[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY]

Pivalophenones from Friedel–Crafts and Grignard Reactions[1]

BY D. E. PEARSON

The purpose of this work was to obtain considerable amounts of pivalophenone by an easier and more economical route than that of Marvel and co-workers[2] (pivalyl chloride plus phenylmagnesium bromide, 67%). First attempts, *via* a Friedel–Crafts route, resulted in some rather unusual reactions, which corroborated and extended those reported by Rothstein and Saville.[3] The Friedel–Crafts reactions of pivalyl chloride can be summarized as

$$(CH_3)_3CCOCl \xrightarrow{AlCl_3} HCl + CO + (CH_3)_2C{=}CH_2 \quad (1)$$

$$(CH_3)_3CCOCl \xrightarrow[ARH]{AlCl_3} ARCOC(CH_3)_3 + HCl \quad (2)$$

If the aromatic nucleus is activated as in anisole, the reaction *via* equation 2 takes place almost exclusively.[3] If more weakly activated, as in toluene[3] and ethylbenzene,[3] both processes occur simultaneously. If deactivated, as in nitrobenzene and bromobenzene, the products of equation 1 are obtained practically exclusively. The isobutylene formed (or a precursor of isobutylene) can participate in an ordinary alkylation reaction giving rise to *t*-butyl derivatives. For example, benzene and pivalyl chloride, in the presence of aluminum chloride, yielded the alkylation–acylation product, *p*-*t*-butylpivalophenone.[4]

In any event, it was found more profitable to prepare pivalophenone and substituted pivalophenones from pivalonitrile and the appropriate Grignard reagents.

This research was supported by the Research Corporation of New York and by a grant made available jointly by the Carnegie Foundation and the Natural Science Research Fund of Vanderbilt University.

Experimental[5]

A. **Pivalyl Chloride.**—Pivalonitrile[6] was hydrolyzed to pivalic acid by the method of Sudborough[7] (b. p. 68–71° at 20 mm., 85%). Pivalyl chloride was obtained from pivalic acid by the excellent method of Brown[8] (84% yield, b. p. 103–106°).

B. **General Procedure for Pivalyl Chloride Alkylations and Acylations.**—An excess of the aromatic compound (0.4 mole) was placed in a three-necked, 200-ml. round-bottomed flask equipped with dropping funnel, hydrogen chloride water-trap and mercury-seal stirrer. The dropping funnel and outlet tube to hydrogen chloride trap were protected with calcium chloride tubes. Aluminum chloride (14 g., 0.1 mole, Eastman Kodak Co. Resublimed) was suspended in the aromatic compound while the flask was cooled to ice-water temperature. Pivalyl chloride (9 g., 0.075 mole), dissolved in 10 ml. of the appropriate aromatic solvent, was added dropwise over a period of 20–60 minutes. As the pivalyl chloride entered the aluminum chloride suspension, evolution of gas took place immediately. The gas was a mixture of hydrogen chloride, carbon monoxide and isobutylene, the proportions of which varied depending on the aromatic compound. Qualitative tests were litmus (for the acid), decoloration of bromine in carbon tetrachloride (for isobutylene) and combustion of a gas sample passed through sulfuric acid (carbon monoxide). After the addition of the pivalyl chloride, the mixture was allowed to stir for a half-hour at ice-water temperature and was then decomposed with 100 ml. of 10% hydrochloric acid mixed with ice. The organic layer was extracted with ether and the combined extracts washed with water, saturated sodium bicarbonate and dried with anhydrous sodium sulfate. The ether extract was concentrated in a small, ST, 30-ml. flask, equipped with 2-in. Vigreux column. The residue was then distilled at reduced pressure directly into tared flasks, partial or complete fractionation being accomplished by slow distillation with oil-bath temperature carefully controlled.

1. ***p*-*t*-Butylpivalophenone (I).**—The starting materials were C. P. benzene, pivalyl chloride and aluminum chloride. Yield was 5.6 g. of I (b. p. 103–106° at 1 mm., 0.0257 mole) and impure I (1.9 g., b. p. 84–103° at 1 mm.), which was converted in 60% yield to pure oxime (m. p. 205–206°, 0.005 mole); 82 total mole % yield. Approximately 0.4 g. of *t*-butylbenzene (b. p. 165–175°, $n^{25}D$ 1.4890, 8%) was also isolated. Runs made at higher temperatures or without stirring or without slow addition of pivalyl chloride gave poorer yields. The ketone was identified by independent synthesis from *p*-*t*-butylphenylmagnesium bromide and pivalonitrile (see below) and comparison of mixed melting points of derivatives. I could be crystallized only from a mixture of methyl alcohol and water.

2. **Mixed Di-*t*-butylbenzenes.**—Pivalyl chloride and *t*-butylbenzene (b. p. 167–169°) were treated as in general procedure with aluminum chloride. A crude mixture of di-*t*-butylbenzenes (b. p. 62–79° at 3 mm., 13 g., 92%) was obtained from which 2 g. of *p*-di-*t*-butylbenzene (m. p. 77–78°, b. p. 72–80° at 3 mm.) and 5.5 g. of a hydrocarbon (b. p. 67–72° at 3 mm., $n^{25}D$ 1.4870–1.4871, insoluble in concentrated sulfuric acid) were isolated. Johnson and Adams[9] report b. p. 78.5° at 4.4 mm., $n^{20}D$ 1.4870, m. p. 10.6° for *m*-di-*t*-butylbenzene. Also traces of a compound, m. p. 166–167°, were isolated in the residue of first distillation but in too small a yield for C–H analysis. Foaming was encountered in all distillations involving *p*-di-*t*-butylbenzene. No ketone could be detected in any fraction with 2,4-dinitrophenylhydrazine.

3. **Reaction of Pivalyl Chloride and Nitrobenzene.**—Under the general procedure, 40 g. of nitrobenzene (b. p. 98–99.5° at 20 mm.) yielded 37 g. of nitrobenzene (b. p. 97–100° at 20 mm., slightly darker than original) with no other detectable fractions.

4. ***p*-Methylpivalophenone (II).**—Toluene was used as the solvent and nucleus to be substituted. A mixture was obtained (12 g., b. p. 33–93° at 0.5 mm.) which was refractionated at 750 mm. (5 fractions, b. p. 195–245°).

---

[1] The experimental results were presented at the American Chemical Society Meeting, April, 1948, Chicago, Ill.

[2] Ford, Thompson and Marvel, THIS JOURNAL, 57, 2619 (1935).

[3] Rothstein and Saville, *J. Chem. Soc.*, 1946–1968 (1949).

[4] Rothstein and Saville[3] report only the formation of *t*-butylbenzene in the above reaction.

[5] All melting points were taken with a partial immersion thermometer (ASTM specification).

[6] Harris and de Atley, British Patent, 583,607 (1946); grateful acknowledgment is made to E. I. du Pont, Electrochemical Division, for a generous sample.

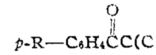
[7] Sudborough, *J. Chem. Soc.*, 67, 602 (1892).

[8] Brown, THIS JOURNAL, 60, 1325 (1938).

[9] Johnson and Adams, U. S. Patent 2,429,691 (1947); *C. A.*, 42, 1605 (1948).

TABLE I

p-SUBSTITUTED PIVALOPHENONES

 $p\text{-R—C}_6\text{H}_4\overset{\text{O}}{\overset{\Vert}{\text{C}}}\text{C(CH}_3)_3$	M. p. or b. p. °C.	Mm.	$n^{25}\text{D}$	$d^{25}{}_{25}$	Yield, %	M. p. hydrazone, °C.	Hydrazone mol. wt.[14] Calcd.	Found
R = H[2,15]	222–224	750	1.5082	0.969	82	....	...	...
I, R = $(CH_3)_3C$[3]	103–106	1	1.5061	0.945	56	129–130.5	232	233
	M. p. 31–34[16]							
II, R = CH_3[3,17]	65–67	1	1.5094	0.954	80	96.5–98	190	190
III, R = Br[18]	84–86	1	1.5493	1.340	30	134.5–136	255	258.5

The fractions were apparently mixtures of II and *p*-*t*-butyltoluene. The amount of ketone was estimated from the oxime yield (3.5 g., m. p. 201–202.5°, 0.18 mole, 24% yield). The hydrocarbon (7.5 g.) isolated from oxime filtrates distilled at 195–208° at 750 mm., $n^{25}\text{D}$ 1.5060, and was evidently still contaminated with II; reported constants of *p*-*t*-butyltoluene, b. p. 190°, $n^{20}\text{D}$ 1.4915.[10] The mixed m. p. of the oxime of II and of the ketone synthesized from *p*-tolylmagnesium bromide and pivalonitrile gave no depression.

5. **Attempted Formation of *p*-Bromopivalophenone (III).**—Bromobenzene (Eastman Kodak White Label) was used as solvent and nucleus to be substituted. No evidence of III was obtained. About 11 g. (73%) of a hydrocarbon mixture (b. p. 45–55° at 0.5 mm.) and 1.5 g. of *p*-*t*-butylpivalophenone (I, b. p. 95–100° at 0.5 mm., 9%, hydrazone m. p. 125–127°, mixed m. p. with authentic sample 125–128°, negative Beilstein test; hydrazone mol. wt. 231.8, calcd. 232). The hydrocarbon mixture was refractionated at 750 mm. into 5 fractions (b. p. 224–230°, $n^{25}\text{D}$ 1.5459–1.5390, $d^{25}{}_{25}$ 1.386–1.368). The refractive indices and densities were too high for *p*-*t*-butylbromobenzene, and the product was assumed to be a mixture of meta and para compounds. A Grignard reagent was prepared from 6 g. of the hydrocarbon mixture and treated with carbon dioxide. Approximately 1.2 g. of acid was obtained which on recrystallization from nitromethane yielded 0.5 g. of acid, m. p. 89–92°, and 1.2 g. of acid, m. p. 92–93° (clear only at 102°); mol. wt. by glass electrode titration 178 (calcd. for *t*-butylbenzoic acid, 178); reported m. p. of *p*-*t*-butylbenzoic acid 165°, of the meta acid 127°,[11] and of the ortho acid 80.3–80.8.[12] Mixed m. p.'s with each of the three of these acids gave significant depressions.[13] Nevertheless, the neutral equivalent is accurate enough to limit possibilities to the butylbenzoic acid series. The most probable structure is *m*- or *p*-isobutylbenzoic acid.

C. **General Procedure for Preparation of Substituted Pivalophenones from Pivalonitrile and the Grignard Reagent.**—The Grignard reagent was prepared from 0.33 g. atom of magnesium, 0.34 mole of bromo compound and 250 ml. of ether distilled from phosphorus pentoxide. Without cooling, pivalonitrile (28 g., 0.33 mole) was added rapidly to the Grignard solution. A slight rise in temperature occurred. The solution was then refluxed for two hours, during which time the crystalline imine-complex separated. The mixture was poured onto cracked ice mixed with 20% hydrochloric acid and allowed to stand overnight for complete hydrolysis. The ketone was extracted with ether, the extracts being washed further with dilute acid, water, saturated bicarbonate solution and then dried with sodium sulfate and distilled. Yields are given in Table I.

Summary

Some substituted pivalophenones were found to be best prepared from pivalonitrile and the appropriate Grignard reagent. It was observed that pivalyl chloride could not be used for such preparations *via* a Friedel–Crafts reaction since alkylation as well as acylation took place.

NASHVILLE, TENN. RECEIVED NOVEMBER 7, 1949

---

[10] Egloff, "Physical Constants of Hydrocarbons," Vol. III, Reinhold Publishing Corp., New York, N. Y., 1946.

[11] Kelbe and Pfeiffer, *Ber.*, **19**, 1726 (1886); *cf.* also Bauer, *ibid.*, **24**, 2832 (1891).

[12] Serijan, Hipsher and Gibbons, THIS JOURNAL, **71**, 873 (1949).

[13] The author is grateful to Drs. Serijan, Hipsher and Gibbons for generous samples of the *m*- and *o*-*t*-butylbenzoic acids.

[14] Determination: About 0.1 g. of hydrazone, weighed accurately, was hydrolyzed with 10 ml. of standard 0.1 *N* acid by standing overnight. The solution was then titrated with standard 0.1 *N* alkali using a glass electrode. Two end-points were obtained corresponding to titration of excess hydrochloric acid (at *p*H 3.4–7) and to titration of hydrazine hydrochloride (at *p*H 9–11). The molecular weight was determined from the hydrazine hydrochloride equivalent.

[15] DeBenneville, *J. Org. Chem.*, **6**, 462 (1941).

[16] Rothstein and Saville[3] do not report this compound as a solid.

[17] Pickard and Vaughan, THIS JOURNAL, **72**, 876 (1950).

[18] Calcd. for $C_{11}H_{13}OBr$: Br, 33.2. Found: Br, 33.0.