

12,500);  $\lambda_{\text{max}}^{\text{CHCl}_3}$  3.4 (m,broad), 3.8(w), 3.96(w), 5.94(s), 6.07(m-s), 7.02(m), 7.22(m-w), 7.41(w), 7.81(s), 8.22 (shoulder), 8.60(m), 8.91(w), 9.21(m), 9.84 (m, typical for tiglic acid), 10.65(m, broad), 11.55(m)  $\mu$ . When the sodium salt of 100 mg. (1.0 mmole) of tiglic acid in 5 cc. of methanol and 1 cc. of water was treated with 500 mg. (2.5 mmole) of S-benzylisothiuronium chloride in 2 cc. of water an immediate precipitation of the S-benzylisothiuronium salt of tiglic acid took place, yield 260 mg. (97%), m.p. 158-159°. Recrystallization from 95% ethanol afforded an analytical sample as colorless needles, m.p. 161.5-162.5°.

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$ : C, 58.62; H, 6.81; N, 10.52; S, 12.04. Found: C, 58.88; H, 6.85; N, 10.54; S, 12.25.

The angelic acid obtained in this work had the following properties: m.p. 44.5-46°;  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  215.5  $\mu$  ( $\epsilon$  9,360);  $\lambda_{\text{max}}^{\text{CHCl}_3}$

3.41(m), 3.8(w, shoulder), 5.92(s), 6.08(m), 6.81(m), 7.0(m, broad), 7.25(w), 7.41(w), 7.93(s, broad), 8.22 (shoulder), 8.45(w), 8.59(m), 8.80(w), 9.20(m), 9.57(m, typical for angelic acid), 10.69(m, broad), 11.68(m)  $\mu$ . When the sodium salt of angelic acid was treated with S-benzylisothiuronium chloride as described above for tiglic acid, no precipitation was observed.

The treatment of a mixture of the sodium salts of 50 mg. of tiglic acid and 50 mg. of angelic acid in 5 cc. of methanol and 1 cc. of water with 500 mg. of S-benzylisothiuronium chloride in 2 cc. of water yielded 131 mg. (98%) of the derivative of tiglic acid, m.p. 153-154°. Recrystallization from 95% ethanol raised the m.p. to 159-160°, undepressed when mixed with the sample obtained from pure tiglic acid.

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[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION]

## Distribution of Isomers in the Acetylation of *t*-Butylbenzene

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*m-t*-Butylacetophenone has been identified as a product in the conventional Friedel-Crafts acetylation of *t*-butylbenzene. Using infrared spectrometric methods, the ratio of *o* : *m* : *p-t*-butylacetophenone was found to be 0:1.8:98.2. Minor amounts of acetophenone, *m*-di-*t*-butylbenzene and di-*t*-butylacetophenone are formed.

It has been assumed that only *para* derivatives are formed in Friedel-Crafts acylations of mono-substituted benzenes.<sup>1</sup> Work by Papa, *et al.*,<sup>2</sup> and others,<sup>3,4</sup> has shown that *meta* orientation does occur in the acylations of  $\alpha$ -substituted toluenes in which the  $\alpha$ -substituents are strongly *meta* directing. However, no examples of *meta* acylation are reported for simple alkyl benzenes.

The synthesis of *p-t*-butylacetophenone by Friedel-Crafts acylation of *t*-butylbenzene with acetyl chloride has been reported previously<sup>5-10</sup> but the isomer distribution was not given. In the current work, the isomer distribution and the minor products were determined by a careful fractional distillation of the reaction products and physical and chemical analyses of various fractions. The identification of *m-t*-butylacetophenone, the first reported formation of a *meta* isomer in the acylation of an alkyl benzene, is important in view of the current interest in orientation in aromatic substitution.<sup>11,12</sup>

### Discussion of Results

The *t*-butylacetophenone was prepared by the conventional means of acetylation<sup>13</sup> of *t*-butylben-

zene; 93.5% of the calculated weight yield was isolated in the various cuts of a fractional distillation (Table I, Fig. 1). The 6.5 weight per cent. loss may be attributed to the loss of low molecular weight material during the reaction (*i.e.*, isobutane), the loss of slightly water-soluble materials in the separation of the reaction mixture, and the loss of portions of the low boiling fractions during distillation. However, it may be assumed that the compositions of the various fractions represent a close approximation to the compositions prior to any loss.

The infrared spectra of *p-t*-butylacetophenone, purified by crystallization to a constant freezing point (Fig. 2), acetophenone and *t*-butylbenzene were used as criteria for determining the percentage of these compounds present in any fraction and for determining the percentage of other compounds by difference.

Tabulation of the distillation data gives the following mole per cent. conversions based on *t*-butylbenzene charged: *t*-butylbenzene (recovered), 1.9; *p-t*-butylacetophenone, 85.9; *m-t*-butylacetophenone, 1.55; acetophenone, 3.05; *m*-di-*t*-butylbenzene, 0.1; di-*t*-butylacetophenone, 2.5 (all high boiling miscellaneous materials are included in this percentage). A total of 94.1 mole per cent. is accounted for. The *para* to *meta* ratio of *t*-butylacetophenones is 98.2/1.8. There is no evidence for an ortho isomer.

This work does not afford a basis for assigning a mechanism for the formation of *m-t*-butylacetophenone, that is, whether it is formed by acetylation in the *meta* position or by some more devious route. There is considerable evidence for migrations of both alkyl and acetyl groups<sup>7,10,14,15</sup> in aromatic ketones in the presence of aluminum

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TABLE I  
DISTILLATION DATA

Cut no.	Reflux ratio	B.p., °C. (22 mm.)	Total wt., g.	<i>p</i> - <i>t</i> -Butylacetophenone (% of cut)	<i>m</i> - <i>t</i> -Butylacetophenone (% of cut)	Acetophenone (% of cut)	Miscellaneous (% of cut)
1	50:1	63.0-98.5	29.4	....	....	37.5 ± 2.5	62.5 ± 2.5 <sup>a</sup>
2	50:1	98.5-99.0	1.9	4 ± 1	....	96 ± 1	....
3	50:1	99.0-99.8	6.7	4 ± 1	....	96 ± 1	....
4	50:1	99.8-117.0	4.3	5	....	95	....
5	50:1	117.0-143.0	10.5	54	8	30	10 <sup>b</sup>
6	50:1	143.0-143.5	2.3	58	22	20	....
7	50:1	143.5-144.8	2.4	69	23	8	....
8	50:1	144.8-146.0	3.2	74	22	4	....
9	50:1	146.0-146.5	4.9	81	18	1	....
10	50:1	146.5-147.0	6.2	82	17	1	....
11	10:1	147.0-148.0	6.2	87	13	0	....
12	10:1	148.0-149.0	19.8	95	5	....	....
13-16	1:1	149.0-150.0	911.5	98.5 ± 0.5	1.5 ± 0.5	....	....
17	1:1	150.0-151.0	91.7	98	0	....	2 <sup>c</sup>
18	1:1	151.0-156.0	47.2	88	0	....	12
19	1:1	156.0-163.0	41.2	74	0	....	26
Bottoms	..	.....	24.8	....	....	....	100
Trap	..	.....	57.8	....	....	....	100 <sup>d</sup>
Loss	..	.....	17.5	....	....	....	100
Totals	..	.....	1289.5	85.8	1.6	2.1	10.5 <sup>e</sup>

<sup>a</sup> *t*-Butylbenzene. <sup>b</sup> *m*-Di-*t*-butylbenzene. <sup>c</sup> *m*-Di-*t*-butylacetophenone. <sup>d</sup> Mostly carbon disulfide and ether. <sup>e</sup> Includes recovered *t*-butylbenzene.

chloride, even at 0°. As the *meta* isomer may be formed by isomerization rather than *meta* acetylation, the stated *meta* content should be considered a maximum for *meta* substitution.

The acetophenone and di-*t*-butyl derivatives are probably formed as a result of disproportionation of *t*-butylbenzene to benzene and *m*-di-*t*-butylbenzene, for it has been shown that *t*-butylbenzene undergoes rapid and extensive disproportionation with HF-BF<sub>3</sub> as catalyst at 0°. The minor extent of this disproportionation in the Friedel-Crafts reaction is explained by the mode of addition of the reagents and by the competitive acetylation reaction, both of which limit the concentration of *t*-butylbenzene in contact with aluminum chloride at any time.

### Experimental

**Acetylation.**—A mixture of 990 g. (7.39 moles) of *t*-butylbenzene (Phillips Pure Grade, benzene-free) and 632 g. (8.08 moles) of acetyl chloride (Baker, C.P.) was added, dropwise, to a stirred mixture of 1,002 g. (7.56 moles) of AlCl<sub>3</sub> (Baker, C.P.) in 1000 ml. of CS<sub>2</sub> (Baker, C.P.) maintained between -5 and +5°. The addition of this mixture was completed in three hours. The reaction mixture was allowed to warm to 15° and then poured onto 4 kg. of ice in 1 liter of concentrated HCl. The organic layer separated and the aqueous layer was extracted with four 1-liter portions of ether. The organic layers were combined, dried over K<sub>2</sub>CO<sub>3</sub>, filtered and distilled, first at atmospheric pressure and then at 20 mm. to remove the solvent; yield 1289.5 g.

**Distillation.**—The organic material was distilled through a 32-inch by 3/4-inch heated column packed with 1/4-inch McMahon saddles.<sup>17</sup> The column was equipped with a vacuum jacketed head with a solenoid controlled variable takeoff valve. The pressure was maintained at 22 mm. of mercury with an electronic manostat. (At this pressure and with the boil-up rate used, about 700 ml./hr., the column should have about 30 theoretical plates at total reflux.) The distilling flask was equipped with a thermometer well, and

boiling sticks were used to facilitate smooth boiling. Table I shows the reflux ratios used, boiling points, and weights for each of the various fractions, as well as the composition of the fractions. Figure 1 shows the over-all distillation curve and an enlarged curve of the first part of the distillation.

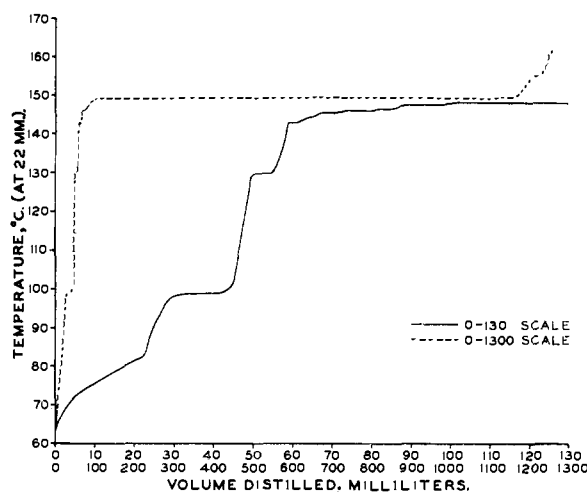


Fig. 1.—Distillation curve of *p*-*t*-butylacetophenone reaction mixture at 22 mm.

The low boiling material, which was collected in a Dry Ice trap, was not analyzed but is believed to be carbon disulfide and ether. It may have contained some *t*-butylbenzene, however, and possibly some benzene. It is assumed that the material lost in the distillation was of a similar low boiling mixture.

Distillation cut 1 was composed of unreacted *t*-butylbenzene and acetophenone. Cuts 2, 3 and 4 are almost pure acetophenone. Cut 5 was shown to contain a small amount of *m*-di-*t*-butylbenzene. Fractions 6 through 10 contain acetophenone, *m*-*t*-butylacetophenone and *p*-*t*-butylacetophenone. The acetophenone content diminishes rapidly in fractions 5 through 10. The *m*-*t*-butylacetophenone diminishes in fractions 9 through 12 but persists even in the long plateau fractions 13 through 16, which are practically pure *p*-*t*-butylacetophenone.

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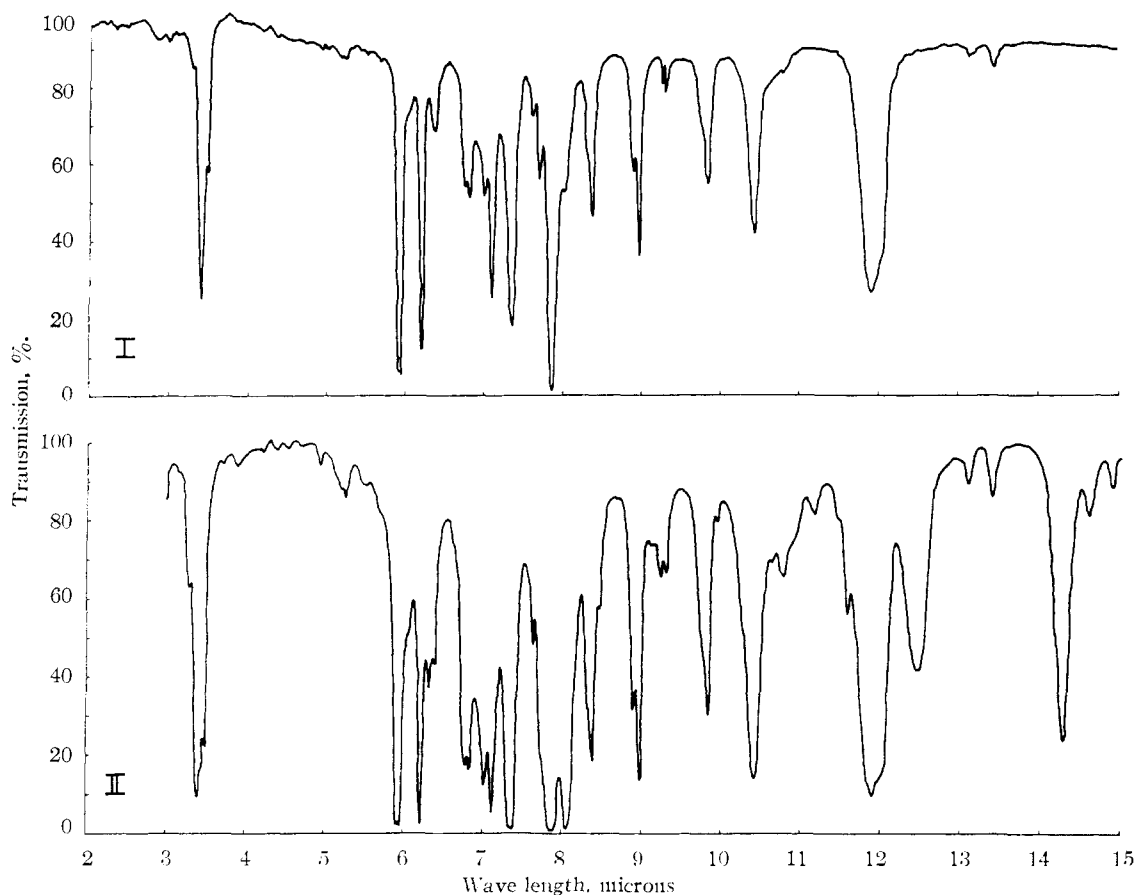


Fig. 2.—Infrared spectra recorded on a model 21, Perkin-Elmer infrared spectrophotometer: I, *p-t*-butylacetophenone, cell length 0.01 mm.; II, 78% *p-t*-butylacetophenone, 22% *m-t*-butylacetophenone, cell length 0.1 mm.

The high boiling cuts (17 and higher) were examined spectroscopically only for *p-t*-butylacetophenone content. Sublimation of the still residue yielded a colorless crystalline compound for which elemental analysis indicated the empirical formula for *di-t*-butylacetophenone.

**Pure *p-t*-Butylacetophenone.**—A 100-g. sample of the composite of fraction 13 through 16 was cooled under nitrogen until crystallization began and then kept at  $15 \pm 1^\circ$  overnight. The supernatant liquid was removed by inverted filtration. The remaining solid was heated to  $16 \pm 1^\circ$  for one hour and then the filtration was repeated. A yield of 89 g. of solid, m.p.  $17.7^\circ$  (cor.), f.p.  $17.5^\circ$  (polymorph f.p.  $5.2^\circ$ ),  $n_D^{20}$  1.5210, was obtained. Recrystallization of this material did not change the melting or freezing points. The infrared spectrum of this material indicated that it was spectroscopically pure *p-t*-butylacetophenone. The combined supernatant liquids, 10 g., were shown by spectroscopic analysis to have a *para/meta* ratio of 85/15. *p-t*-Butylacetophenone semicarbazone was prepared in a conventional manner and recrystallized in ethanol, m.p.  $228.6-229.0^\circ$  (cor.).

*Anal.* Calcd. for  $C_{13}H_{18}N_2O$ : C, 67.12; N, 18.01; H, 8.21. Found: C, 67.33, 67.37; N, 17.92, 18.04; H, 8.17, 8.25.

**Identification of *m-t*-Butylacetophenone.**—Although *m-t*-butylacetophenone was not isolated, it was identified by the following evidence.

1. *m-t*-Butylacetophenone would be expected to boil close to but slightly below the *para* isomer. Distillation cuts 6 through 12 contain a material boiling slightly below *p-t*-butylacetophenone.

2. Cuts 6 through 12 show infrared absorption peaks at 12.5 and  $14.3 \mu$  indicating the presence of a *meta* disubstituted benzene, shown in Fig. 2.

3. Crystallization of cut 12 yielded pure *p-t*-butylaceto-

phenone and a mixture having a *para/meta* ratio of 78/22, by infrared analysis (Fig. 2). The elemental analysis of this mixture was found to be consistent with the empirical formula  $C_{12}H_{16}O$ .

*Anal.* Calcd. for  $C_{12}H_{16}O$ : C, 81.77; H, 9.15. Found: C, 81.72, 81.85; H, 9.20, 9.26.

**Identification of Acetophenone.**—The spectra of fractions 3, 4 and 5 were almost identical with the spectrum of an authentic sample of acetophenone. The semicarbazone was prepared from fraction 3 in the conventional manner and crystallized twice in ethanol, m.p.  $193-195^\circ$ . An authentic acetophenone semicarbazone melted at  $193-195^\circ$  and a mixed melting point of  $193-195^\circ$  was observed.

**Identification of *m-Di-t*-butylbenzene.**—Examination of the distillation curve shows a plateau at  $130^\circ$  (22 mm.) in fraction 5. This fraction was redistilled and the infrared spectrum of the heart cut was obtained. The spectrum indicated the presence of approximately 10% of *m-di-t*-butylbenzene in the original fraction 5. A sample of the redistilled fraction, analyzed by mass spectroscopy showed a prominent peak at mass 190 (dibutylbenzene), but this was different from the known mass spectrum of *p-di-t*-butylbenzene. Thus, the boiling point, infrared spectrum and mass spectrum confirm the presence of a small quantity of *m-di-t*-butylbenzene in fraction 5.

**Identification of *Di-t*-butylacetophenone.**—A colorless, crystalline solid was obtained by sublimation of a portion of the still residue at  $75^\circ$  and 0.28 mm. Recrystallization from methanol yielded a solid, m.p.  $41.0-42.0^\circ$ . A semicarbazone derivative could not be obtained from this material.

*Anal.* Calcd. for  $C_{16}H_{24}O$ : C, 82.6; H, 10.40. Found: C, 82.90, 82.20; H, 10.19, 10.08.

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