isotope shift in dipole moment of this related molecule. Using this assumption, the polarizability anisotropy, $\alpha_{zz} - \alpha_{xx}$, is calculated to be $1.85 \pm 0.05 \times 10^{-24}$ cm.^{3}. Here z refers to the molecular axis and x to a perpendicular axis. This value may be compared with the result[6] 2.27×10^{-24} cm.^{3} obtained rather indirectly from Kerr effect data, refractive indices, etc.

The rotational constant obtained here is $B_0 = 29{,}725.3 \pm 0.1$ Mc., or $B_0 = 0.991527 \pm 0.000003$ cm.$^{-1}$. This agrees with the infrared value[7] of 0.99156 ± 0.00004 cm.$^{-1}$ within the quoted error.

(6) K. G. Denbigh, *Trans. Faraday Soc.*, **36**, 936 (1940).

(7) W. J. Lafferty, E. K. Plyler, and E. D. Tidwell, *J. Chem. Phys.*, **37**, 1981 (1962).

(8) American Chemical Society–Petroleum Research Fund Fellow, 1963–1964.

(9) Alfred P. Sloan Foundation Fellow, 1964.

DEPARTMENT OF CHEMISTRY
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

J. S. MUENTER[8]
V. W. LAURIE[9]

RECEIVED JULY 27, 1964

Hydrogen Abstraction by the Triplet State of Benzophenone[1]

Sir:

The ability of the triplet stage of benzophenone to abstract hydrogen from suitable substrates is well

$$(C_6H_5)_2\dot{C}\text{–}\dot{O} + RH \longrightarrow (C_6H_5)_2\dot{C}\text{–}OH + R\cdot \quad (1)$$

known and recognized as a critical step in the photoreduction of benzophenone.[2] The rate of (1) for various substrates has been estimated by Hammond[3] and by Porter[4] by competitive quenching experiments, although there are some large discrepancies between the two sets of results.

We have been interested in these hydrogen abstraction processes as a method of comparing the reactive properties of triplet states of ketones with those of simple alkoxy radicals. We have employed competitive techniques in which the relative rates of attack on two substrates are compared directly by measuring their relative rates of disappearance when irradiated with benzophenone.

We find that even simple aliphatic hydrocarbons[5] are readily attacked to yield radicals which undergo their expected reactions. In the presence of cyclohexane benzophenone is reduced to benzpinacol, and the cyclohexyl radicals largely dimerize. If CCl_4 is added, cyclohexyl chloride is produced in high yield, together with C_2Cl_6, while addition of benzene gives roughly equal quantities of cyclohexylbenzene and bicyclohexyl. Similarly 2,3-dimethylbutane–CCl_4 gives 2-chloro-2,3-dimethylbutane and 1-chloro-2,3-dimethylbutane in a ratio of 50–5000:1.

Competitive experiments, carried out essentially as in our *t*-butyl hypochlorite work,[6] yield the preliminary relative reactivities shown in Table I. Unless indicated, 4 *M* benzophenone solutions in benzene, 0.1–0.4 *M* in each substrate, were irradiated at 20° through a Nonex filter and sampled periodically for gas chromatographic analysis. For comparison, Hammond[3] reports a relative reactivity cumene:toluene of 3.5, but Porter[4] gives 2-propanol:toluene of only 1.2. However, the two groups differ in their rate constant for the toluene reaction by a factor of 50.[7]

TABLE I
COMPETITIVE HYDROGEN ABSTRACTION EXPERIMENTS

Substrate	Relative reactivity[a] $C_6H_5\dot{C}\text{–}O$	Relative reactivity[a] $t\text{-}C_4H_9O\cdot$ (40°)[6]
Toluene (std.)	1.0	1.0
Cyclohexane	2.1 ± 0.06	6.0
Cumene	3.4 ± 0.2	2.8
2-Propanol	9.3 ± 0.4	..
2-Octanol	9.9 ± 0.6	..
Mesitylene	5.5 ± 0.3	4.1
m-Xylene	3.0 ± 0.2	2.34
p-Fluorotoluene	1.15 ± 0.06	..
p-Chlorotoluene	0.97 ± 0.02	0.71
Anisole	0.50 ± 0.03	..

[a] Experimental errors indicate spread of several determinations.

Our results indicate a reactivity of the benzophenone triplet qualitatively similar to that of the *t*-butoxy radical. However, the reaction appears somewhat more sensitive to the strength of the R–H bond being attacked since cyclohexane is less reactive relative to toluene and (as noted above) a very high $t:p$ selectivity is observed with 2,3-dimethylbutane. The benzophenone triplet also appears to attack selectively points of high electron availability: the substituted toluene data indicate a negative σ-value for the reaction, α-hydrogens of alcohols are particularly reactive, and no photoreduction is produced by solvents such as acetic acid which have weak C–H bonds but strongly electron-withdrawing groups.

An estimate of the energetics of the hydrogen abstraction reaction is of interest and can be obtained from the following thermodynamic cycle which yields the strength of the $(C_6H_5)C\dot{O}$–H bond.

$$(C_6H_5)_2CHOH \longrightarrow (C_6H_5)_2C{=}O + H_2 \qquad +9 \text{ kcal.} \quad (2)$$

$$(C_6H_5)_2C{=}O \longrightarrow (C_6H_5)_2\dot{C}\text{–}\dot{O} \qquad +69 \text{ kcal.} \quad (3)$$

$$H\cdot + (C_6H_5)_2\dot{C}\text{–}OH \longrightarrow (C_6H_5)_2CHOH \qquad -80 \text{ kcal.} \quad (4)$$

$$H_2 \longrightarrow 2H\cdot \qquad +104 \text{ kcal.} \quad (5)$$

$$(C_6H_5)_2\dot{C}\text{–}OH \longrightarrow (C_6H_5)_2\dot{C}\text{–}\dot{O} + H\cdot \qquad +102 \text{ kcal.} \quad (6)$$

The energetics of (2) and (5) are available from standard thermochemical tables, (3) comes from spectral data,[8] while (4) is estimated as a maximum value of the exothermicity of the reaction assuming that the resulting bond is no stronger than that for the benzyl hydrogens of toluene.[9] The resulting bond strength (6) is thus a minimum value. Comparison with $D(t\text{-}C_4H_9O\text{–}H) =$

(1) Support of this work by a grant from the National Science Foundation is gratefully acknowledged.

(2) For general discussion and references, *cf.* G. S. Hammond and N. Turro, *Science*, **142**, 1541 (1963).

(3) G. S. Hammond, W. P. Baker, and W. M. Moore, *J. Am. Chem. Soc.*, **83**, 2795 (1961).

(4) A. Beckett and G. Porter, *Trans. Faraday Soc.*, **59**, 2038 (1963).

(5) The photoreduction of acetone in cyclohexane was reported some time ago [N. C. Yang and D. H. Yang, *J. Am. Chem. Soc.*, **80**, 2913 (1958)]. Very recently photoreduction of substituted benzophenones in cyclohexane has also been described [G. Porter and P. Suppan, *Proc. Chem. Soc.*, 191 (1964)].

(6) C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, **82**, 6108 (1960), and subsequent papers.

(7) Actually, a large part of the difference arises from different assumptions as to the rate of diffusion-controlled quenching in these systems and does not represent an experimental discrepancy.

(8) G. S. Hammond and J. Saltiel, *J. Am. Chem. Soc.*, **84**, 4983 (1962).

(9) D(benzyl-H) is still in question. The value chosen is an arbitrarily weighted average of those reported and is probably uncertain to at least 3 kcal.

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.

DEPARTMENT OF CHEMISTRY
HAVEMEYER HALL
COLUMBIA UNIVERSITY
NEW YORK, NEW YORK 10027

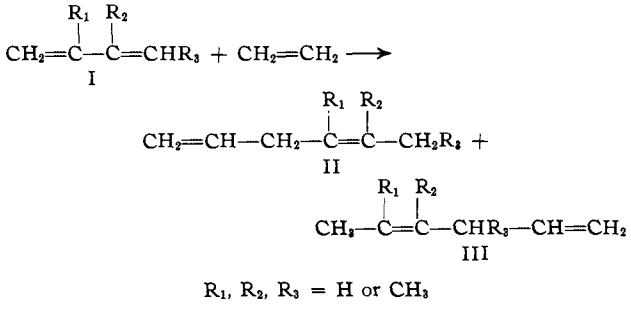
CHEVES WALLING
MORTON J. GIBIAN[11]

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).

BASIC RESEARCH LABORATORIES
TOYO RAYON CO., LTD.
KAMAKURA, JAPAN

GO HATA

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).