

Thus far the discussion has been concerned with the effects of cross-linking on linear polymer molecules. It has been suggested frequently that diene synthetic rubber molecules are highly branched, although no conclusive data bearing on this point are available. As already noted a preponderance of highly branched molecules cannot be produced by cross-linking reactions alone, owing to the intervention of gelation. However, branching reactions such as the one depicted in reaction (4) may conceivably result in highly branched polymer molecules. It may be of interest therefore to consider briefly some of the characteristics to be expected in network structures formed by cross-linking branched molecules.

For a given molecular weight distribution, the same number of cross linkages introduced at random gives rise to the same number of active network elements^{9,19} regardless of whether the molecules are linear or branched (or cross-linked). Hence, elastic modulus should not be affected very much by branching. On the other hand, a network formed from branched molecules will have many more terminal chains,^{9,19} consequently a larger proportion of the structure will not be oriented by stretching. On this basis a vulcanizate formed from branched molecules could be expected to exhibit lower strength than one formed from linear molecules of the same molecular weight. It is important, therefore, to distinguish branching from cross-linking reactions.

Summary

Reaction mechanisms whereby cross-linked and

branched polymer structures may be formed during the polymerization of dienes are discussed. A kinetic treatment of the formation of cross linkages via the occasional addition of a free radical to the unsaturated carbon of a structural unit of a previously polymerized molecule is presented. It is pointed out that the rate of this addition step relative to monomer addition can be deduced from the average chain length and the conversion at which gelation occurs.

Cross linkages introduced by the mechanism under consideration are not distributed at random, but the deviations from a random distribution are unimportant except at high conversions. Conditions are examined under which the cross-linking reaction decreases the total number of molecules more rapidly than they are formed.

Physical properties of polymers (with particular emphasis on vulcanized rubbers) are most conveniently interpreted in terms of (1) the primary molecular weight (*i. e.*, molecular weight in the absence of cross linkages) and its distribution, and (2) the concentration of cross linkages. The actual molecular weight distribution, which may be severely distorted by the presence of cross linkages, is inappropriate for direct correlation with the more important physical properties. The modifiers, or regulators, commonly employed in diene polymerizations suppress gel formation by reducing the primary molecular weight; they do not actually reduce cross-linking. This reduction in molecular weight is not without other undesired consequences, however.

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Perbenzoic Acid Oxidation of 20-Ketopregnanes

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The transformation of 20-ketopregnane derivatives to the corresponding 17-acetoxyetiocholanes by the use of Caro's acid has been described.^{1,2} With allopregnane-20-one, 60-70% of a mixture containing equal parts of allopregnane-21-ol-20-one acetate and androstane-17(α)-ol acetate was obtained. Similar results were found with Δ^5 -pregnene-3(β)-ol-20-one dibromide, allopregnane-3(β)-ol-20-one, and pregnane-3(α)-ol-20-one.

It has also shown³ that perbenzoic acid reacts readily with unsubstituted 3-ketosteroids to give lactones. However, the oxidation of allopregnane-3(β)-ol-20-one acetate with this reagent gave only a few per cent. of androstanediol.

In the course of an investigation in this Labora-

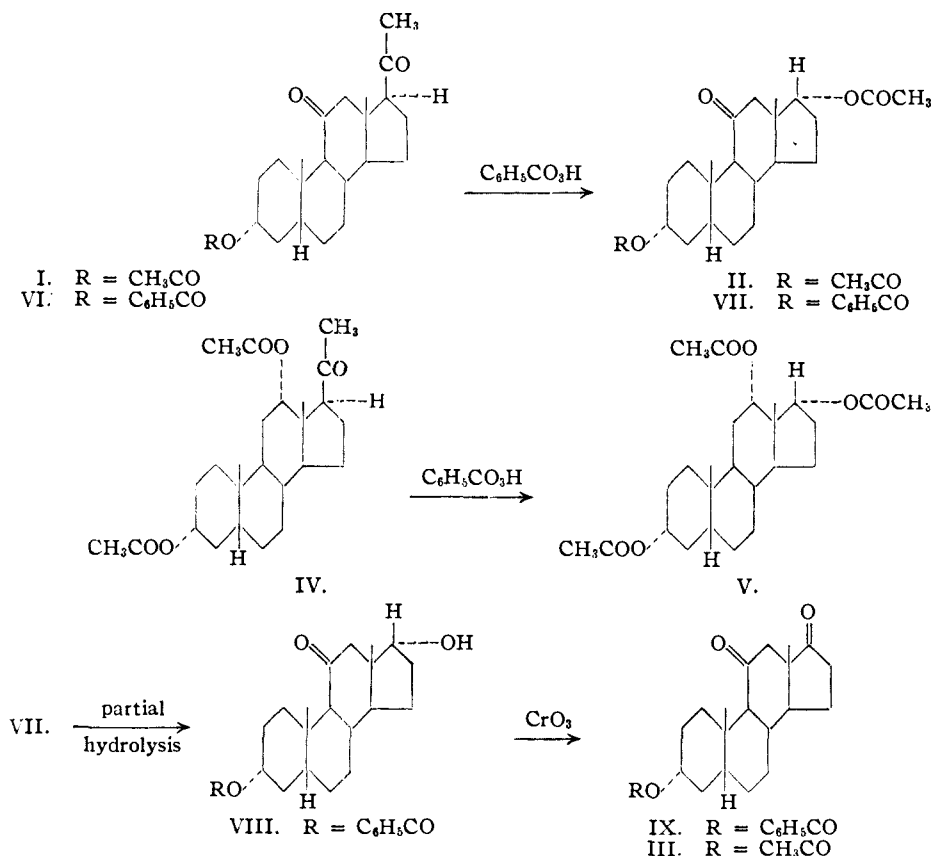
tory on methods of degradation of pregnanes to etiocholanes, the effect of perbenzoic acid on 20-ketopregnanes as a possible preparative method was tested. It was found that in the best case 85% of the 17(α)-acetoxyetiocholane was obtained, but that the yields varied with the 20-ketopregnane used. Neither the 17(β)-acetoxy isomer nor products resulting from oxidation of the C-21 methyl group could be isolated. It was also determined that, as might be anticipated, the rate of oxidation was considerably slower than that reported³ for 3-ketosteroids. After sixteen hours at 16°, the latter reaction was complete, whereas seven to ten days at 25-30° in very concentrated solution was required for the completion of the side chain cleavage.

Four compounds were subjected to the perbenzoic acid oxidation: pregnane-3(α)-ol-11,20-dione acetate (I), pregnane-3(α)-ol-11,20-dione ben-

(1) Marker, *THIS JOURNAL*, **62**, 650 (1940).

(2) Marker, Rohrmann, Wittle, Crooks and Jones, *ibid.*, **62**, 2543 (1940).

(3) Burckhardt and Reichstein, *Helv. Chim. Acta*, **25**, 821, 1434 (1942).



zoate (VI), pregnane-3(α),12(α)-diol-20-one diacetate (IV) and progesterone.⁴ All of these compounds except the last named gave the corresponding 17(α)-acetoxy derivatives, II, VII and V, respectively. Evidently preferential oxidation in Ring A or B occurred with progesterone.^{4a}

In addition, etiocholane-3(α),17(α)-diol-11-one 3-benzoate (VII) was converted by partial hydrolysis to etiocholane-3(α),17(α)-diol-11-one 3-benzoate (VIII). Chromic acid oxidation then readily yielded etiocholane-3(α)-ol-11,17-dione benzoate (IX), thus establishing the structure of the benzoate acetate.

A stereochemical designation of the C-17 hydroxyl group may be tentatively made on the basis of the partial reduction of etiocholane-3(α)-ol-11,17-dione acetate (III). The etiocholane-diolone monoacetate obtained in this way gave, after acetylation, the same etiocholane-diolone diacetate (II) obtained by perbenzoic acid oxidation of pregnane-3(α)-ol-11,20-dione acetate (I). By analogy with the reduction of Δ^5 -androstene-3(β)-ol-17-one and other 17-ketosteroids, the α or "trans" configuration⁵ may be given to the C-17 substituent.

(4) We are indebted to Dr. Erwin Schwenk of the Schering Corporation, Bloomfield, New Jersey, for a sample of pregnenolone from which this compound was prepared.

(4a) Cf. Burckhardt and Reichstein, ref. 3; also Böeseken and Kremer, *Rec. trav. chim.*, **50**, 827 (1931).

(5) Cf. Ruzicka and Goldberg, *Helv. Chim. Acta*, **19**, 99 (1936).

Experimental

All melting points are corrected.

Etiocholane-3(α),17(α)-diol-11-one Diacetate (II) from Pregnane-3(α)-ol-11,20-dione Acetate⁶ (I).—To a solution of 154 mg. of perbenzoic acid (1.12 molar equivalents) in 1.90 cc. of chloroform was added 404 mg. of pregnane-3(α)-ol-11,20-dione acetate (I). After standing at 25–30° for one week, the solution was poured into acidulated potassium iodide solution and the liberated iodine titrated. The perbenzoic acid consumed amounted to 76% of theoretical. The chloroform solution was then diluted with ether, washed with dilute aqueous carbonate solution, then with water, and concentrated to dryness. The residue was crystallized from ether-petroleum ether and gave 250 mg. of etiocholane-3(α),17(α)-diol-11-one diacetate, m. p. 179–180°. The mother liquors were evaporated to dryness and separated into ketonic and non-ketonic fractions with Girard Reagent T. The former amounted to 107 mg. and gave upon crystallization 93 mg. of starting material. The latter furnished an additional 8 mg. of the etiocholane derivative. Total yield was 85% corrected for recovered starting material. A pure sample of etiocholane-3(α),17(α)-diol-11-one diacetate was obtained by recrystallization from a small volume of methanol. It then melted at 180–181°; $[\alpha]_D^{25} +51.5^\circ$ (acetone), $c = 0.9$.

Anal. Calcd. for C₂₂H₃₄O₅: C, 70.73; H, 8.78. Found: C, 70.94; H, 8.91.

Etiocholane-3(α),17(α)-diol-11-one Diacetate (II) from Etiocholane-3(α)-ol-11,17-dione Acetate (III).⁷—A solution of 586 mg. of etiocholane-3(α)-ol-11,17-dione acetate in 50 cc. of glacial acetic acid was shaken with 700 mg. of

(6) v. Euw, Lardon and Reichstein, *Helv. Chim. Acta*, **27**, 821 (1944).

(7) Sarett, *J. Biol. Chem.*, **162**, 601 (1946).

platinum oxide until one mole of hydrogen was consumed in addition to that required for the catalyst. The solution was then filtered, concentrated *in vacuo* nearly to dryness, dissolved in ether, washed with dilute aqueous carbonate, then with water and concentrated to dryness. The oily residue was heated on the steam-bath with pyridine and acetic anhydride for fifteen minutes, cooled and diluted with water. The crystalline precipitate (600 mg.) was crystallized twice from dilute alcohol and twice from benzene-petroleum ether. It then melted at 178–179° and gave no depression with a sample of etiocholane-3(α),17(α)-diol-11-one diacetate prepared by the first described method.

Etiocholane-3(α),17(α)-diol-11-one.—A small sample of etiocholane-3(α),17(α)-diol-11-one diacetate was refluxed for half an hour in 0.5 *N* aqueous methanolic potassium hydroxide. The methanol was then removed *in vacuo*. The crystalline precipitate was washed with water and recrystallized from dilute alcohol. The etiocholane-3(α),17(α)-diol-11-one melted at 254–255°, $[\alpha]_D^{25} +61^\circ$ (acetone), $c = 0.7$.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.41; H, 9.87. Found: C, 74.63; H, 9.88.

Etiocholane-3(α),12(α),17(α)-triol.—A solution of 550 mg. of pregnane-3(α),12(α)-diol-20-one diacetate⁸ in 3.4 cc. of chloroform containing 276 mg. of perbenzoic acid (1.49 molar equivalents) was permitted to stand at 25–30° for ten days. The consumption of perbenzoic acid then amounted to 117%. After working up in the customary manner, 570 mg. of triacetate was obtained, which failed to crystallize. It was therefore saponified by refluxing with 2 *N* aqueous methanolic potassium hydroxide for half an hour. The methanol was removed *in vacuo* and the suspended material extracted with a large volume of ether-ethyl acetate mixture. The ether layer was washed with water, concentrated to a small volume and the solution permitted to crystallize. The yield of triol melting at 231–234° was 250 mg. (61%). Recrystallization from methanol-ether gave fluffy solvated masses of needles, which melted partially at 110–135°, resolidified and melted at 235–236°. For analysis a sample was dissolved in absolute alcohol, the solvent removed *in vacuo* and the amorphous residue dried in a weighing pig at 140°.

Anal. Calcd. for $C_{19}H_{32}O_4$: C, 73.97; H, 10.46. Found: C, 73.75; H, 10.51.

Etiocholane-3(α),12(α),17(α)-triol Triacetate (V).—A small sample of etiocholane-3(α),12(α),17(α)-triol (m. p. 110–135; 235–236°) was heated on the steam-bath with pyridine and acetic anhydride for one hour. The mixture was then worked up as usual. After two recrystallizations from dilute methanol, the pure triacetate melted at 132–133°, $[\alpha]_D^{25} +74^\circ$ (acetone), $c = 0.8$.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.10; H, 8.82. Found: C, 69.46; H, 8.84.

Pregnane-3(α)-ol-11,20-dione Benzoate (VI).—A mixture of 1.0 g. of pregnane-3(α)-ol-11,20-dione, 5 cc. of pyridine and 1.0 cc. of benzoyl chloride was heated on the steam-bath for ten minutes. Water was then added and the mixture was worked up in the usual manner. After two crystallizations from methanol, 1.1 g. of benzoate was obtained, m. p. 154–155°. For analysis the compound was dried in a weighing pig at 140°.

Anal. Calcd. for $C_{25}H_{36}O_4$: C, 77.03; H, 8.32. Found: C, 76.78; H, 8.08.

Etiocholane-3(α),17(α)-diol-11-one 3-Benzoate 17-Acetate (VII).—A solution of 1.0 g. of pregnane-3(α)-ol-

11,20-dione benzoate (VI) in 6.0 cc. of chloroform containing 486 mg. of perbenzoic acid (1.54 molar equivalents) was left in the dark at 25–30° for ten days. At the end of this time, 125% of the theoretical amount of perbenzoic acid was consumed. After the customary working up, an amorphous product was obtained, which was submitted to chromatographic separation on alumina. The fractions eluted with ether-petroleum ether (4:6 and 5:5) were crystallized from methanol and melted at 156–157°. A mixture with starting material melted at 137–150°. A total of 193 mg. of the benzoate acetate was obtained.

Anal. Calcd. for $C_{28}H_{38}O_5$: C, 74.30; H, 8.02. Found: C, 74.41, 74.59; H, 8.10, 8.20.

Etiocholane-3(α),17(α)-diol-11-one 3-Benzoate (VIII).—A solution of 118 mg. of benzoate acetate (VII) in 2 cc. of benzene was treated with 2 cc. of 1.0 *N* methanolic solution of potassium hydroxide. The solution was maintained at 25° for ten minutes, then poured into water, extracted with ether, the ethereal layer washed several times with water and concentrated to dryness. After recrystallization from ether-petroleum ether and from methanol, 70 mg. of the benzoate (VIII) was obtained. It melted at 223–224°.

Anal. Calcd. for $C_{26}H_{34}O_4$: C, 76.06; H, 8.59. Found: C, 75.76; H, 8.40.

Etiocholane-3(α)-ol-11,17-dione Benzoate (IX) from Etiocholane-3(α),17(α)-diol-11-one 3-Benzoate (VIII).—A solution of 75 mg. of etiocholane-3(α),17(α)-diol-11-one 3-benzoate in 2 cc. of 95% acetic acid was treated with a solution of 50 mg. of chromic acid in 0.10 cc. of water. The solution was left at room temperature for one hour and the crystalline ketone then precipitated by careful dilution with water. After recrystallization from alcohol, the etiocholane-3(α)-ol-11,17-dione benzoate melted at 226–227°.

Anal. Calcd. for $C_{26}H_{32}O_4$: C, 76.43; H, 7.90. Found: C, 76.41; H, 7.74.

The esterification of etiocholane-3(α)-ol-11,17-dione with benzoyl chloride in pyridine gave a benzoate identical in melting point and mixed melting point.

Action of Perbenzoic Acid on Progesterone.—From 206 mg. of progesterone treated with perbenzoic acid for one week, 13 mg. of crystals, m. p. 162–171°, was isolated. This substance is evidently different from both Δ^4 -androsterone-17(α or β)-ol-3-one acetate. It was not further investigated.

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Summary

It has been shown that perbenzoic acid reacts with pregnane-3(α)-ol-11,20-dione acetate and with pregnane-3(α),12(α)-diol-20-one diacetate to give the corresponding 17(α)-acetoxy-etiocholanes. With pregnane-3(α)-ol-11,20-dione benzoate, a benzoate acetate was obtained which could be converted by partial saponification and oxidation to etiocholane-3(α)-ol-11,17-dione benzoate.

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(8) The configuration of the C-12 hydroxyl group in desoxycholic acid is taken as α , as has been demonstrated by Gallagher and Long (*J. Biol. Chem.*, **162**, 495 (1946)) and by Sorkin and Reichstein (*Helv. Chim. Acta*, **29**, 1218 (1946)).