cooled to 10°. A cold solution of 0.71 g. of potassium permanganate in 70 ml. of water then was added and the mixture was allowed to warm up to room temperature. After 3.5 hours at room temperature the mixture was filtered through Super-cel and the precipitate was washed well with water. The filtrate was acidified to congo red and the product was filtered, washed with water and dried over sulfuric acid. The crude product, obtained in 94% yield, contained an amorphous impurity. After recrystallization from high-boiling petroleum ether it weighed 0.65 g. (68%) and melted at 106.5–109.5°.

6-Propyl-7-hydroxy-5,8-quinolinequinone (VI) was converted to the phenazine derivative with *o*-phenylenediamine by the procedure used for II (above). The yield was the same. After recrystallization from benzene this phenazine had no definite melting point; it gradually decomposed above 240° and became black at about 250° without melting.

*Anal.* Calcd. for $C_{18}H_{15}NO_3$: C, 74.72; H, 5.23. Found: C, 74.80, 74.90; H, 5.09, 5.04.

**Mannich Reactions.**—To a suspension of 0.025 mole of I in 30 ml. of absolute alcohol a 10% excess of amine was added with cooling. When solution was complete, 2.1 ml. of 40% formaldehyde solution was added with stirring at 5–10°. The reaction then was allowed to continue overnight at room temperature although it appeared to be essentially complete in about 4 hours. The crystalline products, which precipitated from the reaction mixture, melted no more than 2° below the melting points of the purest samples. The diethylamino derivative VIII, however, was best isolated after the addition of anhydrous ether to the suspension; the product was washed well with ether and purified by dissolving in methanol at about 40° and precipitating with anhydrous ether. The hexylamino compound X also was recrystallized from this solvent mixture and the piperidino derivative IX from 95% ethanol and ether. Both VIII and IX were very soluble in water, but the hexylamino compound X was insoluble. The piperidino derivative was slightly hygroscopic. Compound VIII was orange; compounds IX and X were deep red.

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# NOTES

## The Solubility of DDT in Water Determined Radiometrically

BY FRANK H. BABERS

RECEIVED MAY 18, 1955

The solubility of DDT in water has been given by Gauvadan and Poussel[1] as approaching 0.1 p.p.m. at 18°, by Roeder and Weiant[2] as between 0.1 and 0.01 p.p.m., and by West and Campbell[3] as "practically insoluble." Gauvadan and Poussel used a nephelometric method, and Roeder and Weiant used for their calculations the time required for the appearance of symptoms of DDT poisoning in the ventral nerve cord of a roach following treatment with saline-saturated solutions of DDT.

Recently in connection with experiments on the physiological action of DDT on insects, the insecticide labeled with carbon-14 has become available. Because of its physiological interest and the paucity of data on the subject, the water solubility of the material has been determined at three temperatures by radiochemical methods.

### Experimental

A solution of the radioactive DDT was prepared by dissolving 3.046 mg. in 2 ml. of acetone. 300 Microliters were transferred to a 100-ml. flask and the acetone evaporated at room temperature. Water redistilled from glass was added and the flask heated on a steam-bath with shaking for 1 hour. After cooling somewhat, the flask was put in a constant-temperature bath and shaken for at least 1 week. Samples were then removed and centrifuged at the bath temperature, a portion was filtered through a fine sintered-glass funnel, and aliquots of each portion were taken for analysis. To 1 ml. of acetone containing 1 mg. of non-radioactive DDT in an aluminum counting cup 0.5 ml. of the water solution of radioactive DDT was added, and most of the solvent was evaporated with an infrared lamp. One milliliter of acetone was then added, followed by a second 0.5-ml. portion of the DDT–water solution. The sample was then evaporated to dryness and its radioactivity determined in a proportional counter.

The solubility results were not altered by filtration through sintered glass. At least 10 replications were made and the results compared with the activity obtained from 10 samples of known size. Because of the reproducibility of the results, correction for self absorption was not made. Each preparation was about 0.35 mg./cm.$^2$ in thickness. From the results of these experiments, the solubility of DDT in water is 5.9 ± 0.4 micrograms per liter (0.0059 ± 0.0004 p.p.m.) at 2°, 37.4 ± 0.5 micrograms (0.0374 ± 0.0005 p.p.m.) at 25°, and 45 ± 1 micrograms (0.045 ± 0.001 p.p.m.) at 37.5°.

It was found that in very thin layers and microgram qualities DDT is appreciably volatile at room temperatures. This became apparent in preliminary experiments when after 17 samples to which non-radioactive DDT had not been added had been counted, the background of the counting chamber had risen from 59 counts per minute at the start to 311 at the end due to contamination. By the addition of non-radioactive DDT, the sample size was greatly increased and at the same time, the percentage of active DDT decreased so that no further contamination was noted.

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(1) P. Gauvadan and H. Poussel, *Compt. rend.*, **224**, 683 (1947).

(2) K. D. Roeder and E. A. Weiant, *Science*, **103**, 304 (1946).

(3) T. F. West and G. A. Campbell, "DDT and Newer Persistent Insecticides," 2nd Ed. rev., Chapman and Hall, Ltd., London, 632 pp. (1950).

(4) The radioactive material used in these experiments was procured under the authority of the United States Atomic Energy Commission.

## The Uncatalyzed Thermal Addition of Formaldehyde to Olefins

BY NEAL O. BRACE

RECEIVED DECEMBER 10, 1954

The uncatalyzed thermal addition of formaldehyde (from paraformaldehyde) to dialkyl-substituted terminal olefins such as diisobutylene,[1] $\beta$-pinene[2] and methylenecyclohexane,[3] or to an alkyl-

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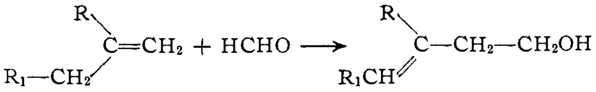
(1) J. J. Ritter, U. S. Patent 2,335,027; *C. A.*, **38**, 2662 (1944).

(2) J. P. Bain, THIS JOURNAL, **68**, 638 (1948).

(3) R. T. Arnold and J. F. Dowdall, *ibid.*, **70**, 2590 (1948).

aryl-substituted olefin such as α-methylstyrene[4] gives a high yield of the terminal carbinol.



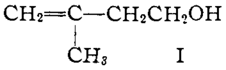
R = alkyl or aryl group; $R_1$ = H or alkyl[5]

We have studied this reaction with isobutylene itself, and with other types of methyl or *n*-alkyl-substituted olefins.[6,7]

When propylene was heated with paraformaldehyde or *s*-trioxane under various conditions no reaction occurred, or only tar and low boiling side-products were obtained. In contrast, anhydrous 99% polymeric formaldehyde gave a moderate yield of distillable product from which 3-buten-1-ol and its formate ester were isolated in about 11% yield.

Likewise, isobutylene gave 3-methyl-3-buten-1-ol (I) in yields of 25–31% as primary condensation product, as well as higher-boiling formals, esters and diols. These reactions, however, required the use of equipment suitable for high pressures (200–1000 atm.).

The products I and II of successive formaldehyde additions still have an "isobutylene-like" structure with which further addition of formaldehyde may occur. Thus, a single reaction mixture gave I in 20% yield and II[7] in 9% yield by direct distillation.



$CH_2{=}C(CH_3)CH_2CH_2OH$

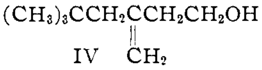
I

$CH_2{=}C(CH_2CH_2OH)_2$

II

$C_{15}H_{31}CH{=}CHCH_2CH_2OH$

III



$(CH_3)_3CCH_2C({=}CH_2)CH_2CH_2OH$

IV

$(CH_3)_3CCH{=}C(CH_2CH_2OH)_2$

V

Acid-catalyzed formaldehyde-exchange of another higher-boiling residue with methanol to distil out volatile methylal and give the free alcohols also afforded II, as well as a higher-boiling mixture of alcohols.

Since formaldehyde is used up in side reactions, such as conversion to formic acid and methanol and is also combined as formal, a high isobutylene to formaldehyde ratio favors higher yields of I, and gives smaller amounts of the high-boiling products. Other conditions such as reaction time and temperature also affect the relative yields of these products.

Thus, 3-hour heating at 200° (544 to 280 atm.) of 3.5 moles of isobutylene (in each case) and 2.5 moles of formaldehyde gave 27% of I and 24.0 g. of liquid higher-boiling residue, while the same quantities when heated at 170° for seven hours (342 to 221 atm.) gave 25% of I and 15.5 g. of higher boiling liquid. Reaction at 225° for two hours with 3.0 moles of formaldehyde (885–850 atm.) gave only 7.8% of I and 70 g. of residue. At 200°, four hours heating with 3.0 moles formaldehyde at 646–323 atm. pressure gave 31% of I and 50.8 g. higher-boiling liquid. Longer heating of 3 *M* amounts of each at lower temperature (*i.e.*, 13 hours at 170°; 16.6% yield I, 22.0 g. of liquid residue) or progressive heating of 3.5 *M* amounts for one hour each at 160, 170, 180, 190 and 200° (27% of I, 24.0 g. of residue) did not improve the conversion to I.

Octadecene-1 was converted to 3-nonadecen-1-ol (III) (and formate ester) having the *trans* structure according to its infrared spectrum.[8] This would be expected from the mode of addition of formaldehyde suggested by Arnold and Dowdall[3] where attack occurs at an α-methylenic group and a carbon atom of the double bond which is furthest removed from this methylene group. The steric requirement of a large R group may be responsible for the resulting *trans* structure.

Whereas Ritter[1] designated the product from diisobutylene and paraformaldehyde as "diisobutenylcarbinol," having the structure (in appended claims) of $(CH_3)_3CCH{=}C(CH_3)CH_2CH_2OH$, Arundale and Mikeska[6] show IV as structure for this product.[9] Infrared absorption spectrum of the product obtained in this work showed a preponderance of terminal olefinic alcohol (strong band at 11.25 μ), while very weak bands at 11.6 and 12.15 μ may have been due to the presence of smaller amounts of the compound possessing the internal double-bond structure. The major product was therefore IV.

A higher-boiling product formed by further addition of formaldehyde to IV also was isolated. Physical properties, infrared spectrum and analysis are consistent with structure V.

Other olefins of varying structure including cyclohexene, α-pinene, 10-hendecenoic acid and methyl oleate were found to react when heated with anhydrous polymeric formaldehyde at 200–225° to give mixtures of carbinol(s) and formate esters. The detailed structures of these products were not ascertained. Bain[2] reported no reaction occurred when α-pinene was heated with paraformaldehyde at 180°.

## Experimental

**Formaldehyde and Propylene.**—In a 440-ml. silver-lined pressure bomb was placed 120 g. (4 moles) of anhydrous 99% polymeric formaldehyde (contained less than 0.10% water and 0.05% acid) and 168 g. (4 moles) of propylene condensed in with Dry Ice cooling. The bomb was sealed and heated while shaking to 235° (autogenous pressure 1035 atm.), and continued for four hours up to 246°. Upon cooling and discharge of volatile gases, 126 g. of liquid product remained. A column having an efficiency of about 20 plates (column A), operated at a reflux ratio of 10/1, was used to separate the liquid fractions.

Methyl formate, b.p. 30–35°, $n^{25}D$ 1.3415, 28.6 g.; methylal and methanol in small amounts were separated. An intermediate fraction, b.p. 70–106, $n^{25}D$ 1.4059, 14.9 g., contained water and 3-buten-1-ol formate. The latter compound and 3-buten-1-ol distilled at 103–108°, $n^{25}D$ 1.4085, 25.0 g. 3-Buten-1-ol alone, b.p. 42–65° (33–20 mm. press.), $n^{25}D$ 1.4187, 4.3 g., next was obtained for a combined yield of 11% on formaldehyde used. Several higher boiling fractions with increasing refractive indices were separated, but were not identified, since they were evidently mixtures of formals, formate esters and alcohols as indicated by infrared spectra.

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[4] T. R. Steadman, U. S. Patent 2,666,795.

[5] In the case of the cyclic compounds R and $R_1$ are part of the same ring.

[6] See E. Arundale and A. Mikeska, *Chem. Rev.*, **51**, 505 (1952), for review of olefin–formaldehyde reactions.

[7] See A. T. Blomquist and J. A. Verdol, THIS JOURNAL, **77**, 78 (1955), for the reaction of isobutylene with paraformaldehyde in acetic acid–acetic anhydride solution.

[8] R. E. Kitson, *Anal. Chem.*, **25**, 1470 (1953).

[9] *Cf.* A. T. Blomquist and J. C. Westfahl, THIS JOURNAL, **74**, 4073 (1952), for products obtained from diisobutylene and paraformaldehyde in glacial acetic acid.

The 3-buten-1-ol and formate-containing fractions (44.0 g.) were combined, dried over calcium sulfate and distilled in column A. Fraction I, b.p. 76–104.5°, 14.3 g., contained a little water; II, b.p. 105–111°, 17.0 g., $n^{25}$D 1.4078, was mostly 3-buten-1-ol formate [literature[10] b.p. 112–113°]; while III, b.p. 111.5–113°, $n^{25}$D 1.4160, $n^{20}$D 1.4182, 4.5 g. was mostly 3-buten-1-ol [literature[10,11] b.p. 112.5–113.5°, $n^{20}$D 1.4200, $n^{25}$D 1.4189].

3-Buten-1-ol was obtained essentially free from ester by alkaline saponification of the crude product from another reaction. The compound distilled at 111–113.5°, $n^{25}$D 1.4155; its infrared spectrum was identical to 3-buten-1-ol prepared by the reaction of gaseous formaldehyde with allylmagnesium chloride.[12,13]

The yield of the desired compound was not increased in experiments where longer reaction times at lower temperature (20 hours at 200°) or sodium bicarbonate or copper powder as catalyst were tried.

**Formaldehyde and Isobutylene.**—Reaction of paraformaldehyde and isobutylene in equimolar amounts at 200° for four hours gave in low yield a complex mixture containing only a small amount of I. In separate experiments activated alumina and di-*t*-butyl peroxide were tried as catalysts. Using 99% anhydrous polymeric formaldehyde, the yield of I was not higher than 31%.

A detailed examination of all the distillable products of the reaction was desired. A liquid product of 155 g. obtained from reaction of 3 *M* amounts at 200° for 5.5 hours was fractionated under reduced pressure in column A. The alcohol and formate ester fractions, b.p. 57–70° (52 mm.), 63.5 g., were combined, dried over calcium oxide and refractionated.

A mixture of I and its formate ester distilled at 126.5–130°, $n^{20}$D 1.4280 to 1.4323, 25.4 g. Compound I had b.p. 130.5°, $n^{20}$D 1.4330, $n^{25}$D 1.4312; 26.5 g. (reported[6] b.p. 130°, $n^{20}$D 1.4329). Infrared spectra of these fractions indicated a terminal olefinic bond (strong band at 11.25 $\mu$). That of I showed nearly complete absence of the carbonyl band at 5.75 $\mu$.

The material, b.p. above 70° (52 mm.), was separated into several fractions. The major constituent, obtained as fractions, b.p. 124–128° (10.0 mm.), $n^{25}$D 1.4713, 10.0 g., and 133–140° (10 mm.), $n^{25}$D 1.4742, 9.1 g., was primarily 3-methylene-1,5-pentanediol II (reported[7] b.p. 110–111° (0.5–0.8 mm.), $n^{20}$D 1.4785) contaminated with some formate ester (yield 9% as monoformate based on formaldehyde charged). Infrared spectra showed strong hydroxyl group absorption at 3.0 $\mu$, carbonyl absorption at 5.75 $\mu$, and strong double bond ($>C{=}CH_2$) absorption at 6.05 and 11.25 $\mu$.

*Anal.* Calcd. for $C_6H_{12}O_2$: C, 62.05; H, 10.41; hydroxyl no., 968. Found: C, 62.2; H, 9.85; hydroxyl no., 624; ester no., 107.

Formaldehyde exchange of the products boiling above 130° at atm. press. with acid in the presence of methanol to distil out volatile methylal and methyl formate was done with a typical residue, in order to determine the amount of combined formaldehyde and obtain the hydroxy compounds present pure if possible. A mixture of 111 g. of residue ($n^{25}$D 1.4600, b.p. above 130°, hydroxyl no. 245, ester no. 33, acid no. 1.9), 100 g. of methanol and 1.0 cc. of concentrated sulfuric acid was heated under an 8-inch packed column with a variable take-off head. Methylal distilled at 40–46° at high reflux (25 cc., 21.8 g., 0.29 mole); then a mixture of methylal and methanol, b.p. 35.5–60° (22 cc.). The residual liquid was neutralized with calcium carbonate and the methanol distilled off.

Fractionation of the remainder (80 g.) gave a number of fractions. Among the compounds identified was II, b.p. 125–132° (10 mm.), $n^{25}$D 1.4714, with an infrared spectrum identical to authentic II, prepared by the method of Blomquist and Verdol.[7]

A higher boiling mixture, b.p. 145–154° (2.5 mm.), $n^{25}$D 1.4770–1.4800, also was obtained which was converted to acetate esters, but could not be characterized satisfactorily.

**Formaldehyde and 1-Octadecene.**—Octadecene-1 (252.5 g., 1 mole) and anhydrous polymeric formaldehyde (30.0 g., 1 mole) were heated in a 440-cc. bomb at 226–251° for six hours. Pressure was less than 12 atm. The liquid product, wt. 256 g., was analyzed; found, 0.119% water, hydroxyl no. 28.8, ester no. 49.6, acid no. 2.2. It was distilled through an 8-inch Heli-grid packed column under reduced pressure to give 173 g. (0.70 mole) of recovered octadecene-1, and 49.2 g. of white solid 3-nonadecene-1-ol and formate, b.p. 179–195° (7.0 mm.) and 162–175° (1.0–2.5 mm.) in three fractions.

*Anal.* Calcd. for $C_{19}H_{38}O$ (alcohol): C, 80.81; H, 13.56; hydroxyl no., 198. Calcd. for $C_{20}H_{38}O_2$ (formate ester): C, 77.5; H, 12.3; ester no., 180. Found, C, 79.3; H, 13.1; hydroxyl no., 85; ester no., 85 (first fraction) and C, 81.0; H, 12.8; hydroxyl no., 106; ester no., 30.0 for last fraction.

The yield of alcohol and ester calculated from the hydroxyl and ester numbers was 0.087 mole carbinol and 0.079 mole ester or 87% on the octadecene-1 used up and 25% on the formaldehyde charged. Infrared analysis showed hydroxyl (band at 3.0 $\mu$) ester group (band at 5.75 $\mu$) and *trans*-RCH=CHR (band at 10.36 $\mu$ and *not* at 11.25 $\mu$) groups present.

**Formaldehyde and Diisobutylene.**—Reaction of 224 g. (2 moles) of diisobutylene (b.p. 102°) and 60 g. (2 moles) of anhydrous polymeric formaldehyde at 200° for six hours gave 266 g. of liquid product.

Distillation gave 32.7 g. of methanol and diisobutylene, b.p. 58–101.5°, $n^{25}$D 1.4622; diisobutylene, b.p. 101.5–102°, 132.0 g. (54.2% recovery); and IV, b.p. 71–74° (7.0 mm.), and 78–85° (8.0 mm.), $n^{25}$D 1.4455, 58.1 g. (a yield of 66% based on diisobutylene used).

*Anal.* Calcd. for $C_9H_{18}O$: C, 76.0; H, 12.7; hydroxyl no., 395. Found: C, 75.3; H, 12.3; hydroxyl no., 325; ester no., 25.0. The product contained about 7.6% 3-neopentyl-3-buten-1-ol formate.

Fractionation of the higher boiling liquid gave the diol V, b.p. 135–144° (8.0 mm.), $n^{25}$D 1.4620, 12.1 g., together with some formate ester, as indicated by the infrared spectrum and analysis.

*Anal.* Calcd. for $C_{10}H_{20}O_2$: C, 69.8; H, 11.7. Found: C, 69.4; H, 11.3.

**Formaldehyde and Other Olefins.**—Cyclohexene, $\alpha$-methylstyrene, $\alpha$-pinene, 10-hendecenoic acid and methyl oleate were heated individually in equimolar amount with anhydrous polymeric formaldehyde. In each case, reaction did occur as shown by functional group analysis and distillation of the liquid products. The products isolated by distillation had infrared spectra and analyses which showed that a mixture of olefinic ester and alcohol was obtained in each case.

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[10] M. H. Palomaa and A. Juvala, *Ber.*, **61B**, 1770 (1928).

[11] E. D. Amstutz, *J. Org. Chem.*, **9**, 310 (1944); *cf.* Ou Kiun-Houo, *Ann. chim.*, **13**, 175 (1940), and S. F. Birch and D. T. McAllan, *J. Chem. Soc.*, 2556 (1951).

[12] M. S. Kharasch and C. F. Fuchs, *J. Org. Chem.*, **9**, 359 (1944).

[13] H. Pariselle, *Ann. chim. phys.*, [8] **24**, 315 (1911).

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## The Reaction of Cortisol 21-Acetate with Lead Tetraacetate[1]

BY SHLOMO BURSTEIN AND RALPH I. DORFMAN

RECEIVED APRIL 4, 1955

In previous publications the occurrence of hydroxylated derivatives of cortisol (hydrocortisone) in guinea pig and in human urine[2-4] has been described. In an attempt to synthesize derivatives of cortisol hydroxylated at C-2 for comparison with unidentified steroids isolated from urine, the reaction of cortisol 21-acetate[5] with lead tetraacetate was studied. Although Rosenkranz, *et al.*,[6] pro-

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[1] This work was supported in part by Research Grant No. NSF-G664, National Science Foundation.

[2] S. Burstein and R. I. Dorfman, *J. Biol. Chem.*, **213**, 581 (1955).

[3] S. Burstein, R. I. Dorfman and E. M. Nadel, *ibid.*, **213**, 597 (1955).

[4] S. Burstein, R. I. Dorfman and E. M. Nadel, *Arch. Biochem. and Biophys.*, **53**, 307 (1954).

[5] Thanks are due to Dr. K. Pfister for the gift of cortisol acetate.

[6] G. Rosenkranz, O. Mancera and F. Sondheimer, THIS JOURNAL, **77**, 145 (1955).