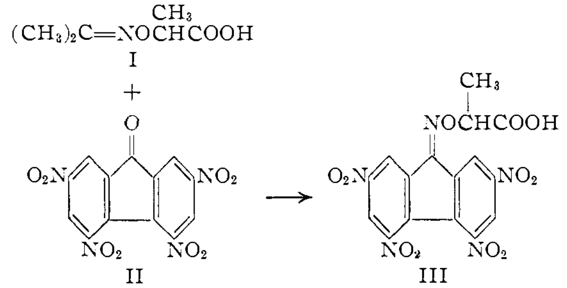
TABLE I

COMPLEXES OF AROMATIC COMPOUNDS WITH 2,4,5,7-TETRANITROFLUORENONE

					Analyses,[b] %					
					Calculated			Found		
	Aromatic component	Color	M.p., °C. (cor.)[a]	Formula	C	H	N	C	H	N
1	Anthracene	Green-black	281–282	$C_{27}H_{14}O_9N_4$	60.2	2.6	10.4	60.2	2.7	10.3
2	Phenanthrene	Orange-red	236–237	$C_{27}H_{14}O_9N_4$	60.2	2.6	10.4	60.2	2.7	10.3
3	Fluoranthene	Orange	230–232	$C_{29}H_{14}O_9N_4$	61.9	2.5	10.0	61.8	2.8	9.9
4	Fluorene	Red-brown	228–231	$C_{26}H_{14}O_9N_4$	59.3	2.7	10.6	58.8	2.9	10.9
5	Acenaphthene	Dark wine-red	210–212	$C_{25}H_{14}O_9N_4$			10.9			11.0
6	2-Methylnaphthalene	Orange	190–192	$C_{24}H_{14}O_9N_4$	57.4	2.8	11.2	57.5	2.9	11.2
7	Naphthalene	Bright orange	206–208	$C_{23}H_{12}O_9N_4$			11.5			11.4
8	4,5-Dimethylphenanthrene	Dark red	191–192	$C_{29}H_{28}O_9N_4$			9.9			9.8
9	1,12-Dimethylbenzo[c]phenanthrene	Wine-black	176–177	$C_{33}H_{24}O_9N_4$	64.3	3.3		64.3	3.3	
10	Pentamethylbenzene	Orange	140–150	$C_{24}H_{24}O_9N_4$			11.0			10.8
11	Hexamethylbenzene	Dark red	171 up	$C_{25}H_{26}O_9N_4$			10.6			10.6
12	1-Acetoxyacenaphthene	Brick red	170–172	$C_{27}H_6O_{11}N_4$			9.9			9.9

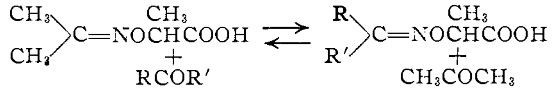
[a] The m.p. of the corresponding TNF derivatives, ref. 7, are: 1, 194°; 2, 197°; 3, 216°; 4, 179°; 5, 176°; 6, 126° (TNF complex contains 2 moles of TNF): 7, 154°; 8, 122° (M. S. Newman and H. S. Whitehouse, THIS JOURNAL, **71**, 3664 (1949)); 9, 134.1–135.4°, *Anal.* Calcd. for $C_{33}H_{21}O_7N_3$: C, 69.4; H, 3.7. Found: C, 69.6; H, 3.6; 10, 103–107° dec., *Anal.* Calcd. for $C_{24}H_{21}O_7N_3$: C, 62.6; H, 4.6; N, 9.1. Found: C, 62.1; H, 4.4; N, 9.0; 11, 121–123°, *Anal.* Calcd. for $C_{27}H_{17}O_9N_3$: N, 8.0. Found: N, 8.2. [b] All analyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

by about the same procedure used for the preparation of the corresponding acetic acid derivative.[14]



In using aminoöxyacetic acid to condense with ketones previous investigators hydrolyzed isopropylideneaminoöxyacetic acid to aminoöxyacetic acid and then condensed the latter with ketones.

We have found that direct interchange of ketone residues may be effected by heating I in acetic acid with II in the presence of hydrated *p*-toluenesulfonic acid. In this way several α-(isopropylideneaminoöxy)-propionic acids have been prepared, the acetone formed usually being removed as formed (see Table II).



$$\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}\!\!>\!\text{C}{=}\text{NO}\overset{\text{CH}_3}{\text{CH}}\text{COOH} + \text{RCOR}' \rightleftarrows \begin{matrix} \text{R} \\ \text{R}' \end{matrix}\!\!>\!\text{C}{=}\text{NO}\overset{\text{CH}_3}{\text{CH}}\text{COOH} + \text{CH}_3\text{COCH}_3$$

TABLE II

PREPARATION OF α-(ISOPROPYLIDENEAMINOÖXY)-PROPIONIC DERIVATIVES BY INTERCHANGE

Ketone	Solvent, % HOAc by volume[a]	Mole I / mole ketone	Mole $CH_3C_6H_4SO_3H$ / mole ketone	Time, hr.	Yield, %
Benzophenone	90	1.3	0.26	7	65[b]
Fluorenone	67	1.1	1.15	7	97[c]
Fluorenone	100	1.1	1.15	7	95[c]
TNF[d]	96	1.5[c,e]	0.95	5	78[c]
TENF, III	93	8.7	.02	2.5	89[c]
	96	7.4	.02	2	95[f]
	93	1.5[g]	1.08	5.5	80[h]
	99	1.3[i]	0.15	9.5	57[h]

[a] All reactions were run at reflux, hence at slightly different temperatures. [b] Acetone removed by distillation through small packed column. [c] Acetone removed by air current. [d] 2,4,7-Trinitrofluorenone. [e] III, $[\alpha]^{20}\text{D}$ +32.0° used. [f] Acetone not removed. [g] III, $[\alpha]^{28}\text{D}$ −30.6° used. [h] Acetone removed by current of nitrogen. [i] III, $[\alpha]^{26}\text{D}$ +30.8° used.

From the limited study of the interchange which we have made we cannot conclude whether the interchange is direct or is preceded by hydrolysis of I to α-aminoöxypropionic acid followed by condensation of the latter with ketone. In one experiment, a solution of III (α −0.77°) in 95% acetic acid containing *p*-toluenesulfonic acid was refluxed. The rotation increased to −3.97° after 16 hours. During the last 11 hours of this treatment an air current, presaturated with solvent by passing through refluxing 95% acetic acid, was passed through the reaction mixture. Acetone was detected in the effluent gas and identified as its 2,4-dinitrophenylhydrazone. The remaining solution afforded an 83% yield of α-(fluorenylideneaminooxy)-propionic acid on treatment with fluorenone. This experiment shows that the hydrolysis–recondensation mechanism is possible under the reaction conditions but does not rule out a faster or concurrent direct interchange. The large increase in negative rotation on heating the partly resolved III (α −0.77°) undoubtedly is due to the formation of free α-aminoöxypropionic acid.

By the interchange method we have prepared both (+) and (−)-III, the (+)-III corresponding to (−)-α-(isopropylideneaminoöxy)propionic acid. Since resolution of (±)-I proved fairly easy with (−)-ephedrine, optically active forms of III were prepared only by interchange with active forms of I and not by resolution of inactive III.

In preliminary work, unsuccessful attempts were made to prepare derivatives of 2,4,7-trinitrofluorenone, TNF, in which the 9-carbon was asymmetric. Although the reduction of *m*-nitrobenzaldehyde to *m*-nitrobenzyl alcohol has been carried out with so-

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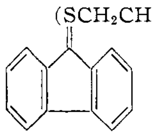
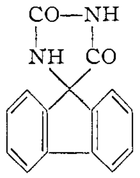
[14] (a) E. Borek and H. T. Clarke, THIS JOURNAL, **58**, 2020 (1936); (b) H. S. Anker and H. T. Clarke, *Org. Syntheses*, **27**, 15 (1947); (c) M. Anchel and R. Schoenheimer, *J. Biol. Chem.*, **114**, 539 (1936).

dium borohydride,[15] we were unable to reduce TNF to any crystalline product by this or any other method. When fluorenone was reduced with sodium borohydride in methanol the product initially formed was undoubtedly a borate ester with peculiar melting point behavior. However, by refluxing with a solution of potassium fluoride in aqueous dioxane the boric acid produced was converted to fluoroborate ion[16] and the isolation of 9-fluorenol in 86% yield was facilitated. When this technique was applied to TNF reduction mixtures it was still impossible to obtain a crystalline product.

It also proved impossible to prepare a 1,3-oxathiolane from TNF and 2-mercaptoethanol, in spite of the success with other ketones.[17] Furthermore, attempts to convert TNF and fluorenone into oxathiolanes by interchange with 2-ethyl-2-methyl-1,3-oxathiolane[17c,18] failed. When fluorenone was treated with excess 2-mercaptoethanol in dioxane[17a] the bis-2-hydroxyethyl mercaptole IV was formed in 76% yield[19] but TNF yielded no mercaptole.


IV


V

An attempt to prepare a trinitro derivative of spiro-(fluorene-9,4′-imidizolidine)-2′,5′-dione (V)[20] by nitration led only to II. Nitration of 9,9′-difluorenyl disulfide,[21] prepared by an improved procedure, afforded only II and TNF.

Experimental[22]

9-Fluorenol.—To a solution of 0.18 g. of fluorenone in 28 ml. of acetonitrile was added a solution of 0.04 g. of sodium borohydride in 2 ml. of methanol Within ten minutes the reduction was complete as judged by loss of yellow color. Addition of 7 drops of 10% sulfuric acid caused the formation of colorless needles. These were collected and more similar but partly amorphous material was obtained from further dilution of the filtrate. No definite melting points could be obtained with these solids. After refluxing the combined solids with 20 ml. of 20% aqueous potassium fluoride containing 5 ml. of dioxane for 6 hours there was isolated 0.156 g. (86%) of colorless leaves of 9-fluorenol, m.p. 154–155°.

Fluorenone-bis-2-hydroxyethyl Mercaptole (IV).—A mixture of 5 g. of freshly fused and powdered zinc chloride, 5 g. of anhydrous sodium sulfate, 1.8 g. of fluorenone, 5.6 g. of 2-mercaptoethanol and 5 ml. of dioxane was stirred for ten hours. By suitable procedure 2.57 g. (79%) of IV, m.p. 84–85°, was obtained. A sample, twice recrystallized from benzene, melted at 85.5–86.0°.

9,9′-Difluorenyl Disulfide.—A solution of 3 g. of fluorenone in 40 ml. of alcohol was saturated alternately thrice with hydrogen sulfide and twice with ammonia, each saturation being completed with cooling. After adding 0.5 g. of sulfur powder, the mixture was allowed to stand for six days in a stoppered flask with occasional shaking. The solid was collected and recrystallized from isopropyl alcohol to yield 2.95 g. (90%) of colorless needles, m.p. 170–171° with darkening.

Spiro-(fluorene-9,4′-imidizolidine)-2′,5′-dione (V).—A mixture of 12 g. of fluorenone, 36 g. of ammonium carbonate, 15 g. of potassium cyanide, 80 ml. of water and 60 ml. of methanol was refluxed for 14 hours, during which 30 ml. of water was added. The dark solution was cooled and poured into 600 ml. of 3% sodium hydroxide. About 7 g. of fluorenone was recovered and, on acidification, 6.4 g. of V was obtained. Recrystallization from acetic acid (charcoal, Darco-G60) afforded 4.8 g. of hard colorless prisms, m.p. 352–356° dec.[20b] Additional V from the mother liquors brought the conversion to 38% (yield 91%).

Anal. Calcd. for $C_{15}H_{10}O_2N_2$: C, 72.0; H, 4.0; N, 11.2. Found: C, 71.8; H, 4.1; N, 10.9.

2,4,5,7-Tetranitrofluorenone (II).—To a gently refluxing solution of 1300 ml. of 90% fuming nitric acid in 770 ml. of concd. sulfuric acid in a 5-l. three-necked flask fitted with an all-glass addition funnel and two condensers was added during one hour a solution (deep purple-brown) of 73 g. of fluorenone, m.p. 82–84°, in 840 ml. of concd. sulfuric acid. After the fluorenone addition was complete a solution of 950 ml. of fuming nitric acid in 1120 ml. of concd. sulfuric acid was added dropwise during 8.5 hours to the gently refluxing reaction mixture. After turning off the heating jacket and allowing to stand for ten hours, the reaction mixture was poured into 5 gallons of water in two 3-gallon crocks. This operation must be carried out in the hood. The light yellow precipitate was washed twice by decantation, collected on a suction filter, and sucked dry without use of a rubber dam. After drying for several days *in vacuo* over calcium chloride the solid was dissolved in 1.6 l. of acetic acid containing 100 ml. of acetic anhydride. The hot solution was filtered through a fluted filter and cooled rapidly to yield 85.6 g. (60%) of TENF, m.p. 253.0–254.5° cor. Additional material to bring the yield to 77% may be obtained by recrystallization of further crops from the mother liquor. TENF, II, crystallizes with one-half a mole of acetic acid which is readily lost on heating *in vacuo*.

Anal. Calcd. for $(C_{13}H_4O_9N_4)_2\cdot CH_3COOH$: C, 43.1; H, 1.6; N, 14.4. Found: C, 43.8, 43.1; H, 2.03, 1.9; N, 14.1, 14.3.

Complexes of II, General Procedure.-One equivalent each of II and of hydrocarbon were dissolved separately in minimal quantities of hot glacial acetic acid. On mixing deep colors were formed immediately and on cooling crystals separated. These were recrystallized from acetic acid and dried *in vacuo* over potassium hydroxide and phosphorus pentoxide at room temperature for a day or more. The properties and analyses are listed in Table I.

α-(Isopropylideneaminoöxy)-propionic Acid (I).[23]—A mixture of 230 g. of α-bromopropionic acid, and 170 g. of ice was carefully neutralized with 150 g. of 40% sodium hydroxide. Additional ice (*ca.* 160 g.) was periodically added to keep the temperature below 15°. A considerable quantity of the sodium salt of α-bromopropionic acid separated. To this slurry was added a suspension of 87 g. of acetoxime in 150 ml. of 40% sodium hydroxide, the temperature being kept below 20°. The stirred mixture was then brought to room temperature. The almost clear solution was then dropped slowly (two hours) through a series of three Liebig condensers inclined about 22° from the horizontal and having jacket lengths of 29, 58 and 29 cm., respectively. The upper two were heated with steam, the last cooled with tap water. The clear, colorless reaction

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(15) S. Chaikin and W. G. Brown, This Journal, **71**, 122 (1949).

(16) See F. Feigl, "Spot Tests," Nordemann Publishing Co., New York, N. Y., 2nd Ed., p. 225.

(17) (a) G. Rosenkranz, St. Kaufmann and J. Romo, This Journal, **71**, 3689 (1949); (b) J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 4961 (1951); (c) C. Djerassi and M. Gorman, *ibid.*, **75**, 3705 (1953).

(18) Compare with interchanges using 2,2-dimethyl-1,3-oxathiolane, H. J. Dauben, B. Loken and H. Ringold, *ibid.*, **76**, 1359 (1954).

(19) After we had obtained IV its preparation in 36% yield by a slightly different method was reported by M. Romero and J. Romo, *Bol. inst. quim. univ. nacl. auton. Mex.*, **4**, 3 (1952); *C. A.*, **47**, 10498a (1953).

(20) (a) A. Novelli, *Anales asoc. quim. Argentina*, **29**, 83 (1941); *C. A.*, **35**, 6576 (1941); (b) H. R. Henze and R. J. Speer, This Journal, **64**, 522 (1942), report a m.p. of 324–325° dec.

(21) E. Bergmann and J. Hervey, *Ber.*, **62**, 914 (1929); W. Manchot and P. Krische, *Ann.*, **337**, 186 (1904).

(22) All m.p.'s corrected unless otherwise noted (b) in which case they were taken on a Fisher hot-stage apparatus. All analyses by Galbraith Laboratories, Knoxville, Tenn., unless otherwise noted.

(23) This preparation is modeled after that of aminoöxyacetic acid, ref. 14b.

product was then extracted with three 170-ml. portions of ether to remove unreacted acetone oxime. The aqueous layer was then made acid to congo red with hydrochloric acid, saturated with sodium sulfate and extracted several times with ether and ether–benzene (continuous extraction is also effective). After removal of solvents on the steam-bath, a further quantity of volatile material, b.p. 90–110° at 12 mm. was then distilled and discarded. The fraction boiling at 64–75° at 0.1–0.2 mm. was diluted with 30 ml. of petroleum ether, b.p. 35–40° (Skellysolve F), and 20 ml. of acetone, seeded, and allowed to stand overnight at room temperature. The resulting large colorless crystals were filtered, washed with 70 ml. of 4:1 Skellysolve F–acetone in several portions and dried *in vacuo* over calcium chloride and soda-lime. This crop weighed 52 g. (30%) and melted at 57–61° with softening at 52°. Concentration of the filtrate to about 100 ml. afforded an additional 15 g. (8.7%) of similar material. Further small quantities are obtainable by distillation of the material remaining in the mother liquors and recrystallization.

Even the purest samples of I (including both of the pure enantiomorphs, see below) melt over a range of approximately 3°. The racemate is hygroscopic, the pure enantiomorphs less so.

The analytical sample, m.p. 57.8–60.8°, was recrystallized from petroleum ether, b.p. 60–70° (Skellysolve B), followed by sublimation at 55° at 1–2 mm.

Anal. Calcd. for $C_6H_{11}O_3N$: C, 49.6; H, 7.6; N, 9.7. Found: C, 49.2; H, 7.6; N, 9.7.

Resolution of I.—To a warm solution of 12.8 g. of hydrated (−)-ephedrine, m.p. 40–43°, and 20.3 g. (2 equiv.) of racemic I was added 100 ml. of Skellysolve B. The crystals which had separated after 22 hours at 0–5° were collected, washed with cold mixed solvent and dried *in vacuo*. This material, m.p. 121–123°, $[\alpha]^{27}\text{D}$ −25.0° ± 0.1° (*c* 2.8, water) weighed 5.7 g. (26%). After two recrystallizations very little change was observed in m.p. or rotation. For analysis a thrice-recrystallized salt, m.p. 123–124.5° with sintering at 120°, $[\alpha]^{26}\text{D}$ −25.5 ± 0.1° (*c* 3.25, water) was used.

Anal. Calcd. for $C_{16}H_{26}O_4N_2$: C, 61.9; H, 8.4; N, 9.0. Found: C, 61.7; H, 8.3; N, 9.0.

In a larger run, a solution of 183.5 g. of racemic I and 174 g. of (−)-ephedrine in 1 l. of hot benzene was diluted with 1 l. of cyclohexane and allowed to stand at room temperature for three days. The colorless crystals, after washing with mixed solvent and air drying, weighed 161 g. (82.5%) and melted at 116–119°. The filtrate was used for recovery of the (−)-acid (see below).

A sample of the best (−)-salt was dissolved in strong, but not saturated, sodium chloride solution (8 ml. per g.) and acidified to congo red with sulfuric acid. After continuous extraction with ether for two hours, the ether extract was percolated through dry sodium sulfate and concentrated under an air stream to yield colorless crystals, m.p. 83.0–84.5°, $[\alpha]^{26}\text{D}$ +30.8 ± 0.1° (*c* 7.57, water).

On a larger scale, 161 g. of the ephedrine salt, m.p. 116–119°, was treated with a solution of 40 ml. of concd. hydrochloric acid in 600 ml. of water, and the free acid isolated as above was crystallized in five crops from acetone–Skellysolve B. A total of 56.4 g. (75%) of acid, m.p. 81–85°, $[\alpha]^{29-30}\text{D}$ +30.4 ± 0.6°, was obtained. After recrystallization the best sample was sublimed *in vacuo* to yield colorless crystals, m.p. 83.5–85.5°.

Anal. Calcd. for $C_6H_{11}O_3N$: C, 49.6; H, 7.6; N, 9.7. Found: C, 49.6; H, 7.4; N, 9.8.

The above mentioned filtrate from the crystals, m.p. 116–119°, was treated essentially as the crystals were to yield 19.5 g. of crystals of crude (−)-I, m.p. 79–85°. Recrystallization from 10 ml. of hot acetone diluted with 50 ml. of Skellysolve B afforded 18 g. (29%) of colorless (−)-I, m.p. 82.9–85.4°, $[\alpha]^{30}\text{D}$ −29.8 ± 0.03°.

Preparation of (+)- **and** (−)-*α*-(2,**4,5,7-Tetranitro-9-fluorenylideneaminoöxy**)**-propionic Acid** (III).—A stirred suspension of 46.3 g. of II, 28 g. of (−)-I, 5 g. of *p*-toluenesulfonic acid and 350 ml. of acetic acid was refluxed into a small packed column suitable for removal of the acetone formed. After 2.5, 3 and 4 hours of refluxing additions of 5, 3 and 3 ml. of water were made. After six hours a small sample was almost completely soluble in saturated sodium bicarbonate solution and the mixture was diluted with 60 ml. of water and cooled. After two days the solid was collected, washed with dilute acetic acid, partly dried and recrystallized from 350 ml. of propionic acid diluted when hot with 300 ml. of water. On cooling there was obtained 48 g. of (+)-III, m.p. 151–155°, $[\alpha]^{25}\text{D}$ +86.7° (*c* 0.567, dioxane), $[\alpha]^{25}_{5461}$ +111.5°. This product contained solvent of crystallization for on drying over potassium hydroxide *in vacuo* for 18 hours the sample lost about 10.7% of its weight. The yield of pure non-solvated (+)-III was thus 75% and its specific rotation on a solvent free basis was $[\alpha]^{25}\text{D}$ +97.1°. The melting point is also affected by solvation. When a solvated form (propionic acid or 1,4-dichlorobutane) is heated it may melt in the range 151–157° but, if solvent is lost readily before melting at the lower point, a melting point near 200° dec. is observed. Melted (+)-III-resolidifies and remelts near 200°. When acetic acid is the solvent, the solvated form melts near 123°, then resolidifies and remelts near 200°.

In a similar way (−)-III, $[\alpha]^{29}\text{D}$ −91.4 ± 0.2° (*c* 1.6, dioxane) was obtained in about the same yield from (+)-I and II. A recrystallized sample, which showed the same m.p. behavior as (+)-III, had $[\alpha]^{29}\text{D}$ −97.1 ± 0.7°.

Racemic III was prepared from II and racemic I in good yield. When pure and made solvent free by drying at 100° at 1.5 mm. for 3 hours over phosphorus pentoxide, III melted at 215–217°.

Anal. Calcd. for $C_{16}H_9O_{11}N_5$: C, 43.0; H, 2.0; N, 15.7. Found: C, 42.8; H, 2.1; N, 15.8.

Methyl (±)-*α*-(**2,4,5,7-Tetranitro-9-fluorenylideneaminooxy**)**-propionate.**—Esterification of 0.5 g. of (±)-III with 4 g. of methanol and sulfuric acid at reflux for 3 hours yielded the methyl ester of III as yellow crystals, m.p. 161.0–164.5°, from 3:1 methanol–chloroform and from butyl chloride.

Anal. Calcd. for $C_{17}H_{11}O_{11}N_5$: C, 44.3; H, 2.4; N, 15.2. Found: C, 44.3; H, 2.7; N, 15.2.

The methyl ester carbonyl absorption was at 5.70 μ compared to 5.85 μ for the free acid. The ester is less photosensitive than the free acid.

α-(**9-Fluorenylideneaminoöxy**)**-propionic Acid.**—A solution of 0.70 g. of racemic I, 0.87 g. of fluorenone and 0.1 g. of *p*-toluenesulfonic acid in 15 ml. of 70% acetic acid was refluxed for seven hours during which a slow stream of air which had been passed through 70% acetic acid was passed through the mixture. After addition of 5 ml. of water, cooling, and drying there was obtained 1.17 g. of yellow crystals, m.p. 182.5–186.0°. The analytical sample, recrystallized from benzene, melted at 186.0–187.8°.

Anal. Calcd. for $C_{16}H_{13}O_3N$: N, 5.2. Found: N, 5.3.

When the above reaction was carried out in glacial acetic acid for the same time an almost identical result was obtained.

α-(**Diphenylmethyleneaminoöxy**)**-propionic Acid.**—In a similar way this compound was obtained from racemic I and benzophenone in 65% yield. The analytical sample, colorless crystals, melted at 143.0–144.5°.

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.4; H, 5.6; N, 5.2. Found: C, 71.2; H, 5.7; N, 5.1.

(−)-*α*-(2,**4,7-Trinitro-9-fluorenylideneaminoöxy**)**-propionic Acid.**—Similarly (5 instead of 7 hours of refluxing) TNF yielded 86.5% of product from (+)-I. All fractions had rather wide melting ranges in the region 180–220°, probably because the product was a mixture of geometrical isomers. The analytical sample $[\alpha]^{23}\text{D}$ −71.1° ± 0.5° (*c* 1.61, dioxane) melted at 188–199° after recrystallization from alcohol. The crystals were strongly solvated but lost solvent (9.9%) on drying over phosphorus pentoxide for 23 hours at 100°.

Anal. Calcd. for $C_{16}H_{10}O_9N_4$: C, 47.8; H, 2.5; N, 13.9. Found: C, 47.6; H, 2.7; N, 13.7.

Complexes of III. (a) **Fluoranthene.**—A warmed solution of 0.1 g. of fluoranthene and 0.11 g. of (±)-III in 2.5 ml. of acetic acid deposited orange crystals of complex, m.p. 222–225°. After recrystallization from 2 ml. of acetic acid the m.p. was 225–227°.

Anal. Calcd. for $C_{32}H_{19}O_{11}N_5$: C, 59.3; H, 2.8. Found: C, 59.2; H, 3.0.

(**b**) **Phenanthrene.**—Similarly to the above there was obtained orange yellow crystals of the phenanthrene complex of III which crystallized from acetic acid with one molecule of acetic acid. On heating, the recrystallized complex melted near 190° then solidified and remelted at 201–202°.

Anal. Calcd. for $C_{30}H_{19}O_{11}N_5{\cdot}CH_3CO_2H$: C, 56.1; H, 3.4. Found: C, 56.2; H, 3.6.

(c) **1-Naphthyl (2-Butyl) Ether.**—A solution containing 0.26 g. of 1-naphthyl 2-butyl ether,[24] m.p. 29.0–31.5°, and 0.13 g. of (±)-III in 3 ml. of acetic acid deposited a gummy red solid. This was triturated with 2 ml. of Skellysolve B and washed with two small portions of Skellysolve B and of Skellysolve F. After drying at room temperature *in vacuo* over phosphorus pentoxide the analytical sample melted at 155–158°.

Anal. Calcd. for $C_{30}H_{25}O_{12}N_5$: C, 55.6; H, 3.9; N, 10.8. Found: C, 55.6; H, 4.1; N, 11.2.

(d) **Methyl α-(1-Anthryl)-propionate.**—Prepared from 0.25 g. of ester and 0.25 g. of (±)-III in 3 ml. of acetic acid this complex weighed 0.34 g. (87%). Recrystallization from acetic acid afforded the complex as dark brown leaflets with metallic luster, m.p. 191.0–192.5°.

Anal. Calcd. for $C_{34}H_{25}O_{13}N_5$: C, 57.4; H, 3.5; N, 9.8. Found: C, 57.3; H, 3.7; N, 9.7.

(e) **Miscellaneous.**—Complexes with benzo[c]phenanthrene, red, m.p. 215–217°, anthracene, green black, m.p. 258°, and acenaphthene, red, m.p. 190–195°, were also formed. These complexes were not analyzed or otherwise examined. No crystalline complex of 1,12-dimethylbenzo[c]phenanthrene[25] could be obtained although evidence of complex formation was provided by the red color of solutions of the components in various solvents.

Resolution of 1-Naphthyl 2-Butyl Ether.—A hot solution of 0.589 g. of ether and 0.994 g. of (−)-III in 1 ml. of acetic acid on cooling solidified to a pasty mass. After trituration with 4 ml. of Skellysolve B the purplish complex was collected and washed with 4 ml. of Skellysolve B. After drying *in vacuo* 0.81 g. (94%) of complex, m.p. 137–141°, was obtained. The comparable complex formed from (±)-III (see above) melted at 155–158°. The 1-naphthyl 2-butyl ether from the complex and from the filtrate was recovered after removing the (−)-III by washing with bicarbonate solution. The crude ether obtained from the solid complex was obtained in two fractions, 0.158 g., $[\alpha]^{31}_{\mathrm{D}}$ −7.8 ± 0.2° (*c* 6.4, ethyl acetate) and 0.0508 g., $[\alpha]^{29}_{\mathrm{D}}$ −7.4 ± 0.5° (*c* 2.03, ethyl acetate), by evaporative distillation onto a cold finger at low pressure. There was a negligible residue from this vaporization. The infrared spectra of these fractions were identical to that of the racemic ether. The ether recovered from the filtrate was purified in the same way and afforded a product, $[\alpha]^{32}_{\mathrm{D}}$ +6.4 ± 0.09° (*c* 11, ethyl acetate). For this determination the entire distillate was used. From the bicarbonate extracts the (−)-III was recovered in 65% yield, $[\alpha]^{26}_{\mathrm{D}}$ −92.2 ± 0.3°.

Resolution of Methyl α-(1-Anthryl)-propionate.—A hot acetic acid solution of 0.330 g. of (+)-III, $[\alpha]^{23}_{\mathrm{D}}$ +84.1° (or 93° if allowance for solvation with acetic acid is made, see above) and 0.368 g. of ester,[26] m.p. 91–92°, deposited 0.521 g. of complex, m.p. 196–200°. The comparable complex from ester and (±)-III (see above) melted at 191–192.5°. The ester, recovered from the complex after washing out III with bicarbonate solution, was crystallized from 2 ml. of Skellysolve B to yield 0.126 g., $[\alpha]^{29}_{\mathrm{D}}$ +36.8 ± 0.1° (*c* 4.3, dioxane). The residue in the filtrate from this ester amounted to 0.0409 g., m.p. 88–91°, $[\alpha]^{24}_{\mathrm{D}}$ +101 ± 0.8° (*c* 1.32, dioxane). The ester, recovered from the filtrate from the original solid complex, afforded 0.150 g. of tan solid, m.p. 85–89°, $[\alpha]^{27}_{\mathrm{D}}$ −66.0 ± 0.1° (*c* 5, dioxane). On recrystallization of this solid from Skellysolve F containing a little chloroform there was obtained 0.0546 g. of tan solid, m.p. 89–90°, $[\alpha]^{28}_{\mathrm{D}}$ −28.0, and from the filtrate, 0.0274 g. of ester, m.p. 88.5–91.0°, $[\alpha]^{19.5}_{\mathrm{D}}$ −80.4 ± 0.8°. It is thus apparent that racemic ester is less soluble than the (+)- or (−)-forms.

COLUMBUS 10, OHIO

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[26] We are indebted to Mrs. T. Miwa for the preparation of this ester.

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Dehydronorcamphor from α-Acetoxyacrylonitrile

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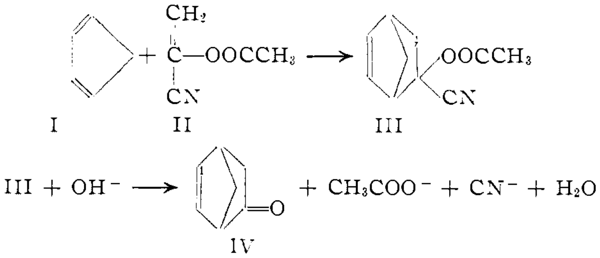
The addition of α-acetoxyacrylonitrile to cyclopentadiene, followed by alkaline hydrolysis of the adduct, leads to dehydronorcamphor in a two-step preparation with 51% over-all yield. Previous reports on derivatives of this ketone are supplemented by determination of the ultraviolet absorption spectrum of the ketone itself in ethanol and in isoöctane. Compared to norcamphor the absorption maximum is shifted 13.5 mμ to longer wave lengths, with a tenfold increase in intensity.

Dehydronorcamphor (IV) has been prepared previously by the oxidation of dehydronorborneol.[1–3] It does not result from the direct addition of ketene to cyclopentadiene. However, α-acetoxyacrylonitrile (II), which should be an excellent dienophile, is readily obtained as the principal product of ketene with hydrogen cyanide under appropriate conditions.[4–6] Under other conditions,[7] the formation of this product can be very largely suppressed. In view of the availability of α-acetoxyacrylonitrile and its increasing industrial interest,[8,9] we have investigated its use as a dienophile. It appears that the use of this compound represents a superior way of introducing the elements of ketene into a diene synthesis.



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