104 kcal.[10] suggests that the energetics of hydrogen abstraction by the benzophenone triplet and the *t*-butoxy radical must be very similar.

We are extending our experiments to other substrates and triplet states of other ketones and find, for example, that the acetophenone triplet shows similar but significantly different selectivities.

(10) P. Gray and A. Williams, *Chem. Rev.*, **59**, 239 (1959).
(11) National Science Foundation Cooperative Fellow, 1963–1964.

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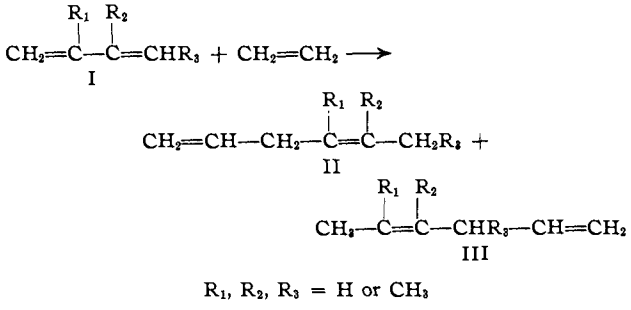
RECEIVED JULY 15, 1964

Stereospecific Synthesis of 1,4-Dienes

Sir:

We wish to report the novel synthesis of 1,4-dienes II and III by the reaction of 1,3-dienes I with ethylene in the presence of a catalyst consisting of iron compounds and organoaluminum compounds. This reaction affords either of the possible geometrical isomers of the 1,4-dienes selectively.



R_1, R_2, R_3 = H or CH_3

In a typical example, 25 ml. of toluene, 0.003 mole of iron(III) acetylacetonate, 0.012 mole of triethylaluminum, and 0.6 mole of 1,3-butadiene were placed in a stainless steel autoclave (100 ml.). The resulting mixture was stirred for 1.5 hr. at 30° under ethylene pressure (40 kg./cm.^{2}). After the usual work-up, the reaction products were separated by preparative gas chromatography. 1-*cis*-4-Hexadiene, b.p. 66.5°, n^{20}D 1.4147, was obtained in 35% yield and identified by comparison of its infrared spectrum and gas chromatographic retention time with an authentic sample.[1] In addition, small amounts of 2,4-hexadiene and 1,3-hexadiene were obtained.

For 1,3-pentadiene and isoprene, there are two possible sites of addition. The reaction of 1,3-pentadiene with ethylene at 50° afforded 3-methyl-1-*cis*-4-hexadiene, b.p. 83°, n^{20}D 1.4169, and 1-*cis*-4-heptadiene, b.p. 93°, n^{20}D 1.4209, in a ratio of 7:3, *i.e.*, ethylene adds more easily to the 4- position of 1,3-pentadiene than to the 1- position. The terminal double bond of the former compound was reduced by addition of an equivalent amount of diisobutylaluminum hydride, followed by hydrolysis to give 4-methyl-*cis*-2-hexene. The absence of the *trans* isomer[2] was confirmed by gas chromatographic analysis. The latter compound was identified by comparing it with an authentic sample.[1] 1-*trans*-3-Pentadiene reacts faster than the *cis* isomer. The unreacted 1,3-pentadiene was found to be rich in the *cis* isomer.

The reaction of isoprene with ethylene at 20° gave 4-methyl-1,4-hexadiene (one geometrical isomer), b.p. 88–89°, n^{20}D 1.4248, and 5-methyl-1,4-hexadiene, b.p. 88–89°, n^{20}D 1.4256, in a ratio of 6:4. As the reaction temperature was raised, the ratio approached 1:1. The terminal double bonds of 4-methyl- and 5-methyl-1,4-hexadiene were reduced by diisobutylaluminum hydride to afford one geometrical isomer of 3-methyl-2-hexene and 2-methyl-2-hexene,[3] respectively. A mixture of geometrical isomers of 3-methyl-2-hexene was prepared by the Wittig reaction of 2-pentanone with ethylidenetriphenylphosphorane. The isomers were separated by gas chromatography using a squalane column (4 m.) at 60°. The infrared spectrum and gas chromatographic retention time of the first eluted component were identical with those of the reduction product of 4-methyl-1,4-hexadiene. Investigation of its geometry is underway.

In a similar way, the reaction of 2,3-dimethyl-1,3-butadiene with ethylene gave 4,5-dimethyl-1,4-hexadiene, b.p. 119–120°, n^{20}D 1.4408.

The steric course and orientation of the reaction are being investigated. A detailed description of these reactions will be published later.

(1) Mixtures of *cis* and *trans* isomers of 1,4-hexadiene and 1,4-heptadiene were prepared by the known method [B. H. Shoemaker and C. E. Boord, *J. Am. Chem. Soc.*, **53**, 1505 (1931)]. The *cis* isomers of both 1,4-dienes were separated by gas chromatography using a silver nitrate–benzyl cyanide column (2.5 m.).
(2) F. J. Soday and C. E. Boord, *ibid.*, **55**, 3293 (1933).
(3) M. D. Sutherland, *ibid.*, **75**, 5944 (1953).

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RECEIVED JULY 21, 1964

An Approach to an Improved Antiinflammatory Steroid. The Synthesis of 11β,17-Dihydroxy-3,20-dione-1,4-pregnadien-21-yl 2-Acetamido-2-deoxy-β-D-glucopyranoside[1]

Sir:

When cortisone is used in the treatment of inflammation, a number of effects also occur which are undesirable in this therapy, such as negative nitrogen balance, osteoporosis, adrenal atrophy, formation of ulcers, and retention of sodium chloride. Numerous synthetic steroids have been prepared[2] in an attempt to obtain a therapeutically active drug which will not cause these side effects. However, mineralocorticoid activity is the only effect, undesired in antiinflammatory therapy, which has been dissociated.

It seemed possible to reduce all of these side effects if an inactive steroid could be prepared which is preferentially converted into an active drug at the site of its therapeutic action.

Connective tissue has an active metabolism of hyaluronic acid.[3] An indication of higher activity of β-D-glucuronidase in the synovial fluid of joints from patients with rheumatoid arthritis than in liver was given by Bollet.[4] Very recently a striking increase

(1) The authors are indebted to Drs. G. Boxer and K. Meyer for many stimulating discussions.
(2) L. H. Sarett, A. A. Patchett, and S. L. Steelman, *Fortschr. Arzneimittelforsch.*, **5**, 11 (1963).
(3) See, *e.g.*, E. Buddecke, *Angew. Chem.*, **72**, 663 (1960).
(4) A. J. Bollet, J. F. Goodwin, and A. K. Brown, *J. Clin. Invest.*, **38**, 451 (1959).