the two pure isomeric esters. A linear dependence of refractive index on composition was assumed. While this method is subject to distortion by small amounts of impurities and is not so accurate as that employing the ultraviolet spectra, it has the advantages of speed and simplicity and was also employed in roughly estimating the composition of the mixtures of unsaturated acids obtained from equilibrations.

Equilibrations of mixed esters were performed according to a previously described procedure.[2]

A. Ethyl 4-isopropyl-3-methyl-2(and -3)-octenoates. Run I. A solution of 3.4*N* sodium glycolate was prepared in a metal flask by dissolving 5.8 g. of sodium in 75 ml. of anhydrous ethylene glycol. This had been previously dried by distilling 150 ml. of glycol from over sodium into the metal flask and then redistilling half of this quantity to remove last traces of water. To the sodium glycolate solution was added 10 g. of a mixture of ethyl 4-isopropyl-2-methyl-2(and -3)-octenoates (n_{D}^{25} 1.4410) containing *ca.* 27% of the conjugated isomer. The resulting mixture was refluxed for 36 hours, cooled, and diluted with water, then refluxed an additional hour to saponify the glycol esters. The reaction mixture was poured into water, acidified, and worked up in the usual manner. The mixed acids, which were distilled rapidly, weighed 8.1 g. and had b.p. 115–124°/1 mm., n_{D}^{25} 1.4602. A small sample taken just prior to distillation had n_{D}^{25} 1.4605, showing that no separation of isomers had occurred during distillation. From the refractive index of the distilled mixture it was estimated to contain 72% of the conjugated isomer. The ultraviolet absorption spectrum (Fig. 2, Curve II) has ϵ_{220} 11,270, from which the mixture may be calculated to contain 78% of the α,β-unsaturated isomer.

Run 2. The second run was performed in the same manner as the first. A mixture of 10 g. of mixed γ-isopropyl unsaturated esters (n_{D}^{25} 1.4488), containing 67% of conjugated isomer, and 75 ml. of 3.4*N* sodium glycolate solution was heated for 39 hr. under reflux, then diluted with water and worked up as before. The mixed unsaturated acids obtained weighed 8.1 g. and had b.p. 114–130°/1 mm., n_{D}^{25} 1.4602. From the refractive index the mixture was estimated to contain 72% of the conjugated isomer. The ultraviolet absorption spectrum (Fig. 2, Curve III) has ϵ_{220} 11,170, from which it may be calculated that the mixture contains 77% of the α,β-unsaturated isomer.

B. Ethyl 4-tert-butyl-2-methyl-2(and -3)-octenoates. The same procedure was employed as that described above for the γ-isopropyl esters. A mixture of 10 g. of mixed γ-*tert*-butyl esters (n_{D}^{25} 1.4413), containing *ca.* 16% of the conjugated isomer, and 75 ml. of 3.4*N* sodium glycolate solution was heated for 41 hr. under reflux and worked up as above. The isomerized product was distilled to give 7.9 g. of a solid mixture of acids, b.p. 115–135°/0.9 mm. The ultraviolet spectrum had ϵ_{220} 12,200, from which the mixture may be calculated to contain 86% of the conjugated isomer. The shape of the absorption spectrum between 205 and 230 mμ also agrees well with that calculated for a hypothetical mixture containing 86% of the conjugated acid.

URBANA, ILL.

[CONTRIBUTION FROM KOPPERS CO., INC., MONOMER FELLOWSHIP AT MELLON INSTITUTE]

Isomerization Accompanying the Acetylation of *p*-*t*-Butyltoluene

W. J. HEINTZELMAN AND B. B. CORSON

Received Aug. 6, 1956

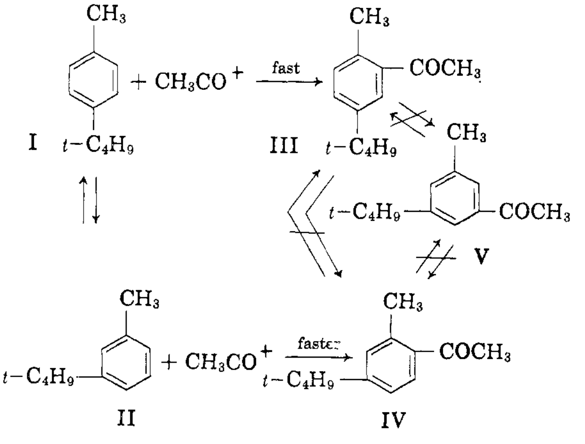
By suitable choice of the order of addition of the reactants, the acetylation of *p-t*-butyltoluene can be directed to give either 2-methyl-4-*t*-butylacetophenone or 2-methyl-5-*t*-butylacetophenone.

There is considerable confusion in the literature concerning the orientation of the ketones resulting from the aluminum chloride catalyzed acetylation of certain *p*-dialkylbenzenes in which one or both of the alkyl groups are secondary or tertiary. It has been variously reported that the product is a 2,4-dialkylacetophenone,[1–5] a 2,5-dialkylacetophenone,[5,6] and a mixture of 2,4- and 2,5-dialkylacetophenones.[7] These conclusions were based on nonquantitative data—the isolation of ketone derivatives, often in small yield.

We have investigated the acetylation of *p-t*-butyltoluene under a variety of conditions and determined the composition of the acetylated products by means of infrared spectrometry. Our results support a mechanism in which the rate-determining step is the ionization of acetyl chloride and the rate of acetylation of *p-t*-butyltoluene is slower than the rate of acetylation of *m-t*-butyltoluene.

It was further shown that 2-methyl-4-*t*-butylacetophenone (IV) and 2-methyl-5-*t*-butylacetophe-

$$CH_3COCl + AlCl_3 \xrightleftharpoons{\text{slow}} CH_3CO^+ + AlCl_4^-$$



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[1] Newton, *J. Am. Chem. Soc.*, **65**, 2444 (1943).

[2] Nightingale and Hucker, *J. Org. Chem.*, **18**, 1529 (1953).

[3] Pines and Shaw, *J. Org. Chem.*, **20**, 373 (1955).

[4] Royals and Prasad, *J. Am. Chem. Soc.*, **77**, 1696 (1955).

[5] Watts and Taylor, *J. Chem. Soc.*, 1123, 5054 (1952).

[6] Hennion and McLeese, *J. Am. Chem. Soc.*, **64**, 2421 (1942).

[7] Nightingale and Shackelford, *J. Am. Chem. Soc.*, **78**, 133 (1956).

TABLE I

ACETYLATION OF *p*-*t*-BUTYLTOLUENE

(CH_3COCl-$AlCl_3$/$C_4H_9C_6H_4CH_3$ mole ratio = 1.1/1)

	Hours				Methyl-*t*-butylacetophenone		
		After			%	% Comp'n	
Expt.	Addition	addition	T°C.	Solvent	Yield	2,4-	2,5-
	Procedure A: $C_4H_9C_6H_4CH_3$–CH_3COCl Mixture Added to $AlCl_3$						
1	1.5	6.0	25–30	CS_2	85	97	3
2	1.5	1.5	25–30	CCl_4	62	94	6
3	1.5	1.5	0–10	CS_2	70	74	26
4[a]	1.5	10.0	0–10	CS_2	45	45	55
5[b]	1.5	1.5	25–30	CCl_4	73	97	3
	Procedure B: $C_4H_9C_6H_4CH_3$ Added to CH_3COCl-$AlCl_3$ Mixture						
6	1.5	1.5	25–30	CCl_4	56	51	49
7	0.3	1.5	0–10	CCl_4	67	36	64
8	1.5	1.5	0–10	CCl_4	75	29	71
9[c]	1.5	1.5	0–10	CCl_4	60	24	76
10	1.5	1.5	0–10	$C_6H_5NO_2$	28	13	87
11	1.5	1.5	0–10	$C_6H_5NO_2$	37	7	93
12[d]	1.5	1.5	0–10	CCl_4	61	9	91

[a] Ferric chloride was substituted for aluminum chloride. [b] *t*-Butyltoluene (*m*-*p* = 65–35) was substituted for *p*-*t*-butyltoluene. [c] Previous to addition of the *p*-*t*-butyltoluene, the acetyl chloride–aluminum chloride mixture was aged for 1 hour. [d] Aluminum chloride–acetyl chloride to *p*-*t*-butyltoluene mole ratio was 3.

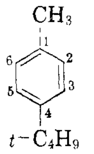
none (III) result from the acetylation of the corresponding *t*-butyltoluenes and not from the rearrangement of an isomeric methyl-*t*-butylacetophenone since neither 2-methyl-4-*t*-butylacetophenone (IV) nor 2-methyl-5-*t*-butylacetophenone (III) nor 3-methyl-5-*t*-butylacetophenone (V) is isomerized under acetylation conditions. Presumably, the presence of the acetyl group deactivates the ring sufficiently to stabilize the positions of the alkyl groups.

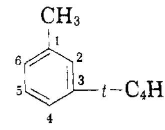
In accordance with this mechanism we can direct the acetylation reaction to give either 2-methyl-4-*t*-butylacetophenone (IV) or 2-methyl-5-*t*-butylacetophenone (III), depending upon the order of addition of the reactants.

When the order of addition of reactants restricts the ionization of acetyl chloride and favors the isomerization of *p*-*t*-butyltoluene, the composition of the product depends upon the relative rates of acetylation of *m*- and *p*-*t*-butyltoluenes. In experiments 1 to 3 of Table I, mixtures of *p*-*t*-butyltoluene and acetyl chloride were added to suspensions of aluminum chloride in nonpolar solvents. The relatively slow ionization of acetyl chloride allowed the major portion of the *p*-*t*-butyltoluene to isomerize to *m*-*t*-butyltoluene prior to acetylation with the result that the ketone products contained 74% to 97% of 2-methyl-4-*t*-butylacetophenone.

Inasmuch as the equilibrium composition of *t*-butyltoluene is 67% *meta*- 33% *para*-,[8] it is evident that *m*-*t*-butyltoluene acetylates faster than *p*-*t*-butyltoluene. If it were not so, the acetylation of *p*-*t*-butyltoluene under isomerizing conditions could not produce a ketone mixture containing more than 67% of 2-methyl-4-*t*-butylacetophenone.

The greater reactivity of *m*-*t*-butyltoluene can be attributed to the combined effects of the hyperconjugation of the methyl group and the induction of the *t*-butyl group activating the 6-position. No position in *p*-*t*-butyltoluene is similarly activated; positions 2- and 4-of *m*-*t*-butyltoluene are similarly activated but are relatively sterically hindered.





When the order of addition of the reactants favors the ionization of acetyl chloride and restricts the isomerization of *p*-*t*-butyltoluene, the product is mainly 2-methyl-5-*t*-butylacetophenone. In experiments 6 to 9 of Table I, *p*-*t*-butyltoluene was added to a preformed mixture of acetyl chloride and aluminum chloride in a nonpolar solvent. Under these conditions of increased CH_3CO^+ concentration, the rate of acetylation was accelerated with respect to the isomerization of *p*-*t*-butyltoluene, with the result that the ketones produced contained 49% to 71% of 2-methyl-5-*t*-butylacetophenone.

Furthermore, when *p*-*t*-butyltoluene was added to mixtures of acetyl chloride and aluminum chloride in a polar solvent (experiments 10, 11 of Table I), the resulting ketone products contained 87% to 93% of 2-methyl-5-*t*-butylacetophenone. Thus, the polar solvent aided the ionization of acetyl chloride, thereby increasing the concentration of CH_3CO^+, with the result that the rate of acetylation was accelerated. Similarly (experiment 12 of Table I), increasing the CH_3CO^+ concentration by using a 2 molar excess of aluminum chloride–acetyl chloride

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(8) Schlatter and Clark, *J. Am. Chem. Soc.*, **75**, 361 (1953).

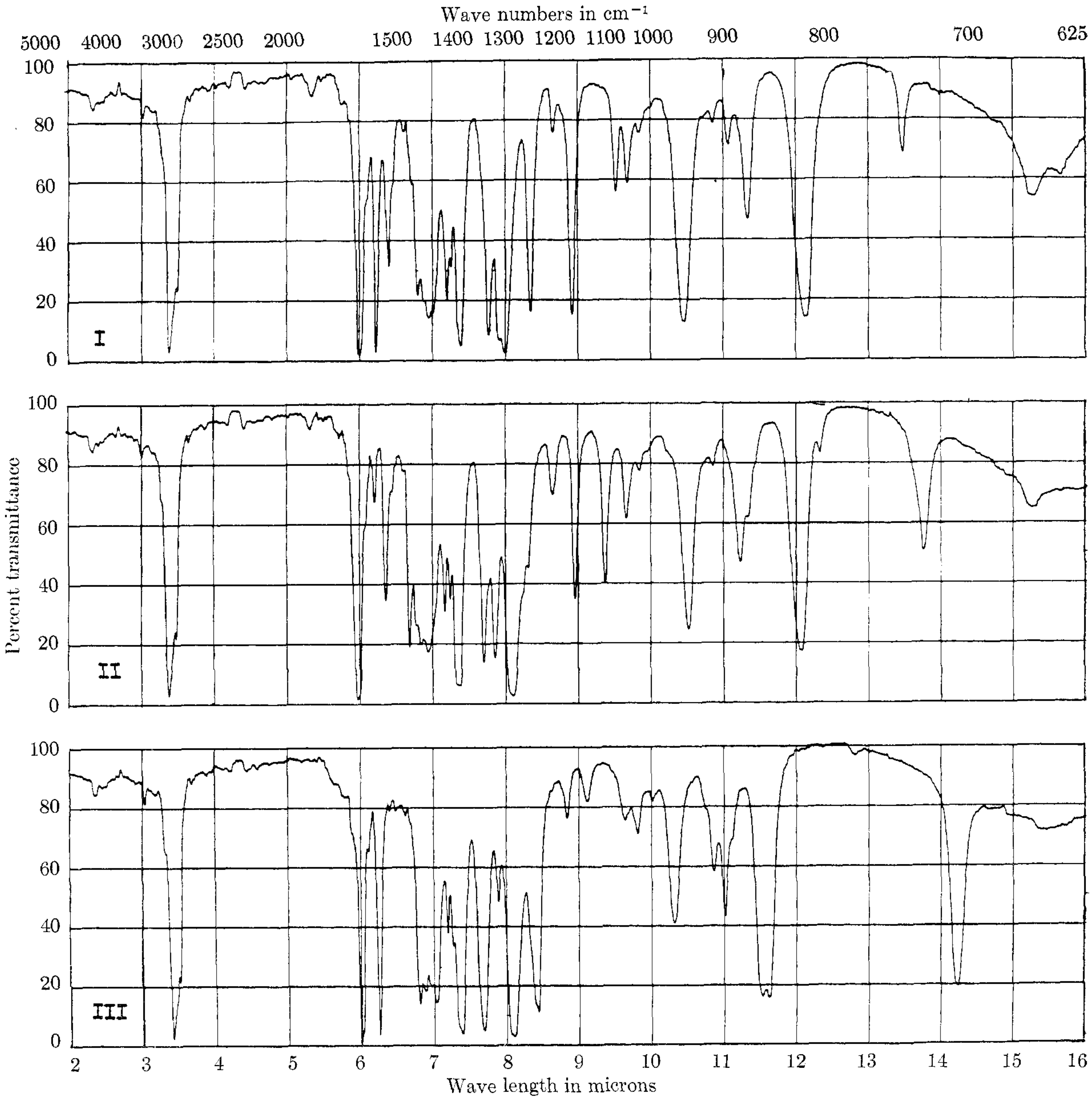
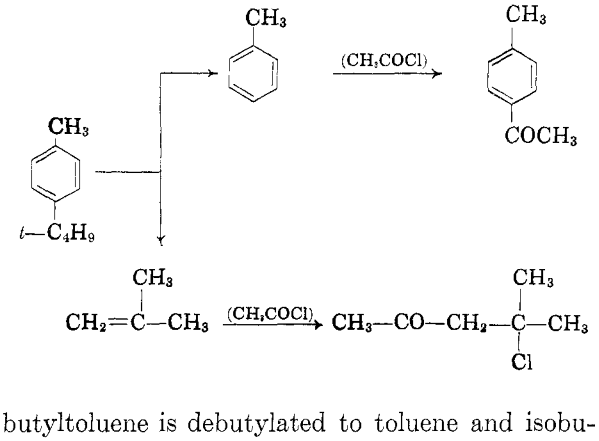


Fig. 1.—Infrared spectra measured on a Baird infrared spectrophotometer Model A with a sodium chloride prism, undiluted sample, 0.028 mm. cell thickness: I, 2-methyl-4-*t*-butylacetophenone; II, 2-methyl-5-*t*-butylacetophenone; III, 3-methyl-5-*t*-butylacetophenone.

gave a ketone mixture containing 91% of 2-methyl-5-*t*-butylacetophenone.

It is to be noted that whereas Nightingale and Shackelford[7] reported that the acetylation of *p*-cymene and *p*-*sec*-butyltoluene in the presence of ferric chloride as catalyst gave no 2,4-dialkylacetophenone, we obtained a ketone from *p*-*t*-butyltoluene under their conditions which contained 45% of 2-methyl-4-*t*-butylacetophenone (experiment 4 of Table I).

In all of the acetylation experiments there was obtained in addition to the methyl-*t*-butylacetophenones a certain amount of low boiling by-product which was shown (experiment 2 of Table I) to be a mixture of *p*-methylacetophenone, *t*-butyltoluene and mesityl oxide. Evidently a portion of the *t*-butyltoluene is debutylated to toluene and isobutylene both of which then react with acetyl chloride



to give, respectively, *p*-methylacetophenone and 4-chloro-4-methyl-2-pentanone. The latter is subsequently dehydrohalogenated to mesityl oxide.[9]

EXPERIMENTAL

Melting points are corrected.

p-t-Butyltoluene. Isobutylene (560 g., 10 moles) was passed into a stirred, 0–10° mixture of 920 g. (10 moles) of toluene and 100 ml. of concentrated sulfuric acid during 3 hr. After stirring the mixture for an additional hour at 0–10°, the hydrocarbon layer was washed with water, refluxed for 1 hour with 300 ml. of 20% aqueous sodium hydroxide and washed again with water. The dried hydrocarbon was distilled through a 23-plate column at 5/1 reflux ratio to give 1129 g. (76% yield) of *t*-butyltoluene; b.p. 185–195°/750 mm., *o-m-p* ratio 0–7–93. Redistillation of this isomer mixture through a 45-plate column at 25/1 reflux ratio gave 740 g. of material which was recrystallized from ethanol 4 times and finally redistilled through a 23-plate column at 10/1 reflux ratio to give 420 g. of *p-t*-butyltoluene; b.p. 191.5°/740 mm., t_f[10] −52.69° (99.7 mole % pure), n_D^{25} 1.4896, d_4^{25} 0.8574. The reported constants[11] are: b.p. 192.76°/760 mm., t_f −52.515°, n_D^{25} 1.4895, d_4^{25} 0.8573. Its infrared spectrum was identical with that of an authentic sample.[12]

Acetylation procedure A. To a stirred mixture of 200 ml. of solvent and 51 g. (0.38 mole) of anhydrous aluminum chloride was added a mixture of 30 g. (0.38 mole) of acetyl chloride and 51 g. (0.35 mole) of *t*-butyltoluene. After stirring for an additional time, the product was poured into a mixture of 40 ml. of concentrated hydrochloric acid and 120 g. of crushed ice. The organic layer, combined with two carbon tetrachloride extracts of the aqueous layer, was washed successively with water, 5% aqueous sodium carbonate, and water. The solvent was stripped off and the residue was distilled through a 27-plate column at 20 mm. at 5/1 reflux ratio. The fraction distilling at 140–150°/20 mm., was taken for analysis.

Acetylation procedure B. To a stirred mixture of 200 ml. of solvent and 51 g. (0.38 mole) of anhydrous aluminum chloride was added 30 g. (0.38 mole) of acetyl chloride during 15 min. To this mixture was added 51 g. (0.35 mole) of *t*-butyltoluene; the mixture was stirred for an additional 1.5 hr. then worked up as in method *A*.

Composition of low boiling by-product. In order to obtain sufficient low boiling by-product to establish its composition, experiment 2 of Table I was repeated on a seven-fold scale. The crude product was steam distilled until practically no more organic material came over. The organic portion of the distillate was distilled through a 23-plate column at 10/1 reflux ratio until, when nearly all of the carbon tetrachloride had distilled, hydrogen chloride started to be evolved. The distillation was stopped and the residue was stirred and heated to 70° with 400 cc. of 5% alcoholic potassium hydroxide during 1 hr. The mixture was diluted with water, and the organic layer, after washing with water, was distilled through a 23-plate column at 10/1 reflux ratio to give four main fractions: (*a*) 14.3 g., b.p. 125–128°/740 mm., identified as mesityl oxide by its infrared spectrum and by the m.p. and mixture m.p. (both 197–198°) of its 2,4-dinitrophenylhydrazone[13]; (*b*) 16.2 g., 185–187°/740 mm., identified by its infrared spectrum as *p-t*-butyltoluene contaminated with a small amount of *m-t*-butyltoluene; (*c*) 17.3 g., b.p. 116–127°/20 mm., identified as *p*-methylacetophenone by its infrared spectrum and by the m.p. and mixture m.p. (both 259–260°) of its 2,4-dinitrophenylhydrazone[13]; (*d*) 79.3 g. of methyl-*t*-butylacetophenone, b.p. 141–148°/20 mm.

The organic residue from the steam distillation was stirred with 5% alcoholic potassium hydroxide at 70° and distilled as above to give an additional 122 g. of methyl-*t*-butylacetophenone.

2-Methyl-4-t-butylacetophenone (spectrometric standard). *t*-Butyltoluene (250 g., 1.7 moles, *o–m–p* ratio 0–7–93) was acetylated by procedure A to give 225 g. (70% yield) of crude 2-methyl-4-*t*-butylacetophenone, t_f 9.47° (88–94 mole % pure). Six crystallizations of this ketone from methanol at −25°, followed by distillation through a 23-plate column at 10/1 reflux ratio gave 146 g. of 2-methyl-4-*t*-butylacetophenone; b.p. 146.5°/20 mm., t_f 11.90° (99.0–99.4 mole % pure).

2-Methyl-5-t-butylacetophenone (spectrometric standard). *t*-Butyltoluene (157 g., 1.1 moles, *o–m–p* ratio 0–7–93) was acetylated by procedure B to give 142 g. (70% yield) of mixed ketones. After cooling overnight at −6°, the mixture was filtered and the solid was recrystallized 3 times from methanol at −6° and finally distilled through a 10-cm. Vigreux column to give 51 g. of 2-methyl-5-*t*-butylacetophenone; b.p. 146°/20 mm., t_f 30.72° (99.4–99.8 mole % pure).

3-Methyl-5-t-butylacetophenone (spectrometric standard). To a 0–10° mixture of 1179 g. (10 moles) of ethyltoluene (*o–m–p* ratio 0–70–30) and 71 g. (0.4 mole) of ferric chloride was added 555 g. (6.0 moles) of *t*-butyl chloride during 1 hr. After stirring for an additional hour the product was poured into a mixture of 150 ml. of concentrated hydrochloric acid and 900 g. of crushed ice and the mixture was steam distilled. The hydrocarbon distillate was redistilled through a 23-plate column at 5/1 reflux ratio to give 319 g. (30% yield) of 3-ethyl-5-*t*-butyltoluene; b.p. 214–216°/740 mm., t_f −33.14° (87–94 mole % pure).

The 3-ethyl-5-*t*-butyltoluene was oxidized as follows: Oxygen was bubbled through a stirred mixture of 142 g. (0.8 mole) of the hydrocarbon and 3.4 g. of 10% manganese naphthenate for 11 hr. at 120–125°. The mixture was cooled, filtered, washed with 10% aqueous sodium hydroxide, refiltered, washed with water, and dried. Distillation through a 27-plate column at 5/1 reflux ratio gave 64 g. of 3-ethyl-5-*t*-butyltoluene (b.p. 108–112°/20 mm.) plus 37 g. of a mixture of 3-methyl-5-*t*-butylacetophenone and the corresponding carbinol (b.p. 140–150°/20 mm.). This ketone-carbinol mixture was prepared to the amount of 120 g.

Anal. Calc'd for $C_{13}H_{18}O$: Carbonyl, 14.7. Found: Carbonyl, 9.9. Calc'd for $C_{13}H_{20}O$: Hydroxyl, 8.9. Found: Hydroxyl, 2.1.

The ketone-carbinol mixture was oxidized as follows: A solution of 60 g. (0.2 mole) of sodium dichromate, 50 ml. of concentrated sulfuric acid, and 300 ml. of water was added with stirring to 120 g. (0.63 mole) of the ketone-carbinol mixture during 1 hr. The temperature did not exceed 50°. The reaction mixture was stirred for an additional 0.3 hr., then extracted with ether. The extract, after washing with dilute sodium hydroxide solution, was stripped of ether and the residue was distilled through a 27-plate column at 5/1 reflux ratio to give 92 g. (77% yield) of crude 3-methyl-5-*t*-butylacetophenone (b.p. 141–150°/20 mm.).

Anal. Calc'd for $C_{13}H_{18}O$: Carbonyl, 14.7. Found: Carbonyl, 12.5.

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(9) Konakoff, *J. Russ. Chem. Soc.*, **26**, 5 (1894); Krapivin, *Chem. Abstr.*, **5**, 1281 (1911).

(10) t_f = freezing temperature determined by extrapolation of freezing curve; temperatures measured by platinum resistance thermometer and G-2 Mueller bridge which had been certified by National Bureau of Standards and checked prior to use at the triple point of water and with a National Bureau of Standards benzoic cell.

(11) Rossini, *et al.*, *Selected Values of Physical Properties of Hydrocarbons*, Carnegie Press, Pittsburgh 13, Pa., 1953, p. 73.

(12) Authentic sample obtained from American Petroleum Institute, Carnegie Institute of Technology, Pittsburgh 13, Pa.

(13) Huntress and Mulliken, *Identification of Pure Organic Compounds, Order I*, John Wiley & Sons, N. Y., 1941.

TABLE II

PROPERTIES AND DERIVATIVES OF METHYL-*t*-BUTYLACETOPHENONES

Acetophenone	B.P., °C./20 Mm.[a]	T_f, °C.	Purity, Mole %	Semicarbazone, M.P., °C.		Derived Benzoic Acid			
						M.P., °C.		Equiv. Wt.	
				Found	Lit.	Found	Lit.	Found	Calc'd
2-Methyl-4-*t*-butyl-	146	11.90	99.0–99.4	195–196	197[5]	142–143	143–144[5]	192.6	192.3
2-Methyl-5-*t*-butyl-	146	30.72	99.4–99.8	180–181	183[4]	98–99	101[5]	192.7	192.3
3-Methyl-5-*t*-butyl-	148	46.14[b]	99.0–99.5	177–178	...	163–164	162[14]	192.0	192.3

[a] Uncorrected. [b] Reported m.p. 47°.[14]

A mixture of 90 g. (0.47 mole) of 3-methyl-5-*t*-butylacetophenone, 71 g. (0.64 mole) of semicarbazide hydrochloride, 95 g. (1.2 moles) of sodium acetate, 280 ml. of water, and 350 ml. of ethanol was refluxed for 1 hour. The solution was cooled to room temperature and filtered. The solid was crystallized 5 times from ethanol to give 50 g. (43% yield) of semicarbazone; m.p. 177–178°, white needles.

Anal. Calc'd for $C_{14}H_{21}N_3O$: N, 16.99. Found: N, 16.69.

The semicarbazone was hydrolyzed by refluxing for 1 hr. with 400 ml. of 20% hydrochloric acid, and the regenerated ketone was extracted with ether. Distillation of the concentrated ether extract through a 27-plate column at 5/1 reflux ratio gave 35 g. (91% yield) of 3-methyl-5-*t*-butylacetophenone; b.p. 148°/20 mm., t_f 46.14° (99.0–99.5 mole % pure).

Anal. Calc'd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.94; H, 9.71.

Hydrobromite oxidation of dialkylacetophenones. The structures of the dialkylacetophenones (99+ mole % pure) were established by oxidation to known dialkylbenzoic acids. The general procedure follows: To a stirred, 0–10° mixture of 150 ml. of 5% aqueous sodium hydroxide and 10 g. (0.13 mole) of bromine was added 4.0 g. (0.02 mole) of dialkylacetophenone during 1 hr. The mixture was subsequently stirred for 9 hr. at 60°. The reaction mixture was cooled and extracted with ether to remove residual ketone. The aqueous layer was acidified and extracted with ether. The extract of the aqueous layer was concentrated and the solid residue was crystallized or sublimed to give about a 75% yield of methyl-*t*-butylbenzoic acid.

Nonisomerization of methyl-t-butylacetophenones. A mixture of 10 g. (0.05 mole) of 2-methyl-4-*t*-butylacetophenone (99.0–99.4 mole % pure), 10 g. (0.08 mole) of aluminum chloride and 100 ml. of carbon tetrachloride was stirred at 30° for 3 hr., then poured into an ice–hydrochloric acid mixture. The organic layer was washed successively with water, 5% aqueous sodium carbonate, and water. Carbon tetrachloride was stripped off, and the residue was distilled through a 10-cm. Vigreux column to give 7.9 g. (79% yield) of ketone whose infrared absorption spectrum was that of 2-methyl-4-*t*-butylacetophenone.

Similar treatment of 2-methyl-5-*t*-butylacetophenone (99.4–99.8 mole % pure) and 3-methyl-5-*t*-butylacetophenone (99.0–99.5 mole % pure) showed that these ketones also were not isomerized under the conditions employed, which were the conditions used in the acetylation of *p-t*-butyltoluene.

PITTSBURGH 13, PA.

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(14) Baur-Thurgau, *Ber.*, **31**, 1345 (1898).

[CONTRIBUTION FROM THE COURTAULD INSTITUTE OF BIOCHEMISTRY]

Constant *Ortho* Effect with an Interacting Substituent

A. E. KELLIE,[1] D. G. O'SULLIVAN, AND P. W. SADLER

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Infrared spectra of a number of substituted anthranilic acids were determined in chloroform and in potassium bromide disks. The extensive hydrogen bonding present in chloroform solution appears to involve both carboxyl and amino groups, but the infrared results suggest that in the solid state hydrogen bonding is confined to the carboxyl groups. No evidence exists for the presence of zwitter ion structures in these compounds. Carbonyl frequencies are linearly related to the σ values of the substituent groups. In spite of the broadening of the carbonyl bands produced by hydrogen bonding, the relation with σ values is readily appreciated from the solution data, but is less apparent from data obtained with solids. Comparison of the spectra of substituted benzoic and anthranilic acids shows that the amino group exerts a constant influence on the carbonyl stretching frequency.

A second substituent R in a benzene ring produces an effect on the reactivity and other properties of the first substituent Y which is dependent on the nature and position of R. If the latter group is present in the *meta* or *para* position with respect to Y, its effect on Y is usually related to the σ value of the R group.[2,3] In multiple substitution, σ constants of the substituents are additive, since in any reaction series in which only the original substituent is modified, the entropy changes are presumably constant. Although σ values cannot be allocated to substituents in the *ortho* position to Y, this essential additivity property is likely to be preserved. Thus the presence of a further substituent X in the *ortho* position to group Y should produce a constant effect on the properties and reactivity of group Y in a series of substituted compounds.[3,4]

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(1) British Empire Cancer Campaign Research Fellow.

(2) L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940, p. 188.

(3) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(4) H. H. Jaffé, *Science*, **118**, 246 (1953).