Another preparation of **3** produced enough pure compound by column chromatography for elemental analysis.

Anal. Calcd for $C_{10}H_{10}$: C, 92.26; H, 7.74. Found: C, 92.09; H, 7.74.

Benzobicyclo[2.2.0]hex-5-en-*exo*-2-ol (8).—**4** (150 mg) was converted to **2** as described above. Olefin **2** was immediately transferred to a reaction vessel containing 1 ml of tetrahydrofuran (distilled from $LiAlH_4$) at 5–10°. To this was added 0.45 ml of a 0.45 *M* diborane solution in tetrahydrofuran. After stirring for 1 hr, water was added dropwise to destroy excess diborane followed by 0.1 ml of 3 *N* aqueous sodium hydroxide and 0.1 ml of 30% hydrogen peroxide. Stirring was continued for 1 hr. The reaction mixture was extracted with 20 ml of ether, which was separated and washed with four 5-ml portions of saturated, aqueous brine. The organic layer was dried ($MgSO_4$) at 0°, the ether was removed on a rotatory evaporator, and the liquid residue was chromatographed on activity II, basic alumina to give 17 mg (15% based on **4**) of **8**: ir (neat) 3260, 2950, 1460, 1060, and 745 cm^{-1}; nmr (CCl_4, internal TMS) τ 2.85 (m center, aromatic A_2B_2, 4), 5.75 (t center, C_2H, 1), 6.15 (m center, bridgehead H's, 2), 6.87 (s, OH, 1), and 7.6–7.85 (m, CH_2, 2).

Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.90. Found: C, C, 81.98; H, 6.81.

Registry No.—**2**, 20847-82-9; **3**, 20847-83-0; **4**, 20902-25-4; **8**, 33905-59-8.

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Synthesis of Angularly Substituted Tetrahydro- and Hexahydrofluorenes[1]

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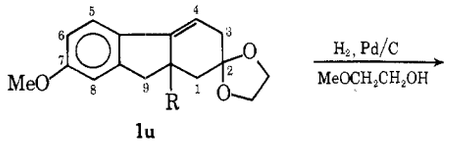
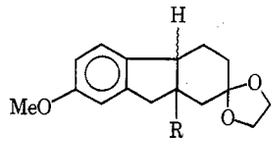
A series of 7-methoxy-2,2-ethylenedioxy-1,2,3,9a-tetrahydrofluorenes has been synthesized in which the 9a substituent has been transformed from COOEt into CHO, CHNOH, COOLi, COONa, $CONH_2$, CN, and COMe as well as into the previously reported groups COOMe, CH_2OH, and COOH. For each substituent the cis and trans compounds resulting from olefin reduction have been synthesized by routes which establish their stereochemistry. The influence of the stereochemistry at C-4a on the course of reactions at the group attached at C-9a is discussed.

In the hydrogenation of olefins over heterogeneous catalysts, the stereochemistry of reduction has been found to be influenced not only by the bulk of neighboring functional groups but by attractive interactions between certain of these groups and the catalyst surface.[3] These interactions, in contrast to steric effects, are responsible for addition of hydrogen cis with respect to the group involved. Our study of this phenomenon[3] required us to synthesize a series of compounds **1u**, in which the angular group R represented a



1u



1c = cis; **1t** = trans

variety of common functional groups, as well as requiring us to prepare authentic samples of the corresponding cis (**1c**) and trans (**1t**) reduction products.

We report here these syntheses, which were accomplished by transformations of the unsaturated carboethoxy compound (**2u**) and which illustrate reactivities and limitations in a system which is both severely crowded and acid sensitive. The results are instructive as to the relative usefulness in such an environment of a number of the existing methods for functional group transformation.

The only cases for which we had already made entire sets consisting of all three compounds (**u**, **c**, and **t**) for a given functional group were carbomethoxy (**3**) and hydroxymethyl (**4**). Since the stereochemistry of each of these materials was unequivocally known,[3] they were in practice the starting or reference points for our synthetic sequences. As these sequences in many instances parallelled each other for our three series of compounds (Schemes I–III) we shall usually discuss the transformations in the unsaturated series as being typical of all three.

We had synthesized the previously reported cis aldehyde (and established its stereochemistry)[4] by oxidation of the *cis*-hydroxymethyl compound **4c** with CrO_3 in pyridine.[5] The same procedure was successful for preparation of **5u** and **5t**; however, yields were consistently poor and we found that greatly improved yields for the entire aldehyde set could be obtained with the procedure employing dicyclohexylcarbodiimide and dimethyl sulfoxide.[6] Treatment of the aldehyde **5u** with hydroxylamine in ethanol proceeded smoothly to give the oxime **6u**.[7]

The unsaturated carboxylic acid **7u** had been produced as previously described[3] from the corresponding ester by saponification. The trans acid could also be obtained by saponification, albeit under more drastic conditions than were required for **2u**, and the stereochemistry of **7t** was thus related unequivocally to the trans series. As none of the reduction methods tried on the unsaturated ester **3u** gave appreciable quantities of cis ester, we could not prepare the cis acid by an analogous saponification. However, metal–ammonia reduction of the acid **7u** provided **7c** in good yield and

(1) Abstracted in part from the Ph.D. thesis of R. E. N.
(2) NASA Predoctoral Trainee, 1966–1967.
(3) H. W. Thompson, *J. Org. Chem.*, **36**, 2577 (1971).
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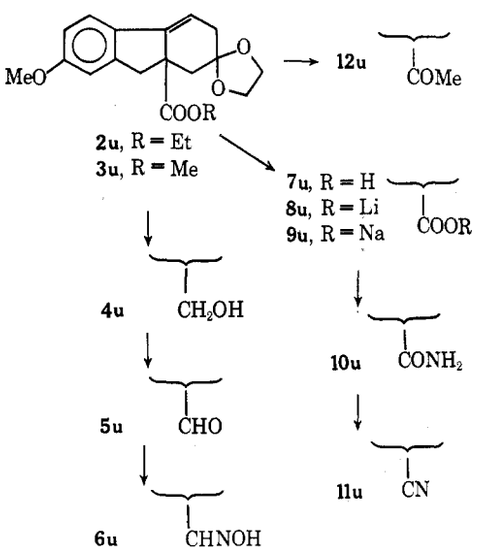
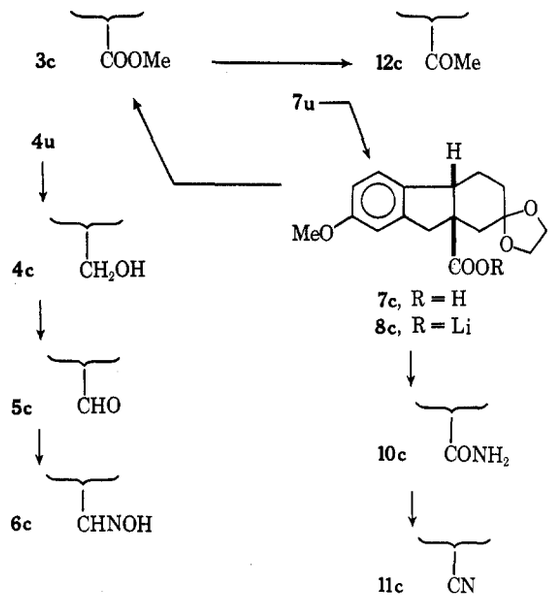
(7) The same procedure was used to obtain the cis and trans isomers.

SCHEME I
UNSATURATED SERIES



SCHEME II
CIS SERIES



the methyl ester was in turn prepared from **7c** by treatment with diazomethane.[3]

The acid **7u**, in addition to being the starting point for the above compounds and for the nitrogen-bearing compounds of the unsaturated series (Scheme I), was converted to its sodium and lithium carboxylates by careful treatment with exactly or slightly less than equivalent amounts of the corresponding metal hydrides, followed by removal of excess **7u** by trituration with hot benzene until the ir spectrum showed complete loss of carbonyl stretching absorption.[7]

In order to prepare the amide **10u** we attempted ester ammonolysis under a variety of conditions, ranging from anhydrous ethanolic ammonia (no reaction) to potassium amide in liquid ammonia (very poor yields). Of several procedures involving conversion of carboxylic acid salts into reactive intermediates,[8,9] the most successful was treatment of the lithium carboxylate **8u** with oxalyl chloride in pyridine solution,[9] followed by reaction with liquid ammonia; this provided **10u**[7] in a yield of 52%. Dehydration of the carboxamide to the corresponding nitrile (**11u**) proceeded readily in THF–pyridine on treatment with thionyl chloride.[7,10]

Our attempts to convert the carboxylic acid to the acetyl compound by direct methylation of the lithium salt **8u** with methyllithium[11] resulted in poor yields of **12u** and isolation of mixtures either rich in starting material or in tertiary alcohol. Alternate pathways involving treatment of the aldehyde **5u** with methyl Grignard followed by oxidation,[6] and treatment of the acid chloride with cadmium reagent, proved equally unpromising. The sequence which proved successful for the synthesis of **12u** and **12c** was the condensation of DMSO anion with an ester followed by reductive cleavage of the α carbon–sulfur bond with aluminum amalgam.[12] However, this was not successful for synthesis of the *trans*-methyl ketone from **2t**, the only ketonic product isolated being, not **12t**, but **12c**, evidently due to removal of the tertiary benzylic proton under the very strongly basic reaction conditions. This and the subsequently described isomerization in the methyl set of compounds provide additional evidence for the correctness of our stereochemical assignments, as the cis compounds are known, both from the data of others[13] and from metal–ammonia reduction of **4u** and **7u**, to be the more stable thermodynamically. The *trans*-methyl ketone **12t** fortunately became available by catalytic hydrogenation of **12u** and its stereochemistry was demonstrated by haloform cleavage to the trans acid.

Although we have not yet been able to synthesize the set in its entirety, we explored a number of reactions aimed at complete reduction of the angular function to a methyl group, including (1) $LiAlH_4$ treatment of **4u** tosylate and **4c** mesylate in ether, pyridine, THF, and DME under a variety of conditions; (2) LiH + $LiAlH_4$ treatment of **4u** tosylate and **4c** mesylate in THF;[14] (3) Li–NH_3 treatment of **4u** tosylate and **4c** mesylate;[15] (4) $LiAlH_4$ and $NaBH_4$ treatment of **5u** tosylhydrazone;[16] (5) PBr_3 treatment of **4u** in pyridine at 0 and 60°; (6) $(COCl)_2$ + pyridine treatment of **4u**.[17] The only reaction which gave angular group reduction without other disruptions of the molecule was Wolff–Kishner reduction[15,18] of the trans aldehyde **5t**. Curiously, the similar reduction of **5c** failed, as did the at-

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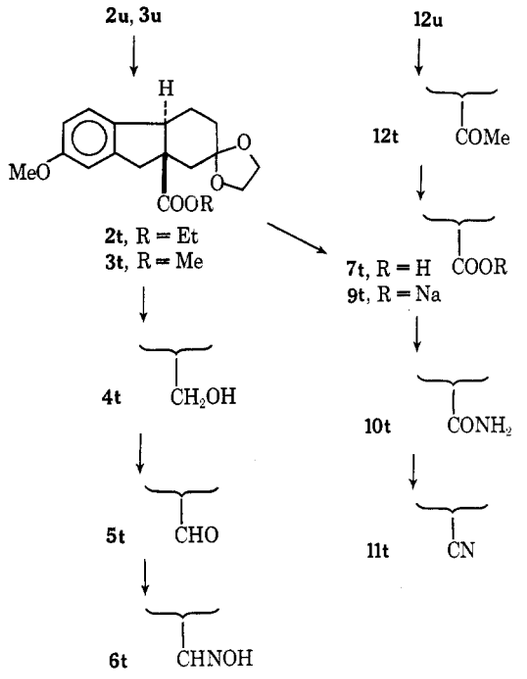
tempt with **5u** and with the mild Wolff–Kishner conditions (KO-*tert*-Bu + DMSO) introduced by Cram.[19] While we were able to isomerize the *trans*-methyl compound to cis by use of potassium amide, our attempts to utilize the former to make the unsaturated compound by benzylic bromination (NBS) led to introduction of bromine but apparently only at the benzylic methylene group, since we were unable to dehydrobrominate the product.

Because some amines are known to be catalyst poisons and hence interact strongly with catalyst surfaces, we particularly desired to obtain the aminomethyl set of compounds. Reduction of the three carboxamides (**10**) with $LiAlH_4$, using a variety of conditions and solvents, led to aminomethyl compound only from **10u** and then in disastrously low yield. The other compounds isolated in all cases were starting materials and carboxaldehydes (**5**), which arise from failure either of the intermediate iminate to undergo reduction or of the aluminoxyaminate precursor to form iminate by oxygen elimination. Further unsuccessful attempts to produce the aminomethyl compounds involved (1) $LiAlH_4$ treatment of the nitriles (**11**); (2) $LiAlH_4$ treatment of the aldoximes (**6**); (3) catalytic hydrogenation of the aldoximes (**6**) with Raney cobalt[20] at 40 atm and 65° and with 5% Rh/Al_2O_3[21] at 1 atm and 25°; (4) KNH_2 treatment of **4u** tosylate in refluxing ammonia, benzene and toluene; (5) NaN_3 treatment of **4u** tosylate and **4c** mesylate.[22]

In general our experience bore out the idea suggested by models that steric hindrance at the neopentyl carbon is greatest in the trans and least in the cis compounds. This is consistent with the behavior of the trans ester **2t** in the presence of DMSO anion; in the conversion of **7** into its acid chloride, reaction with the trans material would not proceed at the temperatures which sufficed for the unsaturated and cis compounds. In addition we observed that reactions involving attack at the neopentyl carbon invariably failed when that carbon was tetrahedrally hybridized. Although additions to a carbonyl group at this center did proceed in many instances, evidently the five coordination required for SN2 displacements at an already tetrahedral neopentyl carbon is excessively difficult in this crowded steric environment. Substitutions of the SN2 type at neopentyl carbons are normally very difficult but have been effected in some instances.[23] However, we are not aware of any reports of successful SN2 reactions at ring-juncture neopentyl carbons of this sort.[15] One attempt at such a displacement in this system, by acetylide on the tosylate of **4c**, has already been recorded.[4] Several more attempts were made in the present work with amide, azide, and borohydride, all with equal lack of success. Displacements with aluminohydride were in several instances apparently successful but led to loss of ketal and/or olefin as well.

SCHEME III
TRANS SERIES



Experimental Section[24]

CrO_3–Pyridine Preparation of Unsaturated Aldehyde 5u.—To a solution of unsaturated alcohol **4u** (879 mg, 3.05 mmol) in 15 ml of pyridine containing 1% water was added 43 ml of a saturated solution of CrO_3 in the same solvent. The flask, flushed with N_2 and stoppered, was allowed to stand at room temperature for 24 hr with stirring, after which 29 ml more of the CrO_3 solution was added and the mixture was stirred for an additional 48 hr under N_2. The reaction was worked up by addition of ether and filtration. The filtrate was passed through a short column of basic alumina, then concentrated and chromatographed, providing *ca.* 170 mg of tan solid, which was sublimed at 150° (0.01 mm) and recrystallized from pentane to give 160 mg (18%) of **5u** as light tan crystals: mp 154–156°; ir 2700, 1715, 1610, 1585, 935 cm^{-1} (ketal) with no absorption in the 3600–3200 cm^{-1} region; uv 218 nm (ε 11,900), 265 (12,900), 298 (5150); nmr δ 1.9 (1 H, d, J = 13 Hz), 2.55 (1 H d, J = 13 Hz), 2.5–2.9 (3 H complex), 3.2 (1 H, d, J = 16 Hz), 3.8 (3 H s), 3.95 (4 H m), 6.1 (1 H t, J = 4 Hz), 6.65–6.9 (2 H m), 7.35 (1 H d, J = 9.5 Hz), 9.75 (1 H s).

Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.34; H, 6.37.

DCC–DMSO Preparation of 5u.—Solid dicyclohexylcarbodiimide (1.24 g, 6.0 mmol) was added to a solution of unsaturated alcohol **4u** (576 mg, 2.0 mmol) in 6 ml of dry 1:1 DMSO–benzene which contained dry pyridine (0.16 ml, 2.0 mmol) and trifluoroacetic acid (0.08 ml, 1.0 mmol). The flask was flushed with N_2 and stoppered and the suspension was stirred for 48 hr at room temperature, after which 25 ml of ether and a solution of anhydrous oxalic acid (540 mg, 6.0 mmol) in 5.0 ml of MeOH were added; gas was evolved and the suspension was stirred for 30 min. Water and ether were added and urea was removed by filtration. Separation and extraction of the filtrate provided an

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(24) Melting points were determined with a Mel-Temp apparatus and are uncorrected; infrared (ir) spectra were taken, using a Beckman IR-10 or a Perkin-Elmer 457 spectrometer, on $CHCl_3$ solutions unless otherwise specified; ultraviolet (uv) spectra were determined with a Cary Model 14 spectrophotometer and employing 95% EtOH as solvent; nmr spectra were taken using a Varian A-60 or A-60A spectrometer and $CDCl_3$ solutions (CH_2Cl_2 and/or Me_4Si internal standard); mass spectra were obtained from a Perkin-Elmer Model 270 mass spectrometer; unless otherwise specified $MgSO_4$ was the drying agent and Florisil was the chromatograph absorbent employed; microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.; the abbreviations DCC, DME, DMSO, and THF refer to dicyclohexylcarbodiimide, dimethoxyethane, dimethyl sulfoxide, and tetrahydrofuran, respectively.

organic residue, chromatographed to give 400 mg (70%) of **5u**, crystallizing from pentane as a crude tan solid, mp 147–152°.

DCC–DMSO Preparation of Cis Aldehyde 5c.—By the procedure described in detail above for **5u**, cis alcohol **4c** (353 mg, 1.22 mmol) was oxidized over 24 hr. After work-up, the crude aldehyde was chromatographed and appropriate fractions were combined. Sublimation at 160° (0.01 mm) and recrystallization from pentane yielded 300 mg (85%) of **5c** as a white solid: mp 69–71.5° (lit.[4] mp 69.5–72°); ir (CCl_4) 2700, 1725, 1610, 935 cm^{-1}, no absorption in the 3600–3200 cm^{-1} region; nmr δ 1.25–2.3 (6 H complex), 2.75 (1 H d, J = 16 Hz), 3.05 (1 H d, J = 16 Hz), 3.55 (1 H t, J = 5 Hz), 3.8 (3 H s), 3.95 (4 H s), 6.65–6.9 (2 H m), 7.1 (1 H q, J = 1, 9.5 Hz), 9.85 (1 H s).

CrO_3–Pyridine Preparation of Trans Aldehyde 5t.—By the procedure described in detail above for **5u**, trans alcohol **4t** (430 mg, 1.48 mmol) was oxidized over 72 hr. The crude oxidation product was chromatographed and appropriate fractions were combined and crystallized, yielding 95 mg of yellow-brown solid, mp 124–126°, which was sublimed at 170° (0.01 mm) and recrystallized from hexane to give 90 mg (21%) of **5t** as white crystals: mp 128.5–130°; ir (CCl_4) 2740, 1720, 1615, 935 cm^{-1}, no OH absorption in the 3600–3200 cm^{-1} region; uv 227 nm (ε 6800), 285 (2930), 290 s (2520); nmr δ 1.6–3.2 (9 H complex), 3.8 (3 H s), 3.9 (4 H m), 6.6–6.85 (2 H m), 7.1 (1 H q, J = 1, 9 Hz), 9.65 (1 H s).

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.70; H, 7.00.

DCC–DMSO Preparation of 5t.—By the procedure described in detail above for **5u**, trans alcohol **4t** (500 mg, 1.73 mmol) was oxidized over 48 hr. The crude product was chromatographed and appropriate fractions were combined and crystallized from hexane to give 350 mg (71%) of **5t** as crude yellow crystals, mp 127–133°.

Unsaturated Aldoxime 6u.—By the general oximation procedure of Shriner, Fuson, and Curtin,[25] unsaturated aldehyde **5u** (500 mg, 1.75 mmol) was added to a suspension of $NH_2OH \cdot HCl$ (665 mg, 9.5 mmol) and NaOH (400 mg, 10 mmol) in 35 ml of absolute EtOH and refluxed for 18 hr under N_2. The mixture was concentrated under vacuum; the residue was taken up in 50 ml of water and acidified to pH 3–4 with saturated aqueous oxalic acid. Extraction with CH_2Cl_2 and concentration gave 474 mg of brown oily solid. Sublimation at 180° (0.01 mm) and recrystallizations from ether–CH_2Cl_2 provided 400 mg (76%) of **6u** as pale yellow needles: mp 172–174°; ir *ca.* 3350 (broad), 1610, 1585, 935 cm^{-1}, no C=O absorption; uv 261 nm (ε 15,300), 300 (4640); nmr δ 1.95 (1 H d, J = 13 Hz), 2.2–2.95 (4 H complex), 3.25 (1 H d, J = 16 Hz), 3.75 (3 H s), 3.95 (4 H s), 5.85 (1 H t, J = 4 Hz), 6.6–6.85 (2 H m), 7.25 (1 H d, J = 9 Hz), 7.55 (1 H s).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36. Found: C, 67.61; H, 6.46.

Cis Aldoxime 6c.—By the procedure described in detail above for **6u**, cis aldehyde **5c** (320 mg, 1.11 mmol) was oximated over 8 hr to yield 330 mg of crude oily product, which was sublimed at 180° (0.01 mm) and crystallized from ether–pentane to yield 270 mg (80%) of **6c** as a white solid: mp 93–94°; ir *ca.* 3350 (broad), 1610, 1590, 930 cm^{-1}, no C=O absorption; uv 228 nm (ε 8180), 283 (2730), 288 s (2420); nmr δ 1.2–2.35 (6 H complex), 2.7 (1 H d, J = 16 Hz), 2.9–3.5 (2 H m), 3.75 (3 H s), 3.9 (4 H s), 6.6–7.15 (3 H m), 7.8 (1 H s).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98. Found: C, 67.23; H, 6.99.

Trans Aldoxime 6t.—By the procedure described in detail above for **6u**, trans aldehyde **5t** (350 mg, 1.22 mmol) was oximated over 18 hr to give 376 mg of crude solid. Sublimation at 180° (0.01 mm) and recrystallizations from CH_2Cl_2 yielded 225 mg (61%) of **6t** as white crystals: mp 195–197°; ir *ca.* 3350 (broad), 1615, 1590, 930 cm^{-1}, no C=O absorption; uv 228 nm (ε 8370), 282 (2760), 288 s (2450); nmr δ 1.0–3.0 (8 H complex) 3.1 (1 H d, J = 14.5 Hz), 3.75 (3 H s), 3.9 (4 H s), 6.5–7.1 (3 H complex), 7.5 (1 H s), 7.55 (1 H, broad).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98. Found: C, 67.20; H, 6.91.

Trans Carboxylic Acid 7t.—A solution of trans ethyl ester **2t** (1.8 g, 5.42 mmol) and KOH (4.0 g, 71 mmol) in 180 ml of 2-methoxyethanol was refluxed under N_2. After 24 hr the cooled mixture was acidified to pH 3–4 with saturated aqueous oxalic acid, then diluted with more water and extracted with CH_2Cl_2. Sublimation of the extraction residue at 150° (0.01 mm) and recrystallizations from absolute EtOH yielded 1.2 g (73%) of **7t** as white crystals: mp 198–200°; ir 3600–2300 (broad), 1715, 1610, 1585, 945 cm^{-1}; uv 219 nm (ε 7050), 228 (7210), 283 (2820), 290 s (2440); nmr δ 1.8 (1 H d, J = 13 Hz), 1.85–2.95 (7 H complex), 3.1 (1 H d, J = 15.5 Hz), 3.8 (3 H s), 3.9 (4 H m), 6.6–6.85 (2 H m), 7.05 (1 H d, J = 9 Hz), 10.6 (1 H s, broad).

Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.04; H, 6.60.

Identical material could be obtained in purified yields of *ca.* 75–80% by catalytic hydrogenation of **7u** under the conditions previously specified.[3]

Unsaturated Lithium Carboxylate 8u.—Unsaturated carboxylic acid **7u** (141 mg, 0.466 mmol) was added to a stirred suspension of LiH (3.4 mg, 0.425 mmol) in dry DME and the mixture was refluxed for 2 hr under N_2. The mixture was cooled in an ice–salt bath and the insoluble Li salt was removed by filtration. The solid was washed three times with 10-ml portions of hot benzene and then once with cold anhydrous ether; the solid was dried for 1 hr at room temperature under vacuum (1.0 mm) to give 111 mg (85%) of **8u** as an off-white solid displaying no C=O absorption in its ir spectrum (KBr).

Cis Lithium Carboxylate 8c.—By the procedure described above for **8u**, cis carboxylic acid **7c** (150 mg, 0.496 mmol) was converted to its lithium salt, which was purified to give 117 mg (76%) of **8c** as an off-white solid, whose ir spectrum (KBr) lacked C=O absorption.

Unsaturated Sodium Carboxylate 9u.—Unsaturated carboxylic acid **7u** (145 mg, 0.471 mmol) was added to a stirred suspension of 0.471 mmol of NaH (20.2 mg of 56% oil dispersion washed twice with pentane) in dry DME (25 ml) under N_2. The mixture was refluxed for 2 hr, then cooled and concentrated to dryness under vacuum. The solid residue was purified as described for the lithium salt to give 136 mg (93%) of **9u** as a light tan solid having no C=O absorption in its ir spectrum (KBr).

Trans Sodium Carboxylate 9t.—By the procedure described above for **9u**, trans carboxylic acid **7t** (150 mg, 0.496 mmol) was converted to its Na salt and the product was isolated and purified to give 110 mg (69%) of **9t** as an off-white solid whose ir spectrum (KBr) showed no C=O absorption.

Unsaturated Carboxamide 10u.—Unsaturated carboxylic acid **7u** (501 mg, 1.66 mmol) was added to a stirred solution of $LiOH \cdot H_2O$ (69.8 mg, 1.66 mmol) in 70 ml of MeOH and the solution was stirred overnight at room temperature and then concentrated to dryness under vacuum. The residual solid was taken up in 75 ml of dry benzene and the solution was reduced to 1/3 volume by distillation at atmospheric pressure. To the stirred ice-cold benzene solution of the Li salt under N_2 was added dry pyridine (*ca.* 0.1 ml) and then oxalyl chloride (0.34 ml, 4.0 mmol). The resultant yellow suspension was allowed to warm to room temperature and then heated to 40–50° and stirred for 2 hr. Excess oxalyl chloride was removed under slight vacuum and the suspension of acid chloride was cooled to room temperature. The flask was then equipped with a Dry Ice condenser and anhydrous NH_3 (*ca.* 125 ml) was distilled into it. The suspension was stirred at reflux for 4 hr, the NH_3 was then allowed to evaporate, and the residue was extracted with water and CH_2Cl_2. Concentration of extracts gave 359 mg of crude yellow solid, which was chromatographed. Appropriate fractions were combined, sublimed at 170° (0.01 mm), and crystallized from 1:1 cyclohexane–benzene to give 260 mg (52%) of **10u** as white crystals: mp 161.5–163°; ir *ca.* 3530, *ca.* 3410, 1675, 1610, 1580, 940 cm^{-1}; uv 261 nm (ε 20,600), 300 (5930), 308 s (5170); nmr δ 1.7 (1 H d, J = 13 Hz), 2.6 (2 H t, J = *ca.* 3.5 Hz), 2.9 (1 H d, J = 16 Hz), 2.95 (1 H d, J = 13 Hz), 3.3 (1 H d, J = 16 Hz), 3.8 (3 H s), 4.0 (4 H s), 5.65 (2 H, broad), 6.0 (1 H t, J = 4 Hz), 6.65–6.9 (2 H m), 7.35 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36. Found: C, 67.89; H, 6.37.

Cis Carboxamide 10c.—By the procedure described in detail above for **10u**, cis carboxylic acid **7c** (518 mg, 1.71 mmol) was converted to the corresponding carboxamide, which was chromatographed. Appropriately combined fractions were purified by sublimation at 170° (0.01 mm) and recrystallizations from CH_2Cl_2 to give 400 mg (77%) of **10c** as white crystals: mp 178.5–179°; ir *ca.* 3480, *ca.* 3330, 1665, 1610, 1585, 925 cm^{-1}; uv 220 nm (ε 6740), 228 (7070), 282 (2680), 288 s (2390); nmr δ 1.3–2.3 (6 H complex), 2.8 (1 Hd, J = 16 Hz), 3.4–3.8 (2 H complex), 3.8 (3 H

(25) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964.

s), 3.95 (4 H m), *ca.* 5.8–7.3 (2 H, very broad), 6.65–6.9 (2 H m), 7.05 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; mol wt, 303. Found: C, 67.13; H, 7.01; mol wt (mass spectrum), 303.

Trans Carboxamide 10t.—To a stirred suspension of LiH (8.0 mg, 1.0 mmol) in 40 ml of dry DME was added trans carboxylic acid **7t** (304 mg, 1.0 mmol) and the suspension was refluxed for 2 hr under N_2. The stirred mixture was cooled in an ice–salt bath and dry pyridine (*ca.* 0.1 ml) was added, followed by oxalyl chloride (0.60 ml, 7.0 mmol). The resultant yellow suspension was heated for 7 hr with stirring under N_2 at 45–55°; the mixture was then cooled; and excess oxalyl chloride was removed under slight vacuum.

The acid chloride (ir 1740, 1770 cm^{-1}) was treated with *ca.* 250 ml of anhydrous NH_3 for 6 hr as described for **10u**. Work-up provided 341 mg of crude oily product, which was chromatographed. Sublimation of appropriately combined fractions at 170° (0.01 mm) and recrystallizations from ether–$CHCl_3$ gave 55 mg (18%) of **10t** as fine white needles: mp 178–179.5°; ir 3500, 3400, 1665, 1610, 1580, 930 cm^{-1}; uv 220 nm (ϵ 6230), 228 (6670), 282 (2660), 288 s (2350); nmr δ 1.4–2.5 (6 H complex), 2.5–3.5 (3 H complex), 3.75 (3 H s), 3.95 (4 H s), 5.1 (2 H s, broad), 6.6–6.9 (2 H m), 7.05 (1 H d, J = 8 Hz).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; mol wt, 303. Found: C, 67.20; H, 7.01; mol wt (mass spectrum), 303.

Unsaturated Nitrile 11u.—To a stirred solution of unsaturated carboxamide **10u** (150 mg, 0.5 mmol) and dry pyridine (2.43 ml, 30 mmol) in 115 ml of dry THF under N_2 was added 0.55 ml (7.5 mmol) of $SOCl_2$ by syringe. The mixture was refluxed for 5 hr and cooled in an ice bath, and excess $SOCl_2$ was decomposed with aqueous NaOH. The extraction residue was chromatographed and appropriately combined fractions were sublimed at 175° (0.01 mm) and recrystallized from ether–$CHCl_3$ to give 91 mg (64%) of **11u** as white needles: mp 149.5–151°; ir (CCl_4) 2230, 1610, 940 cm^{-1}, no C=O absorption; uv 212 nm (ϵ 20,400), 261 (20,200), 298 (5650), 305 (5110); nmr δ 1.85 (1 H d, J = 13 Hz), 2.5 (1 H d, J = 13 Hz), 2.5–2.9 (2 H m), 2.9 (1 H d, J = 15.5 Hz), 3.4 (1 H d, J = 15.5 Hz), 3.8 (3 H s), 4.05 (4 H m), 5.95 (1 H t, J = 4 Hz), 6.65–7.0 (2 H m), 7.35 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05. Found: C, 71.83; H, 6.04.

Cis Nitrile 11c.—By the procedure described in detail above for **11u**, cis carboxamide **10c** (152 mg, 0.50 mmol) was dehydrated over 5 hr. The crude oily product was chromatographed and appropriate fractions were combined, recrystallized from pentane–ether, sublimed at 175° (0.01 mm), and recrystallized from ether to give 51 mg (36%) of **11c** as white shiny plates: mp 82–83°; ir (CCl_4) 2230, 1610, 935 cm^{-1}, no C=O absorption; uv 229 nm (ϵ 8420), 281 (2620), 288 s (2410); nmr δ 1.3–2.5 (6 H complex), 2.9 (1 H d, J = 15.5 Hz), 3.3 (1 H d, J = 15.5 Hz), 3.45 (1 H t, J = 4 Hz), 3.75 (3 H s), 3.95 (4 H m), 6.6–6.85 (2 H m), 7.0 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found: C, 71.53; H, 6.69.

Trans Nitrile 11t.—By the procedure described above for **11u**, trans carboxamide **10t** (238 mg, 0.786 mmol) was dehydrated over 8 hr and the crude oily product was chromatographed. Appropriately combined fractions were sublimed at 180° (0.01 mm) and recrystallized from ether–$CHCl_3$ to give 126 mg (56%) of **11t** as white crystals: mp 144–145°; ir 2230, 1615, 1585, 950 cm^{-1}, no C=O absorption; uv 229 nm (ϵ 7840), 283 (2510), 289 s (2280); nmr δ 1.5–2.8 (7 H complex), 2.8 (1 H d, J = 15 Hz), 3.2 (1 H d, J = 15 Hz), 3.75 (3 H s), 4.0 (4 H m), 6.6–6.9 (2 H m), 7.1 (1 H d, J = 8 Hz).

Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found: C, 71.62; H, 6.70.

Unsaturated Methyl Ketone 12u.—Dry DMSO (3 ml) was added under N_2 to a flask containing 2.0 mmol of NaH (86 mg of 56% oil dispersion, washed twice with pentane) and the suspension was heated at 65–70° for 45 min with stirring until H_2 evolution ceased. The solution was cooled in an ice bath and 3 ml of dry THF was added, followed by unsaturated ester **2u** (330 mg, 1.0 mmol) in dry THF (3 ml). The green solution was stirred at room temperature for 2 hr under N_2; then excess DMSO anion was decomposed by careful addition of saturated aqueous Na_2SO_4 (1.0 ml) and the mixture was poured into 500 ml of water and acidified to *ca.* pH 4 with saturated aqueous oxalic acid. Extraction provided the β-keto sulfoxide as a brown viscous oil.

To a stirred solution of the crude β-keto sulfoxide in 1:10 water–THF (20 ml) was added Al·Hg prepared by dipping strips of Al foil (270 mg, 10 mg-atoms) into 2% aqueous $HgCl_2$ for *ca.* 1 min, then washing the strips in absolute EtOH, rinsing them in anhydrous ether, and cutting them into small rectangles directly into the reaction flask. The mixture was stirred at reflux for 2 hr under N_2, during which time gas was evolved, then cooled and filtered through Celite; the residue was washed thoroughly with 1:10 water–THF. The filtrate was concentrated to 5 ml, diluted with 50 ml of water, and extracted three times with ether; the extracts were combined and concentrated and the residual oil was passed in ether through a short column of Florisil. The eluate was concentrated and crystallized on standing; the crystalline material was sublimed at 170° (0.01 mm) and recrystallized from hexane–ether to give 110 mg (37%) of **12u** as white prisms: mp 123–125°; ir 1700, 1610, 1585, 1350, 935 cm^{-1}; uv 261 nm (ϵ 18,500), 301 (4140), 309 s (3660); nmr δ 1.75 (1 H d, J = 13 Hz), 2.0 (3 H s), 2.55 (2 H t, J = *ca.* 4 Hz), 2.8 (1 H d, J = 13 Hz), 3.0 (1 H d, J = 17 Hz), 3.1 (1 H d, J = 17 Hz), 3.75 (3 H s), 3.9 (4 H m), 5.95 (1 H t, J = 4 Hz), 6.65–6.9 (2 H m), 7.4 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.82; H, 6.73.

***cis*-Methyl Ketone 12c.**—By the procedure described in detail above for **12u**, *cis*-methyl ester **3c** (500 mg, 1.58 mmol) was converted to the β-keto sulfoxide, which was reductively cleaved with Al·Hg to give a crude oily product. This material was passed in 1:1 ether–CH_2Cl_2 through a short column of Florisil and the eluate was concentrated and crystallized from ether–pentane. The crystalline material was sublimed at 170° (0.01 mm) and recrystallized from ether–pentane to give 102 mg (21%) of **12c** as fine white needles: mp 114–116°; ir 1700, 1610, 1585, 1350, 925 cm^{-1}; uv 218 nm (ϵ 8340), 227 (6110), 282 (2780), 288 s (2450); nmr δ 1.15–2.35 (6 H complex), 2.2 (3 H s), 2.7 (1 H d, J = 15 Hz), 2.85 (1 H d, J = 15 Hz), 3.65 (1 H m), 3.75 (3 H s), 3.85 (4 H s), 6.6–6.85 (2 H m), 7.05 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.71; H, 7.41.

***trans*-Methyl Ketone 12t.**—Unsaturated methyl ketone **12u** (173 mg, 0.563 mmol) was hydrogenated with stirring at room temperature and atmospheric pressure over 31.3 mg of 5% Pd/C catalyst in 9.2 ml of 2-methoxyethanol. After 2 hr the reaction mixture was filtered and concentrated under vacuum to give crystalline material which was recrystallized three times from anhydrous ether yielding 95.2 mg (56%) of **12t** as white needles: mp 130–131°; ir 1700, 1620, 1590, 950 cm^{-1}; uv 219 nm (ϵ 7300), 228 (7260), 283 (3020), 290 s (2570); nmr δ of 1.5–3.1 (9 H complex), 2.0 (3 H s), 3.7 (3 H s), 3.9 (4 H m), 6.55–6.85 (2 H m), 7.0 (1 H d, J = 9 Hz).

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.72; H, 7.39.

Iodoform Cleavage[25] of *trans*-Methyl Ketone 12t.—*trans*-Methyl ketone **12t** (60.4 mg, 0.20 mmol) was dissolved in 10 ml of dioxane and heated to 60° under N_2. A 10% NaOH solution (1.0 ml) was added, followed by slow addition of a solution of 2.0 g of KI and 1.0 g of I_2 in 8.0 ml of water until a deep brown color persisted (*ca.* 2.1 ml required). Just enough 10% aqueous NaOH was then added to decolorize the solution and the mixture was heated at 80° for 8 hr under N_2. When the cooled solution was poured into 25 ml of water an immediate yellow precipitate formed and was removed by filtration and recrystallized from absolute EtOH to give 59 mg (75%) of CHI_3, mp 117–119° (lit.[25] mp 119–121°). The aqueous filtrate was acidified to pH 3–4 with saturated aqueous oxalic acid and extracted to give material which was crystallized from ether, providing 39 mg (64%) of **7t** as white shiny plates, mp 198–200°; all spectral data are identical with those of trans carboxylic acid **7t** and a mixture melting point with authentic **7t** was undepressed.

***trans*-9a-Methyl Compound.**—To a solution of trans carboxaldehyde **5t** (400 mg, 1.39 mmol) in 10 ml of triethylene glycol was added 85% hydrazine monohydrate (4.0 ml) and the mixture was heated at 110–115° for 1 hr under N_2. The condenser was then removed and 2.0 g (36 mmol) of KOH was cautiously added to the mixture, which was heated to 190° and the condenser and N_2 source were reconnected. The temperature was maintained at 190–200° for 2.5 hr, after which the cooled mixture was dissolved in 50 ml of water and the pH was adjusted to 8

with saturated aqueous oxalic acid. The aqueous solution was extracted to give 184 mg of crude oily product, which was passed in ether through a short column of Florisil. Sublimation at 65–70° (0.01 mm) and recrystallizations from pentane yielded 99 mg (26%) of white crystals: mp 54–55°; ir 1610, 1580, 1350, 925 cm^{-1}, no C=O absorption; uv 219 nm (ϵ 6960), 228 (7550), 282 (2720), 288 s (2360); nmr δ 0.85 (3 H s), 1.1–2.85 (9 H complex), 3.75 (3 H s), 3.9 (4 H m), 6.5–7.1 (3 H complex).

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.41; H, 8.16.

***cis*-9a-Methyl Compound.**—Potassium amide was prepared by addition of 39 mg (1.0 mg-atom) of K to 15 ml of anhydrous NH_3 containing *ca.* 1 mg of $FeCl_3$ in a flask equipped with a Dry Ice condenser. The suspension was stirred for 30 min, during which time the color changed from blue to gray-black; to this was added a solution of 50 mg of *trans*-methyl compound (0.183 mmol) in 5 ml of dry THF. The mixture was refluxed for 4 hr and worked up by addition of excess solid NH_4Cl. The usual work-up provided 48 mg of crude oily product, which was chromatographed. Appropriately combined fractions were sublimed at 90° (0.01 mm) and recrystallized from pentane to give 25 mg (50%) of white needles; mp 93–94°; ir 1610, 1585, 1355 m, 925 cm^{-1}, no C=O absorption; uv 220 s nm (ϵ 7570), 228 (7850), 282 (2780), 228 s (2440); nmr δ 1.1–2.9 (9 H complex), 1.25 (3 H s), 3.7 (3 H s), 3.8 (4 H m), 6.45–6.65 (2 H m), 6.9 (1 H d, J = 8.5 Hz).

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.34; H, 8.17.

***p*-Toluenesulfonate Ester of Unsaturated Alcohol 4u.**—To a cold solution of unsaturated alcohol **4u** (1.0 g, 3.47 mmol) in dry pyridine (10 ml) was added *p*-toluenesulfonyl chloride (820 mg, 4.31 mmol) and the flask was flushed with N_2 and stoppered; the mixture was stirred for 4–5 hr at 0° and then at room temperature for 24 hr. The mixture was recooled to 0° and neutralized with dilute aqueous HCl. Extraction of the diluted mixture provided material which was crystallized from ether to give 563 mg (37%) of tan solid, mp 109–112°, ir 1350 cm^{-1}, no OH absorption in the 3600–3200 cm^{-1} region.

The *p*-toluenesulfonate ester of cis alcohol 4c and its preparation have been described previously.[4]

Methanesulfonate Ester of Cis Alcohol 4c.—To a stirred, ice-cold solution of cis alcohol **4c** (1.5 g, 5.28 mmol) in dry pyridine (10 ml) was added freshly distilled methanesulfonyl chloride (0.63 ml, 7.0 mmol) and the flask was flushed with N_2 and stoppered; the solution was stirred for 4–5 hr in an ice bath at 0° and then at room temperature for 32 hr. The mixture was recooled to 0° and neutralized with dilute aqueous HCl. Extraction of the diluted solution gave a viscous yellow oil, which failed to crystallize from a variety of solvents: ir 1370, 1350 cm^{-1}, no OH absorption in the 3600–3200 cm^{-1} region.

Registry No.—**4c** (methanesulfonate), 33885-17-5; **4u** (tosylate), 33885-18-6; **5c**, 13673-64-8; **5t**, 33885-20-0; **5u**, 33885-21-1; **6c**, 33885-22-2; **6t**, 33885-23-3; **6u**, 33885-24-4; **7t**, 33872-69-4; *cis*-9a-methyl compound, 33885-25-5; *trans*-9a-methyl compound, 33885-26-6; **10c**, 33885-27-7; **10t**, 33885-25-8; **10u**, 33885-29-9; **11c**, 33885-30-2; **11t**, 33885-31-3; **11u**, 33885-32-4; **12c**, 33885-33-5; **12t**, 33885-34-6; **12u**, 33885-35-7.

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The Resolution and Absolute Configuration of 7-Methylhexahelicene

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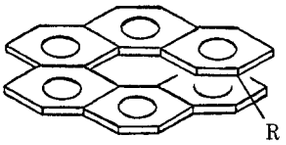
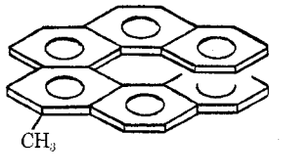
rac-7-Methylhexahelicene (**3**) is brominated to the bromomethyl derivative **4** which on treatment with trimethylphosphine is converted into the racemic quaternary phosphonium bromide **5**. By salt formation with silver D(−)-hydrogendibenzoyltartrate and recrystallization of same, a pure diastereoisomeric salt (−)-**6**$^+$·D(−)-HDBT$^-$ is isolated and converted into (−)-**5** by treatment with tetraethylammonium bromide. Aqueous alkaline treatment of (−)-**6**$^+$·D(−)-HDBT$^-$ affords (−)-**3**. All steps proceed in high yield. The above reactions provide a new method of resolution for methyl derivatives of dissymetric aromatic hydrocarbons.

When the work herein reported was started the absolute configuration of hexahelicene (**1**)[2] had not been



1, R = H
2, R = Br



(−)-3

established. Recently, the assignment of the left-handed helix (−)-**1**, as shown in the formula, has been established by X-ray analysis of (−)-2-bromohexahelicene (**2**).[3]

Because of the difficulty experienced in resolution of hexahelicene[2,4] by the use of α-(2,4,5,7-tetranitro-9-fluorenylidenaminooxy)propionic acid (TAPA),[5] a new method for the resolution of a helicene was sought which would involve a compound whose absolute configuration could be established by X-ray crystallographic methods. This method has been discovered and is described herein. However, since the problem of the helicenes has been solved[3] the X-ray work has not been carried out. Our method is outlined in Chart I.[6]

Bromination of 7-methylhexahelicene (**3**)[7] to 7-

(1) Postdoctoral fellow supported by Grant G12445X of the National Science Foundation.

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(4) M. S. Newman, R. S. Darlak, and L. Tsai, *J. Amer. Chem. Soc.*, **89**, 6191 (1967).

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(6) Ag$^+$D(−)-HDBT$^-$ is silver D(−)-hydrogendibenzoyltartrate, a compound first used for resolution of an asymmetric tetracovalent phosphorus compound by D. M. Coyne, W. E. McEwen, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, **78**, 3061 (1956). Both the D(−)- and L(+)-dibenzoyltartaric acids can be obtained from the Norse Laboratories, Inc., Santa Barbara, Calif. 93103.

(7) 7-Methylhexahelicene was first prepared here (unpublished work) by Dr. David J. Collins in 1959.