only two centers (C-2 and C-19) remains ambiguous because all others are fixed in this bridged system.

Experimental[22]

Isolation of Alkaloids from the Tree Bark of *Aspidosperma quebracho blanco*.—The powdered bark (100 g.) was refluxed with 3 portions of 500 ml. of ethanol for 2 hr. each. After-filtering, the combined ethanolic solutions were evaporated under reduced pressure and the brown residue was extracted three times with 100-ml. portions of hot chloroform. The chloroform solution was extracted first with 1 *N* sodium hydroxide and then with dilute sulfuric acid. The aqueous acidic solution was made slightly alkaline and immediately extracted with several portions of chloroform. After drying and evaporation of the solvent, 0.70 g. of crude alkaloids was obtained. The gas chromatogram shown in Fig. 1 was obtained with a small amount of this material.

For the isolation of the individual components of this mixture, three such portions were combined (total 1.959 g.) and chromatographed on 185 g. of alumina (act. II). Elution was started with petroleum ether–benzene 5:3 and changed gradually to pure chloroform which eluted yohimbine (see Table I). About 60% of the starting material had been recovered at that point. The more polar substances remaining on the column were not further investigated.

Most of these fractions (185 in all) still represented mixtures of a few compounds which could be obtained pure on further separation by gas chromatography (80-cm. column, 10% Apiezon L on Chromosorb W, 250°, 14 lb. helium). Frequently, it was necessary to combine adjacent fractions of the alumina chromatogram before gas chromatography. The individual fractions were collected simply by inserting into the exit tube of the gas chromatograph an unsealed melting point capillary on the cold parts of which the substance condensed immediately. The capillary containing the sample was transferred directly into the inlet system of the mass spectrometer to obtain the mass spectrum of the fraction or, alternatively, rinsed with ethanol to obtain a solution for ultraviolet spectroscopy. Melting points were also obtained in some instances from the gas chromatographic fractions, except for the major alkaloids which could be obtained crystalline from the alumina chromatogram (for physical data of these fractions see Table I).

Isolation of (−)-Pyrifolidine (384A).—The fractions emerging from the alumina column immediately after the bulk of 354A were found by mass spectrometry to consist of a difficult to-separate mixture of 354A and 384A. To facilitate separation, the mixture was hydrolyzed with boiling hydrochloric acid (10%, 4 hr.). The reaction mixture was then made alkaline and extracted with ether. After drying and evaporation of the solvent, the product (187 mg.) was chromatographed on alumina. Benzene eluted 312A (96.8 mg., m.p. 109–110°). Benzene–chloroform 19:1 eluted 342A (10.6 mg., m.p. 144–147°) which was dissolved in 0.5 ml. of pyridine and 0.5 ml. of acetic anhydride. After 15 minutes reflux, the mixture was evaporated, digested with dilute sodium hydroxide, and extracted with ether. The ether phase was dried and evaporated to yield 9.0 mg. of 384A, m.p. 148–150°, $[\alpha]^{28}D$ −93° ($CHCl_3$, *c* 0.90) (pyrifolidine from *A. pyrifolium*[15]: m.p. 147.5–150°, $[\alpha]D$ +90°).

Reduction of 1,2-Dehydroaspidospermidine (280A) with Lithium Aluminum Deuteride.—The purest fractions of 280A obtained from the alumina chromatogram were combined (12 mg.) and treated with 20 mg. of $LiAlD_4$ in 1 ml. of tetrahydrofuran in a sealed tube. On work-up, 9 mg. of crude material was obtained which was purified by gas chromatography. The mass spectrum of the collected material (282A-2-*d*) exhibited the major peaks at *m/e* 131, 144, 145, 152, 254 and 283.

Catalytic Reduction of Aspidospermatidine (266B) and 12-Methoxyaspidospermatidine (206B).—Fractions containing both 266B and 296B were combined (48 mg.; ratio 1:1 as determined by gas chromatography), dissolved in 2 ml. of methanol and hydrogenated on 20% Pd-on-charcoal for 2 hr. The filtrate, on evaporation, yielded 44 mg. of an oil which was separated by gas chromatography into two components. The one emerging first showed a molecular weight of 268 (Fig. 5c), the second 298 (characteristic peaks in the mass spectrum at *m/e* 138, 160, 174, 242, 257, 298).

Hydrolysis of Aspidospermatine (338B).—Aspidospermatine, 3 mg., was heated to reflux with 2 ml. of 10% hydrochloric acid for 4 hr. After cooling, the solution was made alkaline with bicarbonate and extracted with ether. After drying and evaporation of the solvent, the residue was distilled at 0.05 mm. (180–200° bath). The mass spectrum of the oil so obtained was identical with that of deacetylaspidospermatine (296B) shown in Fig. 4c.

Catalytic Reduction of Aspidospermatine (338B).—Aspidospermatine (4 mg.) was hydrogenated in 2 ml. of methanol with 10 mg. of 20% Pd-on-charcoal. After 40 min. the catalyst was filtered off, the solvent evaporated, and the residue purified by gas chromatography (one peak). The mass spectrum (major peaks at *m/e* 138, 160, 174, 299 and 340) of the collected material was identical with that of dihydroaspidospermatine (340B) isolated from the alkaloid mixture (see Table I).

Zinc Dust Distillation of the Aspidospermatine Group.—The mixture (25 mg.) of 268B and 298B obtained on catalytic hydrogenation of 266B and 296B (see above) was thoroughly mixed with 1 g. of zinc dust, transferred into a glass ampoule and covered with 1 g. of zinc dust and glass wool. The ampoule was evacuated, sealed and heated for 1 hr. to 400–410° in a horizontal furnace. The volatile degradation products condensed in the part of the tube extending from the furnace. After cooling and opening of the tube, the more volatile components were separated on a gas chromatographic column (2.5 m., 16% silicon oil 550 on Chromosorb W, 110°, 10 lb. helium), and the individual fractions collected. The lower boiling ones were found on the basis of their mass spectra to consist mainly of 3-ethylpyridine and small amounts of 3-methyl-5-ethylpyridine and 3,5-diethylpyridine. The higher boiling fractions seemed to consist of indoles and carbazoles.

Reduction with Perdeuteriohydrazine.—A sample (19 mg.) of deacetylaspidospermatine (296B) still containing some aspidospermatidine (266B) was heated to 90–100° with perdeuteriohydrazine in dioxane–D_2O. The progress of the reduction was followed by mass spectrometry (withdrawing a small sample in 1-day intervals). After 4 days the reduction was essentially complete. The reaction mixture was then concentrated under reduced pressure, extracted with ether, the solvent removed, and the residue purified by gas chromatography which permitted the isolation of a pure specimen of deuteriated dihydrodeacetylaspidospermatine (298B). Its mass spectrum showed a molecular weight of 300 and peaks at *m/e* 259, 270, 271, and the most intense at *m/e* 140.

Acknowledgments.—We are indebted to Dr. G. F. Smith for a sample of decarbomethoxydihydroakuammicine (VI); to S. B. Penick and Company for a supply of powdered quebracho bark; to the Petroleum Research Fund of the American Chemical Society and, in part, to the Upjohn Company, for financial support.

(22) Mass spectra were determined with a CEC 21-103C mass spectrometer, equipped with a heated inlet system operated at 140°. Ionizing potential 70 e.v.

COMMUNICATIONS TO THE EDITOR

CYANOETHYLATIONS AND MICHAEL ADDITIONS. I. THE SYNTHESIS OF ALLYLIC CYCLOHEXENOLS BY γ-CYANOETHYLATION OF AN α,β-UNSATURATED ALDEHYDE[1,2]

Sir:

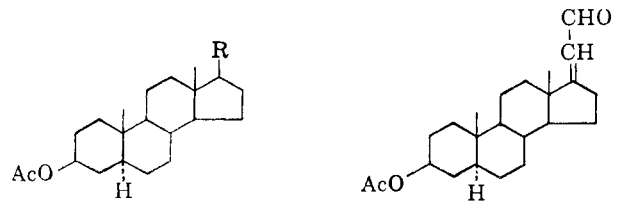
Cyanoethylations of α,β-unsaturated carbonyl compounds are reported to occur, similarly to mechanistically related alkylations,[3] in position α to the carbonyl function, on the originally unsaturated carbon atom,[4a–d] even in the absence of a hydrogen substituent in this position.[4b,c] We now wish to record the *first*

(1) Paper XXII in the series on Steroids and Related Products; for Paper XXI, see S. Rakhit, R. Deghenghi and Ch. R. Engel, *Can. J. Chem.*, **41** (1963) (in press).

(2) Abbreviated from the doctoral thesis of J. Lessard to be submitted to the School of Graduate Studies, Laval University, Quebec; presented, in part, at the 2nd International Symposium on the Chemistry of Natural Products, Prague, August–September, 1962.

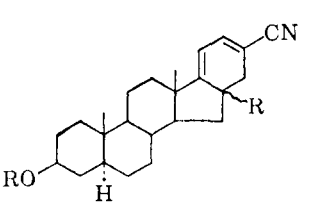
(3) *Cf.*, *e.g.*, (a) J.-M. Conia, *Bull. Soc. Chim. France*, 690 (1954); J.-M. Conia and A. Le Craz, *ibid.*, 1327 (1960); (b) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives and R. B. Kelly, *J. Am. Chem. Soc.*, **76**, 2852 (1954); (c) H. J. Ringold and S. K. Malhotra, *ibid.*, **84**, 3402 (1962).

(4) *Cf.*, *e.g.*, (a) H. A. Bruson and T. W. Riener, *ibid.*, **65**, 18 (1943); (b) H. A. Bruson and T. W. Riener, *ibid.*, **66**, 56 (1944); (c) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, *ibid.*, **74**, 4223 (1952); (d) S. Julia, *Bull. Soc. Chim. France*, 780 (1954).

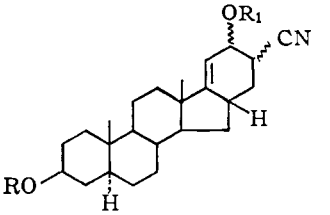


I, R = O
II, R = OH, $-C\equiv C-OC_2H_5$
III, R = OH, $-CH=CH-OC_2H_5$

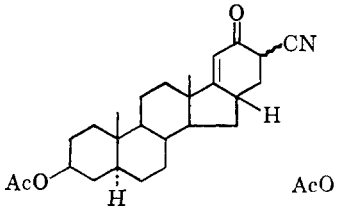
IV



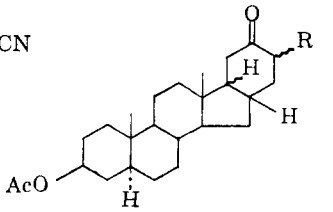
V, R = H, R_1 = —H
VI, R = Ac, R_1 = —H
VII, R = H, R_1 = ···H
VIII, R = Ac, R_1 = ···H



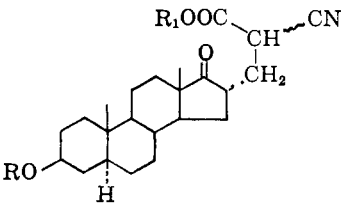
IXA; IXB, R = R_1 = H
XA; XB, R = Ac, R_1 = H
XIA; XIB, R = R_1 = Ac



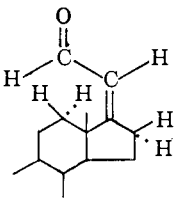
XIIA, XIIB



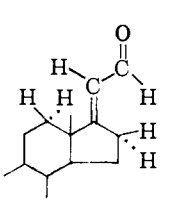
XIII, R = H
XIVA, R = CN



XVA, R = R_1 = H
XVIA, R = H, R_1 = CH_3
XVIIA, R = Ac, R_1 = CH_3



A



B

example of a γ-cyanoethylation of an α,β-unsaturated carbonyl compound which results, by a subsequent aldol cyclization, in the *formation of a functionalized six-membered ring.*

3β-Acetoxy-5α-pregn-17-en-21-al (IV) [m.p. 160–161°, $[\alpha]^{23}D$ 36° (*c* 1.00),[5] λ_{max}^{EtOH} 242 mμ (log ε 4.3), $\nu_{max}^{CHCl_3}$ 2760, 1728, 1672, 1642 (shoulder), 1610, 1252 cm.$^{-1}$; found: C, 76.99; H, 9.52] was obtained in 75% yield from 3β-acetoxy-5α-androstan-17-one (I) by the method described by Heusser, *et al.*, in the Δ^5 series,[6] *via* 3β-acetoxy-17α-ethoxyethinyl-5α-androstan-17β-ol (II) [m.p. 130.5–131.5° dec., $[\alpha]^{23}D$ −46° (*c* 1.00), $\nu_{max}^{CHCl_3}$ 3640, 2260, 1728, 1259–1250 (split) cm.$^{-1}$; found: C, 74.61; H, 9.47] and the ethoxyvinyl derivative III [m.p. 130.5–132°, $[\alpha]^{23}D$ 19° (*c* 0.696), ν_{max}^{KBr} 3560, 1730, 1678, 1245 cm.$^{-1}$; found: C, 74.55; H, 9.82]. Treatment of aldehyde IV with 1 to 1.4 moles of acrylonitrile in benzene, at 55°, in the presence of *t*-sodium amylate gave, in approximately 8% yield, 3β-acetoxy-16α-ethyl-16[2]-cyano-16[2],21-cyclo-5α-pregna-17,21-diene (VI) [m.p. 184–187°, $[\alpha]^{23}D$ −214° (*c* 0.55), λ_{max}^{EtOH} 297 mμ (log ε 4.02), ν_{max}^{KBr} 2210, 1735, 1655, 1575, 1258 cm.$^{-1}$; found: C, 79.59; H, 8.95; N, 3.63], accompanied by very small quantities of its 16-epimer VIII (m.p. 209–214°, $[\alpha]^{23}D$ 124° (*c* 0.992), λ_{max}^{EtOH} 297 mμ (log ε 4.01), ν_{max}^{KBr} 2200, 1735, 1650, 1565, 1255 cm.$^{-1}$], and, in approximately 75% yield, a 2:1 mixture of the isomeric allylic alcohols XA [m.p. 219–221°, $[\alpha]^{25}D$ 15° (*c* 0.986), ν_{max}^{KBr} 3480, 2250, 1735, 1250 cm.$^{-1}$; found: C, 76.00; H, 8.92; N, 3.61] and XB [m.p. 210–211°, $[\alpha]^{25}D$ −24° (*c* 0.96), ν_{max}^{KBr} 3510, 2240, 1735, 1245 cm.$^{-1}$; found: C, 75.99; H, 8.81; N, 3.36]. Since, in contrast to its epimer VIII, the predominantly formed diene VI is markedly levorotatory, it can be assigned the 16β-hydrogen configuration,[7] which also follows from the greater accessibility of the 16-position from the α-side. The acetoxy alcohols XA and XB were acetylated readily to the diacetates XIA [m.p. 169–170° dec., $[\alpha]^{25}D$ 23° (*c* 0.971), ν_{max}^{KBr} 2250, 1755, 1735, 1245, 1220 cm.$^{-1}$; found: C, 74.01; H, 8.68; N, 3.06] and XIB [m.p. 218.5–219.5°, $[\alpha]^{23}D$ 65° (*c* 0.838), ν_{max}^{KBr} 2250, 1740 (broad), 1250, 1225 cm.$^{-1}$; found: C, 74.25; H, 8.70; N, 3.20] and oxidized with chromic acid and sulfuric acid in acetone to the six-membered-ring ketones XIIA [m.p. 252–253°, $[\alpha]^{24}D$ −18° (*c* 0.87), λ_{max}^{EtOH} 237 mμ (log ε 4.17), ν_{max}^{KBr} 2245, 1732, 1682, 1641, 1255 cm.$^{-1}$; found: C, 76.50; H, 8.64; N, 3.59] and XIIB [m.p. 199–200°, $[\alpha]^{25}D$ −47° (*c* 1.00), λ_{max}^{EtOH} 238 mμ (log ε 4.2), ν_{max}^{KBr} 2245, 1736, 1685, 1641, 1245 cm.$^{-1}$; found: C. 75.72; H, 9.01; N, 3.59]. Upon fusion or digestion in various solvents (*e.g.*, ethyl acetate–acetic acid, dioxane–ethanol), ketone XIIB is converted to ketone XIIA, which can be explained by the facile enolization of the keto function toward the nitrile group, provided that the difference between the ketones results from a difference of configuration in 16[2]. This is borne out by the transformation of both acetoxy alcohols XA and XB (XA at room temperature in 57% yield, XB at 50° in 15.5% yield) with *p*-toluenesulfonyl chloride and pyridine into the same levorotatory diene VI; this establishes the 16β-ring fusion for both alcohols and their derivatives. Since the high frequency of the carbonyl absorption in the infrared of ketones XIIA and XIIB (and also of ketone XIVA) points to an equatorial conformation of their nitrile groups, one of them should have a half-chair conformation with an α-orientation of the nitrile group, and the other, a half-boat conformation with a β-orientation of the nitrile function. The result of the dehydration of alcohols XA and XB and the partial transformation of their acetates by alkali into diene V point to a *cis* relationship between their hydroxy and nitrile functions. Ketones XIIA and XIIB are reduced with palladium on calcium carbonate in dioxane–ethanol to the saturated keto nitrile XIVA [m.p. 212.5–213°, $[\alpha]^{23}D$ −94° (*c* 1.02), ν_{max}^{KBr} 2250, 1735, 1730, 1245 cm.$^{-1}$; found: C, 75.85; H, 8.99; N, 3.49] which, upon hydrolysis with hydrochloric acid–acetic acid, decarboxylation and reacetylation, affords the unsubstituted ketone XIII [m.p. 166–168°, $[\alpha]^{25}D$ −102° (*c* 1.04), ν_{max}^{KBr} 1731, 1718, 1243 cm.$^{-1}$; found: C, 77.87; H, 10.03]. Ozonolysis of the unsaturated ketones XIIA and XIIB, in ethyl acetate–acetic acid, yielded 2ξ-cyano-3-(3β-hydroxy-17-oxo-5α-androstan-16α-yl)-propanoic acid (XV) [m.p. 183–189°, ν_{max}^{KBr} 3450, 3400–2600, 2250, 1750–1720, 1035 cm.$^{-1}$], fully characterized as the acetoxy methyl ester XVII [m.p. 162–163.5°, $[\alpha]^{25}D$ 65°, (*c* 1.02), λ_{max}^{EtOH} 284 mμ (log ε 1.78), ν_{max}^{KBr} 2245, 1757, 1736, 1728, 1290, 1245, 1198 cm.$^{-1}$; found: C, 70.14; H, 8.51; N, 3.36].

(5) All rotations were taken in chloroform.

(6) H. Heusser, K. Eichenberger and Pl. A. Plattner, *Helv. Chim. Acta*, **33**, 370 (1950).

(7) *Cf.* D. K. Fukushima and T. F. Gallagher, *J. Am. Chem. Soc.*, **73**, 196 (1951); G. E. Arth, D. B. R. Johnston, J. Fried, W. W. Spooncer, D. R. Hoff and L. H. Sarett, *ibid.*, **80**, 3160 (1958); D. Taub, R. D. Hoffsommer, H. L. Slates, C. H. Kuo and N. L. Wendler, *ibid.*, **82**, 4012 (1960).

Cyanoethylation of aldehyde IV with sodium hydroxide in aqueous *t*-butyl alcohol gave a higher proportion of diene V and of alcohol IXB; alcohol IXA was not isolated.

We tentatively suggest that steric factors are the principal cause of the reported γ-cyanoethylation: position 20 of the thermodynamically favored *s-trans* aldehyde (*cf.* partial formula B) (as well as of the *s-cis* isomer) is sterically hindered and, therefore, the attack on its mesomeric anion should take place preferably in position 16. Furthermore, the geometry of the *s-trans* aldehyde and of the derived anion is particularly well suited for the aldol cyclization of the intermediate addition product, leading to a stable six-membered ring. A detailed discussion will follow in a subsequent paper of this series. We shall also illustrate the scope and the limitations of the above-described reaction sequence on the basis of cyanoethylations with various types of α,β-unsaturated aldehydes.

We sincerely thank Mrs. J. Capitaine and Mr. D. Capitaine for their expert assistance and the National Research Council of Canada for supporting this project.

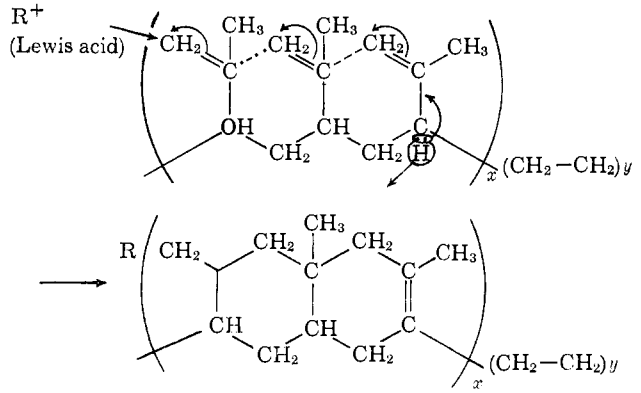
DEPARTMENT OF CHEMISTRY CH. R. ENGEL
LAVAL UNIVERSITY
QUEBEC, QUEBEC, CANADA J. LESSARD

RECEIVED NOVEMBER 26, 1962

THE PREPARATION AND CYCLIZATION OF A NOVEL COPOLYMER OF ETHYLENE AND ISOPRENE

Sir:

We wish to report the preparation of a novel copolymer of ethylene and isoprene, where the isoprene was copolymerized primarily through the 3,4 unsaturation.[1] The resultant copolymer contained blocks of isoprene units principally in the form of isopropenyl groups separated by methylene groups. Lewis acids such as boron trifluoride or phosphorus oxychloride eliminated isopropenyl unsaturation *via* what we believe to be a cyclization mechanism, to give a unique product containing *linearly*[2] fused cyclohexane units. For example, the cyclization of three lateral isopropenyl groups in an ethylene–isoprene copolymer probably takes place as shown.



The proposed structures of the products rely on the method of formation, X-ray and infrared analysis, and elemental analysis of nitrogen dioxide adducts.

The polymerizations were carried out by adding ethylene (100–300 cc./min.) and isoprene (0.5–2.0 cc./min.) to a stirred mixture of 1.5 l. of tetrachloroethylene, 5 of mmoles vanadyl trichloride, and 15 mmoles of aluminum triisobutyl, in the absence of oxygen and moisture. After 1.5 hours, the reaction was terminated by the addition of 50 ml. of methanol. The solid product was filtered off, washed successively with methanol and tetrachloroethylene, and then dried. This catalyst system polymerizes ethylene rapidly but is sluggish toward 1,4 addition polymerization of butadiene, which may help explain the preferential 3,4 polymerization of isoprene.

Over 95% of the isoprene units incorporated into the copolymer took the form of isopropenyl unsaturation (880 cm.$^{-1}$) due to polymerization through the 3,4 unsaturation; only a trace of 1,4-isoprene unsaturation (835 cm.$^{-1}$) was observed. Analysis of the isopropenyl unsaturation in the product showed that 10:1 mole ratio ethylene–isoprene mixtures produced copolymers which had a mole ratio of approximately 25:1. The unsaturation could not be removed by repeated precipitation from perchloroethylene, which suggests that the product was a copolymer and not an intimate mixture of homopolymers. X-Ray goniometer scans showed that the polyethylene crystallinity was virtually undisturbed, indicating the absence of random copolymer; this coupled with the ease of cyclization suggests that the isoprene was incorporated as a block.

Treatment of 1.5 l. of a 0.2% solution of the copolymer in perchloroethylene at 90° with 2 ml. of phosphorus oxychloride eliminated essentially all of the isopropenyl unsaturation in three minutes. Phosphorus could not be detected in the solid product, which was isolated by cooling, filtration, washing with methanol and drying. The formation of isopropylidene unsaturation instead of a polycyclic can be ruled out because (a) C=C stretching frequencies (1600–1650 cm.$^{-1}$ region) which were present in the untreated copolymer were absent after treatment with Lewis acid and (b) treatment of the product with the double bond reagents bromine or nitrogen dioxide gave adducts with a very low, non-stoichiometric bromine or nitrogen content. The isopropenyl groups of the uncyclized polymer are ideally situated for intramolecular cyclization of fused six-membered rings. This reaction is analogous to the rapid cationic polymerization of isobutylene.

Treatment of the cyclized 25:1 ethylene–isoprene copolymer with excess nitrogen dioxide gave an adduct which contained a maximum of 0.28% nitrogen. If the proposed cyclization mechanism is valid and nitrogen dioxide addition to the terminal unsaturated group in a block of fused rings was quantitative, this nitrogen content implies that there is one terminal unsaturated group remaining after cyclization of 13 isoprene units. In other words, the average block length in a 25:1 copolymer is 12 fused cyclohexane units.

Films of the cyclized ethylene–isoprene copolymer (2–6 mils, melt pressed at 175°) showed moduli (3% elongation) of 58 to 131 kp.s.i., an average elongation of about 100%, a tensile strength of 3 to 9 kp.s.i., and a pneumatic impact strength of 2–7 kg.-cm./mil. Polyethylene controls had moduli of about 100 kp.s.i., an elongation of 125%, pneumatic impact strengths of 1.5–2 kg.-cm./mil, and tensile strengths of 3 kp.s.i. or less.

Forthcoming reports from our laboratory will discuss the work in detail as well as the preparation and structure proof of cyclized poly(3,4-isoprene) polymers.

FILM DEPARTMENT
EXPERIMENTAL STATION LABORATORY STANLEY TOCKER
E. I. DU PONT DE NEMOURS & CO., INC.
WILMINGTON 98, DELAWARE

RECEIVED OCTOBER 29, 1962

(1) After this work was completed, G. Natta and L. Porri reported the preparation of 3,4-polyisoprene (French Patent 1,154,938) using tetra-isopropyl titanate and aluminum triethyl as catalyst.

(2) The acid catalyzed cyclization of natural rubber (poly-1,3-isoprene) has been reported to give an *angular* polycycloisoprene with tricyclic and bicyclic segments, as evidenced by identification of aromatized fragments (F. T. Wallenberger, *Monatsh.*, **93**, 74, 1962). N.m.r. studies by M. A. Golub and J. Heller suggested that the structure is primarily bicyclic (*Chem. Eng. News*, October 15, 1962, p. 44).