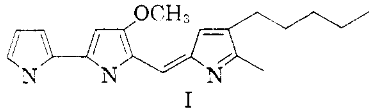
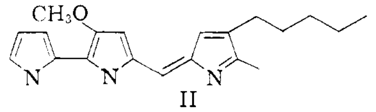
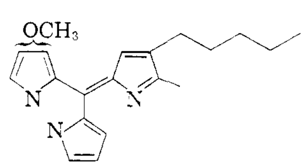


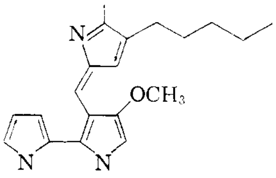
I



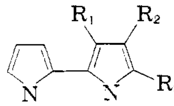
II



III



IV



	R_1	R_2	R_3
V	H	H	H
VI	H	OCH_3	$COOC_2H_5$
VII	H	OCH_3	CHO
VIII	OCH_3	H	$COOCH_3$
IX	OCH_3	H	CHO

methoxypyrrole-2-carboxylic acid, which was decarboxylated to ethyl 4-methoxypyrrole-3-carboxylate (m.p. 107–109°), identical with material prepared from ethyl 1-ethoxycarbonyl-4-methoxy-Δ^3-pyrroline-3-carboxylate.[7]

Condensation of Δ^1-pyrroline with ethyl 3-methoxypyrrole-2-carboxylate gave ethyl 3-methoxy-5-(2′-pyrrolidinyl)-pyrrole-2-carboxylate which was dehydrogenated to ethyl 4-methoxy-2,2′-bipyrrole-5-carboxylate (VI), m.p. 214° (found: C, 61.2; H, 6.2). With hydrazine, VI formed a hydrazide, whose tosylate was heated with sodium carbonate to give 4-methoxy-2,2′-bipyrrole-5-carboxaldehyde (VII), m.p. 265° dec. (found: C, 63.5; H, 5.6); $\lambda_{\max}^{\text{MeOH}}$ 251 mμ (ϵ 14,700), 361 (40,300). This compound appears identical with the natural prodigiosin precursor, reported[6] m.p. > 250°; $\lambda_{\max}^{\text{EtOH}}$ 254 mμ (ϵ 13,000), 363 (35,000). 2-Methyl-3-amylpyrrole[3d] and VII in methanolic hydrochloric acid[5] produce a deep red solution of the hydrochloride of I. Chromatography of the free base (I) on alumina gave a pure sample of synthetic prodigiosin whose infrared as well as ultraviolet and visible spectra under both acidic and alkaline conditions were identical with those of natural prodigiosin.[10,11]

Synthesis of the isomeric prodigiosin II proceeded in a similar sequence from methyl 4-methoxypyrrole-2-carboxylate,[7] m.p. 86° (found: C, 54.2; H, 6.0; OCH_3, 39.9). Condensation with Δ^1-pyrroline gave methyl 4-methoxy-5-(2′-pyrrolidinyl)-pyrrole-2-carboxylate which was dehydrogenated to methyl 3-methoxy-2,2′-bipyrrole-5-carboxylate (VIII), m.p. 178° (found: C, 60.2; H, 5.5; N, 12.8; OCH_3, 28.0). This was converted to the isomer of the prodigiosin precursor, 3-methoxy-2,2′-bipyrrole-5-carboxaldehyde (IX), m.p. 186° (found: C, 63.3; H, 5.5); $\lambda_{\max}^{\text{MeOH}}$ 236 mμ (ϵ 12,400), 386 (26,800). Condensation of IX with 2-methyl-3-amylpyrrole gave II. In acid solution prodigiosin (I) absorbs at 535 mμ while the isomer II has its maximum at 585 mμ.

---

[10] We are indebted to Dr. M. C. Bachman of the Commercial Solvents Corporation for a sample of natural prodigiosin.

[11] The demonstration of a pyrryldipyrrylmethene nucleus for prodigiosin eliminates the one postulated, natural occurrence of a tripyrrylmethene and thus removes any support such an occurrence might give to the intermediacy of a tripyrrylmethene in porphyrin biosynthesis [D. Shemin, C. S. Russel, and T. Abramsky, *J. Biol. Chem.*, **215**, 613 (1955)]. However, prodigiosin now becomes the second natural substance containing a 2,2′-dipyrrole skeleton, vitamin B_{12} being the other [R. Bonnett, J. R. Cannon, V. M. Clark, A. W. Johnson, L. F. J. Parker, E. L. Smith and A. Todd, *J. Chem. Soc.*, 1158 (1957)].

[12] Public Health Service Predoctoral Research Fellow of the National Heart Institute.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA
H. RAPOPORT
K. G. HOLDEN[12]

RECEIVED JULY 20, 1960

ALTERNATING COPOLYMERS OF DIMETHYLKETENE WITH KETONES

Sir:

High polymers in which the monomeric units are, at least in part, originated by the opening of the carbonyl bond of a ketone were not known up to now.

During our work on the polymerization of cumulative double bonds, we have found that by direct polymerization of mixtures of dimethylketene and acetone in the presence of lithium alkyls it is possible to obtain in good yields macromolecular products containing both monomers.

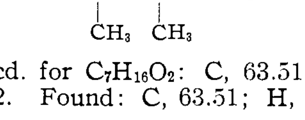
By adding, at −60°, 1.4 millimoles of butyllithium to a solution of dimethylketene (8 g.) and acetone (8 g.) in toluene (20 ml.), rapid polymerization takes place. After precipitation with methyl alcohol, 8 g. of a white solid polymer (I) is isolated. This product shows an intrinsic viscosity in chloroform at 30° of approximately 0.4, is soluble in boiling benzene and dioxane, and proves to be highly crystalline on X-ray examination. This result indicates that the polymer possesses a high regularity of structure.

The analysis of (I) demonstrates that dimethylketene and acetone are present in a molar ratio of 1:1.

Anal. Calcd. for $C_4H_6OC_3H_6O$: C, 65.60; H, 9.44. Found: C, 65.98; H, 9.55.

After reduction of the polymer, dissolved in tetrahydrofuran, with $LiAlH_4$, we have isolated in good yields (78%) a product (II) having m.p. 138–140°.

Composition analysis and molecular weight of (II) agree with the formula

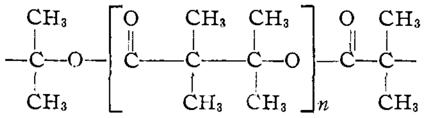


$$HO-\underset{CH_3}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}}-\underset{CH_3}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}}-CH_2OH$$

Anal. Calcd. for $C_7H_{16}O_2$: C, 63.51; H, 12.18; mol. wt., 132. Found: C, 63.51; H, 12.12; mol. wt., 138.

The structure of this glycol also has been confirmed by comparison with the product obtained by reduction of tetramethyl-β-propiolactone with $LiAlH_4$.

The results of the reduction of (I) indicate that it consists of an alternating copolymer of the two monomers, having the chemical structure



$$-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-\text{O}-\left[\overset{\text{O}}{\overset{\|}{\text{C}}}-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-\text{O}\right]_n-\overset{\text{O}}{\overset{\|}{\text{C}}}-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-$$

The presence of ester groups is also confirmed by a strong absorption band at 5.80 μ.

Polymerization of mixtures containing acetone and dimethylketene in molar ratios higher than one always leads to the product described above.

Starting from mixtures in which dimethylketene prevails, some homopolymer of this monomer is present in the polymerizate.

When polymerizing mixtures of dimethylketene and acetophenone, an alternating copolymer also is produced which, however, proves to be amorphous on X-ray examination.

It is known that by treating ketenes with ketones in the presence of Friedel-Crafts catalysts, β-lactones are obtained.[1] Some β-lactones, such as β-propiolactone and β-butyrolactone, yield polyesters on heating.[2] We have observed, however, that under the same conditions tetramethyl-β-propiolactone loses quantitatively carbon dioxide. Even in the presence of lithium alkyls, this lactone does not yield a polyester. These results demonstrate that the alternating copolymerization of dimethylketene with acetone does not take place through successive reactions, with formation of a β-lactone as a stable intermediate product.

(1) H. J. Hagemeyer, Jr., *Ind. Eng. Chem.*, **41**, 765 (1949).

(2) T. L. Gresham, J. E. Jansen and F. W. Shaver, THIS JOURNAL, **70**, 998 (1948).

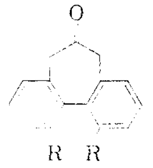
ISTITUTO DI CHIMICA INDUSTRIALE GIULIO NATTA
POLITECNICO DI GIORGIO MAZZANTI
MILANO GIANFRANCO PREGAGLIA
MILANO, ITALY MARCO BINAGHI

RECEIVED SEPTEMBER 5, 1960

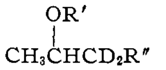
ON THE MAGNITUDE OF POSSIBLE STERIC SECONDARY KINETIC DEUTERIUM ISOTOPE EFFECTS: (+)-(S)-2-PROPANOL-1-d_3

Sir:

It has been suggested[1] that some secondary deuterium isotope effects may to an important degree be accounted for by changes in non-bonded interaction due to differences in vibrational amplitudes of hydrogen and deuterium. A direct and sensitive test of differential non-bonded interaction is available in the partial asymmetric Meerwein–Ponndorf–Verley reduction[2] of Ia which, unlike Ib, has extraordinary optical rotatory power in a region of low absorption.[3] Thus, optical purities of less than 0.01% are still detectable beyond experimental error since (S)-Ia, with $[\alpha]^{27}{}_{435}$ − 1922° (benzene), has $\alpha^{27}{}_{435}$ − 384° (c 10, l 2). Table I shows rate ratios observed in partial reductions of racemic Ia with carbinols (+)-(S)-$AlkCHOHCH_3$ at 63° in dioxane, and the corresponding values of $\Delta\Delta F^{\ddagger}$.



I



$$\overset{\text{OR}'}{\overset{|}{\text{CH}_3\text{CHCD}_2\text{R}''}}$$

II

IIa, R′ = CH_2Ph, R″ = OH
IIb, R′ = CH_2Ph, R″ = Bros
Ia, R = CH_3 IIc, R′ = CH_2Ph, R″ = D
Ib, R = NO_2 IId. R′ = H, R″ = D

With (+)-(S)-2-propanol-1-d_3 (IId, 2.9 atoms of D) the reducing agent, residual (after 29% reduction) Ia had $\alpha^{25}{}_{435}$ 0.00 ± 0.01° (c 8.84, l 2, benzene); it can be shown that k_R/k_S 1.0000 ± 0.0002 and $\Delta\Delta F^{\ddagger}$ not more than ~0.0001 kcal./m. We conclude that differences in non-bonded interaction between CH_3 and CD_3 are not capable of giving rise to secondary kinetic deuterium isotope effects in this and possibly other systems.

TABLE I

Alk	k_R/k_S[a]	$\Delta\Delta F^{\ddagger}$, kcal./m.
CH_3[b]	1.00	0.00
C_2H_5	1.29	.17
n-C_3H_7	1.31	.18
i-C_4H_9	1.58	.31
n-C_6H_{13}	1.59	.31
neo-C_5H_{11}[c]	1.87	.42
i-C_3H_7	1.92	.44
t-C_4H_9	2.91	.72

[a] Unreduced Ia always (−) at 435 mμ. [b] Standard group. [c] Resolved *via* brucine salt of acid phthalate. Carbinol has $[\alpha]^{27}D$ +24.8° (neat), acid phthalate $[\alpha]^{25}D$ +77.4° (chf.).

IId was prepared as follows. The (−)-methyl ester of (+)-(S)-lactic acid was converted ($PhCH_2Br/Ag_2O$) to methyl O-benzyl lactate (b.p. 89–91° (1 mm.), $n^{25}D$ 1.4918, $\alpha^{26}D$ −78.4° (l 1, neat); found: C, 68.03; H, 7.25) which was reduced ($LiAlD_4$) to IIa (b.p. 106° (2 mm.), $n^{25}D$ 1.5106, $\alpha^{27}D$ + 28.6° (l 1, neat); found at. % excess D (= 100D/(D+H)): 14.09, 14.15). Reduction of the brosylate (IIb, m.p. 59–60°, $[\alpha]^{26}D$ −4.2° (c 2.3, benzene); found at. % excess D: 11.70, 11.52) with $LiAlD_4$ to IIc (b.p. 79°(16 mm), $n^{25}D$ 1.4829, $\alpha^{26}D$ +1.2°, $\alpha^{26}{}_{365}$ +3.7° (l 1, neat); found at. % excess D: 20.65, 20.50) followed by catalytic (5% Pd/C) hydrogenolysis in toluene–HCl, afforded IId (b.p. 82–82.5°, $n^{25}D$ 1.3737, $\alpha^{25}D$ + 0.27°, $\alpha^{25}{}_{365}$ + 0.98° (l 1, neat); found at. % excess D: 36.00, 36.22), purified *via* the acid phthalate (m.p. 79–81.5°, $[\alpha]^{27}D$ + 0.2° $[\alpha]^{27}{}_{365}$ + 1.2° (c 4, chf.); found at. % excess D: 24.30, 24.21).

The optical activity of IIc, IId and the acid phthalate of IId is in line with that observed[4] for citric acid-2-d_2. If deuterium is less polarizable than hydrogen, the (+)-sign of (S)-IId is in accord with the atomic asymmetry rule,[5] provided that the

(1) L. S. Bartell, *Tetrahedron Letters*, No. 6, 13 (1960).

(2) K. Mislow, *Angew. Chem.*, **70**, 683 (1958).

(3) K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg and C. Djerassi, THIS JOURNAL, **82**, 4740 (1960).

(4) C. Martius and G. Schorre, *Ann.*, **570**, 140 (1950).

(5) J. H. Brewster, THIS JOURNAL, **81**, 5475 (1959); *Tetrahedron Letters*, No. 20, 23 (1959); private communication.