We are presently exploring the syntheses and properties of these and related compounds.

Experimental Section

The following instruments were employed for spectral determinations: nmr, Bruker HFX and Varian A-60; mass spectrum, Hitachi RMU-7; uv, Cary 14; ir, Perkin-Elmer 337. Melting points were measured with an oil bath and are uncorrected. Gas-liquid chromatography was carried out on a Hewlett-Packard 700 fitted with a 10 ft × $^1/_8$ in. column packed with 12% Squalane on 80-100 Chromosorb W, AWDMSC; separation parameters: column temperature, 100°; injection block temperature, 135°; carrier gas flow rate 30 cm^3/min. The microanalysis was performed by Chemalytics, Inc.

1,3-Di-*tert*-butylpropargyl Alcohol (1).—The procedure of Corey and Borden[1a] was used to give 1: mp 38.5-40.0°;[1b] ir (carbon tetrachloride solution) 3480, 2970, 2260 cm^{-1}; pmr (carbon tetrachloride solution, internal TMS) δ 0.95 (s, 9 H), 1.22 (s, 9 H), 2.21 (s, 1 H), 4.07 (s, 1 H).

Reaction of 1 with Thionyl Chloride.—To a vented flask containing 168 mg (1.0 mmol) of 1 and protected from moisture was added, *via* syringe, 145 mg (1.2 mmol) of thionyl chloride, and the resulting mixture was stirred for 15 hr at 25°. Ether (5 ml) was added, and the solution was washed with three 1-ml portions of saturated aqueous sodium chloride solution. The ether solution was dried over molecular sieves, and then the solvent was removed, leaving 150 mg (81%) of a liquid mixture of the propargyl chloride (retention time 3.8 min) and the allenic chloride (retention time 4.2 min) in the ratio 74:26. A pmr spectrum (carbon tetrachloride solution, internal TMS) of the mixture yielded the following: 1,3-di-*tert*-butylpropargyl chloride, δ 1.13 (s, 9 H), 1.30 (s, 9 H), 4.44 (s, 1 H); di-*tert*-butylchloroallene, δ 1.14 (s), 1.28 (s), 5.70 (s).

Reaction of 1 with Phosphorus Tribromide, Neat.—Using a procedure exactly analogous to the above, 1.68 g (10 mmol) of 1 was allowed to react with 1.22 g (4.5 mmol) of phosphorus tribromide for 17 hr at 25°. Work-up as before left 2.22 g of an oil containing finely divided crystalline material constituting about one-fifth of the total volume. The mixture was transferred to a Craig tube and cooled to −20° overnight to cause precipitation of any of the solid still in solution. Centrifugation effectively separated the oil from the moist solid (*vide infra*).

The oil (1.85 g, 80%) was found to be a mixture of the propargyl bromide (retention time 5.95 min) and the allenic bromide (retention time 6.60 min) in the ratio 17:3. A pmr spectrum (carbon tetrachloride solution, internal TMS) showed the following: 1,3-di-*tert*-butylpropargyl bromide, δ 1.16 (s, 9 H), 1.30 (s, 9 H), 4.52 (s, 1 H); 1-bromo-1,3-di-*tert*-butylallene, δ 1.13 (s, 9 H), 1.22 (s, 9 H), 5.44 (s, 1 H). The mixture of bromides distilled at 60-63° (3.5 mm), with enrichment of the allenic isomer. The fact that the allenic isomer is indeed thermodynamically favored was confirmed by the observation that a 95% pure sample of the propargyl bromide (isolated by preparative glpc) was transformed into a 48:52 mixture (propargyl: allenic bromide) after 48 hr at 83°.

Isolation of Phosphorus Heterocycle 4.—The above moist solid (350 mg), which seemed to react with metallic surfaces (*e.g.*, spatulas), was recrystallized from heptane-chloroform (3:1 *v/v*), then sublimed at 75° (0.15 mm) to yield stable, colorless, amorphous crystals (115 mg, 5% overall), mp 133.2-134.4°. Once purified, the compound is stable indefinitely if kept dry. Exposure to moist air appears to slowly (over weeks) hydrolyze the bromide. The various spectra of 4 are given in the text.

Anal. Calcd for $C_{11}H_{20}O_2PBr$: C, 44.76; H, 6.83; P, 10.49. Found: C, 44.88; H, 6.50; P, 10.66.

Reaction of 1 with Phosphorus Tribromide in Chloroform.—To a solution of 2.70 g (10 mmol) of phosphorus tribromide in 50 ml of chloroform under nitrogen was added dropwise a solution of 1.68 g (10 mmol) of 1 in 20 ml of chloroform. After stirring for 18.8 hr at 25°, the solution was washed twice with 10-ml portions of saturated sodium chloride solution and dried at 0° over molecular sieves. Removal of solvent left 2.54 g of product mixture, which gave 1.75 g of liquid bromide product mixture and 540 mg (20%) of 4, which was purified as above to yield ~260 mg (10% overall) of analytically pure material.

Reaction of 4 with Silver Perchlorate in Methanol.—To a solution of 44.2 mg (0.15 mmol) of 4 in 1.0 ml of dry methanol was added a solution of 31.2 mg (0.15 mmol) of silver perchlorate (Caution!) in 1.0 ml of methanol, and the solution was stirred at 25° for 20 min. Precipitation of silver bromide began immediately upon addition. The mixture was centrifuged, and the supernatant was removed and saved. The silver bromide was washed with methanol (which was added to the supernatant) and dried to give 23.8 mg (84%). The methanol solution was rotary evaporated, and the residue was redissolved in 2 ml of ether and then dried over molecular sieves. Removal of solvent left 37 mg (99%) of a clear, colorless liquid with freezing point below −20°: ir (chloroform solution) 2970 (s), 1615 (w), 1470 (s), 1370 (m), 1310 (m), 1285 (w), 1250 (vs), 1060 (vs), 1020 (s), 980 (s), 915 (m), 880 (s), 860 (m), 835 (m), 665 cm^{-1} (m); pmr (deuteriochloroform solution, internal TMS) δ 0.99 (s, 9 H), 1.27 (s, 9 H), 3.70 (d, J_{POCH} = 12 Hz, 3 H), 4.32 (d of d, $J_{\mathrm{PH_1}}$ = 12, $J_{\mathrm{H_1H_2}}$ = 1.7 Hz, 1 H), 6.59 (d of d, $J_{\mathrm{PH_2}}$ = 46.5, $J_{\mathrm{H_2H_1}}$ = 1.7 Hz, 1 H).

Registry No.—**1**, 30338-48-8; **4b**, 30338-49-9; **6b**, 30338-50-2; thionyl chloride, 7719-09-7; phosphorus tribromide, 7789-60-8.

Acknowledgments.—We wish to thank Professor Barry Trost for a helpful discussion. Acknowledgment is made to the Donors of the Petroleum Research Fund of the American Chemical Society for support of this work.

Catalytic Dehydrogenation of Estr-4-en-3-ones

E. FARKAS* AND N. J. BACH

The Lilly Research Laboratories, Eli Lilly and Company,
Indianapolis, Indiana 46206

Received February 1, 1971

The catalytic dehydrogenation of cyclic enones and diones has found extensive use in both synthesis and structure determination. Most such dehydrogenations are conducted at high temperatures and/or long reaction times.[1,2] During the study of the reactions of several steroids with unnatural stereochemistry[3,4] some unusually facile dehydrogenations were observed. Reasons for these high reactivities were explored.

The reaction of 17β-hydroxy-10α-estr-4-en-3-one[3] (1) with 5% palladium-carbon at 80° in ethanol for 2 min yielded approximately a 1:1 mixture of estradiol (2) and 17β-hydroxy-5α,10α-estran-3-one (3). Similarly, 17β-hydroxy-17α-methyl-9β-estr-4-en-3-one[4] (4) showed complete disappearance of the 243-nm wavelength chromophore in 2 min. On the other hand, neither the natural 9α,10β nor the 9β,10α series of estr-4-en-3-ones gave appreciable amounts of dehydrogenation products after 2 hr at these mild conditions. In the latter case, only traces of dehydrogenation material were observed even after 24 hr.

The two compounds which give ready dehydrogenation both contain 9,10 cis hydrogens, and it was attractive to propose that these hydrogens were removed catalytically to give intermediate estra-4,9(10)-dien-3-

---

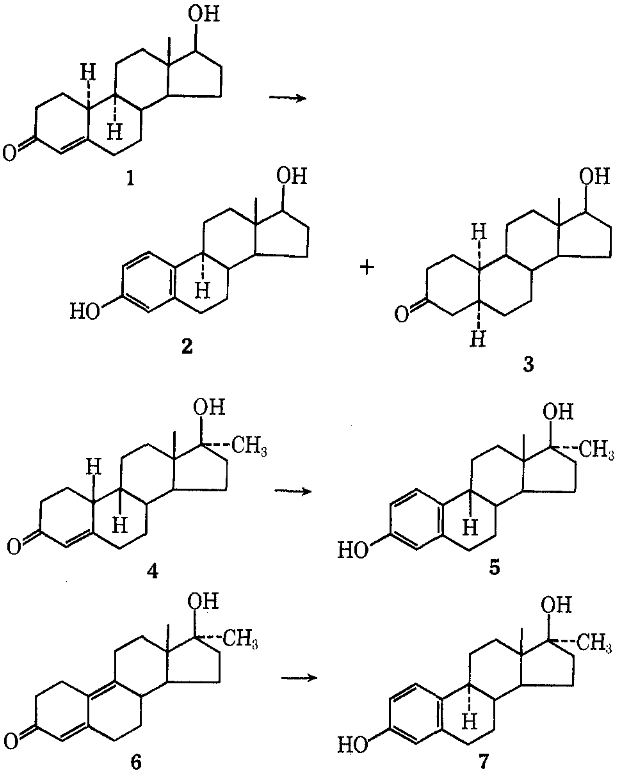
[1] A. J. Birch, G. A. Hughes, G. Kruger, and G. S. R. Subba Rao, *J. Chem. Soc.*, 5889 (1964).

[2] R. B. Turner and J. A. Meschino, *J. Amer. Chem. Soc.*, **80**, 4862 (1958).

[3] E. Farkas, J. M. Owen, M. Debono, R. M. Molloy, and M. M. Marsh, *Tetrahedron Lett.*, 1023 (1966).

[4] E. Farkas, J. M. Owen, and D. J. O'Toole, *J. Org. Chem.*, **34**, 3022 (1969).

ones.[5] This class of compounds was reported to aromatize catalytically by isomerization of the double bond.[6] Thus, 17β-hydroxy-17α-methyl-estra-4,9(10)-dien-3-one (**6**) was treated using our mild dehydrogenation conditions; the isomerization proceeded considerably slower, but a good yield of 17α-methylestradiol was obtained after 0.5 hr of reaction.

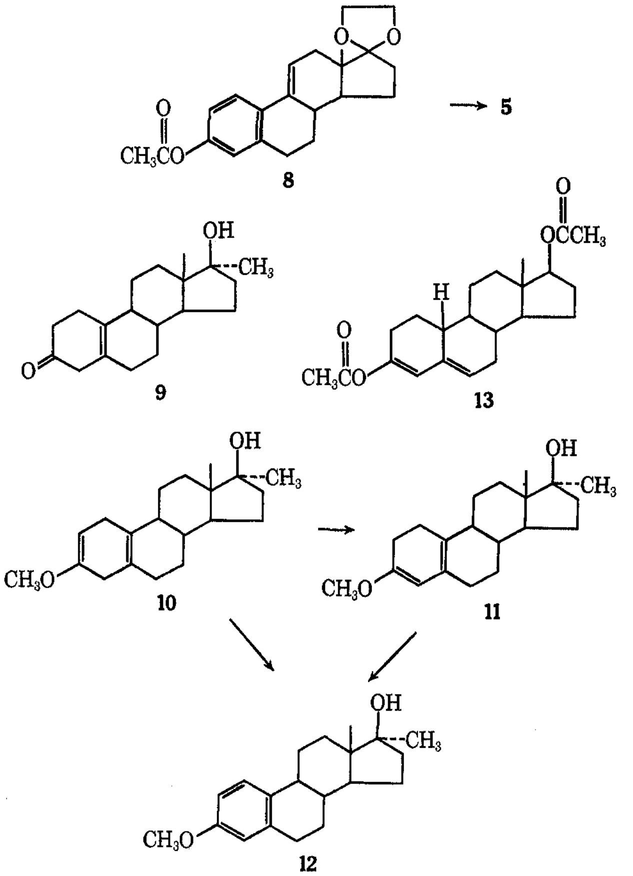


The dienone was eliminated as an intermediate in the dehydrogenation of the reactive enones when the aromatic product from the $9\beta,10\beta$ compound was examined. A 50% yield of 17α-methyl-9β-estradiol (**5**) was isolated on reaction of **4**; no trace of the 9α isomer was detected. The structural assignment of the 9β compound was made on the basis of its nmr spectrum, which showed the chemical shifts of the two methyl group protons at about δ 0.95. The 17α-methyl protons resonance is shifted upfield when compared with the same protons of the 9α isomer (δ 1.27) as expected, because the stereochemistry of the 9β isomer positions the 17α-methyl protons in the shielding cone of the aromatic A ring.

In order to confirm the structural assignment, **5** was synthesized *via* the reduction[7] of the ketal **8**.[8] After hydrolysis of the protective groups, the two isomers were separated, and the 9β-17-ketone was treated with methyl Grignard reagent to yield **5**.

Previous chemical studies[3,4] demonstrated the ease of enolization of the $9\alpha,10\alpha$- and $9\beta,10\beta$-estr-4-en-3-ones as evidenced by ready epimerization at C_{10}. In addition, in the 9β series the deconjugated 9β-estr-5(10)-en-3-one also formed easily *via* the enol. The deconjugated 17β-hydroxy-17α-methylestr-5(10)-en-3-one (**9**) was examined as a possible intermediate; only a small amount of aromatization was obtained after 4 hr under the standard dehydrogenation conditions.

In order to examine the approximate reactivity of the dienol in this reaction, dienol ethers **10** and **11**[9] were allowed to react in order to determine the ease of dehydrogenation. A good yield of aromatic ether **12** was obtained in 0.75 hr from either compound. On the other hand, the heteroannular dienol acetate **13** showed no appreciable aromatization over a 4-hr period.



The results of these studies suggest that a homoannular dienol, either conjugated or unconjugated, stabilized by interaction with the catalyst is an intermediate in the dehydrogenation reaction. The 5(10)-en-3-one apparently does not readily enolize under these reaction conditions. The normal $9\alpha,10\beta$-estr-4-en-3-ones are known to yield the heteroannular dienol as the thermodynamic product;[10] there are also indications that this heteroannular dienol is also formed as the kinetic product.[11]

Experimental Section

Melting points are uncorrected. The uv spectra were obtained using a Cary 15 spectrophotometer. Nmr spectra were obtained using a Varian HA-60 spectrometer with TMS as the internal standard.

Dehydrogenation of 17β-Hydroxy-10α-estr-4-en-3-one (1).—In a small flask was placed 0.1 g of **1** in 15 ml of EtOH, and the solution was heated to 80°. After flushing well with N_2, 0.025 g of 5% Pd–C was added with vigorous stirring while maintaining the N_2 atmosphere. A small aliquot was removed after 2 min;

---

[5] M. Perelman, E. Farkas, E. J. Fornefeld, R. J. Kraay, and R. T. Rapala, *J. Amer. Chem. Soc.*, **82**, 2402 (1960).

[6] L. Velluz, G. Nomine, J. Mathieu, E. Toromanoff, D. Bertin, M. Vignau, and J. Tessier, *C. R. Acad. Sci.*, **250**, 1510 (1960).

[7] G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, and H. Smith, *J. Chem. Soc.*, 5072 (1963).

[8] A. Bowers, J. Edwards, and P. Crabbe, U. S. Patent 3,207,753 (1965).

[9] A. J. Birch, J. M. H. Graves, and J. B. Siddall, *J. Chem. Soc.*, 4234 (1963).

[10] S. K. Malhotra and H. J. Ringold, *J. Amer. Chem. Soc.*, **86**, 1997 (1964).

[11] H. J. Ringold and A. Turner, *Chem. Ind. (London)*, 211 (1962); see ref 5.

no appreciable uv chromophore at 240 nm remained. The catalyst was filtered and the solvent was removed under vacuum. Nmr analysis of the residue confirmed the presence of two compounds as an approximate 1:1 mixture.

The residue (0.095 g) was chromatographed using 8 g of basic Al_2O_3. The fraction eluted with Et_2O was crystallized from hexane to give 0.036 g, mp 146–148°. Mixture melting point determination with an authentic sample of 17β-hydroxy-5α,10α-estran-3-one showed no depression. The fraction eluted with EtOAc was crystallized from hexane–$CHCl_3$ to give 0.052 g, mp 178–180°. Mixture melting point determination with an authentic estradiol sample again showed no depression. Both compounds gave nmr spectra identical with those of the authentic samples.

Dehydrogenation of 19-Nortestosterone.—Using the above procedure, 0.05 g of the compound was treated with 0.013 g of Pd–C. Occasionally a small aliquot was removed for monitoring by uv; after 4 hr no appreciable change in the uv maximum was noted. Tlc confirmed the presence of primarily starting material.

Dehydrogenation of 17β-Hydroxy-17α-methyl-9β,10α-estr-4-en-3-one.—Using the above procedure 0.04 g of the 9β,10α compound was treated with 0.010 g of 5% Pd–C. Monitoring the reaction by uv indicated no appreciable change from starting material. After 24 hr of reaction, still no appreciable change in uv was observed. The catalyst was filtered and the solvent was evaporated. Tlc of the residue revealed in addition to starting material only a trace of a more polar substance.

Dehydrogenation of 17β-Hydroxy-17α-methyl-9β,10β-estr-4-en-3-one (4).—Using the standard procedure 0.1 g of **4** was treated with 0.025 g of 5% Pd–C. Uv analysis after 5 min showed no starting material present. After filtration and removal of solvent, the residue was crystallized from isopropyl ether to give 0.050 g of **5**: mp 215–216°; nmr ($CDCl_3$) δ 0.95 and 0.96 (s, 3 H each, C-17 and C-18 Me).

Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.43; H, 9.32.

17α-Methyl-9β-estradiol (5).—To a mixture of 0.3 g of 5% Pd–C in 36 ml of AcOH and 4 ml of Ac_2O was added 0.61 g of **8**.[7] One equivalent of H_2 was taken up in 15 min in a calibrated atmospheric hydrogenation apparatus. The catalyst was filtered and the solvent was evaporated *in vacuo*. The residue was dissolved in 20 ml of MeOH containing 2 ml of HCl and refluxed for 1 hr. The solution was poured into ice water and the mixture was extracted thoroughly with EtOAc. The combined organic layer was washed in turn with water, saturated $NaHCO_3$ solution, and NaCl solution. After drying (Na_2SO_4) the solvent was evaporated *in vacuo*, and the residue was crystallized from EtOAc–hexane. The first crop of 0.16 g, mp 259–261°, proved to be estrone. The succeeding three crops, 0.195 g, mp 185–190°, were largely the 9β estrone.

To 15 ml of MeMgBr (*ca.* 5 mol) in 30 ml of THF was slowly added a solution of 0.195 g of the 9β ketone in 25 ml of THF. The mixture was stirred under N_2 at the reflux for 18 hr. After the mixture was cooled, excess saturated NH_4Cl solution was added and the mixture was extracted thoroughly with EtOAc. The combined organic layer was washed in turn with water and saturated NaCl solution. After drying (Na_2SO_4) the solvent was evaporated *in vacuo* and the residue was crystallized from benzene to give 0.16 g, mp 216–218°, of **5**. Mixture melting point with material previously obtained by dehydrogenation gave mp 215–218°. The nmr spectra were virtually identical.

Aromatization of 17β-Hydroxy-17α-methylestra-4,9(10)-dien-3-one (6).—A solution of 0.29 g of **6** in 100 ml of 3A EtOH was flushed with N_2 and heated to 80°. Then 0.075 g of 5% Pd–C was added and the mixture was stirred while heating continued. The extent of aromatization was followed by uv; most of the chromophore disappeared in 0.5 hr. The catalyst was filtered and the solvent was evaporated *in vacuo*. The residue was crystallized from Et_2O to give 0.19 g of **7**, mp 191–193°. Nmr spectrum of the mother liquor showed no trace of the 9β isomer.

Dehydrogenation of 17β-Hydroxy-17α-methylestr-5(10)-en-3-one (9).—Following the usual procedure, 0.29 g of **9** in 100 ml of 3A EtOH was treated with 0.075 g of catalyst for 4 hr. The reaction rate was monitored by uv; no large amount of aromatic formation was observed. The catalyst was filtered and the solvent was evaporated *in vacuo*. Tlc of the residue showed one major spot for the starting material with a trace of impurity.

Dehydrogenation of 1,4-Dihydro-17α-methylestradiol 3-Methyl Ether (10).—Using the standard procedure, 0.29 g of **10** in 100 ml of 3A EtOH and 0.075 g of catalyst were used. The rate of reaction was followed by uv; reaction was stopped at 0.75 hr. After usual handling tlc was run on residue, which indicated that two compounds were formed. The residue was chromatographed on 50 g of Florisil using benzene–EtOAc (10:1) as solvent. The first crystalline fraction was recrystallized from MeOH to give 17α-methylestradiol 3-methyl ether (**12**), 0.160 g, mp 99–103°. The second fraction of 0.045 g was not crystalline but nmr analysis showed that this was mainly **9**.

Dehydrogenation of 1,2-Dihydro-17α-methylestradiol 3-Methyl Ether (11).—Following the procedure of Birch,[9] 0.2 g of **10** was converted primarily to **11** as evidenced by the large uv maximum at 272 nm. This material without isolation was treated with 0.025 g of 5% Pd–C in the usual way. After work-up as for **10**, 0.13 g of **12**, mp 100–102°, was obtained.

Dehydrogenation of Estra-3,5-diene-3,17β-diol Diacetate (13).—Following the usual conditions, 0.1 g of **13**[12] was treated with 0.025 g of 5% Pd–C. The reaction was monitored by uv and showed no appreciable change in uv chromophore in up to 4 hr. Tlc analysis of the residue showed that only starting material was present.

Registry No.—**1**, 5670-56-4; **4**, 20708-78-5; **5**, 30541-88-9; **6**, 14531-89-6; **7**, 302-76-1; **12**, 15236-73-4.

Acknowledgment.—We wish to acknowledge the assistance of our colleagues in microanalysis and physical chemistry who obtained the data used in this paper.

(12) R. Villotti, C. Djerassi, and H. J. Ringold, *J. Amer. Chem. Soc.*, **81**, 4566 (1959).

Oxidation and Reduction Reactions Involving Cobalt–Cyano Complexes

K. H. Shin and L. J. Kehoe*

Research Laboratories, Ethyl Corporation,
Ferndale, Michigan 48220

Received November 6, 1970

The catalytic activity of cobalt–cyano complexes has received considerable attention[1,2] since Iguchi first observed that solutions of such complexes absorbed molecular hydrogen and transferred it to a substrate.[3] Recent publications concerned with the oxidation[4,5] and reduction[5,6] of organic compounds promoted by cobalt–cyano complexes prompt us to report related work. Our observations are presented to clarify and expand these recent reports.

This note describes the epoxidation of allyl alcohol by reacting $[(CN)_5CoOOCo(CN)_5]^{6-}$ (**1**) with hydrochloric acid in the presence of tungstic acid, the oxidation of 1-octene by **1** in acetic acid solvent, and the reduction of sodium methacrylate in the presence of $[Co(CN)_5]^{3-}$ (**2**) using water as the hydrogen source.

By utilizing a catalyst such as tungstic acid or sodium tungstate we found that allyl alcohol can be epoxidized, under a nitrogen atmosphere, with **1** as the oxygen source. After 1.5 hr at 70–75° and at a pH of 4.5–5.5, a 70% yield of glycidol (based on consumed active oxy-

(1) J. Kwiatek, *Catal. Rev.*, **1**, 37 (1967).

(2) B. M. Chadwick and A. G. Sharpe, *Advan. Inorg. Chem. Radiochem.*, **8**, 83 (1966).

(3) M. Iguchi, *J. Chem. Soc. Jap.*, **63**, 634 (1942); *Chem. Abstr.*, **41**, 2975d (1943).

(4) T. Asai and T. Hara, *Bull. Chem. Soc., Jap.*, **42**, 3580 (1969).

(5) G. Pregaglia, D. Morelli, F. Conti, G. Gregorio, and R. Ugo, *Discuss. Faraday Soc.*, **46**, 110 (1968).

(6) K. Tarama and T. Funabiki, *Bull Chem. Soc. Jap.*, **41**, 1744 (1968).