Condensed Cyclobutane Aromatic Compounds. XXIX. Benzocyclobutadienequinone. Ring Cleavage Reactions with Some Nitrogenous Carbonyl Reagents

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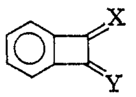
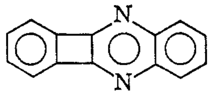
Benzocyclobutadienequinone (I) was found to react with several nitrogenous carbonyl reagents to give ring cleavage products rather than normal carbonyl derivatives. Thus, depending on the conditions, dione I gave phthalaldehydic acid oxime (IX), phthalimide (X), or ethyl *o*-cyanoacetate (XI) with hydroxylamine, and either phthaldehydic acid tosylhydrazone (XIII) or 2-tosylphthalazone (XIV) with tosylhydrazine; dione I also gave phthalazone when treated with hydrazine and it was converted into a bisethylene ketal (XV) and a monoethylene ketal (XVI); both the azine (XVIII) and the tosylhydrazone (XIX) of the monoketal were prepared.

Benzocyclobutadienequinone (1,2-benzocyclobutenedione, I) has been found to react normally with 2,4-dinitrophenylhydrazine and with *o*-phenylenediamine to give bis-2,4-dinitrophenylhydrazone (II) and the quinoxaline analog, 5,10-diazabenzo[*b*]biphenylene (III), respectively.[2] It was of interest, therefore, to investigate the synthesis of the monoxime (IV), monohydrazone (V), and monotosylhydrazone (VI) of dione I, all of which are logical precursors to the unknown diazobenzocyclobutenone (VII), a reasonable starting material for the synthesis of benzocyclopropene derivatives.[3]



I, $X = Y = O$
II, $X = Y = NNHC_6H_3\text{-}2,4\text{-}(NO_2)_2$
IV, $X = O$; $Y = NOH$
V, $X = O$; $Y = NNH_2$
VI, $X = O$; $Y = NNHSO_2C_7H_7$
VII, $X = O$; $Y = N_2$
VIII, $X = Y = NOH$


III

Dione I was subjected to the action of hydroxylamine under various conditions in attempts to prepare either the monooxime (IV) or the dioxime (VIII). Under all conditions tried, the only products isolated were those resulting from cleavage of the four-membered ring. Dione I reacted rapidly and exothermally with aqueous alkaline hydroxylamine at room temperature to yield, after acidification, phthalaldehydic acid oxime (IX). The speed of this reaction, compared to the noticeably slower cleavage of I to phthalaldehydic acid by 5% sodium hydroxide under similar conditions,[2] suggests that phthalaldehydic acid is probably not an intermediate. A more likely mechanism, involving initial formation of IV and its cleavage by hydroxide ion, is illustrated in Chart I. In contrast, dione I was recovered quantitatively after treatment with hydroxylamine acetate for 1 hr at room temperature. Reaction of I with the same reagent in boiling ethanol for 1 day led to the formation of phthalimide (X), which may be viewed as the normal Beckmann rearrangement product of monooxime IV. Hydroxylamine hydrochloride reacted slowly with I in ethanol to give either phthalimide (X) or ethyl *o*-cyanoacetate (XI). (The latter is the product of a second-order Beckmann rearrangement of monoxime IV.) The relative amounts of products X and XI varied with reaction conditions (*e.g.*, the amount of hydroxylamine hydrochloride used), but the exact factors determining this variation were not determined.

Dione I reacted rapidly with an equimolar amount of free hydrazine or slowly with hydrazine dihydrochloride. In either case, the only product isolated was phthalazone (XII), rather than the desired monohydrazone (V) of I. Hydrazone V is a possible intermediate in this reaction but proof of this hypothesis was not obtained.

The reaction of I with *p*-toluenesulfonylhydrazine (tosylhydrazine) took place under alkaline conditions to give phthalaldehydic acid tosylhydrazone (XIII); XIII was also synthesized by the action of tosylhydrazine on phthalaldehydic acid. In the absence of added base, dione I reacted with 1 equiv of tosylhydrazine to give a product of the composition $C_{15}H_{12}N_2O_3S$ which was assigned the structure of 2-tosylphthalazone (XIV) rather than that of the monotosylhydrazone (VI) of dione I. The infrared spectrum of this compound showed no band attributable to an NH stretching vibration, and its carbonyl function absorbed at 1695 cm^{-1}, a frequency more characteristic of an amide grouping than of a cyclobutenone. The compound was quite stable to sulfuric acid, a property also inconsistent with structure VI, but it was hydrolyzed by base to phthalaldehydic acid tosylhydrazone (XIII). The dehydration of tosylhydrazone XIII to 2-tosylphthalazone (XIV) could not be achieved using sulfuric acid, polyphosphoric acid, or acetic anhydride as the dehydrating agent. The desired cyclization took place smoothly, however, when excess acetyl chloride was added to a suspension of XIII in methanol. The resulting 2-tosylphthalazone was identical in all respects with the tosylhydrazine reaction product of dione I.

An indirect approach to the synthesis of the monohydrazones V and VI was investigated briefly. In this scheme, one of the carbonyls of dione I was to be blocked by ketal formation before reaction with hydrazine or tosylhydrazine, and the resulting monchydrazone ketal was then to be subjected to partial acid hydrolysis. Dione I reacted readily with excess ethylene glycol in the presence of *p*-toluenesulfonic acid to give the bisethyleneketal (XV). When the reaction was carried out using only 1 equiv of ethylene glycol, however, the monoethyleneketal XVI was obtained. The structures of XV and XVI were confirmed by their spectral prop-

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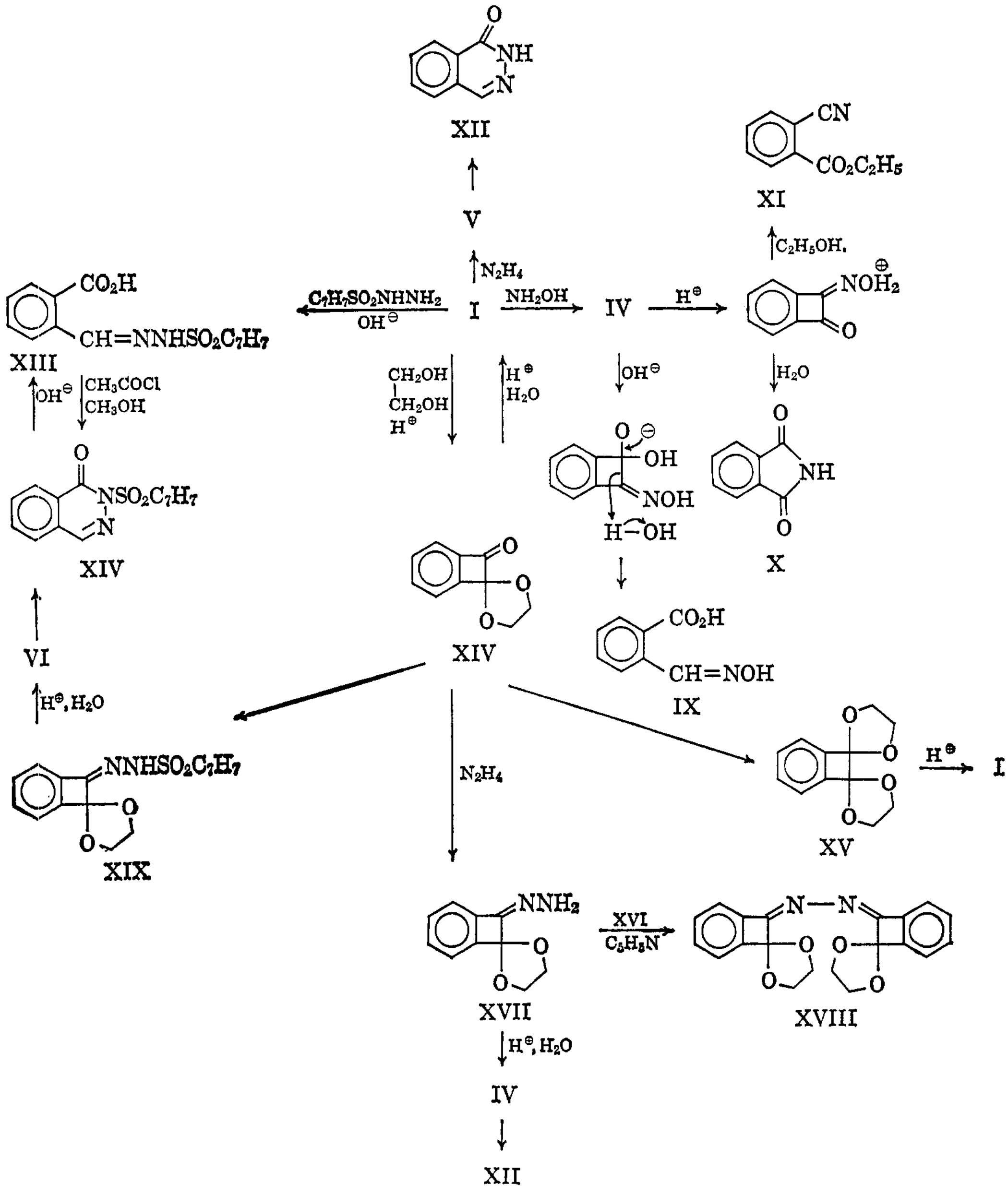
(1) Department of Chemistry, Wayne State University, Detroit, Mich.

(2) M. P. Cava, D. R. Napier, and R. J. Pohl, *J. Am. Chem. Soc.*, **85**, 2076 (1963).

(3) Recently, both a benzocyclopropene derivative and the parent hydrocarbon have been synthesized: (a) R. Anet and F. A. L. Anet, *J. Am. Chem. Soc.*, **86**, 525 (1964); (b) E. Vogel, W. Grimme, and S. Korte, *Tetrahedron Letters*, 3625 (1965).

Chart I



erties, as well as by their acid hydrolysis to I. Monoketal XVI reacted slowly with hydrazine dihydrochloride in hot ethanol: the only compound isolated was phthalazone (XII), the product of both ketal hydrolysis and rearrangement of the presumed intermediate XVII. The reaction of monoketal XVI with hydrazine dihydrochloride proceeded without complication in pyridine solution to yield the azine XVIII, rather than the hydrazone XVII. The structure of XVIII was confirmed by acid hydrolysis to dione I, although no intermediate in this reaction could be isolated. Tosylhydrazine reacted cleanly with monoketal XVI to give the corresponding monotosylhydrazone (XIX). However, acid hydrolysis of XIX afforded the rearrangement product, 2-tosylphthalazone (XIV), rather than the desired monotosylhydrazone (VI) of I.

Experimental Section[4]

Reactions of Benzocyclobutadienequinone (I) with Hydroxylamine. A.—A solution of dione I (264 mg, 2 mmoles) and hydroxylamine hydrochloride (138 mg, 2 mmoles) in 95% ethanol (10 ml) was heated for 1 hr on the steam bath, during which time the original yellow color faded. After standing overnight at room temperature, long white needles of phthalimide (X, 162 mg, 55%) separated; this material was identified as X by its melting point (230-235°) and infrared spectrum. Concentration of the mother liquors yielded colorless crystals (44 mg, 13%) of ethyl *o*-cyanoacetate (XI), mp 50-55°; recrystallization from ethyl acetate–hexane afforded pure XI as plates, mp 61-63°, the infrared spectrum of which was identical with that of an authentic sample.[5]

B.—A solution of dione I (264 mg, 2 mmoles), hydroxylamine hydrochloride (138 mg, 2 mmoles) and sodium acetate (164 mg, 2 mmoles) in a mixture of ethanol (10 ml) and water (1 ml) was stirred for 1 hr at room temperature. Evaporation of the ethanol *in vacuo* and trituration of the residual yellow solid with water resulted in quantitative recovery of I (246 mg), identified by its infrared spectrum. Repetition of the above experiment under refluxing conditions for 24 hr afforded, after crystalliza-

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[4] All melting points were determined on a Fisher-Johns melting point block and are uncorrected. Microanalyses were carried out by Midwest Microlab, Inc., Indianapolis, Ind.; Schwartzkopf Laboratories, Woodside, N. Y.; and Dr. A. Bernhardt, Mülheim, Germany. Infrared spectra were measured in potassium bromide pellets using a Perkin-Elmer Model 237 recording spectrophotometer. Ultraviolet absorption spectra were measured in 95% ethanol solution using a Perkin-Elmer Model 202 spectrophotometer.

(5) L. A. Carpino, *J. Am. Chem. Soc.* **84**, 2196 (1962).

tion from ethyl acetate–hexane, white crystals of phthalimide (X, 60 mg, 20%), mp 220–230°, identified by its infrared spectrum.

C.—Powdered dione I (264 mg, 2 mmoles) was added to a solution of hydroxylamine hydrochloride (138 mg, 2 mmoles) and potassium hydroxide (224 mg, 4 mmoles) in water (10 ml) at room temperature. The dione dissolved completely within 2 min and the solution became noticeably warm. The orange solution was filtered and acidified with dilute hydrochloric acid to give white needles (116 mg, 35%) of phthalaldehydic acid oxime (IX), mp 130–132°. The infrared spectrum of this product was identical with that of a sample prepared as described below.

Phthalaldehydic Acid Oxime (IX).—Phthalaldehydic acid (126 mg) and an excess of hydroxylamine hydrochloride were dissolved in a mixture of methanol (2 ml) and water (10 ml) and the mixture was kept at room temperature for 15 min. The resulting precipitate (102 mg, 69%) of crude oxime IX crystallized from ethyl acetate as prismatic clusters: mp 128–130°; ν_{max} 3500–2500 (broad hydroxyl), 1680 (carboxyl carbonyl), 1570 (C=N) cm^{-1}.

Anal. Calcd for $C_8H_7NO_3$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.36; H, 4.44; N, 8.57.

Reactions of Benzocyclobutadienequinone (I) with Hydrazine. A.—A solution of dione I (264 mg, 2 mmoles) and hydrazine dihydrochloride (208 mg, 2 mmoles) in 95% ethanol (20 ml) was refluxed for 20 hr. The ethanol was removed *in vacuo* and a small amount (2 ml) of water was added. The yellow solid was recrystallized from methanol (charcoal decolorization) to give colorless needles of phthalazone (XII, 99 mg, 34%), mp 178–184°. Recrystallization from water gave pure XII, mp 186–187°, the infrared spectrum of which was identical with that of an authentic sample.[6]

B.—Hydrazine (0.04 ml) was added to a solution of dione I (132 mg, 1 mmole) in ethanol (10 ml). The solution, which immediately became colorless, was concentrated *in vacuo* to yield white needles of phthalazone (XII, 92 mg, 63%), mp 186–187°, identified by its infrared spectrum.

Phthalaldehydic Acid Tosylhydrazone (XIII).—A solution of phthalaldehydic acid (300 mg), tosylhydrazine (372 mg), and concentrated hydrochloric acid (1 drop) in ethanol (20 ml) was heated for 30 min on the steam bath and then allowed to stand for 12 hr at room temperature. The resulting prisms of tosylhydrazone XII (370 mg, 58%), mp 189–195° dec, were directly pure: ν_{max} 3300–2800 (carboxyl OH), 1705 (carboxyl carbonyl) cm^{-1}.

Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.80; S, 10.07. Found: C, 56.82; H, 4.29; N, 8.71; S, 10.39.

2-Tosylphthalazone (XIV).—Acetyl chloride (5 ml) was added dropwise at a slow rate to a solution of phthalaldehydic acid tosylhydrazone (XIII, 305 mg) in warm methanol (15 ml). The resulting solution was heated on the steam bath for several minutes and then kept at room temperature for 1 hr, during which time 2-tosylphthalazone (XIV, 246 mg, 86%) separated as white plates, mp 199–202°. The analytical sample, mp 205–207°, was obtained by crystallization from dimethyl sulfoxide: ν_{max} 1695 (amide carbonyl), 1600 (C=N) cm^{-1}.

Anal. Calcd for $C_{15}H_{12}N_2O_3S$: C, 59.99; H, 4.03; N, 9.33; S, 10.68. Found: C, 60.11; H, 3.99; N, 9.35; S, 10.65.

Basic Hydrolysis of 2-Tosylphthalazone (XIV).—A mixture of 2-tosylphthalazone (25 mg) and 2.5% aqueous potassium hydroxide (10 ml) was heated on the steam bath for a short time during which the solid dissolved. Acidification of the cooled solution with hydrochloric acid afforded a crystalline precipitate of phthalaldehydic acid tosylhydrazone (XIII, 26 mg), mp 165–172°, identified by its infrared spectrum.

Reactions of Benzocyclobutadienequinone (I) with Tosylhydrazine. A.—A solution of dione I (264 mg, 2 mmoles) and tosylhydrazine (372 mg, 2 mmoles) in methanol (10 ml) was refluxed for 10 hr. The solvent was removed *in vacuo* and the residue was allowed to stand for some time with a small amount of ethanol (1 ml). Recrystallization of the resulting crystals from ethyl acetate afforded 2-tosylphthalazone (XIV, 311 mg, 52%), mp 205–207°, having an identical infrared spectrum with material prepared from phthalaldehydic acid tosylhydrazone.

B.—Dione I (132 mg, 1 mmole) was added at room temperature to a stirred solution of tosylhydrazine (186 mg, 1 mmole) and potassium hydroxide (56 mg, 1 mmole) in water (10 ml). After 2 hr, the resulting solution was acidified with concentrated hydrochloric acid to give phthalaldehydic acid tosylhydrazone (XIII, 224 mg, 70%), mp 153–157° dec. A portion of the product melted at 185–192° dec after recrystallization from aqueous ethanol and was conclusively identified as XIII by its infrared spectrum.

Reactions of Benzocyclobutadienequinone (I) with Ethylene Glycol. Ketals XV and XVI. A.—A solution of dione I (264 mg, 2 mmoles), excess ethylene glycol (1 ml), and a trace of *p*-toluenesulfonic acid in benzene (30 ml) was refluxed for 10 hr while the water produced in the reaction was removed azeotropically. The solvent was evaporated *in vacuo* and the residue was decolorized by charcoal treatment in chloroform. Evaporation of the filtered chloroform solution gave ketal XV (341 mg, 77%, mp 128–130°), which crystallized from benzene–hexane as white platelets: mp 143–147°; λ_{max} 256.5 mμ (log ϵ 3.08), 262.5 (3.22), and 269 (3.18); ν_{max} 3020 (aromatic H), 2950 (ketal methylenes), 1060–990 (ketal) cm^{-1}.

Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.60; H, 5.68.

Hydrolysis of bisketal XV was effected as follows. A mixture of XV (25 mg), water (5 ml), and concentrated hydrochloric acid (4 drops) was heated on the steam bath for 1 hr and then kept at room temperature for 24 hr. The resulting yellow solid was identified as dione I (10 mg, 67%) by melting point and infrared determinations.

B.—A solution of dione I (1.980 g), ethylene glycol (1.000 g), and *p*-toluenesulfonic acid (300 mg) in benzene (50 ml) was refluxed for 4 hr while the water produced in the reaction was removed azeotropically. The resulting product, dissolved in a small amount of benzene, was purified by chromatography on alumina (neutral, grade I); elution of the column with 1:1 benzene–ethyl acetate afforded monoketal XVI (2.071 g, 78%), mp 103–106°. Recrystallization from benzene-hexane gave pure XVI as slightly yellow flaky needles: mp 109–112°; λ_{max} 241 mμ (log ϵ 4.20), 279 (3.62), and 286 (3.59); ν_{max} 3020 (aromatic H), 2950 (ketal methylenes), 1770 (cyclobutenone carbonyl), 1060–990 (ketal) cm^{-1}.

Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.59; H, 4.71.

Acid hydrolysis of monoketal XVI gave dione I in 68% yield when carried out as described for the hydrolysis of bisketal XV.

Tosylhydrazone (XIX) of Monoketal XVI.—A solution of monoketal XVI (176 mg) and tosylhydrazine (190 mg) in 95% ethanol (10 ml) was allowed to stand at room temperature overnight. The resulting colorless crystals of tosylhydrazone XIX (308 mg, 90%, mp 178–182° dec) were recrystallized from chloroform–methanol–hexane to give the analytical sample as colorless needles: mp 181–185° dec; λ_{max} 297 mμ (log 4.28), shoulder at 246 (4.32); ν_{max} 3240 (NH), 1060–990 (ketal) cm^{-1}.

Anal. Calcd for $C_{17}H_{16}N_2O_4S$: C, 59.30; H, 4.65; N, 8.14; S, 9.30. Found: C, 59.55; H, 4.95; N, 8.07; S, 9.18.

Hydrolysis of Tosylhydrazone XIX.—A mixture of the tosylhydrazone ketal XIX (100 mg), water (5 ml), methanol (5 ml), and concentrated hydrochloric acid (10 drops) was warmed on the steam bath for 1 hr, and then allowed to stand 4 hr at room temperature. The white crystalline precipitate was identified as 2-tosylphthalazone (XIV, 50 mg, 57%), mp 201–205°, having an infrared spectrum identical with that of an authentic sample.

Azine (XVIII) of Monoketal XVI.—A solution of monoketal XVI (352 mg) and hydrazine dihydrochloride (220 mg) in pyridine (5 ml) was allowed to stand at room temperature for 2 days. Addition of water gave a yellow precipitate which was washed with water and 95% ethanol and then dried. The resulting azine XVIII (227 mg, 65%), mp 215–218°, was crystallized from a large volume of methanol to give the analytical sample as yellow flakes: mp 220–221.5°; λ_{max} 262 mμ (log ϵ 4.19), 305 (4.30), and 316 (4.25); ν_{max} 3020 (aromatic H), 2950 (ketal methylene), 1700 (C=N), and 1060–990 (ketal) cm^{-1}.

Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 69.11; H, 5.01; N, 7.71.

Azine XVIII was hydrolyzed almost quantitatively to dione I when treated with dilute boiling aqueous hydrochloric acid for several minutes.

Reaction of Hydrazine Dihydrochloride with Monoketal XVI.—A mixture of monoketal XVI (176 mg), hydrazine dihydrochloride (330 mg), and absolute ethanol (20 ml) was refluxed for 24

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(6) S. Gabriel and A. Naumann, *Ber.*, **26**, 521 (1893).

hr. Evaporation of the solvent and trituration of the residue with water yielded crude phthalazone (XII, 75 mg, 52%) which, after recrystallization from methanol–ether–hexane, melted at 182° and was identical by infrared comparison with an authentic sample.

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Photochlorination of 2,4-Dimethylpentane, 2,2,4-Trimethylpentane, and 2,2,4,4-Tetramethylpentane[1]

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The methine hydrogens of 2,4-dimethylpentane and 2,2,4-trimethylpentane possess unusually low reactivity toward the free or complexed chlorine atom. This result has been explained in terms of conformational effects in the hydrocarbons that shield the methine hydrogen atoms from radical attack.

The low reactivity of the tertiary hydrogen atom of 2,2,4-trimethylpentane (isooctane) in autoxidation has been deduced from rate and product studies,[2] and in the attack of methyl radicals by product isolation.[3] The over-all abnormally low reactivity of 2,4-dimethylpentane and isooctane toward *t*-butoxy[4] and phenyl radicals[5] has been interpreted in terms of conformational effects which essentially shield the tertiary hydrogen atoms from attack by radical species. The present results on over-all reactivity and substitution products in photochlorination support this conclusion. These results also provide additional examples of specific solvent effects in the reaction of chlorine atoms with carbon hydrogen bonds.[6]

Results

2,4-Dimethylpentane.—Photochlorination of 99 mole % minimum 2,4-dimethylpentane in carbon tetrachloride, 4 *M* benzene, or 12 *M* carbon disulfide with 5 mole % of chlorine at 40° [7] produced three monochlorides that could be separated by gas–liquid partition chromatography (glpc) at 50° on a 100 m × 1/16 in. i.d. copper Golay column coated with polypropylene glycol. The relative retention times were 1:1.16:1.25. The chloride with the lowest retention time was 2-chloro-2,4-dimethylpentane as ascertained by comparison with the retention time of the tertiary chloride produced by treatment of 2,4-dimethyl-2-pentanol with hydrogen chloride at room temperature. The chloride with the longest retention time was the primary chloride, 1-chloro-2,4-dimethylpentane, since the same chloride was produced by treatment of 2,4-dimethyl-1-pentanol with thionyl chloride. The chloride with the intermediate retention time was assigned to the secondary chloride, 3-chloro-2,4-dimethylpentane. The composition of the monochlorides produced is summarized in Table I and average yields listed in Chart I.

TABLE I

COMPOSITION OF MONOCHLORIDES FORMED IN CHLORINATION OF METHYLPENTANES AT 40°

Solvent	Chlorides (% of total monochlorides)		
	Primary	Secondary	Tertiary
	2,4-Dimethylpentane		
CCl_4[a]	55.1	22.9	22.0
	55.5	23.0	21.5
	54.3	23.2	22.5
4 *M* C_6H_6[a]	33.5	30.2	36.3
	33.4	30.6	36.0
	33.1	30.9	36.0
12 *M* CS_2[b]	10.5	35.8	53.7
	11.1	35.2	53.7
	12.3	36.5	51.2
	9.6	35.0	55.4
	2,2,4-Trimethylpentane		
CCl_4[a]	70.6	24.6	4.8
	70.6	24.6	4.8
	70.2	24.4	5.4
	70.1	24.4	5.5
	67.4	26.0	6.6
	67.4	26.0	6.6
4 *M* C_6H_6[a]	50.5	39.7	9.8
	49.5	40.9	9.6
	51.1	40.1	8.8
12 *M* CS_2[b]	19.3	59.8	20.9
	20.7	57.1	22.2
	20.8	55.8	23.4
	22.6	51.5	25.9
	22.1	53.0	24.9
	2,2,4,4-Tetramethylpentane		
CCl_4[a]	81.8	18.2	
	82.6	17.4	
	81.1	18.9	
4 *M* C_6H_6[a]	52.5	47.6	
	52.0	48.0	
	51.5	48.5	

[a] *Ca.* 5 mole % chlorination. [b] *Ca.* 2 mole % chlorination.

Competitive chlorinations with cyclohexane were performed in carbon tetrachloride, benzene, and carbon disulfide solutions. The relative reactivities of cyclohexane and 2,4-dimethylpentane summarized in Table II are based on the rates of disappearance of the two hydrocarbons as measured by glpc.

2,2,4-Trimethylpentane.—Photochlorination of 99 mole % minimum 2,2,4-trimethylpentane produced four monochlorides, which at 50° on a polypropylene glycol column had relative retention times of 1:1.09:

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[1] Directive Effects in Aliphatic Substitutions. XXIX. For part XXVIII, see G. A. Russell and Y. R. Vinson, *J. Org. Chem.*, **31**, 1994 (1966).

[2] J. P. Wibaut and A. Strang, *Koninkl. Ned. Akad. Wetenschap, Proc.*, **B54**, 229 (1951); C. E. Frank and A. V. Blackham, *Ind. Eng. Chem.*, **46**, 212 (1954); F. F. Rust and D. O. Collamer, *J. Am. Chem. Soc.*, **76**, 1055 (1954).

[3] A. L. J. Beckwith, *J. Chem. Soc.*, 2248 (1962).

[4] J. H. T. Brook, *Trans. Faraday Soc.*, **53**, 327 (1957).

[5] R. F. Bridger and G. A. Russell, *J. Am. Chem. Soc.*, **85**, 3754 (1963).

[6] G. A. Russell, *ibid.*, **80**, 4987, 4997, 5002 (1958).

[7] For experimental details of the technique, see G. A. Russell, A. Ito, and D. G. Hendry, *ibid.*, **85**, 2976 (1963).