the infrared spectrum of the crude product showed the band characteristic of the C=N double bond.

The physical constants of the above four products are given in Table I.

The infrared spectra were measured in approximately 10% solutions in carbon tetrachloride using a Perkin-Elmer infrared spectrometer model 12C, equipped with a rock salt prism. The refractive indices were determined with a Bausch and Lomb precision refractometer.

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[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION]

t-Alkyl Groups. I. Orientation of *t*-Alkylation Products of Toluene and Ethylbenzene

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RECEIVED JULY 28, 1952

t-Butyltoluenes obtained by alkylation ranged in composition from the 67% meta, 33% para equilibrium ratio to 7% meta, 93% para. Recurrence of this latter composition strongly suggests that it is a true limiting value. *o*-*t*-Butyl or *o*-*t*-amyl derivatives of toluene and ethylbenzene were not found in any of the *t*-alkylation products investigated, but ortho derivatives were found when *n*- and *s*-alkyl groups were introduced. Controversial *t*-alkylations were repeated and the products analyzed by infrared spectrometric methods.

The object of this research was to obtain accurate analyses of *t*-alkylation products of toluene and ethylbenzene in preparation for study of the factors controlling orientation in these alkylations. For completeness a number of cases were reinvestigated which were the subject of controversy or which were in apparent disagreement with our findings. These studies were greatly facilitated by the use of infrared spectrometry in the analysis of the hydrocarbon mixtures. This technique is rapid, accurate and not subject to the errors inherent in most of the methods formerly available for solving this otherwise very difficult analytical problem.

A series of alkylations of toluene with a variety of *t*-butylating agents and catalysts are summarized in Table I, along with several *t*-amylations of toluene and *t*-butylations of ethylbenzene. Alkylations of toluene with other than *t*-alkylating agents are presented in Table II. A clear cut difference between *t*-alkyl groups and other alkyl groups in the ortho-alkylation of alkylbenzenes is evident on comparing the isomer analyses in Table I with those in Table II. No appreciable amount of ortho-isomer was detected in the products from the *t*-butylation or *t*-amylation of toluene or ethylbenzene.[1] On the other hand, all three isomers were obtained in all cases where other than *t*-alkylating agents were used. It is of interest that even the diisopropylbenzene fraction from the alkylation of benzene with propylene over a "solid phosphoric acid" catalyst has been shown to contain an appreciable amount of ortho isomer.[2]

t-Butylation of toluene (Table I) gave *t*-butyltoluene fractions ranging in composition from 67 ± 3% meta, 33 ± 3% para to 7 ± 3% meta, 93 ± 3% para with several cases at each extreme. Isomerization experiments (Table IV) showed the former composition to be the equilibrium ratio. Recurrence of the latter composition strongly suggests that it too is a true limiting value. In the intermediate region between the composition limits indicated above, the meta–para ratio appears to be quite sensitive to small variations in the amount of catalyst and in the alkylation procedure.

The recurrence of the 7% meta, 93% para *t*-butyltoluene ratio under mild alkylating conditions suggests that this is the initial product and that other product compositions result from isomerization of this. The data in this paper, however, do not exclude the possibility that different meta–para ratios may result from alkylation in the very different environments existing in the catalyst and hydrocarbon phases or at the interface between hydrocarbon and catalyst phase. Likewise, the data do not preclude the possibility that the meta component in this initial product may result entirely or in part from attack of the alkylating agent on the ortho position followed either by rearrangement of the *o*-*t*-butyltoluene or of the alkylation intermediate.

Several *t*-alkylations which had been reported to give only the meta or the para isomer were repeated (expts. 8, 9, 10, 15) and were found to give mixtures of meta and para isomers falling in the range defined above.[3] Similarly, although selective *p*-alkylation has been claimed in alkylations with other than *t*-alkylating agents, those repeated here (Table II) gave considerable quantities of all three isomers. This result is in essential agreement with reports of recent studies in which spectrometric analytical methods were used.[4]

The *t*-amylations of toluene and *t*-butylations of ethylbenzene reported in Table I are not adequate to establish the limiting compositions of the alkylates in these systems. However, these limits must fall outside of the 72–20% meta and 28–80% para ranges in the former case and the 45–15% meta and 55–85% para ranges in the latter.

Several isomerization experiments were carried out in order to obtain information on the relative ease of isomerization of the *t*-butyltoluene isomers and to determine the equilibrium composition for comparison with the isomer ratios in the alkylation products. These are summarized in Tables III

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(1) This result is consistent with reports of similar alkylations by (a) E. Noelting, *Chimie & industrie*, **6**, 719 (1921); (b) K. T. Serijan, H. F. Hipsher and L. C. Gibbons, THIS JOURNAL, **71**, 873 (1949).

(2) F. W. Melpolder, J. E. Woodbridge and C. E. Headington, *ibid.*, **70**, 935 (1948).

(3) This general result is in accordance with J. H. Simons and H. Hart, *ibid.*, **69**, 979 (1947), and Serijan, *et al.*, reference 1b.

(4) (a) F. E. Condon, *ibid.*, **71**, 3544 (1949); (b) W. M. Kutz, J. E. Nickels, J. J. McGovern and B. B. Corson, *J. Org. Chem.*, **16**, 699 (1951).

TABLE I

t-ALKYLATION OF TOLUENE AND ETHYLBENZENE

				Alkylation conditions						Monoalkylated product			
Expt. No.	Alkylating agent (I), moles		Aromatic hydrocarbon (II), moles/mole of (I)	Catalyst (III), moles/mole of (I)		Total time, hr.	Temp., °C.	Method	Procedure	Yield,[a] %	Wt., %[b] of total alkylate	Isomer analysis[c]	
												Vol. % *m*-	Vol. % *p*-
	Toluene alkylations										*t*-Butyltoluenes		
1	Isobutene[d]	4.5	5.5	UOP No. 2 solid phosphoric acid	....	6.0	170	A	I + II over III at 1.05 liq. vol./vol. of catalyst/hr. (300 p.s.i.g.)	54(87)	97	14	86
2	Isobutene	0.9	1.1	Liq. HF	31.7	0.7	0–5	B	I (gas) into II + III (40 min.)	11	82	62	38
3	Isobutene[d]	2.88	5.0	Liq. HF	5.5	2.0	1–8	B	I + II to III (1–8°, 85 min.), stirred 1–3°, 35 min.	88	97.5	52	48
4	Isobutene	7.0	1.4	Liq. HF	1.3	4.0	0–6	B	1 + II to III (0–6°, 3 hr.); stirred 0–3°, 1 hr.	61	86[f]	44	56
5	Isobutene	2.0	3.0	Liq. HF[g]	0.6	1.5	2–4	B	I (gas) into II + III (1.5 hr.)	56	95+	7	93
6	Isobutene	2.0	3.0	80% Aq. HF; HF·H$_2$O	4.0 1.1	2.0	0–5	B	1 (gas) into II + III (90 min.), stirred 30 min.	83	98+	7.7[e]	92.3
7	Isobutene	0.7	1.4	$FeCl_3$	0.036	1.6	80–90	C	I (gas) into II + III (80–90°; 36 min.), stirred 80°, 1 hr.	35[h]	95+	7	93
8[t]	*t*-BuCl	4.0	1.8	Liq. HF	2.3	3.5	0–2	B	I to II + III (2 hr.), stirred 1.5 hr.	82(84)	98	12	88
9[t]	*t*-BuCl	4.03	1.8	Liq. HF	1.8	3.5	0–2	B	I to II + III (2 hr.), stirred 1.5 hr.	71(78)	96	15	85
10[t]	*t*-BuCl	0.54	1.0	$FeCl_3$	0.004	0.05	18–28	D	III to I + II in one portion	72(88)	98	10	90
11[t]	*t*-BuCl	.27	5.0	$FeCl_3$	.2	4.6	0–3	C[i]	I to II + III (38 min.), stirred 4 hr.	84	91	70	30
12[t]	*t*-BuCl	.27	5.0	$FeCl_3$	.2	4.5	0–3	C[i]	I to II + III (30 min.), stirred 4 hr.	82	93	67	33
13[t]	*t*-BuCl	.27	5.0	$AlCl_3$	.3	4.9	0–3	C[i]	I to II + III (53 min.), stirred 4 hr.	75	85	70	30
14[t]	*t*-BuCl	.27	5.0	$AlCl_3$ + Nitrobenzene	.3 .6	4.5	0–2	C[i]	I to II + III (25 min.), stirred 4 hr.	90[j]	95+	15	85
15[t]	*t*-BuOH	1.0	4.0	BF_3	1.0	6.5	4–72	Ref. 16	III into I + II (4–18°, 1 hr.), heated slowly to 72°, 3.5 hr., stirred 72°, 2 hr.	61	69	41	59
16	*t*-BuOH	1.0	4.0	BF_3 (III) P_2O_5 (IV)	1.0 0.25	(7.0)	10–75	Ref. 16	III into I + II (10°, 30 min.), IV added, stirred 20°, 30 min., let stand 16 hr., stirred 75°, 6 hr.	48	61	61	39
17	*t*-BuOH	0.33	3.0	H_2SO_4 (sp. g. 1.84)	5.8	1.3	35–50	C	III to I + II (35–50°, 45 min.), stirred 35–40°, 30 min.	27[k]	75	7	93[k]
18	*t*-BuOH	.50	1.4	H_3PO_4 (100%)	4.2	8.5	80–82	C	I + II + III stirred	27[l]	91	7	93
19[t]	Diisobutylene	1.0	2.5	$FeCl_3$	0.09	4.8	33–50	C	I to II + III (40–50°, 49 min.), stirred 33–40°, 4 hr.	10.5	44[m]	12	88
20	Diisobutylene	2.5	1.0	$FeCl_3$	.04	4.8	33–50	C	I to II + III (40–50°, 48 min.), stirred 33–40°, 4 hr.	7.5[n]	53[m]	12	88
21	1,2-Dimethyl-4-*t*-Butylbenzene	1.0	5.0	Liq. HF	8.0	6.0	0–2	B	I + II + III stirred	66	...[p]	52	48
											t-Amyltoluenes		
22	*t*-AmCl	4.0	2.0	Liq. HF	3.8	5.0	0–2	B	I to II + III (5.0 hr.)	94	98	20	80
23	*t*-AmCl	2.5	2.0	$FeCl_3$	0.2	7.0	0–4	C	I to II + III (1.5 hr.), stirred 5.5 hr.	78	86[q]	72	28
24	*t*-AmCl	0.24	5.7	$AlCl_3$ + Nitrobenzene	.3 .6	4.5	0–3	C[i]	I to II + III (30 min.), stirred 4 hr.	86	90+[r]	27	73
	Ethylbenzene alkylations										*t*-Butylethylbenzenes		
25	Isobutene	6.0	1.1	Liq. HF	1.1	1.2	0–5	B	I + II to III (40 min.), stirred 30 min.	66	85[s]	15	85
26	*t*-BuCl	2.0	1.0	Liq. HF	4.5	2.8	0–2	B	I to II + III (85 mm), stirred 85 min.	69	80[s]	15	85
27[t]	*t*-BuCl	0.44	4.3	$FeCl_3$	0.07	30	−11 to −10	E	III to I + II in one portion. stirred 30 hr.	88	91	45	55

[a] Yields are based on the actual weights of products distilling in the following ranges at 760 mm. pressure: *t*-butyltoluenes, 185–195°; *t*-amyltoluenes, 206–216°; *t*-butylethylbenzenes, 203–214°. They are referred to product theoretically obtainable from the alkylating agent used. Figures in parentheses are corrected for recovered alkylating agent. [b] The total alkylate is defined as product distilling above a point 5° below the boiling point of the lowest boiling component of the monoalkylated product. [c] Infrared analyses, accuracy better than ±3 units; in expt. 6 ± 0.3 units. No more than 1% ortho isomer was detected in any product and in most cases it is known to be below 0.2%. [d] Commercial grade, approximately 95% purity. [e] The low yield in this experiment is due largely to manipulation losses during the procedure used in removing the relatively large amount of hydrogen fluoride. [f] The high boiling product contained 70% 3,5-di-*t*-butyltoluene: b.p. 162.6° at 100 mm., n^{20}_D 1.4904 (supercooled liquid), m.p. 31.5–32.0°. [g] The toluene was saturated with hydrogen fluoride at room temperature. A small catalyst phase separated on cooling to 0°. [h] Low refractive indices of the transition cuts between toluene and *t*-butyltoluenes indicate the presence of non-aromatic hydrocarbons (about 10% as much as the *t*-butyltoluene fraction), probably triisobutylene. Diisobutylene also appears to be present in the early part of the toluene plateau. [i] The toluene was dried with calcium hydride, the apparatus carefully dried and moisture excluded with a calcium chloride tube. Except for the reactor, method essentially as described by Shoesmith and McGechen.[6] [j] The nitrobenzene was not removed by reduction as described in the original description.[6] Product analyzed contained 6% nitrobenzene; yield corrected for this. [k] The sulfuric acid layer increased in weight from 200 to 242.1 g. Selective sulfonation may have affected the isomer distribution in this case. [l] The phosphoric acid layer increased in weight from 200 to 214.0 g. The product appeared to contain a small amount of diisobutylene and tetraisobutylene and a considerable quantity of triisobutylene (10.6 g.). This fraction, collected from 101.8–115.7° at 100 mm., (n^{20}_D 1.4340), distilled mainly at 108–109° at 100 mm. pressure. [m] The following product components were estimated from the distillation curve and the bromine numbers and refractive indices of the individual distillation cuts. The isomer ratio in the *t*-butyltoluene fraction was determined spectrometrically.

	n^{20}_D Used in calculations	Expt. 19, g.	Exp. 20, g.
Diisobutylene	1.410	195.1	29.7
Toluene	1.497		180.8
Triisobutylene	1.430	12.4	17.5
t-Butyltoluenes	1.492	38.8	31.6
Tetraisobutylene	1.450	60.4	207.4
High boiling products	...	49.2	35.9
		355.9	502.9

These experiments were carried out because of the report by Noelting[1a] that the ferric chloride catalyzed alkylation of toluene with diisobutylene gave *p*-*t*-butyltoluene. He gave no experimental details. [n] Yield based on toluene. [p] The product composition estimated from the distillation curve is

	g.	Wt. %
Toluene	243.5	56.1
o-Xylene	70.4	16.2
t-Butyltoluenes	99.9	23.1
1,2-Dimethyl-4-*t*-butylbenzene	19.9	4.6
High boiling products		
	433.7	100.0

Ultraviolet analysis of the *o*-xylene fraction distilling from 144–154° showed that no *m*- or *p*-xylene were present. Freezing point analysis gave 97.7% *o*-xylene. [q] Hydrocarbons steam distilled from the reaction mixture after addition of 1.2 *N* hydrochloric acid, but before separation and treatment with alkali. The *t*-amyltoluenes obtained from this experiment contained isomeric dialkylbenzenes boiling slightly below *m*-*t*-amyltoluene. As these are not easily removed by fractional distillation, they interfere seriously with isolation of pure *m*-*t*-amyltoluene from the reaction product by this method. [r] Nitrobenzene removed from product by reduction with tin and hydrochloric acid before distillation. [s] The high boiling products contained the following percentages of 3,5-di-*t*-butylethylbenzene: expt. 25, 60%; expt. 26, 70%. This compound has apparently not been reported previously. Center cut product,' obtained on fractionation at 20 mm. pressure through an 85 cm. × 25 mm. heated column packed with $^3/_{32}$ inch Pyrex helices and equipped with an intermittent takeoff device, had the following properties: b.p. 130.0° at 20 mm., n^{20}_D 1.4890; d^{20}_4 0.8575. *Anal.* Calcd. for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 88.02; H, 11.83. The 1,3,5-arrangement of the alkyl groups was shown spectrometrically. The ultraviolet spectrum showed the presence of 1–2% of the corresponding 3,5-di-*t*-butylstyrene. This was removed by adsorption on a silica gel column. The refractive index was reduced to n^{20}_D 1.4884 by this treatment. [t] Repetition of a previously described experiment.

and IV. In some experiments toluene was added to diminish the amount of 3,5-di-*t*-butyltoluene formed by disproportionation of the *t*-butyltoluenes under the isomerization conditions. Rapid isomerization of *o*-*t*-butyltoluene under alkylating conditions was observed when a mixture of *o*-*t*-butyltoluene, toluene and isobutene was added to liquid hydrogen fluoride at 0–2° (expt. 35, Table III); no more than 0.2% of the added *o*-*t*-butyltoluene remained in the product. The para isomer does not isomerize as readily (compare expt. 36 with expts. 3 and 4), but complete isomerization to the equilibrium mixture can be effected without difficulty using hydrogen fluoride (expts. 40, 41, Table IV).

Aluminum bromide at 25° is an effective isomerizing agent, but its use in expt. 39 gave *t*-butyltoluenes containing a small amount of other close-boiling aromatic hydrocarbons.

Ferric chloride reportedly does not isomerize *t*-butyltoluenes at 100°.[5] This result appears to be confirmed by expt. 7 (Table I) in which product having the 7% meta, 93% para composition was obtained by the ferric chloride catalyzed alkylation of toluene with isobutene at 80–90°. On the other hand, two ferric chloride catalyzed alkylations of toluene with *t*-butyl chloride at 0° gave the equilibrium composition (expts. 11, 12, Table I). This result could be due to alkylation giving the 67% meta, 33% para composition directly or to alkylation giving the 7% meta, 93% para composition or some intermediate composition which is then isomerized by the *t*-butyl chloride-activated ferric chloride.

Controversial *t*-alkylations of toluene and ethylbenzene are summarized in Table V. Most of the contradictory reports can be explained by failure to observe minor constituents in mixtures containing a predominant amount of one isomer and to the confusion which resulted when methods of analysis involving sulfonation were applied to mixtures of *t*-butyltoluenes.

Although it has been suggested that the results from Shoesmith and McGechen's[6] analytical methods for *t*-butyltoluene isomers are questionable due to the possibility of isomerization of the mixture during the sulfonation stage,[7] this view

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(5) R. Pajeau, *Bull. soc. chim.*, [5] **12**, 637 (1945).

(6) J. B. Shoesmith and J. F. McGechen, *J. Chem. Soc.*, 2231 (1930).

(7) (a) N. G. Buu-Hoi and P. Cagniant, *Bull. soc. chim.*, [5] **9**, 887 (1942); (b) C. C. Price in "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 47.

TABLE II

ALKYLATION OF TOLUENE TO GIVE ETHYL, ISOPROPYL AND *s*-BUTYL DERIVATIVES

Expt. No.	Alkylating agent (I), moles		Toluene (II), moles/mole of (I)	Catalyst (III), moles/mole of (I)		Total time, hr.	Temp., °C.	Method	Procedure	Yield,[a] %	Monoalkylated product: Wt. %[b] of total alkylate	Isomer analysis[c]: Vol., % *o*-	Vol., % *m*-	Vol., % *p*-
											Ethyltoluenes			
28[d]	EtOH	1.0	8.0	BF_3 (III) P_2O_5 (IV)	1.0 0.25	30.5	90–95	Ref. 16	III into I + II (16–54°, 10 min.), stirred 50–44°, 20 min., IV added, stirred 90–95°, 30 hr.	70	79	45	30	25
											Cymenes			
29	Propylene	5.0	5.6	UOP No. 2 solid phosphoric acid	..	6.0	155	A	I + II over III at 0.97 liq. vol./vol. of catalyst/hr. (300 p.s.i.g.)	63(82)	85	40	25	35
30	Propylene	3.0	5.0	Liq. HF	3.0	2.1	0–6	B	I into II + III (97 min.), stirred 30 min.	93	95	41	26	33
31[d]	*i*-PrOH	1.0	4.0	BF_3	1.0	9.0	25–75	Ref. 16	III into I + II (25–50°, 20 min.), stirred 40–70°, 3 hr., 70–75°, 6 hr.	35	49	32	28	40
32[d]	*i*-PrOH	1.0	4.0	BF_3 (III) P_2O_5 (IV)	1.0 0.25	7.5	25–70	Ref. 16	III into I + II (25–50°, 20 min.), cooled to 0°, IV added, stirred 0–70°, 3 hr., 70°, 4 hr.	72	79	29	30	41
											s-Butyltoluenes			
33	2-Butene	2.0	4.0	Liq. HF	4.3	3.5	0–6	B	I + II to III (2.5 hr.), stirred 1 hr.	89	92	36	33	31
34	1-Butene	2.0	3.0	Liq. HF	4.3	3.5	0–4	B	I + II to III (2.5 hr.), stirred 1 hr.	92	95	35	33	32

[a] Yields are based on the amount of alkylating agent. Figures in parentheses are corrected for recovered alkylating agent. [b] The total alkylate is defined as product distilling above a point 5° below the boiling point of the lowest boiling component of the monoalkylated product. [c] Infrared analyses, accuracy ±3 units. [d] Repetition of a previously described experiment.

TABLE III

t-BUTYLATION OF MIXTURES OF TOLUENE AND ONE *t*-BUTYLTOLUENE ISOMER

Expt. No.:	35	36
Reactants, moles		
I, Isobutene	0.5	0.5
II, Toluene	1.0	1.0
III, *o*-*t*-Butyltoluene	0.101	....
IV, *p*-*t*-Butyltoluene	....	0.101
V, Liq. HF	4.0	4.0
Alkylation conditions: Method B		
Total time, min.	57	48
Temp., °C.	0–2	0–2
Time of addn. of I + II + III (or IV) to V (min.)	27	15
Time of stirring after addn. (min.)	30	33
t-Butyltoluenes:		
Yield, %	70	68
Wt. % of total alkylate	91	91
Isomer analysis:[a]		
Vol. % *m*-	45	35
Vol. % *p*-	55	65

[a] In expt. 35, the transition cut distilling from 195–210° at the end of the *t*-butyltoluene fraction was found to contain 1–2% of *o*-dialkylbenzene. This corresponds to less than 0.04% of the total *t*-butyltoluene fraction or less than 0.2% of the added *o*-*t*-butyltoluene. Analysis of the transition cuts from expt. 36 indicated the presence of *o*-dialkylbenzenes corresponding to less than 0.01% of the total *t*-butyltoluene fraction.

has not been universally accepted[8] and no experimental data to confirm or refute it have been presented. For this reason a sample of *p*-*t*-butyltoluene was submitted to the two analytical processes used by Shoesmith and McGechen. Pure *p*-*t*-butyltoluene analyzed by the partial sulfonation method gave approximately 60% meta, 40% para isomer; complete sulfonation followed by separation of the barium sulfonates gave 65% meta, 35% para. Spectrometric inspection of the unsulfonated oil from the partial sulfonation procedure indicated that it contained 5–10% of *m*-*t*-butyltoluene, 30–40% of *p*-*t*-butyltoluene and approximately 50% of 3,5-di-*t*-butyltoluene. The hydrocarbon fraction recovered by steam distilling the sulfonated portion from 50% sulfuric acid contained approximately equal amounts of *m*- and *p*-*t*-butyltoluene and a considerable quantity of a monoalkylbenzene, probably toluene. The two barium sulfonate fractions from the second analytical method were not investigated for homogeneity.

The results described above show conclusively that extensive isomerization and disproportionation occur during the analytical method used by Shoesmith and McGechen and that analyses obtained in this way are invalid.

Experimental Part

All melting and boiling points are corrected.

Materials.—The following materials were used in the alkylation and isomerization experiments. One or two exceptions are specifically mentioned in the tables. Toluene (J. T. Baker Chemical Co., C.p. grade); ethylbenzene, 1-butene and 2-butene (Phillips Petroleum Co., 99 mole per cent. minimum purity); *t*-butyl chloride, *t*-amyl chloride and *t*-butyl alcohol (Eastman Kodak Co., center cut fractionated products with less than 0.1° distilling range);

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(8) A. W. Francis, *Chem. Revs.*, **43**, 257 (1948).

TABLE IV

ISOMERIZATION OF *t*-BUTYLTOLUENES

Expt. No.	37				38				39		40		41	
Reactants, moles														
Toluene	2.0				2.0				..		0.674		...	
t-Butyltoluenes	1.0				1.0				2.15		0.337		0.337	
Catalyst	$AlBr_3$				$AlBr_3$				$AlBr_3$		liq. HF		liq. HF	
	0.05				0.05				0.12		2.8		5.6	
Isomerization conditions:														
Method	F				F				G		B		B	
Temp., °C.	25–30				25–30				25		0		0	
Reaction time, hr.	0	24	48	144	0	24	48	120	0	144	0	4	0	4
Composition of *t*-butyltoluenes in hydrocarbon phase:[a]														
%, *m*-	18	66	67	67	93	67	67	67	67	67[b]	0	65	0	65
%, *p*-	82	34	33	33	7	33	33	33	33	33	100	35	100	35

[a] Infrared spectrometric analyses, ±3 units. [b] Small quantities of isomeric hydrocarbons were formed which prevented more accurate determination of the isomer ratio in this product.

diisobutylene (Shell Chemical Co., fractionated, b.p. 103.2–104.2°); hydrogen fluoride (Harshaw Chemical Co., anhydrous 99%); ferric chloride (Eimer and Amend, C.p. anhydrous, sublimed); UOP No. 2 "solid phosphoric acid" (Universal Oil Products Co.); boron trifluoride (Harshaw Chemical Co., anhydrous 97%), 100% phosphoric acid (prepared by adding the calculated amount of C.p. phosphorus pentoxide to C.p. 85% phosphoric acid); other catalysts and reagents were standard reagent grades.

1,2-Dimethyl-4-*t*-butylbenzene (b.p. 215.1° at 760 mm., m.p. −25.6°, $n^{20}{}_D$ 1.4992, $d^{20}{}_4$ 0.8733) was prepared by the hydrogen fluoride catalyzed alkylation of 95% *o*-xylene (Oronite Chemical Co.) with isobutene (essentially as described for the alkylation of toluene in expt. 3, Table I) followed by fractionation of the product. *o*-*t*-Butyltoluene was obtained by a small scale modification of the procedure of Serijan, Hipsher and Gibbons[1b] and a product with identical properties obtained. *t*-Butyltoluenes used in the isomerization experiments were analyzed, fractionated products from various *t*-butylations summarized in Table I.

Yields.—The reported yields are not intended for use in a comparative sense, because the experiments differed widely in scale and in the manner in which the products were worked up. They are useful only in establishing minimum yields. The weight per cent. of monoalkylated product in total alkylated product, is a better index of freedom from side reactions.

Spectrometric Standards, Infrared and Ultraviolet Spectra.—The isomeric ethyltoluenes and cymenes were obtained from the National Bureau of Standards. *o*-*t*-Butyltoluene was prepared as indicated in the section on materials. *Meta* and *para*-*t*-butyltoluenes, *t*-amyltoluenes and *t*-butylethylbenzenes were obtained by repeated fractional distillation through a 13 mm. × 3 ft. Podbielniak Heligrid column, supplemented in some cases by low temperature crystallization until fractions with constant physical properties and adequate spectrometric purity were obtained. The physical properties of these samples are given in Table VI. Spectra are shown in Figs. 1 and 2.

Analytical Methods.—The crude alkylation products which had been treated to remove catalysts were fractionally distilled at atmospheric or 100 mm. pressure through 75 cm. × 14 mm. electrically-heated columns packed with $^3/_{32}$ inch "Pyrex" helices and equipped with intermittent takeoff distillation heads. The alkylate samples taken for analysis distilled from 2–5° below the boiling point of the meta isomer to 2–5° above the boiling point of the para isomer. In many cases the higher-boiling transition cuts, in which the ortho isomers would be expected to concentrate, were also investigated. Numerous distillation cuts were taken, especially in the larger runs, and the refractive indices determined as an index of the amount and distribution of polymeric olefins and other non-aromatic hydrocarbons in the products.

Although material balances in some of the smaller experiments were not very good, losses of the meta and para isomers are very probably proportional because of their similar properties. For this reason the ratio of meta and para isomers in the isolated monoalkylated product is probably a true index of the isomer ratio in the original alkylate.

The analyses of the dialkylbenzene mixtures for the percentages of position isomers were carried out using a routine, quantitative infrared spectrometric method. For the majority of these analyses, spectra were obtained from 2 to 15 μ and the absorbancies of the "aromatic" absorption peaks in the 12 to 15 μ range were measured (Table VI). The instruments were frequently recalibrated against the pure isomers present in the mixture being analyzed. As the pure *s*-butyltoluene isomers were not available, the cymene calibration was used in calculating these analyses. By scanning the spectrum through the entire rock salt region, any abnormalities in individual spectra were easily observed. Ultraviolet spectra were also recorded in order to determine differences which would not be apparent in the infrared analyses.

The routine analyses have an accuracy of better than ± 3 units. The 7% meta, 93% para limiting composition is believed to be accurate to ± 1 unit; the product from expt. 6, which is representative of this group, was determined more accurately as 7.7 ± 0.3% meta and 92.3 ± 0.3% para isomer. Here the sample was bracketed with synthetic mixtures of very nearly the same composition and the analysis was corrected for small amounts of *m*- and *p*-*t*-butyltoluenes in the low boiling and high boiling transition cuts by analyzing these as three component mixtures containing toluene and 3,5-di-*t*-butyltoluene, respectively. Traces of compounds other than *t*-butyltoluenes in the product from the aluminum bromide catalyzed isomerization reduced the absolute accuracy of this determination to about ± 3 units. *o*-*t*-Butyltoluene was detectable in concentrations of as little as 0.2% in mixtures of *t*-butyltoluenes by the infrared technique used in this work.

Procedures. Method A. Alkylation with Olefins over U.O.P. Phosphoric Acid.—The olefin and toluene were premixed in a steel cylinder, pressured with nitrogen and fed through a metering pump to the top of a vertical, stainless steel reactor tube. Here the mixture passed through a preheater section into the catalyst chamber (2 in. i.d., 9 in. long) containing 500 cc. of UOP No. 2 "solid phosphoric acid" catalyst (4–10 mesh). It was then cooled and discharged through a pressure loading device into a degassing device in series with a gasometer and gas condensing system. The preheater section and catalyst bed were separately heated by automatically controlled, aluminum bronze, block furnaces. Catalyst-bed temperatures were measured by a thermocouple placed in a thermowell located in the center of the catalyst bed.

The olefin dissolved in the liquid product was determined by distillation through a low-temperature Podbielniak column. The gas condensed at −78° in the gas condensing system was assumed to be unchanged olefin. The liquid product was distilled without further treatment.

Method B. Hydrogen Fluoride Catalyzed Alkylations.[8a]—The hydrogen fluoride catalyzed alkylations were carried out in ice-cooled, copper flasks equipped with stainless steel stirrer, thermocouple-well, copper gas-outlet tube and in-

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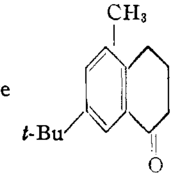
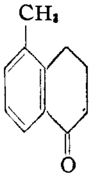
[8a] The procedure used was a modification of those described by Simons and Archer[17] and W. S. Calcott, J. M. Tinker and V. Weinmayr, THIS JOURNAL, **61**, 1010 (1939).

TABLE V

CONTROVERSIAL *t*-ALKYLATIONS OF TOLUENE AND ETHYLBENZENE

	Alkylation procedure		Isomer analysis		
Reactants	Expt. No.	Ref.	Method	Result	Ref.
Toluene, *t*-BuCl, $AlCl_3$	13	6	Identical with product from toluene, *i*-BuBr, $AlBr_3$[a] which gave isophthalic acid on chromic acid oxidn.	*m*[b]	9[c]
			Sepn. of Ba sulfonates[d]	62% *m*, 38% *p*	6
			Sequence of reactions gave 	Pure *m*	7a[c]
			Raman spectra	*m*, *p* (mainly *m*)	5
			Infrared spectra	70% *m*, 30% *p*	Expt. 13
Toluene, *t*-BuCl, $FeCl_3$	10	11	Oxidn. gave *p*-*t*-butylbenzoic acid ("in very good yield") and terephthalic acid; trinitro-deriv. could not be prepared	*p*[e,f]	11
			Parallel sequence of reactions to those used in *m*-structure proof gave  (*t*-Bu group lost in last step)	Pure *p*	7a
			Identity with synthetic product obtained by independent method	*p*-	12
			Infrared spectra	10% *m*, 90% *p*	Expt. 10
	12	6	Selective sulfonation[d]	70% *m*, 28% *p*	6
			Sepn. of Ba sulfonates[d]	67% *m*, 33% *p*	6
			Raman spectra	*m*, *p*, (mainly *p*)	5[c,g]
			Infrared spectra	67% *m*, 33% *p*	Expt. 12
Toluene, *t*-BuCl, $AlCl_3$–nitrobenzene complex	15	6	Selective sulfonation[d]	67% *m*, 33% *p*	6
			Infrared spectra	15% *m*, 85% *p*	Expt. 14
Toluene, *t*-BuOH, BF_3	15	15	Oxidn. to terephthalic acid	*p*	16
			Distillation	55% *m*, 45% *p*	1b
			Infrared spectra	41% *m*, 59% *p*	Expt. 15
Toluene, *t*-BuCl, HF	8, 9	17, 18	Oxidn. to *p*-*t*-butybenzoic acid	*p*-	17, 18
			Infrared spectra	12% *m*, 88% *p*	Expt. 8
				15% *m*, 85% *p*	Expt. 9
Ethylbenzene, *t*-BuCl, $FeCl_3$	27	19	Product did not give trinitro deriv.	(mainly *p*)[h]	19
			Infrared spectra	45% *m*, 55% *p*	Expt. 27[i]

[a] Kelbe and Pfeiffer[10] showed conclusively that *m*- and *p*- "isobutyl" benzoic acids were obtained on dil. nitric acid oxidation of this product. These "isobutyl" derivatives were then subsequently shown by Baur,[9b] Bialobrzeski[11] and Konovalof[13] to be *t*-butyl derivatives. The latter author, by an independent method, also showed that this alkylation product was a *m*-*p* mixture. [b] Noelting[1a] states that in later investigations Baur found this product to be mainly *m*-*t*-butyltoluene containing some *p*-isomer. [c] Alkylation procedure incompletely described. [d] See discussion in text of method of analysis of *t*-butyltoluene mixtures involving sulfonation. [e] Nitration gave nitro derivative with a faint musk-like odor. Verley,[14] studying the product from isobutyl alcohol, toluene and sulfuric acid, noted that a similar faint musk-like odor in the same dinitro derivative disappeared on further recrystallization. This impurity was probably the trinitro derivative from the small amount of *m*-*t*-butyltoluene present. This has an intense musk-like odor. [f] Battegay and Haefely[15] carried out an extensive series of reactions proving the structure of the mononitro derivative obtained from this product. [g] Pajeau[5] used a smaller ratio of ferric chloride to alkylating agent than Shoesmith and McGechen.[6] He apparently obtained a product intermediate in composition between those reported here for expts. 10 and 12. [h] Baur[19] did not assign structure; however, as he also reported that the hydrocarbon (mainly *m*) from the aluminum chloride catalyzed alkylation did give a trinitro derivative with an intense musk-like odor, it is likely that his product was mainly *p*-. [i] Pajeau,[20] alkylating ethylbenzene with a mixture of isobutyl bromide and *t*-butyl bromide in the presence of ferric chloride, reported that he obtained pure *p*-*t*-butylethylbenzene with a Raman spectrum identical with that of the product obtained by reducing *p*-*t*-butylacetophenone.

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(9) (a) W. Kelbe and A. Baur, *Ber.*, **16**, 2559 (1883); (b) A. Baur, *ibid.*, **24**, 2832 (1891).

(10) W. Kelbe and G. Pfeiffer, *ibid.*, **19**, 1723 (1886).

(11) M. Bialobrzeski, *ibid.*, **30**, 1773 (1897).

(12) K. von Auwers, *ibid.*, **49**, 2403 (1916).

(13) M. Konovalof, *J. soc. phys. chim. russe*, **30**, 1036 (1898).

(14) A. Verley, *Bull. soc. chim.*, [3] **19**, 67 (1898).

(15) M. Battegay and P. Haefely, *ibid.*, [4] **35**, 981 (1924).

(16) C. E. Welsh and G. F. Hennion, THIS JOURNAL, **63**, 2603 (1941).

(17) J. H. Simons and S. Archer, *ibid.*, **60**, 2953 (1938).

(18) J. W. Sprauer and J. H. Simons, *ibid.*, **64**, 648 (1942).

(19) A. Baur, *Ber.*, **27**, 1610 (1894).

(20) R. Pajeau, *Bull. soc. chim.*, [5] **13**, 544 (1936).

TABLE VI

PHYSICAL PROPERTIES OF *t*-ALKYL TOLUENES AND *t*-BUTYLETHYLBENZENES

	B.p., °C. at 760 mm.	n^{20}_D	d^{20}_4	M.p., °C.	"Aromatic" absorption peaks, microns *o*-	*m*-	*p*-
o-*t*-Butyltoluene	200.4	1.5076	0.8898	.....	13.2, 13.8		
m-*t*-Butyltoluene	189.3	1.4946	.8659	.....		12.8, 14.2	
p-*t*-Butyltoluene[a]	192.7	1.4919	.8612	.....			12.3, 13.9
m-*t*-Amyltoluene	210.4	1.4975	.8739	.....		12.7, 12.9, 14.2	
p-*t*-Amyltoluene[a]	214.6	1.4958	.8726	−47.83			12.3, 13.9
m-*t*-Butylethylbenzene	205.4	1.4928	.8635	−75.4		12.6, 14.2	
p-*t*-Butylethylbenzene	212.1	1.4933	.8641	−38.35			12.0

[a] A combination of fractional distillation and low temperature recrystallization from methanol was used in the purification of these hydrocarbons.

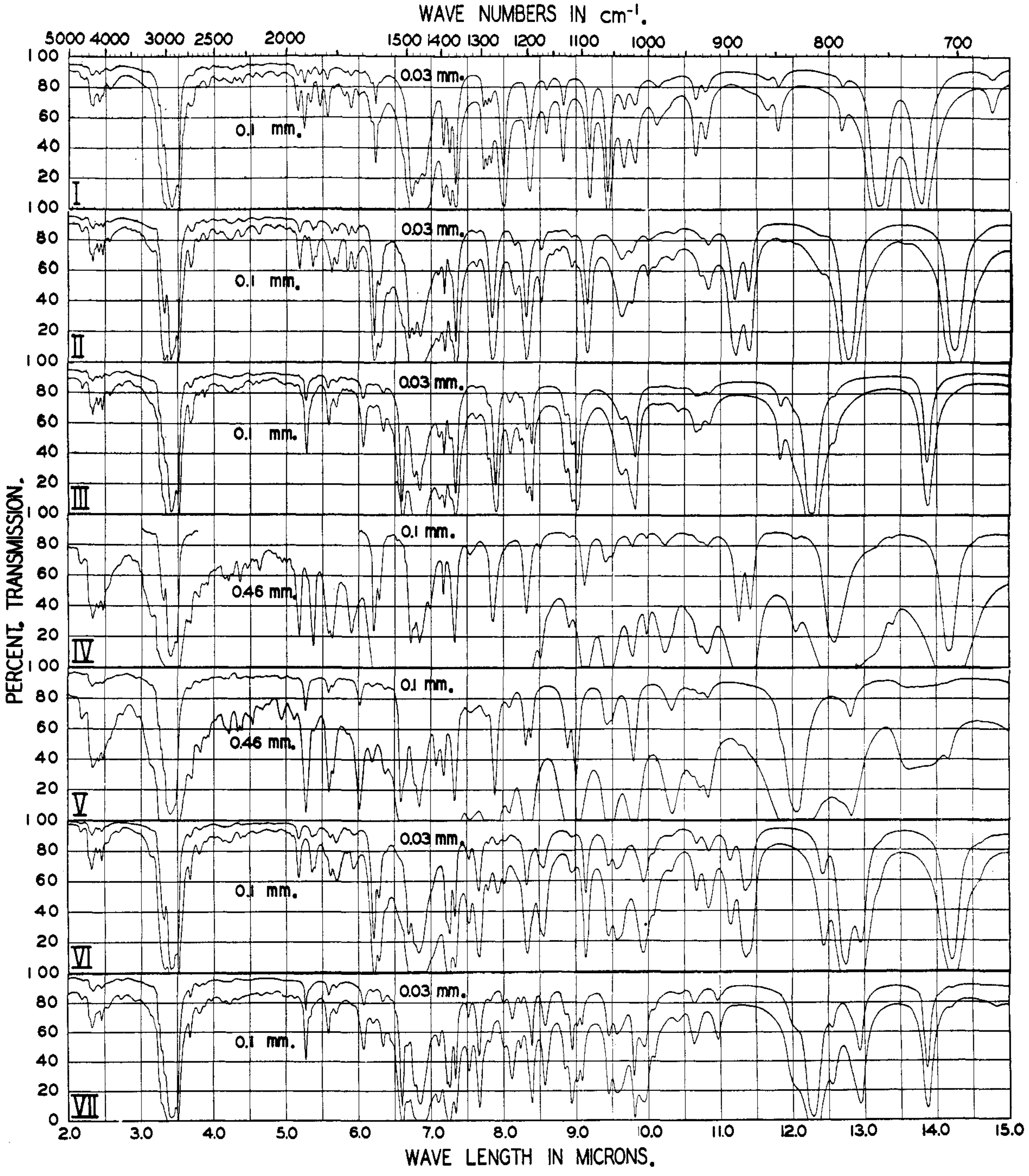

Fig. 1.—Infrared spectra recorded on a model 21, Perkin-Elmer spectrophotometer with a sodium chloride prism; undiluted sample, cell-thicknesses as marked: 1, *o*-*t*-butyltoluene; II, *m*-*t*-butyltoluene; III, *p*-*t*-butyltoluene; IV, *m*-*t*-butylethylbenzene; V, *p*-*t*-butylethylbenzene; VI, *m*-*t*-amyltoluene; VII, *p*-*t*-amyltoluene.

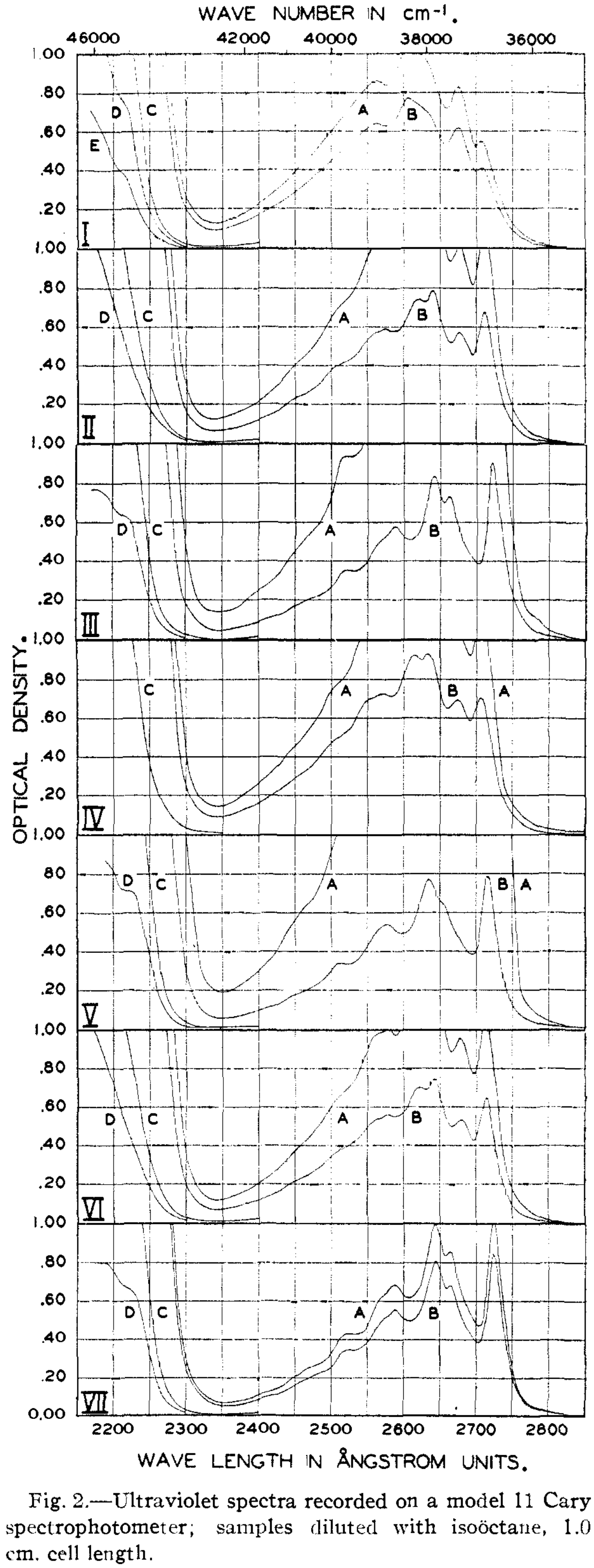

Fig. 2.—Ultraviolet spectra recorded on a model 11 Cary spectrophotometer; samples diluted with isoöctane, 1.0 cm. cell length.

	Compound	Dilutions, g./l. A	B	C	D	E
I	*o-t*-Butyltoluene	0.80	0.592	0.0592	0.0291	0.0145
II	*m-t*-Butyltoluene	.80	.444	.0444	.0222	
III	*p-t*-Butyltoluene	.80	.296	.0296	.0148	
IV	*m-t*-Butylethylbenzene	1.00	.648	.648		
V	*p-t*-Butylethylbenzene	1.00	.324	.0324	.0162	
VI	*m-t*-Amyltoluene	0.80	.444	.0444	.0222	
VII	*p-t*-Amyltoluene	0.40	.324	.0324	.0162	

let tube for addition of reagents. The hydrogen fluoride was added in liquid form from small iron transfer cylinders having a brass valve at each end for convenience in filling. Gases were introduced below the surface of the liquid in the reactor after passing through a calibrated flowmeter; liquids were added through a tube ending above the reactant level. No effort was made to exclude moisture during the operations indicated above.

The catalyst was removed from the products at the end of the reaction period by pouring the two phase reaction product on crushed ice, neutralizing the acid with excess potassium hydroxide, shaking thoroughly, separating and drying the hydrocarbon phase over potassium carbonate.

Method C. Miscellaneous Alkylations.—These alkylations were carried out in small borosilicate glass reaction vessels equipped with stirrer and baffles.[21] The alkylating agent was introduced at the bottom of the reactor; gases after passing through a calibrated flowmeter, liquids together with a slow stream of nitrogen which prevented the alkylating agent and any of the other materials from mixing until they were actually in the body of the reactor. In the ferric chloride and aluminum chloride catalyzed reactions the catalyst was destroyed at the end of the reaction period by adding 1.2 *N* hydrochloric acid. The organic phase was washed with water and dilute sodium carbonate solution and dried over anhydrous potassium carbonate. In the sulfuric acid and phosphoric acid catalyzed reactions, the catalyst layer was drawn off before washing with water and alkali.

Method D. Ferric Chloride Catalyzed Alkylation of Toluene with *t*-Butyl Chloride (Expt. 10).—The procedure used was an attempt to duplicate the experiment of Bialobrzeski.[11]

Toluene (50 g., 0.543 mole, dried over calcium hydride) was placed in a dry one-liter flask with thermometer and 50 g. (0.540 mole) of *t*-butyl chloride added. To this mixture was added 0.30 g. (0.0019 mole) of sublimed, anhydrous ferric chloride[22] in one portion and a reflux condenser attached. Vigorous gas evolution occurred immediately, the temperature rose from 25 to 28° in 10 seconds and then dropped to 18° after one minute, at which time the reaction was almost complete. Three minutes after addition of the catalyst, 200 ml. of water was added and the mixture shaken. The combined product from two runs was steam distilled, separated from the distillate and dried over anhydrous potassium carbonate.

Method E. Ferric Chloride Catalyzed Alkylation of Ethylbenzene with *t*-Butyl Chloride (Expt. 27).—The method used here was an attempt to reproduce an experiment reported by Baur.[19] However, as Baur reported that hydrogen chloride evolution continued for two days while in our experiment the reaction was essentially complete in less than one hour, it appears that our catalyst was more active than his.

The ethylbenzene and *t*-butyl chloride were placed in a dry flask equipped with stirrer, thermometer and reflux condenser. The reactants were protected from moisture with a calcium chloride tube. The mixture was cooled in a bath automatically maintained at −9 to −10° and the ferric chloride added. A vigorous reaction began immediately. Gas evolution was essentially complete in about one hour. After 18 hours, 100 ml. of 1.2 *N* hydrochloric acid was added and the mixture shaken vigorously. The oil was collected in isopentane, washed with 100 ml. of 5% sodium carbonate, dried over anhydrous potassium carbonate and the isopentane removed through a short column.

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(21) The reaction vessels used in several of the experiments listed here are cylindrical reactors with "tru-bore" sealed, axial stirrers carrying four sets of four rectangular vertical blades spaced about 2 cm. apart on the shaft. The reactor tube opposite each set of blades is pressed in to form four vertical baffles, leaving about 1–2 mm. clearance between each blade and the four baffles opposing it. The reactors carry a thermocouple well and an inlet tube at the bottom with a three-way stopcock which permits addition of gas or liquid reactants or allows liquid to be drained from the reactor. Standard taper joints at the top of the reactor permit reflux condenser or other equipment to be attached in the usual manner. The reactors are heated by means of resistance wire wound on the lower part of the reactor and are cooled by immersion in a bath, or in some cases by circulating coolant in a jacket provided for this purpose.

(22) A preliminary experiment using 0.20 g. of ferric chloride was much less vigorous and therefore did not seem to fit Bialobrzeski's description as well as the behavior with 0.30 g.

Method F. Aluminum Bromide Catalyzed Isomerization of *t*-Butyltoluenes (Expts. 37, 38).—The aluminum bromide was added to the mixture of *t*-butyltoluenes and toluene contained in a dry flask equipped with calcium-chloride tube. The mixtures were shaken eight hours each day and allowed to stand at room temperature the rest of the time. At intervals, 100-ml. samples were pipetted from the hydrocarbon phase, shaken with dilute hydrochloric acid, washed with water, dried over anhydrous potassium carbonate and the *t*-butyltoluene fraction, distilling from 185–195°, isolated by distillation through a small twenty-plate column using biphenyl to minimize losses due to column hold-up.

Method G. Aluminum Bromide Catalyzed Isomerization of *t*-Butyltoluenes (Expt. 39).—The isomerization was carried out in a borosilicate glass reaction vessel equipped with stirrer and baffles[22] and provided with a drying tube. The *t*-butyltoluenes and aluminum bromide were stirred eight hours during each 24-hour period. The isomerization was carried out at room temperature for the first three days and at 25 ± 1° during the rest of the six-day period. The heavy catalyst layer was separated, the hydrocarbon layer clarified by centrifuging, washed with dilute hydrochloric acid and water, dried over potassium carbonate and fractionally distilled. The transition cuts and main *t*-butyltoluene fraction were analyzed separately: 109.3–120.2° at 100 mm. (6.4 g.), 120.2–122.0° at 100 mm. (165.9 g.), 122.0–160.2° at 100 mm. (6.4 g.).

RICHMOND, CALIFORNIA

[CONTRIBUTION FROM ABBOTT LABORATORIES]

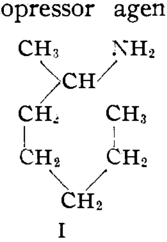
The Synthesis of Some Tertiary Carbinamines as Vasopressor Agents

BY K. E. HAMLIN AND MORRIS FREIFELDER

RECEIVED AUGUST 1, 1952

The synthesis of a series of tertiary carbinamines as vasopressor agents has been accomplished by two methods. The hydrogenation of tertiary nitrocyclanes afforded certain of these amines. In addition, sodium amide cleavage of tertiary alkyl phenyl ketones yielded tertiary carboxamides which were converted by sodium hypobromite to tertiary carbinamines. N-Alkylation of these compounds by a variety of methods is described.

It has been well established that vasopressor action is not confined to members of the phenethylamine series. Indeed, examination of a large group of aliphatic amines has indicated that practical pressor activity is found in those compounds with seven or eight carbon atoms having the amino group in the 2-position.[1a,b] Such pharmacologic effects may also be found in certain alicyclic amines. While cyclohexylamine itself has only mild pressor activity, recently both 1-cyclohexyl- and 1-cyclopentyl-2-methylaminopropane have proved to be valuable medicinal agents in this field.[2a,b] These facts suggested the investigation of certain cyclized analogs of the 2-aminoalkanes (I), *i.e.*, 1-amino-1-methylcyclanes (II) and their derivatives as vasopressor agents. In addition, such compounds may be regarded as tertiary carbinamines, certain examples of which have been found to be useful agents in this field.[3a,b]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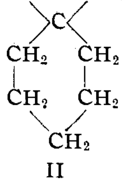
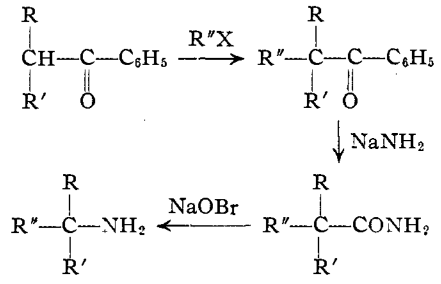

II

The most direct method of preparation of such amines appeared to be the nitration of the appropriate hydrocarbon followed by catalytic hydrogenation of the tertiary nitrocyclane. Several procedures are available whereby hydrocarbons can be nitrated satisfactorily at the tertiary position. Thus 1-methyl-1-nitrocyclohexane has been prepared by Nametkin[4] by nitrating methylcyclohexane with aluminum nitrate. The secondary nitro products were removed by alkali extraction. With minor modifications, this method was used to nitrate the isomeric dimethylcyclohexanes, and hydrogenation using a Raney nickel catalyst provided the corresponding tertiary carbinamines (method A).

This procedure, however, had serious limitations. The synthesis of additional members of the series was necessarily restricted by the available pure hydrocarbons. Also, after conducting numerous nitrations with no untoward effects, during one experiment there resulted a violent exothermic reaction causing considerable damage to the autoclave. As a result, the general method of Haller[5] for the preparation of tertiary carboxamides was investigated. This procedure involves the cleavage of a tertiary alkyl phenyl ketone with sodium amide. The complete reaction sequence may be depicted as



In a model experiment, isobutyrophenone was alkylated with *n*-amyl bromide and the resulting tertiary ketone, where R and R′ represent methyl and R″ represents *n*-amyl, was cleaved with sodium amide in refluxing toluene. The resulting

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(1) (a) E. Rohrmann and H. A. Shonle, THIS JOURNAL, **66**, 1516 (1944); (b) E. E. Swanson and K. K. Chen, *J. Pharmacol.*, **88**, 10 (1946).

(2) (a) E. Macko and E. J. Fellows, *Federation Proc.*, **8**, 318 (1949); (b) E. E. Swanson and K. K. Chen, *J. Pharmacol.*, **93**, 423 (1948).

(3) (a) R. S. Shelton and M. G. Van Campen, Jr., U. S. Patent 2,408,345 (1942); (b) R. S. Shelton and M. G. Van Campen, Jr., U. S. Patent 2,482,377 (1946).

(4) S. Nametkin, *J. Russ. Phys. Chem.* (*Ger.*), **42**, 691 (1909); *Chem. Zentr.*, **81**, II, 1377 (1910).

(5) A. Haller, *Bull. soc. chim.*, **31**, 1073 (1922).