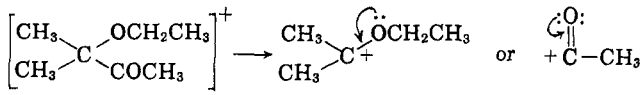
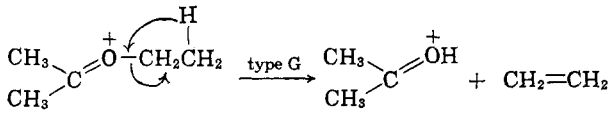


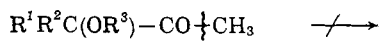
XII, 0% Σ_{39} m/e = 130 XIIA, 14.1% Σ_{39} m/e = 87 XIIB, 14.5% Σ_{39} m/e = 43



XIIA XIIC, 50.0% Σ_{39} m/e = 59

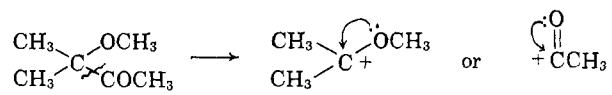
(40.3) $87^+ \longrightarrow 59^+ + 28$

Cleavage of the acyl–carbon bond in the first step of the reaction sequence is in direct contrast to the primary cleavage of an alkyl group in the acetylenic ether series. This cleavage of the molecular ion produces a very stable ion and radical. In contrast fragmentation of the acetylenic ether molecular ion produces an alkyl radical of comparatively high energy. The facility of this rearrangement sequence is reflected in the fact that the ions produced in the decomposition of XII amount to almost 70% of Σ_{39}. It is interesting that in this series the cleavage of the acyl methyl is not an important process even though such a cleavage would be expected to result in the formation



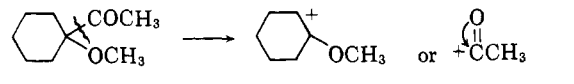
of a very stable acyl ion.[14] Once again the stabilities of the radicals and ions formed in the fragmentation are a deciding factor.

When type-G rearrangement is not structurally possible, such as in the fragmentation of 3-methoxy-3-methyl-2-butanone, the reaction sequence stops at the first step. The result is an increase in the intensity of the oxonium ion (XIA) produced by acyl–carbon cleavage by over 300% (in comparison to XIIA). As in the case of the methyl ethers in the acetylenic ether series, a molecular ion is observed, being 0.05% Σ_{39}.

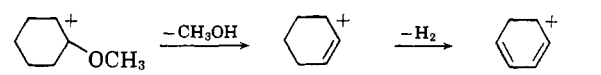


XI, 0.05% Σ_{39} m/e = 116 XIA, 40.8% Σ_{39} m/e = 73 XIB, 24.7% Σ_{39} m/e = 43

In contrast, 1-acetyl-1-methoxycyclohexane undergoes a two-step rearrangement not involving loss of an olefin molecule in the second step. Primary fragmentation involves the cleavage of the acyl–carbon bond



XIII, 0% Σ_{39} m/e = 156 XIIIA, 25.4% Σ_{39} m/e = 113 XIIB, 9.72% Σ_{39} m/e = 43



XIIIA m/e = 113 XIIIC, 15.6% Σ_{39} m/e = 81 XIV, 1.41% Σ_{39} m/e = 79

(58.3) $113^+ \longrightarrow 81^+ + 32$ (77.4) $81^+ \longrightarrow 79^+ + 42$

followed in sequence by the loss of methanol (type-E rearrangement) and a hydrogen molecule from this ion.

All other fragmentation processes in the keto ether series are minor in comparison with the reaction paths described above.

Experimental

All of the α-acetylenic ethers and keto ethers investigated in this work were generously donated by Professor G. F. Hennion of Notre Dame University. The assigned structures[15] have been corroborated by n.m.r. and infrared analysis.

Mass Spectra.—Spectra were obtained on a modified Consolidated 21-103c mass spectrometer operating under the following conditions: ionizing voltage, 70 v. (nominal); ion source temperature, 270°; ionizing current, 50 μa.; magnet current, 0.296 amp.; inlet system, room temperature.

(15) G. F. Hennion and A. P. Boisselle, *J. Org. Chem.*, **26**, 2677 (1961).

Friedel–Crafts Acylation. Positional Selectivity and Reactivity of Acylating Agents

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Received April 6, 1964

The importance of the activity or selectivity of acylating agents in determining orientation has been demonstrated for the substrate 2,3-dimethoxytoluene. Under typical Friedel–Crafts conditions, the reaction is kinetically controlled with substitution at positions 5 and 6. When polyphosphoric acid was used as the solvent and catalyst, exclusive acetylation at position 6 was realized. It was shown, however, that acylation in polyphosphoric acid is thermodynamically controlled when steric factors become important.

In the compound, 2,3-dimethoxytoluene (I), there are two positions of high but unequal reactivity[2] and the results reported in this paper show that the orientation in acylation is determined by the activity or selectivity of the acylating agent. The concepts developed by Brown correlating *ortho*, *meta*, and *para* isomer distribution in aromatic substitutions with the activity of the electrophilic agent[3] can be used to explain the experimental data here reported.

Nitration[4] of I has been shown to give substitution at

(1) Undergraduate research participants sponsored by Robert A. Welch Foundation Scholarships.

(2) Position 6 would be expected to be the most reactive site because of the combined effects of the *ortho* methyl and *para* methoxyl groups. The advantage of position 6 over 5 is further enhanced by steric inhibition to resonance of the 2-methoxyl group.

(3) (a) G. A. Olah, "Friedel-Crafts and Related Reactions," Vol. I, G. A. Olah, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 906; (b) J. E. Leffler and E. Grunwalk, "Rates and Equilibra of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 197.

(4) R. Majima and Y. Okazaki, *Ber.*, **49**, 1482 (1916).

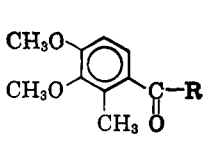
TABLE I
ACID CHLORIDE
RCOCl

R	Carbon disulfide, % Yield	Carbon disulfide, % 5-Isomer[a]	Benzene, % Yield	Benzene, % 5-Isomer[a]	Nitrobenzene, % Yield	Nitrobenzene, % 5-Isomer[a]
CH_3	52	42	57	45	59	41
C_2H_5	54	51	58	53	56	53
$(CH_3)_2CH$	52	58	50	60	55	58

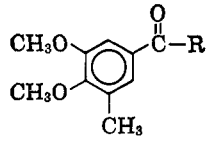
[a] ±1%.

position 5, whereas formylation[5] and acetylation[6,7] are reported to give substitution at the 6-position.

With the highly reactive Friedel–Crafts acylating agent from the acid chloride and aluminum chloride, it was found that substitution in I occurs at both position 5 and 6. The reaction conditions were proved to be nonisomerizing and the isomer distribution is therefore kinetically controlled.



II R = CH_3
III R = C_2H_5
IV R = $(CH_3)_2CH$
V R = $(CH_3)_3C$



VI
VII
VIII
IX

In searching for an acylating agent with higher selectivity and lower reactivity, it was found that exclusive acetylation of I at position 6 (II) can be realized with acetic anhydride in polyphosphoric acid.

In the first experiments the acylations were carried out by the slow addition of aluminum chloride to I and the acid chloride in a solvent (Elbs procedure). The solvents studied were carbon disulfide, benzene, and nitrobenzene. The results obtained are given in Table I, and in each case a mixture resu ted from substitution at the 5- and 6-position. For these solvents no significant difference in isomer distribution was found. With such reactive components, any solvent stabilization of the electrophilic intermediate does not appear to be important. For less reactive benzenoid systems, evidence of solvent stabilization has been reported.[8]

To evaluate the steric requirements imposed by the methyl group *ortho* to position 6 in I, on substitution at this site, the change in isomer distribution for acetyl, propionyl, and isobutyryl chlorides was determined. As can be seen from the data in Table I, the per cent of the 6-isomer decreases with a concurrent increase in the 5-isomer as the size or bulk of the acylating agent in the series increases. Any change in the reactivity within this group of acylating agents because of inductive effects would be masked by the simultaneous increase in bulk.

When trimethylacetyl chloride was used under these conditions, no acylation resulted. This was not unexpected[9] in view of the order of addition. The acylation was successful when an excess of I was used as the solvent. A yield of 31% was obtained and the product contained 67% of the 5-isomer.

(5) R. I. T. Cromartie and J. Harley-Mason, *J. Chem. Soc.*, 1052 (1952).
(6) F. Bruchhausen, *Arch. Pharm.*, **263**, 570 (1925).
(7) E. D. Hornbaker and A. Burger, *J. Am. Chem. Soc.*, **77**, 5314 (1955).
(8) H. C. Brown and F. R. Jensen, *ibid.*, **80**, 2296 (1958).
(9) E. Rochstein and R. W. Saville, *J. Chem. Soc.*, 1946 (1949).

To show that these isomer distributions were due to differences in relative reaction rates and not to relative stabilities realized by thermodynamically controlled isomerizations, all of the respective ketones, except IX, were synthesized, and anhydrous hydrogen chloride was passed through them in the different solvents with an excess of aluminum chloride present. Analysis by g.l.p.c. and infrared proved that isomerization did not take place. In like manner, prepared mixtures of the pure isomeric ketones showed no isomerization. When a threefold excess of aluminum chloride was used, the 5-acyl derivatives in particular suffered to some extent partial ether cleavage and, in part, some were further degraded. The base-soluble fractions were methylated and analysis by infrared and g.l.p.c. showed the absence of the ketone which would result from isomerization.

From studies on the acylation of I (Elbs procedure) using acid anhydrides and aluminum chloride in the solvent benzene, the results in Table II were obtained. In all runs, 2 moles of aluminum chloride were used per mole of anhydride. As before, the per cent of the 5-isomer increased as the bulk of the acylating agent in the series increased. However, a comparison of these isomer distributions with the results from the corresponding acid chlorides shows that in each case when the anhydride was used a significantly higher per cent of the product mixture is the 5-isomer.

TABLE II
ANHYDRIDES *vs.* ACID CHLORIDES

$(RCO)_2O$	Yield, %	5-Isomer,[a] %	RCOCl	Yield, %	5-Isomer,[a] %
CH_3	60	54	CH_3	42	45
C_2H_5	50	67	C_2H_5	51	53
$(CH_3)_2CH$	41	71	$(CH_3)_2CH$	58	60

[a] ±1%.

These results were unexpected since it has been assumed for some time[10,11] that the rate and site of substitution are the same for the acid chloride and monobasic acid anhydrides in the Friedel–Crafts acylation reaction.

When the acylation of I was studied using the organic acid or anhydride with polyphosphoric acid[12–14] as the solvent and catalyst, acetic anhydride at 45° for 1.5 hr. gave only the 6-acyl derivative (II). The results determined for the other acids or anhydrides including trimethylacetic acid are given in Table III.

To determine if isomerization was important, the experiment with acetic anhydride was repeated with a

(10) Ref. 3a, p. 94.
(11) G. Baddeley, *Quart. Rev.* (London), **8**, 370 (1954).
(12) F. Uhlig and H. R. Snyder, "Advances in Organic Chemistry. Methods and Results," Vol. I, R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p. 35.
(13) F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 321 (1958).
(14) P. D. Gardner, *J. Am. Chem. Soc.*, **76**, 4550 (1954).

TABLE III

POLYPHOSPHORIC ACID AS SOLVENT

RCOOH or $(RCO)_2O$	Yield, %	5-Isomer,[a] %
CH_3	70	0
C_2H_5	58	21
$(CH_3)_2CH$	53	25
$(CH_3)_3C$	42	23

[a] ±1%.

reaction time of 18 hr. An increase in yield to 83% was realized but the product contained 7% of the 5-isomer. When the pure 5-acyl derivative (VI) was subjected to the same conditions, it was recovered unchanged. More impressive results were obtained from the isopropyl ketones. With the pure 6-isomer (IV), heating in polyphosphoric acid for 19 hr. gave a product (80%) containing 52% of the 5-isomer. When VIII was heated in the same way for 18 hr., no isomerization occurred. If the time and temperature of the reaction of I with isobutyric anhydride was lowered to 10° and 0.5 hr., a nonhomogeneous system resulted and a marked decrease in both yield (17%) and the per cent of 5-isomer (16%) in the product resulted. The increase in substitution at the 6-position is significant.

It is of interest that the Friedel–Crafts reaction does not involve isomerization, whereas the polyphosphoric acid procedure does. By consideration of models it is obvious that the 5-acyl compounds would be more stable than the corresponding 6-acyl derivatives because of steric factors. One possible explanation for this difference toward isomerization is that in the Friedel–Crafts reaction the product ketone is complexed with aluminum chloride for which it is known the heat of formation[3a] is approximately 20 kcal./mole. Stabilization to this extent is not realized in polyphosphoric acid. For example, at room temperature, the addition of acetophenone to polyphosphoric acid in the same relative quantities as given in the Experimental part resulted in a temperature rise of only a few degrees.

The 6-acyl derivatives of I were prepared by reaction of the Grignard reagent of 6-bromo-2,3-dimethoxytoluene with the appropriate acid chloride or nitrile. The bromo compound was prepared from I by bromination and the structure was established by comparison with the product prepared by the bromination and subsequent methylation of 2-methoxy-3-methylphenol.[6]

The 5-acyl derivatives of I were synthesized except for the pivaloyl by the Fries rearrangement of the appropriate esters of 2-methoxy-6-methylphenol[4] and methylation of the resulting phenolic ketones. Analysis by g.l.p.c. showed approximately 5% of the isomeric 6-acyl compounds. The pure 5-acyl derivatives of I were easily obtained by recrystallization of the intermediate phenolic ketones before methylation. Compound IX was not synthesized and this structure is assigned to the ketone formed with V in the acylations by analogy to the other members of the series.

The acetyl and propionyl derivatives, (II, III, VI, and VII) were converted to the benzoic acids by oxidation with hypobromite.[15] The isobutyryl derivatives were converted to the benzoic acids by halogenation, hydrolysis to the α-hydroxy ketone, and cleavage to the acid by lead tetraacetate.

The 6-acyl derivatives gave the same acid, 2-methyl-3,4-dimethoxybenzoic acid (X), as that prepared by carbonation of the Grignard reagent from 6-bromo-2,3-dimethoxytoluene which had been prepared from 2-methoxy-3-methylphenol.[6] Similarly, the acid derived from the 5-acyl derivatives, 3-methyl-4,5-dimethoxybenzoic acid (XI), was shown to be identical with that prepared from 5-methylvanillin.[16]

A comparison of the infrared spectra of the acyl derivatives (Table IV) shows that the 6-acyl compounds have a characteristic absorption at 1570–1572 and the 5-acyl at 1145–1170 cm.$^{-1}$. The ultraviolet spectra of the isomeric methyl and ethyl ketones (II, III, VI, and VII) were determined to see if inhibition of resonance between the aromatic ring and carbonyl group was caused by the nuclear methyl group in II and III. Differences in the position and intensity of the major absorption band are not significant although the shoulder at 300 mμ in VI and VII is absent in II and III and this may be ascribed to steric effects. Owing to the position of the shoulder and the high intensity value, overlapping of bands is apparent and any quantitative comparisons would be unwarranted.[17]

Experimental[18,19]

Acylation. Elbs Procedure.[20]—The reactions were carried out in a four-neck, 200-ml. round-bottomed flask fitted with a thermometer, stirrer, condenser with drying tube, and an addition tube enclosed in a rubber bag. Anhydrous solvent (60 ml.), 5 g. (0.033 mole) of 2,3-dimethoxytoluene (I), and 0.033 mole of freshly distilled acid chloride or anhydride were placed in the flask. With good stirring, aluminum chloride (4.4 g., 0.033 mole, with the acid chloride and 8.8 g., 0.066 mole, with the anhydride) was slowly tapped into the reaction vessel at a temperature of 25°. This required 10 min. After the addition, the reaction mixture was stirred at this temperature for 30 min. and then decomposed by pouring into ice–hydrochloric acid and 50 ml. of ether. After extraction with ether and washing with cold dilute potassium hydroxide and water, the ether was removed on a steam bath. The product was distilled and collected from 55° at 0.1 mm. Any unreacted I and solvents distilled before this product fraction. The samples were analyzed by g.l.p.c. and infrared.

Polyphosphoric Acid Procedure.—Polyphosphoric acid (100 g.) was added with stirring to a mixture of I (10 g., 0.066 mole) and the anhydride (0.037 mole) or acid (0.074 mole). The flask was then placed in a water bath at 45°. In each case, the temperature initially rose to 5–7° above that of the bath and a color developed. After stirring for 1.5 hr. at this temperature, the reaction flask was rigidly lodged in a beaker and completely covered with ice and water. With rapid stirring, solution of the polyphosphoric acid was complete within 1–2 min. The product was extracted with ether and, after washing with dilute alkali and water, the ether was removed and the product was distilled as in the procedure above.

(15) J. D. Edwards, Jr., and J. L. Cashaw, *J. Am. Chem. Soc.*, **78**, 3821 (1956).

(16) C. Kaiser and A. Burger, *ibid.*, **79**, 4370 (1957).

(17) K. S. Dhami and J. B. Stothers, *Tetrahedron Letters*, **No. 12**, 631 (1964), and references cited therein.

(18) All melting points are reported uncorrected. Microanalyses were performed by the Huffman Laboratories, Inc., Wheatridge, Col., and Galbraith Laboratories, Inc., Knoxville, Tenn. The infrared spectra were determined with a Beckman IR-5 and the ultraviolet spectra on a Bausch and Lomb 505 spectrophotometer in methanol.

(19) The authors (S. E. M. and C. H.) wish to thank Dr. N. Ichikawa and Dr. T. Hase, Visiting Scientists from Osaka City University, for assistance in some of the experimental work.

(20) Because of the insolubility of aluminum chloride in carbon disulfide and benzene, the Elbs procedure was used. Sufficient reagents and solvents were obtained and pooled to complete the study. Each procedure was repeated at least two times and the g.l.p.c. analyses were within 2%.

TABLE IV
SPECTRAL DATA

Compd.	Infrared absorption,[a] cm.$^{-1}$	Ultraviolet spectra from 200 to 350 mμ (ε)
II	1590, 1572, 1450, 1270, 1035, 1148, 973, 805	269 (11,950)
III	1595, 1570, 1250, 1130, 972, 912	267 (11,380)
IV[b]	1590, 1572, 988, 920, 810	
VI	1585, 1335, 1300, 1170, 890, 867	269 (11,160), 299 sh (5340)
VII	1580, 1161, 865, 875	268 (11,010), 300 sh (4680)
VIII[b]	1580, 1145, 1040, 890, 876	
X	1630, 1270, 1080, 1042, 821	
XI	1097, 1333	

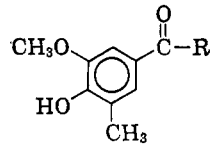
[a] For isomeric compounds common bands are omitted. [b] Liquid film, all others chloroform solutions, 4%; 0.1-mm. matched cells.

TABLE V
5- AND 6-ACYL DERIVATIVES

Compd.	Yield, %	M.p., °C.	B.p. (mm.), °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	2,4-DNPH[a] m.p., °C.
I	25	68–69	80–82 (0.06)	$C_{11}H_{14}O_3$	68.02	68.25	7.27	7.22	173–175
II	40	53–55	79 (0.03)	$C_{12}H_{16}O_3$	69.21	69.15	7.74	7.84	
III	40		103 (0.06)	$C_{13}H_{18}O_3$	70.25	70.06	8.16	8.07	
IV	54	28	81 (0.04)	$C_{14}H_{20}O_3$	71.16	70.88	8.53	8.27	
V	50	44–45	85–87 (0.05)	$C_{11}H_{14}O_3$	68.02	67.95	7.27	7.26	240
VI	52	45–46	96–97 (0.07)	$C_{12}H_{16}O_3$	69.21	69.50	7.74	7.58	199–200
VII	51		99 (0.15)	$C_{13}H_{18}O_3$	70.25	70.30	8.16	8.28	111–112

[a] 2,4-Dinitrophenylhydrazone.

TABLE VI
PHENOLIC KETONES



R	Yield, %	M.p., °C.	Recrystn. solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3	58	94	Ligroin (90–120°)	$C_{10}H_{12}O_3$	66.65	66.77	6.71	6.57
C_2H_5	55	106–108	Benzene	$C_{11}H_{14}O_3$	68.01	67.99	7.28	7.20
$(CH_3)_2CH$	60	52–53	Petr. ether (30–60°)	$C_{12}H_{16}O_3$	69.20	68.98	7.75	7.53
		122–130 (0.35)[a]						

[a] B.p. (mm.)

Analysis by Gas Chromatography.—Initially the analyses were carried out on a Perkin-Elmer[21] Model 226 gas chromatograph with a 200-ft. MBMA Golay column. Later the acetyl and isobutyryl derivatives were analyzed on a Wilkens Aerograph A-700 gas chromatograph, using a 5 ft. × 1/8 in. DEGS column. The propionyl and pivaloyl derivatives were analyzed using a 25 ft. × 1/8 in. XF-1150 column. The method of analysis, peak height, was shown to be valid by preparing known mixtures of the pure isomeric ketones and analyzing. The calculated and found values were within 1%. Complete resolution was obtained in all cases.

6-Bromo-2,3-dimethoxytoluene.—To a well-stirred solution of I (100 g., 0.66 mole) in 200 ml. of carbon tetrachloride at 0°, there was added dropwise 105 g. (0.66 mole) of bromine in 150 ml. of carbon tetrachloride. The resulting solution was concentrated on the steam bath and taken up in ether and extracted with dilute sodium hydroxide and water. After drying, the ether was removed and the product (124 g., 88%) distilled at 85–87° (1.1 mm.)

Anal. Calcd. for $C_9H_{11}BrO_2$: C, 46.77; H, 4.80. Found: C, 47.17; H, 4.83.

6-Acyl Derivatives (II–V).—The reaction of the Grignard reagent of 6-bromo-2,3-dimethoxytoluene with the various acid chlorides was carried out as described[22] for similar compounds except that tetrahydrofuran was used as the solvent. Compound IV was also prepared from the nitrile[23] with tetrahydrofuran as the solvent. See Table V for yields, constants, and analyses.

5-Acyl Derivatives (VI–VIII).—In a flask with a magnetic stirrer, dropping funnel, and condenser with drying tube, there was placed 15 g., (0.11 mole) of 2-methoxy-6-methylphenol.[5,24] The phenol was heated to melting and then 1 ml. of the acid chloride was added. The temperature was increased until hydrogen chloride was liberated and the remainder of the calculated amount of the acid chloride was added dropwise with stirring. After the reaction was complete, the system was placed under a water aspirator vacuum and the residue dissolved in anhydrous carbon disulfide. This was added dropwise with stirring at 35–45° to 29 g. (0.22 mole) of aluminum chloride in 150 ml. of carbon disulfide with the vigorous evolution of hydrogen chloride. The mixture was heated under reflux for 3 hr. and then let stand overnight. It was decomposed with ice–hydrochloric acid and extracted with ether. The ether extract was concentrated and washed with cold, dilute sodium hydroxide. The aqueous phase was acidified, extracted with ether and dried, and the ether was removed on a steam bath. The product was distilled and/or recrystallized (see Table VI). The phenolic ketones were methylated in the conventional manner in methyl alcohol with sodium methylate by the addition of dimethyl sulfate. (See Table V.)

2-Methyl-3,4-dimethoxybenzoic Acid (X).—To 5.5 g. (0.04 mole) of 2-methoxy-3-methylphenol[5] in 50 ml. of carbon tetra-

(21) The authors are indebted to Dr. T. McCoy and Mr. F. Click, Perkin-Elmer Corp., Houston, Texas, for assistance and use of instruments.

(22) J. H. Ford, C. D. Thompson, and C. S. Marvel, *J. Am. Chem. Soc.*, **57**, 2625 (1935).

(23) C. R. Hauser, W. J. Humphlett, and M. J. Weiss, *ibid.*, **70**, 426 (1948).

(24) Prepared by the Huang-Minlon modification of the Wolff–Kishner reaction.

chloride, there was added dropwise at 0° with good stirring a solution of 6.4 g. (0.04 mole) of bromine in 25 ml. of carbon tetrachloride. The solvent was removed on a steam bath and the residue was dried under high vacuum. After the addition of 25 ml. of methanol and 15 g. of dimethyl sulfate, there was added dropwise with stirring 12 g. of potassium hydroxide in 40 ml. of water. The final solution was made basic and extracted with ether. After drying and removing the ether on a steam bath, the product distilled at 88° (1 mm.). Infrared showed that this product was identical with that prepared by the bromination of I. The bromo compound was dissolved in 30 ml. of anhydrous ether and 3 g. of magnesium was added. A solution of 6 g. of ethyl iodide in 15 ml. of ether was added dropwise under gentle reflux, and the resulting mixture was refluxed for 30 min. and then added to a large excess of Dry Ice in a beaker. After 3 hr., excess concentrated hydrochloric acid was added, and the mixture was extracted with ether. The ether extract was washed with a dilute solution of sodium hydroxide and the aqueous phase was acidified and placed in the refrigerator overnight. The crystals were filtered, air-dried, sublimed at 180° (0.05 mm.), and recrystallized from petroleum ether (30–60°) to give colorless crystals, 1 g., m.p. 184°.

Oxidation of Acylphenones.—The methyl and ethyl ketones (II III, VI, and VII) were converted to the corresponding benzoic acids by hypobromite oxidation.[15,25] The isopropyl ketones (IV and VIII) gave the benzoic acids by bromination (hypobromite), hydrolysis by aqueous alkali, and cleavage of the crude anhydrous α-hydroxy ketone by lead tetraacetate.[26] The acids obtained were purified as described above and compounds II, III, and IV gave an acid identical with X. Compounds VI, VII, and VIII gave an acid, m.p. 151–152°. A mixture melting point with the acid prepared from 5-methylvanillin[16,27] showed no depression.

Acknowledgment.—The authors gratefully acknowledge support of this work by the Robert A. Welch Foundation and the Lamar Research Center.

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Synthesis and Study of Pseudo-Aromatic Compounds. II. The Synthesis of Indeno[5′,6′-4,5]-2,7-dicarboethoxytropone

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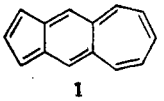
Received March 17, 1964

The synthesis of indeno[5′,6′-4,5]-2,7-dicarboethoxytropone is described. From the n.m.r. and ultraviolet spectra of this compound, as well as its failure to incorporate deuterium from deuterium oxide, it is concluded that it does not enolize to give a substituted anthrazulene.

The fact that simple, molecular-orbital and valence-bond approximation methods fail to satisfactorily predict the π-electronic properties of nonalternant cyclic and polycyclic conjugated polyenes has resulted in the use of rules to qualify these calculations. Thus two rules, Craig's rule[1] and the $4n + 2$[2] rule, are commonly used as criteria to predict aromaticity.

Although the $4n + 2$ rule has no formal validity for polycyclic systems,[1,3] it is still applied to them under the assumption that polycyclic systems are not too severe a perturbation of a monocyclic system.[3,4]

The anthrazulene ring system (**1**) is an interesting example of a nonalternant hydrocarbon which concurs with both the $4n+2$ rule and Craig's rule for aromaticity, but has defied synthesis by routes commonly useful for the synthesis of aromatic systems. Thus, attempted dehydrogenation of indano[5′,6′-1,2]cyclohepta-1,3-diene gave no traceable products and it was concluded that anthrazulene must be nonaromatic.[5,6]



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The fact that anthrazulene has a high-predicted, π-electron delocalization energy (2.245γ,[7] 74.1 kcal./mole; 4.895β,[8] 80.8 kcal./mole) which even after correction for strain energy (21.7 kcal./mole)[8] is still substantially high (52.4, 59.1 kcal./mole), indicated that further study of this ring system would be of value. This paper reports the synthesis of indeno-[5′,6′-4,5]-2,7-dicarboethoxytropone (**8**) which is a tautomer of the anthrazulene ring system.

The dichloromethylation of indane yields three products (**2**) which were detected by hydrogenation to the methylindanes and analysis by vapor phase chromatography. The components were found in a ratio of 60:30:10. Oxidation of the mixture of dichloromethyl compounds with 30% nitric acid, methylation of the resulting carboxylic acids with diazomethane, and separation by column chromatography over alumina, yielded the tetramethyl esters of pyromellitic acid (39%) and prehnitic acid (3%). From these data the predominant dichloromethylindane produced was assumed to be the 5,6-isomer (**2a**) and the product formed in the second highest amount the 4,6-isomer (**2b**). The remaining isomer is most likely the 4,5-isomer (**2c**) although no mellophanic acid was detected as an oxidation product.

Further confirmation of the structural assignment of the most predominant isomer (**2a**) was obtained. The dichloride mixture was recrystallized until the vapor phase chromatographic analysis of the hydrogenation product contained only a single peak which corresponded to the isomer that was originally most abundant. Hydrolysis of this component to the dialcohol and oxidation with chromic acid in acetone gave a lactone[9] and thus showed the *ortho* relationship of the two groups.

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