286. *The Fission of Non-enolisable Ketones by Potassium* tert.*-Butoxide.*

By G. A. Swan.

Benzophenone undergoes fission to benzene and benzoic acid (90% yield) by refluxing an ethereal solution containing water (1 mol.) with potassium *tert.*-butoxide (3 mols.), a small amount of triphenylcarbinol also being formed. This reaction also occurs in dioxan, benzene, or pyridine (at water-bath temperature), but not in *tert.*-butanol as solvent. By refluxing an ethereal solution of benzophenone with potassium ethoxide or *iso*propoxide, reduction to benzhydrol, in good yield, occurs. The fission reaction has been carried out on a number of 4-mono- and 4 : 4′-di-substituted derivatives of benzophenone, as well as on xanthone, anthraquinone, and ω-trimethylacetophenone. The mechanism of the reaction is discussed.

A modification of the Oppenauer method of oxidation of secondary alcohols to ketones has been described by Woodward, Wendler, and Brutschy (*J. Amer. Chem. Soc.*, 1945, **67**, 1425) who thus oxidised quinine to quininone. In this, potassium *tert.*-butoxide is used instead of the customary aluminium compound (which has the disadvantage of forming insoluble complexes with many basic compounds), and benzophenone is used as hydrogen acceptor, the solvent being benzene.

Recently, attempts were made by W. Cocker and C. Lipman (unpublished work) to apply this reaction to the oxidation of a derivative of ψ-santonin, and by the present author to the oxidation of a derivative of an alkaloid; and as in each case the desired product would be acidic, the alkali-soluble fraction of the reaction mixture was investigated. In each case, small amounts of benzoic acid were detected; this unexpected result led the present author to investigate the reaction further. A blank experiment, in which a benzene solution of benzophenone was heated on the water-bath with potassium *tert.*-butoxide in an atmosphere of nitrogen, without any added secondary alcohol, also resulted in the formation of benzoic acid, thus establishing that the latter was a degradation product of the benzophenone.

In these experiments, in which the benzophenone (1 mol.) was in excess with respect to the potassium *tert.*-butoxide (0·5 mol.), and the presence of moisture was carefully excluded, the yield of benzoic acid was very small. However, it has been shown that by using excess of potassium *tert.*-butoxide (3 mols.) and an inert solvent such as benzene, ether, dioxan, or pyridine containing water (1—1·2 mols.), the yield of benzoic acid can be increased to 90%, a small amount of triphenylcarbinol also being formed. When *tert.*-butanol was used as solvent, no benzoic acid could be detected, the benzophenone being recovered unchanged. The results of a number of experiments under varying conditions are shown in the accompanying table. In those experiments in which the yield of benzoic acid was below 90%, unchanged benzophenone was also isolated at the end of the reaction. The results of these and other experiments may be summarised as follows, the numbers of experiments illustrating the generalisations being given in parentheses :

(1) With 3·1 mols. of potassium *tert.*-butoxide, the yield of benzoic acid is small if no water is added, increases to a maximum (90%) when water (1—1·2 mols.) is present, and then falls as more water is added (1—7).

(2) If the amount of potassium *tert.*-butoxide is reduced below 3 mols., the yield of benzoic acid falls (8, 9).

(3) Ether, dioxan, and pyridine are all suitable solvents (4, 10, 11).

(4) No reaction occurs in *tert.*-butanol as solvent (12—14).

(5) If ether is used as solvent, the addition of as little as 1 mol. of *tert.*-butanol has a very marked inhibiting effect on the reaction, lowering the yield from 90% to 50% (when 1 mol. of water is present), but in dioxan the yield is lowered only to 85%. The addition of 3 mols. of *tert.*-butanol lowers the yield to 17% in ether (10, 15—18, 21).

(6) To ensure completion of the reaction, the time of heating was usually 12—17 hours; but, in general, the yield was very little lower with a reaction time of only 2 hours.

(7) Aluminium *tert.*-butoxide or potassium phenoxide when used instead of potassium *tert.*-butoxide does not give the reaction. Potassium ethoxide or *iso*propoxide reduces an ethereal solution of benzophenone to benzhydrol, in good yield, and no benzoic acid is detected.

(8) Experiment 4 was repeated in the following manner: the solution of water in ether was refluxed with the potassium *tert.*-butoxide for 13 hours before the benzophenone was added, after which it was refluxed again for the same period of time. The yield of benzoic acid was unchanged.

Although the product derived from the second benzene nucleus of the benzophenone molecule has not been isolated, this is undoubtedly benzene itself. Thus when treated with potassium *tert.*-butoxide (3 mols.) in dioxan solution containing water (1 mol.), xanthone gave *o*-phenoxybenzoic acid in 89% yield. Similar treatment of anthraquinone yielded a mixture of benzoic with a little phthalic acid, Michler's ketone gave *p*-dimethylaminobenzoic acid and dimethylaniline, and 4 : 4′-dibromo- and 4 : 4′-dimethoxy-benzophenone gave *p*-bromo- and *p*-methoxy-benzoic acid, respectively. Acetophenone and hexamethylacetone failed to react, but ω-trimethylacetophenone yielded trimethylacetic (*not* benzoic) acid. Unsymmetrically substituted derivatives of benzophenone gave mixtures of the two possible acids. Thus 4-bromobenzophenone yielded a mixture of benzoic and *p*-bromobenzoic acid in the approximate molecular ratio of 4 : 1, while 4-methoxybenzophenone gave a mixture of benzoic and anisic acid in approximate equimolecular proportions (the latter predominating slightly). The crude acidic product of the fission of 4-nitrobenzophenone was not amenable to analysis, but appeared to consist mainly of benzoic acid. The above results suggest that an unsymmetrical ketone, R·CO·R′, undergoes fission to RH and $R'\cdot CO_2H$, rather than to $R\cdot CO_2H$ and R′H, if R is electron-attracting or R′ is electron-repelling.

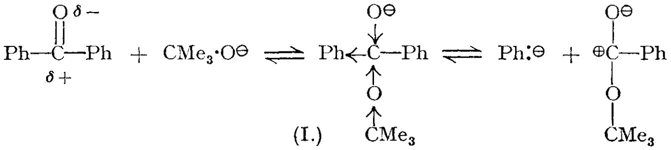
Although this fission of non-enolisable ketones is not a new reaction, the conditions used here are very much milder than those formerly employed. Thus the fission of ketones by alkali fusion has been described by various workers, *e.g.*, Bachmann (*J. Amer. Chem. Soc.*, 1935, **57**, 737), Fedossejew, *et al.* (*Chem. Zentr.*, 1936, II, 1919; 1937, I, 1932, 2369; 1938, I, 585; *Chem. Abstr.*, 1942, **36**, 5471), and Lock (*Ber.*, 1939, **72**, 861). Huntress and Seikel (*J. Amer. Chem. Soc.*, 1939, **61**, 816), studying the alkaline fission of fluorenone and its derivatives, attempted to moderate the conditions used, but the method finally adopted involved the action of caustic alkali in diphenyl ether at 180—200°.

The action of alcoholic potash on benzophenone and its derivatives has been studied extensively by Montagne (*Rec. Trav. chim.*, 1908, **27**, 327; 1922, **41**, 703; and other papers) who found that reduction to the corresponding benzhydrol usually occurs on boiling for long periods of time. In one case, namely that of 2 : 4 : 6-trichlorobenzophenone, fission (to trichlorobenzene and benzoic acid) was observed.

The cleavage of similar ketones (to a hydrocarbon and an amide) by boiling them with sodamide in toluene has been described by Haller and Bauer (*Compt. rend.*, 1908, **147**, 824; 1909, **148**, 127) and by Schönberg (*Annalen*, 1924, **436**, 205), *e.g.*, benzophenone gives benzene and benzamide.

Mechanism of the Fission with Potassium tert.-*Butoxide.*—From the experimental results outlined above, it seems that the presence of *tert.*-butoxide ions and either water molecules or hydroxyl ions (liberated by the action of water on *tert.*-butoxide ions) is necessary for the reaction. Thus, with 3 mols. of potassium *tert.*-butoxide, the maximum yield of benzoic acid is obtained if 1·2 mols. of water is added—presumably because 1 mol. of water or of hydroxyl ion is needed; but if more water is added, the yield is lowered because too much of the potassium *tert.*-butoxide is hydrolysed.

It therefore seems probable that the first stage of the reaction might be the attack by the *tert.*-butoxide ion at the carbonyl group of the ketone to give the anion (I). On account of the electron-repelling effects of the *tert.*-butyl radical and of the $-O^{\ominus}$ atom in (I), there will be a



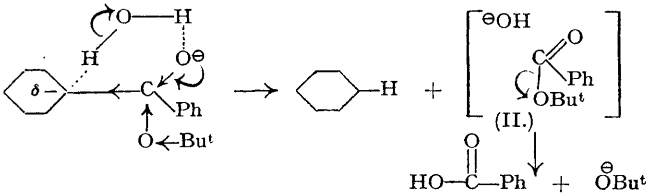
$$\mathrm{Ph{-}\overset{O^{\delta-}}{\overset{\|}{C}}{-}Ph}_{\ \delta+} + \mathrm{CMe_3{\cdot}O^{\ominus}} \rightleftharpoons \mathrm{Ph{\leftarrow}\underset{\underset{\underset{CMe_3}{\uparrow}}{O}}{\underset{\uparrow}{\overset{O^{\ominus}}{\overset{\downarrow}{C}}}}{-}Ph} \rightleftharpoons \mathrm{Ph{:}^{\ominus}} + \mathrm{{}^{\oplus}\underset{\underset{CMe_3}{|}}{\underset{O}{\underset{|}{\overset{O^{\ominus}}{\overset{|}{C}}}}}{-}Ph}$$

(I.)

tendency for the Ph–C bond to break so that the bonding electrons pass to the phenyl group. If the phenyl anion did thus separate, this would account for the formation of small amounts of triphenylcarbinol, which might result from the attack of this anion on a benzophenone molecule.

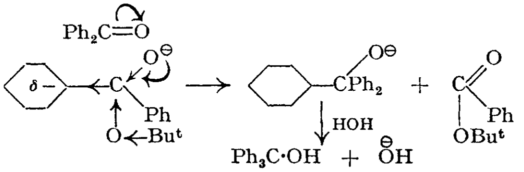
Thus Morton and Fallwell (*J. Amer. Chem. Soc.*, 1938, **60**, 1925) have shown that triphenylcarbinol is formed by the action of sodiumphenyl on sodium benzoate.

The exact mechanism of the reaction is not clear (as the mixture is heterogeneous, it is possible that the reaction may occur at the interface; and it may be of significance that when *tert.*-butanol is used as solvent, and the mixture is homogeneous, no reaction occurs); but that it should be brought about by the interaction of the anion (I) with an hydroxyl ion seems unlikely. Interaction with a water molecule seems more likely, for this might be held in position suitable for reaction by hydrogen-bond formation with the $-O^{\ominus}$ atom and the partial negative charge on the phenyl nucleus.* The phenyl anion need scarcely have an independent existence, but would immediately remove a hydrogen ion from the water molecule, forming a benzene molecule, and leaving an hydroxyl ion, which would then attack the *tert.*-butyl benzoate molecule (II), the *tert.*-butoxyl group separating as an anion, leaving a molecule of benzoic acid. Although, according to Norris and Rigby (*J. Amer. Chem. Soc.*, 1932, **54**, 2088), *tert.*-butyl benzoate is stable to alkali, experiments have shown that it is hydrolysed by refluxing an ethereal solution containing water (1·2 mols.) with potassium *tert.*-butoxide (3 mols.).



Adopting this mechanism, the inhibiting effect of *tert.*-butanol on the reaction might be ascribed to a competition between the water and *tert.*-butanol for hydrogen bond formation with the $-O^{\ominus}$ atom of (I).

The formation of triphenylcarbinol could be formulated in a similar way:



Fission of Benzophenone by Potassium tert.*-Butoxide.*

No. of Expt.	Potassium used for prep. of *tert.*-butoxide.		Benzophenone (1 mol.).	Solvent (c.c.).	Added water.		Added *tert.*-butanol.		Time (hours).	Benzoic acid isolated.	
	G.	Mols.	G.		Mg.	Mols.	G.	Mols.		G.	% of theory.
1	0·2	3·1	0·3	Ether (5)	0	0	0	0	16	0·035	17
2	0·2	3·1	0·3	,, (5)	15	0·5	0	0	6	0·11	55
3	0·2	3·1	0·3	,, (5)	15	0·5	0	0	12	0·12	60
4	0·2	3·1	0·3	,, (5)	30	1·0	0	0	16	0·17	85
5	0·2	3·1	0·3	,, (5)	35	1·2	0	0	16	0·18	90
6	0·2	3·1	0·3	,, (5)	45	1·5	0	0	6	0·15	75
7	0·2	3·1	0·3	,, (5)	60	2·0	0	0	6	0·08	40
8	0·2	2·0	0·45	,, (6)	45	1·0	0	0	13	0·18	60
9	0·2	1·0	0·90	,, (12)	90	1·0	0	0	13	0·04	6
10	0·2	3·1	0·3	Dioxan (5)	30	1·0	0	0	14	0·18	90
11	0·2	3·1	0·3	Pyridine (5)	30	1·0	0	0	14	0·16	80
12	0·2	3·1	0·3	*tert.*-Butanol (6)	0	0	—	—	14	0	0
13	0·2	3·1	0·3	,, (6)	30	1·0	—	—	17	0	0
14	0·2	3·1	0·3	,, (6)	60	2·0	—	—	17	0	0
15	0·2	3·1	0·3	Ether (5)	0	0	0·12	1	16	0	0
16	0·2	3·1	0·3	,, (12)	30	1·0	0·12	1	16	0·10	50
17	0·2	3·1	0·3	,, (4)	30	1·0	0·24	2	17	0·05	25
18	0·2	3·1	0·3	,, (4)	30	1·0	0·36	3	17	0·035	17
19	0·2	3·1	0·3	,, (12)	60	2·0	0·12	1	16	0·06	30
20	0·2	3·1	0·3	,, (12)	90	3·0	0·12	1	16	0·03	15
21	0·2	3·1	0·3	Dioxan (5)	30	1·0	0·12	1	13	0·17	85

* This idea emerged from a discussion with Professor C. C. Price, on his recent visit to this country.

The modes of fission of the few unsymmetrical ketones studied are compatible with the above mechanism. Thus, if in the ketone R·COR′, R is more strongly electron-attracting than R′, one would expect reaction (*A*) to occur more readily than (*B*).

$$(A)\quad \mathrm{R{\cdot}CO{\cdot}R'} \longrightarrow \mathrm{R^{\ominus}} + \mathrm{{}^{\oplus}COR'}$$

$$(B)\quad \mathrm{R{\cdot}CO{\cdot}R'} \longrightarrow \mathrm{RCO^{\oplus}} + \mathrm{{}^{\ominus}R'}$$

The possibility that the reaction might occur by a homolytic fission has also been considered; but this seems unlikely, in view of the above evidence, and the absence among the isolated reaction products of dimerisation products of possible radicals.

EXPERIMENTAL

Commercial *tert.*-butanol was refluxed for 12 hours over barium oxide, and distilled immediately before use. The ether, benzene, and dioxan used as solvents were refluxed over sodium and distilled; pyridine was dried over potassium hydroxide pellets and distilled.

Action of Potassium tert.*-Butoxide on Benzophenone.*—The experiments summarised in the table were carried out as follows. The potassium was dissolved in *tert.*-butanol (6 c.c. for 0·2 g. of potassium), the excess of solvent removed by distillation, and the residue heated for 15 minutes at 150°/12 mm., and allowed to cool. A solution of benzophenone in the solvent, containing the stated amount of water and/or *tert.*-butanol, was added, and the mixture was refluxed from the water-bath for the time stated, cooled, and treated with water.

(*a*) When ether had been used as solvent, the ethereal layer was separated, the alkaline solution again extracted with ether and then acidified (hydrochloric acid), the precipitated benzoic acid taken up in ether, the extract dried (Na_2SO_4), the ether removed, and the residue of practically pure benzoic acid weighed. The ether extract of the alkaline solution was dried (Na_2SO_4) and the ether removed, leaving a residue of triphenylcarbinol and/or unchanged benzophenone. In experiments in which the yield of benzoic acid was 90%, this residue was almost pure triphenylcarbinol and, after being washed with a little light petroleum (b. p. 60—80°) weighed 40 mg. and had m. p. 162° unchanged by recrystallisation from methanol (Found: C, 87·5; H, 6·2. Calc. for $C_{19}H_{16}O$: C, 87·7; H, 6·3%). In experiments in which the yield of benzoic acid was low, this neutral residue was a mixture of a small amount of triphenylcarbinol with unchanged benzophenone. This mixture could be readily separated by passing a solution of it in light petroleum (b. p. 60—80°) through a column of active alumina, the triphenylcarbinol being adsorbed, while the benzophenone passed through; the former could be eluted from the column by benzene–light petroleum (1 : 1).

(*b*) When a solvent miscible with water (*e.g.*, dioxan) had been used, this was removed by evaporation from the water-bath under reduced pressure, the residue treated with water and ether added, the remainder of the working up being carried out as in (*a*).

Action of Potassium tert.*-Butoxide on Other Ketones.*—Unless otherwise stated, in each experiment potassium (0·2 g.) was used for the preparation of the *tert.*-butoxide, dioxan (5 c.c.) was used as solvent, and the time of heating on the water-bath was 13 hours. The reaction was carried out on each of the following ketones, the weight of ketone used being given in parentheses after its name, and this is followed by the name, weight, m. p., and percentage yield of the acidic product isolated.

4 : 4′-*Dibromobenzophenone* (0·56 g.). *p*-Bromobenzoic acid, 0·26 g., m. p. 252° (80%), mixed with authentic specimen, m. p. 251—252°.

4 : 4′-*Dimethoxybenzophenone* (0·4 g.). Anisic acid, 0·20 g., m. p. 180—182° (80%), mixed with authentic specimen, m. p. 181—184°.

4 : 4′-*Bisdimethylaminobenzophenone* (0·44 g.). *p*-Dimethylaminobenzoic acid (isolated by acidification with acetic acid, extraction with chloroform, removal of the chloroform, and washing the residue with water), 90 mg., m. p. 237—239° (33%) (Found: C, 65·7; H, 7·0. Calc. for $C_9H_{11}O_2N$: C, 65·45; H, 6·7%), and unchanged ketone (recovered by extraction with chloroform), 0·25 g.

4-*Bromobenzophenone* (0·42 g.). The crude acidic product was dried in a vacuum desiccator; 0·19 g., m. p. 116—171° (Found: Br, 12·0%). Assuming this to contain only benzoic and *p*-bromobenzoic acid, this corresponds to a mixture containing approx. 20 mols. % of the latter.

4-*Methoxybenzophenone* (0·35 g.). 17 Hours. The crude acidic product weighed 0·2 g. (Found: OMe, 11·9%). Assuming this to contain only benzoic and anisic acid, this corresponds to a mixture containing approx. 53 mols. % of the latter.

Xanthone (0·32 g.). *o*-Phenoxybenzoic acid, 0·31 g., m. p. 108—110° (89%); recrystallised from benzene–light petroleum this afforded pale yellowish plates, m. p. 112—113° (Found: C, 73·5; H, 4·85. Calc. for $C_{13}H_{10}O_3$: C, 73·2; H, 4·65%).

ω-Trimethylacetophenone (Willemart, *Bull. Soc. chim.*, 1935, **2**, 874) (0·26 g.). 16 Hours. Trimethylacetic acid, 50 mg., b. p. 155—165°.

Anthraquinone (0·15 g.). This was dissolved in warm toluene (12 c.c.), the solution cooled rapidly, a solution of water (30 mg.) in ether (4 c.c.) added and the mixture was refluxed for 15 hours (bath temp. 120—130°). The crude acidic product weighed 0·13 g., m. p. 113—155°. By fractional crystallisation from benzene–light petroleum, this afforded phthalic acid (10 mg.) and benzoic acid (80 mg.).

Acetophenone (0·3 g.). This in ether was recovered unchanged.

Hexamethylacetone (Bartlett and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 143). This (0·71 g.) in ether (13 c.c.) containing water (100 mg.) was refluxed for 44 hours with potassium *tert.*-butoxide from potassium (0·63 g.). Unchanged ketone (0·41 g.) was recovered, and the acidic product consisted of only a trace of oil. No improvement in the yield of the latter was obtained by using dioxan as solvent.

Benzil (0·3 g.). In ether (4 c.c.), 44 hours. The crude acidic product weighed 0·27 g. and had m. p. 110—145°; recrystallised from benzene, this afforded benzilic acid, 0·18 g., m. p. 150—151°.

Hydrolysis of tert.-*Butyl Benzoate.*—A solution of *tert.*-butyl benzoate (Norris and Rigby, *loc. cit.*) (0·3 g.) in ether (5 c.c.) containing water (35 mg.) was refluxed with potassium *tert.*-butoxide, from potassium (0·2 g.), for 16 hours. When worked up in the usual manner, this yielded benzoic acid, 0·15 g. (73%).

Action of Potassium Ethoxide and iso*Propoxide on Benzophenone.*—A solution of benzophenone (0·3 g.) in ether (4 c.c.) was refluxed for 13 hours with potassium ethoxide, from potassium (0·2 g.). The main product was benzhydrol (0·25 g.), identified by mixed m. p.; no benzoic acid was detected. A similar result was obtained from potassium *iso*propoxide.

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