of cuprous chloride[40] was added in one portion. While stirring in the ice bath, a solution of 28.4 g. (0.2 mole) of *sec*-butyl crotonate in 125 ml. of ether was added dropwise during 1–1.5 hr. (*With runs on a larger scale, it was found* necessary to increase the amount of ether as solvent, as well as the addition time, proportionally, in order to obtain the maximum yield.) After the addition of the ester had been completed, the reaction mixture was stirred in the ice bath for an additional 10–15 min. and then at room temperature for 1–1.5 hr. It was then poured, under vigorous shaking or swirling, onto ice to which 35 ml. of concentrated hydrochloric acid and 50 ml. of ether had beeen added. The two clear layers were separated and the water layer was extracted with ether. Then the combined ether layers were washed with sodium bicarbonate solution and with water, and dried over anhydrous sodium sulfate. The ether was distilled and the residue fractionated. The products obtained are given in Tables I and II; in the last column of Table I is given certain additional experimental information.

Saponification of sec-butyl 3-methylheptanoate. This ester (40 g., 0.2 mole) was saponified by heating under reflux in a solution of potassium hydroxide (35 g., 0.6 mole) in 95% ethanol (250 ml.) for 6–8 hr., after which time about half of the alcohol was distilled. The corresponding amount of water was added, and the distillation repeated in order to remove any volatile compounds. After pouring into water, acidifying, and extracting with ether, distillation produced 3-methylheptanoic acid in 94% yield, b.p. 116.5–117°/10 mm., n_D^{25} 1.4242 [lit. 121°/15 mm., n_D^{16} 1.4276[16]].

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.62; H, 11.18; neut. equiv., 144.2. Found: C, 66.64; H, 11.05; neut. equiv., 144.4.

The amide, crystallized from heptane, melted at 81.5–82°.

Anal. Calcd. for $C_8H_{17}NO$: C, 67.08; H, 11.97; N, 9.78. Found: C, 67.16; H, 11.88; N, 9.62.

Attempted preparation of product IV. A mixture of 14.2 g. (0.1 mole) of *sec*-butyl crotonate and 20 g. (0.1 mole) of *sec*-butyl 3-methylheptanoate, dissolved in 100 ml. of ether, was added to a stirred suspension of sodium *sec*-butoxide in 100 ml. of ether, prepared from 1.2 g. (0.05 g.-atom) of sodium and 7.4 g. (0.1 mole) of 2-butanol. The mixture was stirred at room temperature for 9 hr., then for 3 hr. under reflux, after which it was worked up in the conventional way. Fractionation gave 17.5 g. (87%) of recovered *sec*-butyl 3-methylheptanoate, b.p. 98–99°/10 mm., n_D^{25} 1.4191, and 9.3 g. (65%) of the dimer of *sec*-butyl crotonate (III), b.p. 120–121°/1.5 mm., n_D^{25} 1.4443.

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92; sap. equiv., 142.2. Found: C, 67.70; H, 10.09; sap. equiv., 253.

The infrared spectrum showed two carbonyl bands at 5.78 μ (1730 cm.$^{-1}$), 5.86 μ (1708 cm.$^{-1}$) and one conjugated carbon-carbon double bond band at 6.10 μ (1640 cm.$^{-1}$). These data show that this compound is different from the isomeric dimer obtained in the attempted ferric chloride catalyzed 1,4- addition of *n*-butylmagnesium bromide to *sec*-butyl crotonate.

Preparation of the anhydride corresponding to product IV from sec-butyl crotonate and n-butylmagnesium bromide [*α-(2-hexyl)-β-methylglutaric anhydride*]. A 10-g. (0.03-mole) sample of IV was saponified under reflux with a solution of 12 g. (0.2 mole) of potassium hydroxide in 95 ml. of ethylene glycol for 72 hr. After dilution with water, washing with ether and boiling to expel volatile compounds, the solution was acidified and the acid extracted with ether. After removal of the ether, the crude liquid acid (7.6 g.) was heated under reflux with acetyl chloride (20 ml.) for 4 hr. The excess of acetyl chloride was removed and the residue distilled to give 3 g. of a colorless oil, b.p. 116°/0.5 mm., n_D^{25} 1.4635.

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50; sap. equiv., 106.2. Found: C, 68.00; H, 9.41; sap. equiv. 107.3.

Acknowledgments. The author wants to express his gratitude to Prof. James Cason for valuable advice and discussion during the course of this research.

The author is further indebted to the Technical University of Denmark and to Danmark-Amerika Fondet for financial support, to the United States Educational Foundation for a Fulbright Travel Grant, and to the University of California at Berkeley for providing excellent working conditions.

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[40] Cuprous chloride was prepared by heating under reflux with copper-metal a solution of commercial cuprous chloride in hydrochloric acid, isolation of the cuprous chloride in the conventional way, drying and storing *in vacuo* over phosphorus pentoxide and sodium hydroxide, applying dry nitrogen whenever the vacuum was released.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MISSOURI]

Some Reactions Effected by Means of Bromomagnesium *t*-Alkoxides[1]

J. L. GUTHRIE[2] AND NORMAN RABJOHN

Received August 27, 1956

It has been found that tribenzoylmethane results in about 10% yield when methyl ketones are caused to react with benzoyl chloride in the presence of bromomagnesium *t*-alkoxides. Bromomagnesium *t*-butoxide has been shown to be effective in bringing about some carbonyl condensations with methyl ketones.

In an attempt to prepare benzoates directly by the action of benzoyl chloride on the reaction mixtures obtained from methyl ketones and Grignard reagents, it was observed[3] that a small amount of a high-melting aromatic compound was formed in several cases. In the present investigation this material has been shown to be tribenzoylmethane.

A detailed study of the reaction product obtained from the treatment of the complex from *n*-dodecylmagnesium bromide and methyl *n*-hexyl ketone with benzoyl chloride afforded 7–18% of tribenzoylmethane, an olefin which might have been produced by the dehydration of methyl-*n*-hexyl-*n*-

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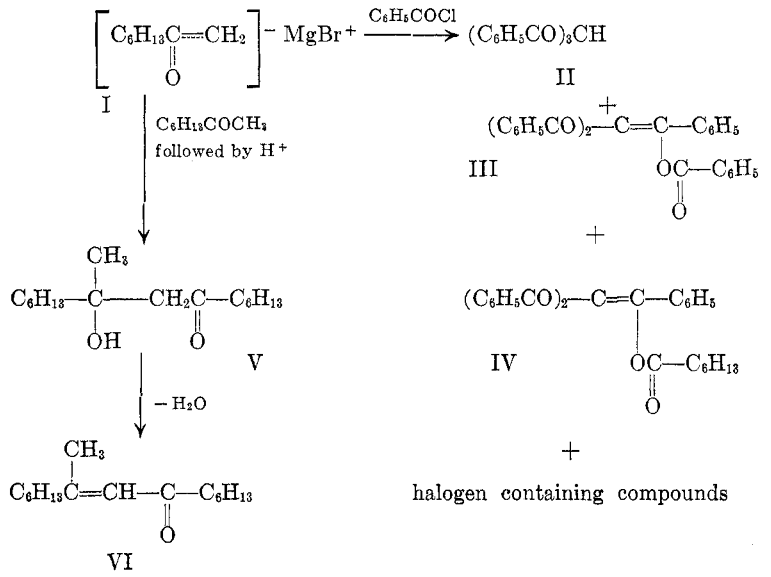
[1] Presented, in part, at the 128th Meeting of the AMERICAN CHEMICAL SOCIETY, Minneapolis, Minn., Sept. 11-16, 1955.

[2] Abstracted from the Ph.D. thesis of J. L. Guthrie, 1956.

[3] These experiments were carried out by G. R. Collins.

dodecylcarbinol, the enol enanthate of tribenzoylmethane and unidentified halogen-containing compounds. In addition, there were isolated unchanged methyl *n*-hexyl ketone, benzoic acid, *n*-tetracosane and much tarry material which could neither be distilled nor induced to crystallize.

These results suggested that the bromomagnesium alkoxide had served as the condensing agent which had brought about the benzoylation of the methyl *n*-hexyl ketone. Accordingly, the latter ketone was treated then with the simpler alkoxide, bromomagnesium *t*-butoxide, and the resulting enolate (I) was caused to react with benzoyl chloride. The reaction mixture was separated to give tribenzoylmethane (II) in 7–15% yields, the enol benzoate of tribenzoylmethane (III), the enol enanthate of tribenzoylmethane (IV), a 16-carbon α,β-unsaturated ketone (VI), which apparently came from the ketol (V), and unidentified halogen-containing compounds.



In order to test the generality of the benzoylation reaction, a number of other methyl ketones were treated with bromomagnesium *t*-butoxide, followed by benzoyl chloride. Acetone, methyl ethyl ketone, and methyl β-phenethyl ketone were converted to tribenzoylmethane in yields of 9.8%, 1.2%, and 9.7%, respectively. Under similar conditions, ethyl *n*-butyl ketone failed to produce any tribenzoylmethane. Acetophenone gave 6.7% of tribenzoylmethane together with 24% of tribenzoylmethane enol benzoate and 2.7% of dibenzoylmethane.

The low yields of tribenzoylmethane obtained from the methyl ketones were due in part, at least, to the decomposition of the ketone enolates by the acid liberated during the course of the benzoylation reaction. However, the addition of basic reagents to the reaction mixtures produced no improvements, and substances such as triethylamine, magnesium carbonate, and powdered magnesium caused the reaction to fail.

Although the mechanism for the formation of tribenzoylmethane from methyl ketones was not determined, it seems reasonable to believe that the bromomagnesium enolates of the methyl ketones suffer benzoylation. Kohler, Tishler, and Potter[4] have benzoylated the magnesium bromide derivatives of a series of selected ketones and observed the formation of diketones in varying yields, with the remainder of the product being composed mainly of benzoates representing O-acylation. Also, Freer and Lachman[5] have reported the mono- and dibenzoylation of acetophenone and methyl *n*-propyl ketone in the presence of sodium ethoxide. However, neither of these groups of investigators apparently observed the formation of tribenzoylmethane.

The formation of the α,β-unsaturated ketone (VI), presumably through an aldol type condensation similar to those first reported by Grignard[6] as being effected by halomagnesium alcoholates and Grignard reagents, suggested that the bromomagnesium enolates, such as I, might be capable of undergoing other reactions like those described by Fuson, Fugate,, and Fisher[7] for the bromomagnesium enolates of hindered carbonyl compounds.

It was found that the enolates of several methyl ketones, prepared by treating the latter with bromomagnesium *t*-butoxide, reacted readily with carbonyl compounds, but poorly or not at all with acetyl chloride, carbon dioxide, ethyl carbonate, or ethyl benzoate, under the conditions employed. The results of the successful carbonyl reactions, the

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(4) Kohler, Tishler, and Potter, *J. Am. Chem. Soc.*, **57**, 2517 (1935).

(5) Freer and Lachman, *Am. Chem. J.*, **19**, 881 (1897).

(6) Grignard, *Ann. chim. et phys.* [7], **24**, 433 (1901); see also, Kharasch and Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, 1954, p. 176.

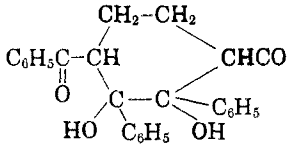
(7) Fuson, Fugate, and Fisher, *J. Am. Chem. Soc.*, **61**, 2362 (1939).

products of which were isolated as α,β-unsaturated ketones, are tabulated below.

Enolate	Addendum	Yield of α,β-Unsaturated Ketone, %
Methyl *n*-hexyl ketone	Methyl *n*-hexyl ketone	65
Acetophenone	Benzaldehyde	60
Acetophenone	Acetophenone	72
Acetomesitylene	Benzaldehyde	75

More recently, Fuson and Hill[8] have reported that the dienolate of 1,4-dimesitoylbutane undergoes condensation with benzil to form 1,4-dimesitoyl-2,3-dihydroxy-2,3-diphenylcyclohexane. In the present work it has been found that a similar type of reaction can be effected between the unhindered diketone, 1,4-dibenzoylbutane, and benzil by means of bromomagnesium *t*-butoxide. The cyclohexane derivative (VII) was cleaved with periodic acid to produce 1,1,4,4-tetrabenzoylbutane (VIII).

$$C_6H_5CO(CH_2)_4COC_6H_5 \xrightarrow[\substack{2.\ C_6H_5COCOC_6H_5\\ 3.\ H^{\oplus}}]{1.\ t\text{-}C_4H_9OMgBr}$$



VII

$$\xrightarrow{HIO_4}$$

$$(C_6H_5CO)_2CH(CH_2)_2CH(COC_6H_5)_2$$

VIII

EXPERIMENTAL[9]

Preparation of the enolate of methyl n-hexyl ketone (I). A solution of ethylmagnesium bromide was prepared from 48.6 g. (2 gram-atoms) of magnesium, 240 g. (2.2 moles) of ethyl bromide, and 500 ml. of anhydrous ether. This was stirred while 149 g. (2 moles) of *t*-butyl alcohol, in an equal volume of anhydrous ether, was added slowly. After all of the alcohol had been added, the alkoxide suspension was stirred vigorously for about 30 min., and 257 g. (2 moles) of methyl *n*-hexyl ketone, in an equal volume of dry ether, was introduced quite rapidly. The precipitate of alkoxide disappeared and a slightly yellowish brown enolate solution resulted. It was allowed to stand for 1 hr. before being used.

Benzoylation of enolate I. A solution of 844 g. (6 moles) of benzoyl chloride, in 500 ml. of absolute ether, was added quite rapidly with stirring to a solution of 2 moles of the enolate. The reaction mixture warmed spontaneously so that the solvent refluxed at a steady rate and a precipitate formed gradually. Stirring was continued for 14 hr. and the mixture was allowed to stand for an additional 16 hr. at which time it was poured into 6 l. of water. It was allowed to stand for 4 hr. with occasional stirring and the precipitate was removed by filtration. There was obtained 30.3 g. of a white solid which melted at 226–231° after one crystallization from benzene. It was shown to be tribenzoylmethane on the basis of its physical and chemical properties and it caused no depression of the melting point of an authentic sample of tribenzoylmethane which had been prepared by the method of Claisen.[10] The filtrate was separated and the water layer was extracted several times with ether. The water layer was distilled until the temperature of the vapor reached 110°, and the distillate was examined but contained no organic compounds. The residue from the distillation was evaporated to dryness and 417 g. of magnesium salts resulted.

The ether layer and extracts were combined and the ether was removed. The residue was distilled at 15 mm. and a fraction was collected to 115°. This was refluxed for 4 hr. with 500 ml. of 3% sodium hydroxide solution and worked up to give 104 g. of methyl *n*-hexyl ketone, n_D^{20} 1.4135, and 3.3 g. of benzoic acid.

The residue from the distillation was stirred for 24 hr. with 2 l. of 12% sodium hydroxide solution, filtered, and 9 g. of tribenzoylmethane was recovered. The filtrate was diluted with ether, separated, and the alkaline solution was acidified with concentrated hydrochloric acid. It was made basic with sodium carbonate and an additional 32.6 g. of tribenzoylmethane precipitated. The basic solution was acidified, the precipitated benzoic acid was removed, and the filtrate was examined but no other compounds could be found.

The organic layer was concentrated and then distilled at 3 mm. to yield 142 g. of material, b.p. 72–155°, and 60 g. of residue. The distillate contained halogen which was removed by boiling with 10% sodium hydroxide solution and finally with 5% alcoholic silver nitrate solution. It was separated into a number of ill-defined fractions which were not identified, but were thought to contain the benzoate of the ketol (V).

The residue (60 g.) was dissolved in a mixture of acetone and petroleum ether (b.p. 60–68°) and after 4 days in a refrigerator, 4 g. of a tan solid precipitated; m.p., 114–116°. After three recrystallizations from aqueous alcohol it melted at 118–120° and did not depress the melting point of an authentic sample of the enol enanthate of tribenzoylmethane (IV). The filtrate was concentrated and distilled at 1 mm. to give a number of wide boiling fractions. The only identifiable materials were benzoic acid and a further 1.3 g. of tribenzoylmethane.

Several experiments similar to the above were performed, but with slight modifications. In general, the results were the same with two exceptions. In the first, a liquid was isolated in three instances which appeared to be a mixture of the ketol (V) and the unsaturated ketone (VI). A sample of this material was distilled from solid sodium carbonate to give 9-methyl-8-pentadecene-7-one (VI); b.p., 118–120°/1 mm., n_D^{20} 1.4562. The ultraviolet absorption spectrum of this material in absolute alcohol showed a maximum at 233 mμ which is in agreement with the findings of Woodward[11] in regard to the spectra of α,β-unsaturated ketones.

In another experiment, there was obtained a 7.3% yield of tribenzoylmethane enol benzoate (III), (m.p. 120–121°) along with 13.8% of tribenzoylmethane. This benzoate was identified by a mixed melting point determination with an authentic sample which was prepared by the benzoylation of tribenzoylmethane with benzoyl chloride in pyridine solution.[10]

Benzoylation of the enolates of other ketones. The enolates were prepared, in the manner indicated previously, from the ketones and bromomagnesium *t*-butoxide, and were benzoylated on a much smaller scale than that of the previous experiment. In most cases the experiments were performed in a cursory fashion and the products of the reactions, other than tribenzoylmethane, were not examined in any detail. The yields of tribenzoylmethane isolated, based on ketone, were: acetone, 9.8%; methyl ethyl ketone, 1.2%;

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[8] Fuson and Hill, *J. Org. Chem.*, **19**, 1575 (1954).

[9] All melting points are uncorrected. The authors are indebted to R. E. Bolin and R. E. Elliott for the semimicro carbon and hydrogen analytical data.

[10] Claisen, *Ann.*, **291**, 90 (1896).

[11] Woodward, *J. Am. Chem. Soc.*, **63**, 1123 (1941).

and methyl β-phenethyl ketone, 9.7%. Acetophenone gave 6.7% of tribenzoylmethane, 24.6% of tribenzoylmethane enol benzoate, and 2.7% of dibenzoylmethane.

A compound, b.p. 185–187°/1 mm., n_D^{20} 1.5638, was isolated from the benozylation of methyl β-phenylethyl ketone and appeared to be an α,β-unsaturated ketone formed by dimerization and subsequent dehydration.

Anal. Calcd. for $C_{20}H_{22}O$: C, 86.28; H, 7.97. Found: C, 86.47; H, 8.14.

Preparation of tribenzoylmethane enol enanthate (IV). To a solution of 20 g. (0.06 mole) of tribenzoylmethane in 100 ml. of dry pyridine was added 18 g. (0.12 mole) of enanthyl chloride. The mixture was allowed to stand for 2 days, was diluted with an equal volume of ether, and filtered. The filtrate was washed with 10% hydrochloric acid, 10% sodium carbonate solution, and water and was dried over anhydrous sodium sulfate. After removing the ether, the oil was distilled until 11 g. of material was collected at 115–160°/2 mm. The residue (21 g.) was dissolved in cyclohexane, and after standing for several days in a refrigerator, there was precipitated 3.4 g. of a tan solid; m.p. 114–116°. It was recrystallized several times from aqueous alcohol and melted at 118–120°.

Anal. Calcd. for $C_{29}H_{28}O_4$: C, 79.07; H, 6.41. Found: C, 79.15; H, 6.70.

The infrared absorption spectrum indicated that O-acylation had occurred.

Reaction of enolate I with methyl n-hexyl ketone. To a solution of 0.5 mole of the enolate in about 300 ml. of ether was added 64.2 g. (0.5 mole) of methyl *n*-hexyl ketone and the mixture was refluxed for 1 hr. After standing overnight, it was decomposed by pouring onto ice and hydrochloric acid. The ether layer was worked up in the usual fashion to give 42.6 g. of unreacted methyl *n*-hexyl ketone and 75 g. of a liquid which boiled at 118–125°/1 mm. A portion (37 g.) of this product was heated for 6 hr. with 1.5 g. of 50% sulfuric acid. It was diluted with ether, washed, dried, concentrated, and distilled to produce 9-methyl-8-pentadecene-7-one (VI) in good yield; b.p. 118–119°/1 mm., n_D^{20} 1.4563.

Anal. Calcd. for $C_{16}H_{30}O$: C, 80.60; H, 12.68. Found: C, 80.38; H, 12.71.

Reaction of the bromomagnesium enolate of acetophenone with benzaldehyde. To a 0.1-molar suspension of magnesium *t*-butoxide in ether was added at once 12 g. (0.1 mole) of acetophenone. The enolate, which appeared as a dense, yellow insoluble oil, was stirred for 1 hr. before 10.6 g. (0.1 mole) of freshly distilled benzaldehyde was added. The reaction mixture was heated at reflux for 13 hr., hydrolyzed with dilute acid, washed, dried, and distilled. There was obtained 12.1 g. (58%) of benzalacetophenone, b.p. 165–170°/2 mm., which melted at 53–55° after one crystallization from ethanol; lit.[12] m.p. 55–57°.

Preparation of dypnone. The bromomagnesium enolate of acetophenone was prepared on a 0.1-molar scale and, after being stirred for 1 hr., an additional 12 g. (0.1 mole) of acetophenone was added. The mixture was stirred for 30 min., 100 ml. of xylene was added, and the ether was removed by distillation until the temperature of the vapors reached 45°. The residue was heated at reflux for 11 hr., hydrolyzed, and purified in the usual way. There was obtained 16.1 g. (72%) of dypnone which boiled at 175–180°/1 mm.; n_D^{20} 1.6312; lit.[13], b.p. 225°/22 mm.

Reaction of the bromomagnesium enolate of acetomesitylene with benzaldehyde. The bromomagnesium enolate was prepared on a 0.1-molar scale and 10.6 g. (0.1 mole) of freshly distilled benzaldehyde was added. The mixture was stirred at room temperature for 3 hr. and then heated at reflux for 3 hr. After hydrolysis, there was obtained 19 g. (75%) of benzalacetomesitylene; b.p. 177–180°/2 mm.; lit.[7], b.p. 215–221°/16 mm.

Preparation of 1,4-dibenzoyl-2,3-dihydroxy-2,3-diphenylcyclohexane (VII). The dienolate was prepared from 0.1 mole of bromomagnesium *t*-butoxide and a solution of 13.3 g. (0.05 mole) of 1,4-dibenzoylbutane in 200 ml. of dry benzene. The mixture was distilled until the ether from the butoxide solution had been removed and the residue was heated at reflux for 1 hr. A solution of 10.5 g. (0.05 mole) of benzil, dissolved in the minimum amount of benzene, was added at once and the mixture was caused to reflux for 5 hr. It was hydrolyzed by means of dilute hydrochloric acid and the organic layer was concentrated to give 12.9 g. of a solid which melted at 220–230°. Several recrystallizations of this material from 95% alcohol gave 7.4 g. (31%) of a white solid; m.p. 231–232°.

Anal. Calcd. for $C_{32}H_{28}O_4$: C, 80.64; H, 5.92. Found: C, 80.58; H, 5.91.

Preparation of 1,1,4,4-tetrabenzoylbutane (VIII). To a solution of 0.5 g. of VII in 50 ml. of purified dioxane was added a solution of 0.55 g. of periodic acid dihydrate in 20 ml. of dioxane and 6 ml. of water. The mixture was heated at reflux for 7 hr., concentrated to about one-half volume, cooled, and filtered. The filtrate was diluted with ether and washed with water, 10% sodium carbonate solution, and water and was dried over anhydrous sodium sulfate. The ether solution was concentrated and there was obtained 0.5 g. of a white solid; m.p., 175–180°. This was recrystallized three times from 95% alcohol and the product melted at 184–185°.

Anal. Calcd. for $C_{32}H_{26}O_4$: C, 80.99; H, 5.52. Found: C, 80.70; H, 5.56.

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(12) Kohler and Chadwell, *Org. Syntheses*, **Coll. Vol. I**, 78 (1941).

(13) Heilbron, *Dictionary of Organic Compounds*, Eyre and Spottiswoode, London, 1934, Vol. I, p. 668.