in acetone and treated with charcoal. Chilling and the addition of water separated a tan solid. Recrystallization from acetone–water gave 5-diethylamino-2,2-dichloro-4-phenyl-3(2H)-furanone (17.2 g., 0.057 mole, 57%), m.p. 119–121°.

Anal. Calcd. for $C_{14}H_{15}Cl_2NO_2$: C, 56.01; H, 5.04; N, 4.67; Cl, 23.62. Found: C, 55.95; H, 5.02; N, 4.76; Cl, 23.65.

Hydrolysis of 5-Diethylamino-2,2-dichloro-4-phenyl-3-(2H)-furanone.—A mixture of 5-diethylamino-2,2-dichloro-4-phenyl-3(2H)-furanone (8.0 g., 0.027 mole), 10% hydrochloric acid (100 ml.), and acetone (20 ml.) was refluxed for 24 hr. The resulting mixture was extracted with ether (2 × 100 ml.) and the ethereal extract was extracted with saturated sodium bicarbonate solution until carbon dioxide was no longer evolved. The bicarbonate solution was acidified with 12 *N* hydrochloric acid and extracted with ether (2 × 100 ml.). The ethereal solution was dried over anhydrous magnesium sulfate and treated with charcoal. Concentration of the solution to a small volume and the addition of hexane produced a white solid. Recrystallization from ether–hexane gave phenylpyruvic acid (2.7 g., 0.016 mole, 59%), m.p. 154–155°; reported m.p. 150–154°.[17] The infrared spectrum was identical with that of an authentic sample.[18]

The aqueous portion of the reaction mixture after extraction with ether was basified with 20% sodium hydroxide solution and *p*-toluenesulfonyl chloride (5 g., 0.026 mole) was added. The mixture was shaken for 24 hr. and chilling separated a white solid. Recrystallization from methanol-water gave N,N-diethyl-*p*-toluenesulfonamide (4.8 g., 0.021 mole, 78%), m.p. 60°; reported m.p. 60°.[16] The infrared spectrum was identical with that of an authentic sample.

Reaction of N,N-Diethyl-2-chloroacetamide and Bromoacetyl Bromide.—A solution of N,N-diethyl-2-chloroacetamide (14.9 g., 0.1 mole) and bromoacetyl bromide (20.1 g., 0.1 mole) in methylene chloride (100 ml.) was stirred for 72 hr. The resulting solution was chilled and water (100 ml.) was added. The methylene chloride solution was separated and dried over anhydrous magnesium sulfate. The methylene chloride was evaporated *in vacuo* and distillation gave a liquid (17.8 g.), b.p. 75–85° (1.0–1.3 mm.). The liquid was washed with saturated sodium bicarbonate solution (50 ml.) and dried over anhydrous magnesium sulfate. Fractional distillation gave a forerun (3.7 g.), b.p. 65–71° (0.65 mm.) and N,N-diethyl-2-bromoacetamide (7.9 g., 0.041 mole, 41%), b.p. 74–75° (0.55 mm.), $n^{26}\text{D}$ 1.4876; reported b.p. 82° (0.6 mm.)[19], $n^{20}\text{D}$ 1.4963.[19] The infrared spectrum was identical with that of an authentic sample. The infrared spectrum of the forerun indicated that it was composed primarily of N,N-diethyl-2-chloroacetamide.

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(17) R. M. Herbst and D. Shemin, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1959, p. 519.

(18) K and K Laboratories, Inc., Jamaica, New York.

(19) W. E. Weaver and W. M. Whaley, *J. Am. Chem. Soc.*, **69**, 515 (1947).

The Dimethyl-*p*-dioxanes and the 2,5-Dibutyl-*p*-dioxanes

R. K. SUMMERBELL, ANNA LOUISE BURLINGAME, DAVID R. DALTON,
AND CECILE KAPLAN DALTON

Chemical Laboratories of Northwestern University, Evanston, Illinois

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The isomeric dimethyl-*p*-dioxanes have been synthesized. Contrary to former reports, their boiling points are consistent with current theory. The boiling points of the 2,5-di-*n*-butyl-*p*-dioxanes are anomalous.

Many of the properties of the disubstituted *p*-dioxanes parallel closely those of the disubstituted cyclohexanes. The preferential formation[1–4] under equilibration conditions of the *trans*-2,3-, *trans*-2,5- and *cis*-2,6-disubstituted *p*-dioxanes, the potentially diequatorial forms of the assumed chair structures,[4] is of fundamental significance. Also, alkali-catalyzed equilibration of the dicarboxylic acid esters resulted in conversions to the theoretically more stable forms.[1,2,4] In contrast, the reported values for the normal boiling points of dimethyl-*p*-dioxanes seem peculiar, since they cover an unexpectedly large span, 114–135°, twice that for the corresponding dimethylcyclohexanes, 119.4–129.5°.[5] To investigate this seeming anomaly, we have prepared the four missing members of the series of seven possible isomers.

The structure and properties of *trans*-2,5-dimethyl-*p*-dioxane (I) are known with certainty, since it was prepared[6] by the lithium aluminum hydride reduction of *trans*-2,5-bis(iodomethyl)-*p*-dioxane,[2] a method that should not cause isomerization.[7] The recently reported[8] 2,2-dimethyl-*p*-dioxane (VII) seems also to have been made under conditions that should give a reasonably pure substance. The material reported as 2,6-dimethyl-*p*-dioxane is presumably the *cis* isomer,[9] as it probably was prepared by reducing a mercury-containing intermediate that was also converted by iodine treatment to a compound later proved[1] to be *cis*-2,6-bis(iodomethyl)-*p*-dioxane. Other reports of the preparation of dimethyl-*p*-dioxanes in the literature could give at best mixtures of isomers,

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(1) R. K. Summerbell and J. R. Stephens, *J. Am. Chem. Soc.*, **76**, 731 (1954).

(2) R. K. Summerbell and J. R. Stephens, *ibid.*, **76**, 6401 (1954).

(3) R. K. Summerbell, G. Lestina, and H. Waite, *ibid.*, **79**, 234 (1957).

(4) R. K. Summerbell and G. Lestina, *ibid.*, **79**, 3878 (1957).

(5) G. A. Haggis and L. N. Owen, *J. Chem. Soc.*, 408 (1953).

(6) E. Augdahl, *Acta Chem. Scand.*, **9**, 1237 (1955).

(7) D. S. Noyce and D. B. Denney, *J. Am. Chem. Soc.*, **72**, 5743 (1950).

(8) R. I. Meltzer, A. D. Lewis, and A. Fischmann, *J. Org. Chem.*, **24**, 1763 (1959).

(9) A. N. Nesmeyanov and I. F. Lutsenko, *Bull. acad. sci. USSR Classe. sci. chim.*, 296 (1943).

and at worst, large proportions of substances that were not even dioxanes.[10,11]

The reasonably convenient availability[1,2,4] of three bis(iodomethyl)-*p*-dioxanes of certain structure made possible the preparation by the method of Augdahl[6] of satisfactory quantities of *trans*-2,5- (I), *cis*-2,6- (II), and *trans*-2,3- (III) dimethyl-*p*-dioxanes. By careful hand-picking of crystals, enough *trans*-2,6-bis(iodomethyl)-*p*-dioxane was obtained to prepare a small sample of the corresponding dioxane (IV) by the same method. Mixtures of *cis*- and *trans*-2,5-dimethyl-*p*-dioxane, prepared by treatment of *trans*-2,5-dichloro-*p*-dioxane[12] with methylmagnesium bromide were submitted to fractional distillation followed by chromatography to give the already known I and its isomer, *cis*-2,5-dimethyl-*p*-dioxane (V). Similar separation of a previously described mixture of 2,3-dimethyl-*p*-dioxanes[13] furnished an additional sample of III and the last isomer, *cis*-2,3-dimethyl-*p*-dioxane (VI).

The properties of the authentic dimethyl-*p*-dioxanes are disappointingly normal. In fact, they constitute a case study of the Dauben–Pitzer version[14] of the Auwers–Skita rules, "that isomers having fully equatorial conformations have lower boiling point, density, and refractive index than isomers whose conformations are partially axial." As to boiling points, the range and the relative values for related isomers parallel almost perfectly the dimethylcyclohexanes. The literature reports of boiling points below 119° or above 131° must refer to mixtures containing rearrangement products such as acetals or ketals. In some cases, the dimethyl-*p*-dioxane content of materials bearing that designation must have been low indeed.

The boiling point behavior of authentic dimethyl-*p*-dioxanes is consistent with the assumption of a chair conformation for the dioxane ring.

Several other 2,5-dialkyldioxanes were prepared by the reaction of Grignard reagents with *trans*-2,5-dichloro-*p*-dioxane, but separation of the isomers was accomplished only with the 2,5-dibutyl-1,4-dioxane (VIII). On distillation, a solid phase, VIIIa, separated from a liquid phase in the condenser. On recrystallization, it melted at 64°. Work-up of the liquid distillate gave a different solid, VIIIb, melting at 20–22°. The isomer VIIIa was synthesized independently by treating *trans*-bis(iodomethyl)*p*-dioxane with sodium allyl and reducing the product catalytically, thus proving the structure to be *trans*-2,5-dibutyl-*p*-dioxane. The *cis* structure is assigned to VIIIb.

TABLE I
PROPERTIES OF DIMETHYL-*p*-DIOXANES

			B.p., °C.	$n^{20}D$	d_{20}
I[b]	*trans*-2,5	e, e	121.4–121.9	1.4147	0.932
V[a]	*cis*-2,5	e, a	125.1	1.4204	.951
II[d]	*cis*-2,6	e, e	121.2–121.7	1.4172	.933
IV[a]	*trans*-2,6	e, a	124.3	1.4220	.936[e]
III	*trans*-2,3	e, e	125.2	1.4195	.934
VI[a]	*cis*-2,3	e, a	130.4	1.4266	.964
VII	2,2		120–121	1.4016	

[a] Prepared in small amount; not rigorously purified. [b] Augdahl (ref. 6) reports b.p.$_{756}$ 121.5°, $n^{22}D$ 1.4147, d_{22} 0.932, m.p. 4.5°. [c] $n^{25}D$ (ref. 8). [d] Also ref. 9. 2,6-dimethyl-*p*-dioxane, b.p. 120–121, sp. gr. $\frac{20}{4}$ 0.9244, $n^{20}D$ 1.4169. [e] This value is probably low, but the sample was dissipated before the anomaly was noticed. A check of this value will be made on material prepared by an alternate synthetic route.

If this assignment is correct, the properties of this pair of isomers is not in agreement with expectations, in that the boiling point of the *cis* (equatorial, axial) is 5° lower than that of the *trans* (diequatorial). The Dauben–Pitzer version of the Auwers–Skita rules would predict the reverse. Such discrepancies, while rare, are not unknown. A recent well established example is that of the esters of 1,3-cyclohexanedicarboxylic acids.[15] According to the rule, the *trans* isomer should boil higher, but in the case of the methyl esters, it boils lower by 12°. Of the two 1,4-diisopropylcyclohexanes, the *trans* isomer boils slightly higher than the *cis*, although refractive index and density follow the rule.[16] It could be that the *trans* structure of our dioxane VIIIa was lost in one of the fairly drastic reactions during synthesis. If so, the results are still curious, as they would represent a transformation from a theoretically more stable to a less stable form.

Experimental

Preparation of I, II, and III.—The method of Augdahl[6] was used; yields: I, 38.3%; II, 49.4%; III, 51.8%. Final distillation was with 100-plate column at 750 mm.

Preparation of *trans*-2,6-Dimethyl-*p*-dioxane (IV).—Several preparations of 2,6-bis(iodomercurimethyl)-*p*-dioxane were run, using mercuric acetate as the condensing agent[1,3] on allyl ether. The mixture of 2,6-bis(iodomethyl)-*p*-dioxane resulting from treatment with iodine was crystallized slowly from methanol, and the crystals of *trans*-2,6-bis(iodomethyl)-*p*-dioxane (m.p. 70°) hand-picked. Repeated crystallization of several batches permitted the accumulation of 10 g. An infrared spectrum indicated the absence of other isomers from recrystallized material, m.p. 71–72°. On reduction of 9.2 g. for 9 days with lithium aluminum hydride, 1.09 g. (38%) of IV was obtained. Boiling point and density determined by micro methods[17] are not as reliable as similar values for I, II and III. The same limitation applies to our values for V and VI.

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(10) E. Augdahl and O. Hassel, *Acta Chem. Scand.*, **9**, 172 (1955). "If dimethyldioxanes are formed where propylene glycol is distilled with sulfuric acid, the amounts are at least insignificant."

(11) A. Noshay and C. C. Price, *J. Org. Chem.*, **23**, 647 (1958).

(12) L. A. Bryan, W. M. Smedley, and R. K. Summerbell, *J. Am. Chem. Soc.*, **72**, 2206 (1950).

(13) R. K. Summerbell and L. N. Bauer, *ibid.*, **58**, 759 (1936).

(14) W. G. Dauben and K. S. Pitzer, "Steric Effects in Organic Chemistry," Melvin S. Newman, ed., J. Wiley and Sons, Inc., New York, N. Y., 1956, p. 21.

(15) N. L. Allinger and R. G. Curby, Jr., *J. Org. Chem.*, **26**, 933 (1961).

(16) A. L. Liberman, T. V. Vasina, and B. A. Kazanskii, *Dokl. Akad. Nauk SSSR* **132**, 130 (1960). *Chem. Abstr.*, **54**, 20, 907 (1960).

(17) S. McElvain, "The Characterization of Organic Compounds," revised ed., Macmillan Co., New York, N. Y., 1953, pp. 31–32.

***cis*-2,3-Dimethyl-*p*-dioxane (VI).**—A mixture of the *cis* and *trans* isomers was prepared by treating *trans*-2,3-dichloro-*p*-dioxane with dimethylcadmium,[13] yield 32%. It was gas chromatographed on a 6 ft. × 3/4 in. column,[18] using tricresyl phosphate as the stationary phase; nitrogen at 30 mm. and a flow rate of 375 cc./min; temperature 60°. The starting sample of 1 cc. was cut into two fractions; the first identical with III, the second assumed to be the *cis* isomer VI.

***cis*-2,5-Dimethyl-*p*-dioxane (V).** (a) **2,5-Dichloro-*p*-dioxane (IX).**—Compound IX was prepared by low temperature chlorination of dioxane in carbon tetrachloride solution as previously described.[12] An induction period was often observed before chlorination started. On one occasion, unchanged chlorine was allowed to accumulate. When the reaction did start, the temperature rose rapidly, and part of the excess chlorine boiled into the atmosphere, creating a dangerous concentration. Light, either visible or ultraviolet, shortens the induction period and also the total time to arrive at the maximum yield, *ca.* 25–30%. The product recrystallized from ether seems to be more stable than that recrystallized from other solvents. Dry box procedures are desirable, the deterioration of the product seeming to be autocatalytic and promoted by a moist atmosphere.

(b) **Reaction with Methylmagnesium Bromide.**—The Grignard reagent was prepared by bubbling methyl bromide into a stirred ether suspension of 1.3 g.-atoms of magnesium turnings until substantially all of the metal had dissolved. The *trans*-2,5-dichloro-*p*-dioxane (0.43 mole) was added portionwise over a period of 1 hr. followed by reflux, 3 hr. Hydrolysis with dilute hydrochloric acid, several ether extractions, drying with sodium sulfate and distillation gave 20.4 g. of mixed 2,5-dimethyl-*p*-dioxanes; yield 41%.

(c) **Isolation of *cis*-2,5-Dimethyl-*p*-dioxane.**—Infrared spectra indicated the presence of much I in the lower boiling fractions and another major product which was concentrated in the higher boiling fractions on distillation through a 20-plate column. On gas chromatography of a 0.5-g. sample of a higher boiling fraction, as described for VI, I came through first, and the compound following was assumed to be V.

Anal. Calcd. for $C_6H_{12}O_2$: C, 62.03; H, 10.41. Found: I: C, 62.04; H, 10.36. II: 62.44; H, 10.05. III: C, 62.00; H, 10.10. IV: C, 61.89; H, 10.31. V: C, 62.38; H, 10.29. VI: C, 61.93; H, 10.21.

Infrared Spectra of Dimethyl-*p*-dioxanes (in μ, $CHCl_3$ Solution.—All absorb in the 3.38–3.50, 6.82–6.9, and 7.20–7.23 regions. Selected strong lines particularly characteristic of each isomer follow. *trans*-2,5-: 7.21, 7.4, 7.84, 8.61, 8.86, 9.05, 9.25, 10.53, 11.86. *cis*-2,5-: 7.84, 8.66, 9.61, 10.09, 10.54, 11.4, 12.16. *cis*-2,6-: 7.50, 7.55, 8.04, 8.66, 9.20, 10.40, 11.21, 11.58, 11.96. *trans*-2,6-: 8.02, 8.60, 8.80, 9.04, 9.20, 9.65, 10.42, 11.32, 11.83. *trans*-2,3-: 7.83, 8.92, 10.71, 10.81, 11.75. *cis*-2,3-: 7.8, 8.55, 8.98, 9.45, 9.93, 10.21, 10.71, 11.00, 11.95.

2,5-Dibutyl-*p*-dioxanes (VIIIa and VIIIb). (a) **From the Grignard Reagent.**—To the Grignard reagent prepared under nitrogen from 0.8 g.-atom of magnesium and 0.8 mole of butyl bromide in 240 ml. of ether was added 43.4 g. (0.28 mole) of *trans*-2,5-dichloro-*p*-dioxane in small portions with cooling. The reaction mixture was stirred for 4 hr., hydrolyzed with dilute acid, and the ether layer was separated and combined with additional ether extracts. Anhydrous magnesium sulfate was used to dry the ether solution and the ether was distilled. Distillation at 29 mm. gave a fraction, b.p. 137–137.5°, from which a crystalline solid, m.p. 64°, separated (VIIIa). Total solid, 5.2 g., 9.4%, b.p. 245° (742 mm.).

Anal. Calcd. for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08; mol. wt., 200.3. Found: C, 72.00; H, 12.33, 12.00; mol. wt. (Rast), 197.

The liquid, 23.5 g. (42% yield) was purified by contact with sodium for 4 days. Redistilled *in vacuo*, it yielded a fraction (VIIIb), b.p. 136–137° (23 mm.), 240.9° (742 mm.), m.p. 20–22°; $n^{20}D$ 1.4417, d_4^{24} 0.893.

Anal. Calcd. for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08; mol. wt., 200.3. Found: C, 72.10; H, 12.28; mol. wt. (Rast), 198.

(b) **From *trans*-2,5-Bis(iodomethyl)-*p*-dioxane.**—Allylsodium in hexane was prepared by the method of Letsinger and Traynham,[19] the reaction of dispersed sodium (0.82 g.-atom) with allyl ether (0.40 mole). *trans*-2,5-Bis(iodomethyl)-*p*-dioxane (0.10 mole) was added in portions. The reaction mixture was stirred for 1 hr. and allowed to stand overnight, diluted with hexane, siphoned onto dry ice, and hydrolyzed with water. The hexane layer was combined with ether extract and distilled. A fraction, b.p. 125–127° (18 mm.), weighed 3.7 g. (19%). The analysis for carbon was low when calculated for dibutenyl-*p*-dioxane, probably indicating some contamination with by-product ether. One gram of the crude product, 0.1 g. of platinum oxide, and 1 ml. of ethanol were hydrogenated at room pressure until 92% of the theoretical amount of hydrogen was absorbed. Evaporation of an ether extract gave 0.60 g. (61%) of VIIIa, m.p. 63°. No trace of VIIIb could be detected.

Other 2,5-Dialkyldioxanes.—Several other alkylmagnesium bromide reagents were allowed to react with *trans*-2,5-dichloro-*p*-dioxane. Yields of the mixed *cis*- and *trans*-2,5-dialkyl-*p*-dioxanes varied from 30 to 70%. The normal boiling point, d_4^{25} and $n^{20}D$ follow: ethyl, 169°, 0.920, 1.4292; *n*-propyl, 211°, 0.909, 1.4362; *n*-amyl, 284°, 0.895, 1.4451; allyl, 212°, 0.943, 1.4601. Analyses, molecular weights, and molar refractivities were satisfactory. Grignard reagents from alkyl iodides gave anomalous results.

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[18] We wish to thank Dr. Howard Zimmerman for permitting us to use this column.

[19] R. L. Letsinger and J. G. Traynham, *J. Am. Chem. Soc.*, **70**, 3342 (1948).