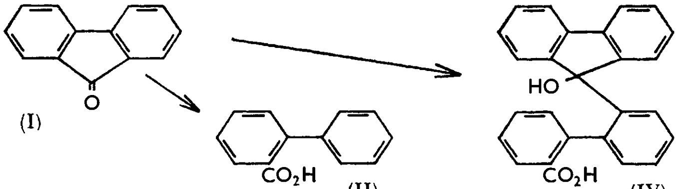
334. *Reactions between Strongly Basic Nucleophiles and Fluorenones.*

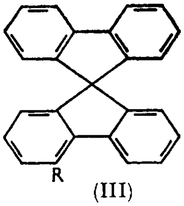
By G. W. Kenner, M. J. T. Robinson, C. M. B. Tylor, and B. R. Webster.

Fusion of fluorenone with either sodium or potassium hydroxide yields the salt of 2′-(9-hydroxy-9-fluorenyl)biphenyl-2-carboxylic acid (IV) in addition to that of biphenyl-2-carboxylic acid. The former is the sole product from the reaction with solid sodium hydroxide in toluene, while solid potassium hydroxide cleaves fluorenone in toluene solution rapidly to potassium biphenyl-2-carboxylate. This exceptionally mild cleavage has also been accomplished with halogenated fluorenones. A novel cyclisation of biphenyl-2-carboxamide to phenanthridone is reported. Mechanisms for all these reactions and the Haller–Bauer cleavage of ketones are suggested.

During another investigation[1] biphenyl-2-carboxylic acid (II) was prepared on a substantial scale from fluorenone (I) by fusion with potassium hydroxide. There was always formed about 10% of a potassium salt sparingly soluble in cold water. This had been noticed by earlier workers[2] who supposed erroneously that it was the salt of biphenyl-2-carboxylic acid. In addition, Schmitz[3] isolated an acidic by-product, m. p. 193°, from the insoluble salt, but he presumed that this resulted from an impurity in the fluorenone because it was not produced from biphenyl-2-carboxylic acid by fusion with potassium hydroxide. We have found that the insoluble potassium salt is obtained in the same yield even from carefully purified fluorenone and that it is the salt of the acid (IV). Consideration of the mechanism of this unexpected reaction has led us to examine the action of alkali-metal amides on fluorenone, and here again interesting results have been obtained.



(I) (II) (IV)



(III)

The structure (IV) of the by-product of m. p. 208—210° in the potassium hydroxide fusion was based on the empirical formula $C_{26}H_{18}O_3$, the presence of a hydroxyl group (infrared spectrum) in its methyl ester, and formation of a methyl ester methyl ether with methanolic sulphuric acid. The same structure had already been assigned by Klinger and Lonnes[4] to an acid of m. p. 177—179°. However the by-product can be obtained in

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[1] Kenner, Murray, and Tylor, *Tetrahedron*, 1957, **1**, 259.

[2] Fittig and Ostermayer, *Annalen*, 1873, **166**, 361; Pictet and Ankersmit, *ibid.*, 1891, **266**, 138.

[3] Schmitz, *Annalen*, 1878, **193**, 115.

[4] Klinger and Lonnes, *Ber.*, 1896, **29**, 2152.

three crystal forms, m. p. 158°, 175—178°, and 208—210°, differing greatly in their infrared spectra (potassium bromide discs). As it is difficult to get reproducible melting points from the lower-melting forms, which readily change to the form of m. p. 208—210° on heating, it is probable that the acid of m. p. 193° described by Schmitz [3] is identical with our by-product. The identity of our compound with that prepared by Klinger and Lonnes from 10-fluorenylidene-9-phenanthrone was confirmed by a repetition of their work. They claimed that their acid formed a lactone on fusion, but our compound gave a mixture of the hexacyclic hydrocarbon (III; R = H) and the corresponding acid (III; R = CO_2H), m. p. 222—224°. The latter was also formed by the action of hydrochloric and acetic acids on the acid (IV), and it could be decarboxylated with soda-lime. Probably the " lactone," m. p. 213—219°, was an impure specimen of this acid.

The proportion of the by-product (IV) from the alkali fusion of fluorenone was not greatly affected by small changes in the reaction conditions: for example, substitution of sodium hydroxide for potassium hydroxide, variation in temperature or the amount of water present, and addition of diphenyl ether as diluent.[5] Soda-lime, chosen as a solid alkali with large surface area, was unreactive, but powdered sodium hydroxide in refluxing toluene during one week converted fluorenone in over 90% yield, after allowance for some recovered fluorenone, into the acid (IV) accompanied by insignificant amounts of biphenyl-2-carboxylic acid. Under the same conditions, reaction with potassium hydroxide was complete in 1 hr. and the product was biphenyl-2-carboxylic acid (97%), in which the amount of by-product (IV) was too small to be detected and probably less than 0·2%. It seemed barely possible that potassium hydroxide, having a lower melting point and higher water content, might be giving a small amount of the molten alkali even at 110°. The reaction was therefore repeated at 80° with ordinary potassium hydroxide, and at room temperature with specially prepared alkali containing relatively little water, but there was no significant change in the product. Therefore the remarkable difference in behaviour of solid sodium and potassium hydroxides must be a consequence of their crystal structures.

There is one recorded analogy for production of the acid (IV). Delange [6] observed that triphenylmethanol accompanied potassium benzoate and benzene as a product of fusion of benzophenone with potassium hydroxide, and Lock and Rödiger [7] also found small quantities of triphenylmethanol. Under our conditions, as much as 30% of triphenylmethanol has been obtained from the fusion. Benzophenone was scarcely attacked by sodium hydroxide in boiling toluene during 8 days, but 4% of triphenylmethanol was obtained after 6 days at 140° in xylene. The reaction with potassium hydroxide in boiling toluene gave benzoic acid and presumably benzene, but it also was very much slower than the reaction with fluorenone. Evidently strain in the 5-membered ring of fluorenone is an important factor in encouraging the alkaline cleavage. Furthermore, fluorenone, being a planar molecule, is doubtless more easily adsorbed than benzophenone.

The mechanism of both cleavages of fluorenone must involve a potential aryl anion, which can react either with a proton source, as in the normal cleavage to biphenyl-2-carboxylic acid, or with fluorenone, as in production of the acid (IV). The obvious first step is addition of hydroxide ion to the carbonyl group giving the anion (V), but it is unlikely that this alone would be sufficiently nucleophilic to generate the potential aryl anion. We suggest that a second molecule of base attacks the proton of the anion (V), setting in train a concerted transfer of electrons through the aryl group to an electrophile which is either the proton source or the second molecule of fluorenone. The rapidity and the course of the reaction with *solid* potassium hydroxide are explained by the assumption that the crystal surface specially favours a cyclic transition state, either as depicted in

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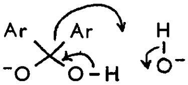
[5] Huntress and Seikel, *J. Amer. Chem. Soc.*, 1939, **61**, 816.

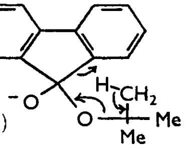
[6] Delange, *Bull. Soc. chim. France*, 1903, **29**, 1131.

[7] Lock and Rödiger, *Ber.*, 1939, **72**, 861.

(VI) or with a larger ring. When these very favourable conditions are absent, as in molten alkali or on the surface of solid sodium hydroxide, the reactive complex survives long enough for a second molecule of fluorenone to compete with proton sources for the potential aryl anion. As a test of this hypothesis, t-butyl alcohol was added to the hydrocarbon solvents to act as an external source of protons; being a considerably weaker acid than water, it was not expected to generate fresh nucleophilic particles, but its adsorption on the alkaline surfaces, with consequent displacement of fluorenone, was foreseen to be a possible influence on the reaction. In fact the rate of reaction with solid potassium hydroxide was greatly decreased by addition of t-butyl alcohol, but the product was still biphenyl-2-carboxylic acid. Evidently competition for the surface was very significant. On the other hand, the reaction between solid sodium hydroxide and fluorenone no longer gave the acid (IV), and the formation of biphenyl-2-carboxylic acid, a by-product from the reaction in absence of t-butyl alcohol, was accelerated. Here again the alcohol must occupy most of the alkaline surface but it is a sufficiently effective proton source to monopolise as much reactive complex as is formed. To sum up, the results of these experiments are regarded as confirmatory evidence for our hypothesis. It should be remarked that, to avoid difficulty in reproducing samples of powdered alkalis, comparisons were always made between simultaneous reactions of divided batches of alkali.


(V)


(VI)


(VII)

One consequence of our hypothesis is that the anion corresponding to (V), formed from the ketone and an alkoxide, should not undergo either cleavage reaction. However, transfer of hydride ion from the alkoxide to the ketone makes such a test experimentally difficult. This transfer is excluded when alkali t-butoxides are the reagents, and at high temperature the alcohol-free t-butoxides do cause fission to the metal salts of biphenyl-2-carboxylic acid. As the t-butyl ester of this acid is unstable under these conditions it might be an intermediate, but we think this unlikely in the absence of a proton donor. Instead we postulate a cyclic transition state (VII), leading directly to isobutene and the carboxylate salt.

The behaviour of some substituted fluorenones under similar conditions has also been examined. The mildness of the treatment with solid potassium hydroxide suggested that this might be a convenient method of preparing substituted biphenyl-2-carboxylic acids. In fact, 2-chloro- and 2,7-dibromo-fluorenone gave excellent yields of 4'-chloro- and 4,4'-dibromo-biphenyl-2-carboxylic acid, but 2-nitrofluorenone formed a dark red complex from which the ketone was regenerated by water. The same acids were obtained very slowly from reactions with solid sodium hydroxide without traces of analogues of the acid (IV). Nor could acids analogous to (IV) be obtained from fusion of these halogenated fluorenones or 1,3-diphenylfluorenone with potassium hydroxide. Probably the negative substituents decrease the nucleophilicity of the potential aryl anion more than its basicity.

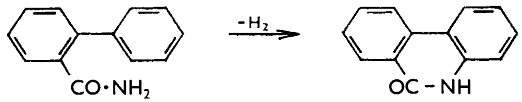
As unexpected results had been obtained from the action of alkali-metal hydroxides on fluorenone, the action of the amides was examined in case there were abnormalities which had been overlooked by earlier workers. The reaction between an excess of sodamide and fluorenone in toluene has been reported[8] as a typical example of the Haller–Bauer reaction,[9] yielding biphenyl-2-carboxamide and also biphenyl. We confirmed this, and we tried an excess of fluorenone in the hope of promoting formation of the amide of acid (IV). In fact, neither the desired reaction nor the Haller–Bauer reaction occurred so long

[8] Haller and Bauer, *Compt. rend.*, 1908, **147**, 824; *Ann. Chim. Phys.*, 1909, **16**, 145.

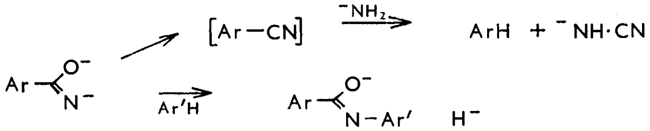
[9] Hamlin and Weston, *Org. Reactions*, 1957, **9**, 1.

as moisture was rigorously excluded. Probably amide ion, being a stronger nucleophile than hydroxide, attaches itself so firmly to the carbonyl group that the three components required by the mechanism analogous to that postulated for the abnormal hydroxide cleavage, namely, addition complex, base, and ketone, cannot co-exist in significant concentrations. As the Haller–Bauer cleavage with an excess of sodamide proceeds under relatively mild conditions, we postulate the annexed mechanism, analogous to that already proposed for the reaction with *solid* potassium hydroxides (VI), in which the ring is not necessarily six-membered.

Three more products, in addition to biphenyl-2-carboxamide and biphenyl, were obtained from fluorenone and an excess of sodamide in liquid ammonia at 100°. One was the imine, but the other two, fluorenone azine and phenanthridone,* were quite unexpected. The source of the azine, a minor product, is still obscure,† but the phenanthridone is formed by dehydrogenation of biphenyl-2-carboxamide:



This conversion was demonstrated in separate experiments, employing potassamide in t-butylamine, where hydrogen could be identified by a mass spectrometer. When fluorenone, instead of biphenyl-2-carboxamide, was allowed to react with sodamide in t-butylamine, the products were phenanthridone, biphenyl, and the t-butylamide of biphenyl-2-carboxylic acid. Neither this amide nor the methylamide undergoes cyclisation to phenanthridone or fission to biphenyl when treated with potassamide for long periods. Primary amides, furthermore, show *two* active hydrogen atoms with Grignard reagents and lithium aluminium hydride, and it is therefore probable that it is the dianion (VIII) which either attacks the unactivated benzene ring or loses oxide ion to a metal cation.[10] The resulting nitrile would be cleaved to cyanamide ion, and this mechanism for the cleavage of amides under Haller–Bauer conditions is more plausible than nucleophilic attack on the carbon atom of an amide monoanion[9].



The following cyclisation[11] is analogous to formation of phenanthridone, except in being an addition instead of a substitution. In this instance too it has been shown that both hydrogen atoms are removed during cyclisation because the reaction is blocked by an additional *N*-alkyl substituent.[12]

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* The production of phenanthridone from fluorenone (or biphenyl-2-carboxamide) and sodamide in toluene has been observed independently by Mr. R. W. Rickards and Mr. P. Hodge (Manchester University).

† It has been pointed out by a Referee that hydrazine might have been formed by reaction between sodamide and ammonia. We had also considered this explanation, amongst others, but we have not discovered any reference to this reaction in the inorganic literature.

[10] Newman and Fukunaga, *J. Amer. Chem. Soc.*, 1960, **82**, 693.

[11] Haller and Bauer, *Compt. rend.*, 1914, **158**, 1086.

[12] Brown and van Gulick, *J. Amer. Chem. Soc.*, 1955, **77**, 1092.

EXPERIMENTAL

Unless otherwise stated, products from reactions between fluorenones and alkali-metal hydroxides and amides were identified by mixed m. p.s and comparisons of infrared spectra with authentic specimens. 4′-Chloro-, 4,4′-dibromo-, and 2′-(9-hydroxy-9-fluorenyl)-biphenyl-2-carboxylic acids, biphenyl-2-carboxamide, fluorenimine, and phenanthridone, were prepared by published methods, and a sample of fluorenone azine was given by Dr. D. Bethell. The *methylamide*, m. p. 169° (Found: C, 79·7; H, 6·2; N, 6·4. $C_{14}H_{13}NO$ requires C, 79·6; H, 6·2; N, 6·6%), and *t-butylamide*, m. p. 112—113° (Found: C, 80·3; H, 7·6; N, 5·6. $C_{17}H_{19}NO$ requires C, 80·6; H, 7·6; N, 5·5%), of biphenyl-2-carboxylic acid were obtained from the acid chloride and the appropriate amine in dry ether.

2′-(9-Hydroxy-9-fluorenyl)biphenyl-2-carboxylic Acid (IV) *and its Derivatives.*—The acid was obtained in three crystal forms, m. p. 158°, 175—178°, and 208—210°, differing greatly in their infrared spectra (KBr discs), but all giving *9,9′-spirobifluorene-4-carboxylic acid* (III; R = CO_2H), m. p. 223—224° (Found: C, 86·8; H, 4·6. $C_{26}H_{16}O_2$ requires C, 86·65; H, 4·5%) [*methyl ester*, m. p. 171—172° (Found: C, 86·3; H, 5·0. $C_{27}H_{18}O_2$ requires C, 86·6; H, 4·8%)], when boiled for 2 min. with hydrochloric acid in acetic acid. The acid (IV) gave with diazomethane a *methyl ester*, m. p. 162°, $\nu_{max.}$ (in $CHCl_3$) 3600 (alcoholic OH) and 1734 cm.$^{-1}$ (aromatic ester C=O) (Found: C, 82·4; H, 5·2; OMe, 7·8. $C_{27}H_{20}O_3$ requires C, 82·6; H, 5·1; OMe, 7·9%), and with methanolic sulphuric acid a *methyl ester methyl ether*, m. p. 174—176°, $\nu_{max.}$ (in $CHCl_3$) 1727 cm.$^{-1}$, but no hydroxyl absorption (Found: C, 82·6; H, 5·4; OMe, 15·3. $C_{28}H_{22}O_3$ requires C, 82·7; H, 5·4; OMe, 15·3%). When the acid (IV) was heated at 220—230° for ½ hr., 9,9′-spirobifluorene (III; R = H),[13] m. p. 197—198° (Found: C, 94·8; H, 5·5. Calc. for $C_{25}H_{16}$: C, 94·9; H, 5·1%), and its 4-carboxylic acid but no lactonic material were obtained. The 4-carboxylic acid gave the parent hydrocarbon when heated with soda-lime.

Reactions between Alkali-metal Hydroxides and Fluorenones.—(a) *Fused alkalis.* In a typical reaction, fluorenone (10 g.) was added during ½ hr. to stirred, fused potassium hydroxide at 180—200°. The temperature was maintained for a further ½ hr. and the pasty mass was then added to cold water (100 ml.) with stirring. The resulting precipitate was washed with water and ether, to remove a little unchanged fluorenone, recrystallised from boiling water, redissolved in hot water, and acidified, yielding the acid (IV) (1·1 g., 10%). The original alkaline filtrate gave, by acidification and crystallisation of the resulting precipitate from carbon tetrachloride, biphenyl-2-carboxylic acid (77%), m. p. 114°. The yield of the acid (IV) was unchanged by adding water to the fused alkali or by using sodium hydroxide, and decreased to 6% when diphenyl ether (150 g.) was used as a diluent. Analogues [1] of the acid (IV) were not detected after alkali fusions of 2-chloro- and 1,3-diphenyl-fluorenone; the product, m. p. 206—208° (Found: C, 85·6; H, 5·3. $C_{25}H_{18}O_2$ requires C, 85·7; H, 5·1%), from the latter was presumed to be *3′,5′-diphenylbiphenyl-2-carboxylic acid* because it was not identical with 2,4,6-triphenylbenzoic acid, m. p. 256°. Benzophenone gave triphenylmethanol (up to 33%) and benzoic acid.

(b) *Solid sodium hydroxide.* Fluorenone (10 g.), finely powdered sodium hydroxide (20 g.), several glass marbles, and boiling toluene (75 ml.) were stirred under reflux for 7 days. The mixture was cooled, treated with water (100 ml.), and filtered. The acid (IV) (94% yield, 68% conversion) was isolated from the insoluble sodium salt. The filtrate and washings (ether and water) were separated, and fluorenone (28%) was recovered from the organic phase; the aqueous solution gave biphenyl-2-carboxylic acid in variable but low yield ($\not>$4%). When t-butyl alcohol (10 ml.) was added to the reaction mixture, and the reaction was stopped after 4 days, none of the acid (IV) was isolated but biphenyl-2-carboxylic acid was obtained in 10% yield. When sodium hydroxide was replaced by soda-lime (30 g.) or 50% sodium hydroxide solution no reaction was detected. In similar reactions with sodium hydroxide 2,7-dibromofluorenone in toluene gave 4,4′-dibromobiphenyl-2-carboxylic acid, m. p. 211—212° (15%), and benzophenone in xylene (3 days) gave benzoic acid (6·7%) and triphenylmethanol (4·2%).

(c) *Solid potassium hydroxide.* When potassium hydroxide (26 g.) replaced sodium hydroxide, the yellow colour of fluorenone faded within ½ hr. but boiling was continued for a total of 4 hr. to complete the reaction. After addition of water no fluorenone could be recovered

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[13] Clarkson and Gomberg, *J. Amer. Chem. Soc.*, 1930, **52**, 2884.

from the toluene layer, and acidification of the aqueous solution gave biphenyl-2-carboxylic acid (97%), m. p. 114°. Sublimation of this acid failed to reveal the presence of any of the far less volatile acid (IV). In similar reactions 2-chloro- and 2,7-dibromo-fluorenones gave 4′-chloro- and 4,4′-dibromo-biphenyl-2-carboxylic acid in 97% and 86% yield, respectively, and benzophenone gave benzoic acid (97%) after 2 days. 2-Nitrofluorenone and solid potassium hydroxide rapidly formed a dark red crystalline complex from which the ketone was recovered quantitatively by the action of water. When boiling benzene, boiling benzene–t-butyl alcohol (10 : 1 v/v), or benzene at room temperature was used as solvent, the yields of biphenyl-2-carboxylic acid were 91%, 1%, and 3%, and the recoveries of fluorenone were 7%, 97%, and 96%, respectively. For a repetition of the last reaction on a reduced scale, potassium hydroxide (containing less than 5% of water) was prepared from potassium (5 g.) and water (2·5 ml.) in dry liquid ammonia, and a 70% yield of biphenyl-2-carboxylic acid was obtained after 6 hr., but whether this increased reactivity of the potassium hydroxide was due to smaller particle size, lower water content, or other factors was not determined.

Action of Alkali-metal t-Butoxides on Fluorenone.—Fluorenone (1 g.) was heated with alcohol-free alkali-metal t-butoxide (2 g.) for 15 min. at 180—200° (sodium or potassium) or 230—250° (lithium). The resulting solid gave biphenyl-2-carboxylic acid (85—90%) and the acid (IV) (1—2%), with no unchanged fluorenone. When fluorenone was used in excess, the yields of acids, based on alkali-metal t-butoxide used, were similar.

Reactions between Metal Amides and Fluorenone.—(a) *Fluorenone in excess.* In an apparatus developed for studying ammonia reactions in the absence of water or oxygen, potassamide was prepared from bright potassium (0·215 g.), liquid ammonia (distilled from sodium in an oxygen-free nitrogen atmosphere), and a small crystal of ferric nitrate. The excess of ammonia was pumped off, the flask was refilled with nitrogen, and a dry deoxygenated solution of fluorenone (3 g., 200% molar excess) in toluene (40 ml.) was added through a glass break-seal. The mixture was magnetically stirred and boiled under reflux for 24 hr., cooled, and treated with water. No acidic product was detected in the aqueous solution, and fluorenone (99%) was recovered from the toluene layer. No carboxamide could be detected.

(b) *Sodamide in liquid ammonia.* Fluorenone (20 g.), sodamide (from sodium, 16 g.), and liquid ammonia (*ca.* 750 ml.) were heated in a 1·5-l. autoclave at 95—100° for 24 hr. After cooling, the ammonia was allowed to evaporate, the residue was treated with water (500 ml.), and the resulting brown solid was collected, washed with water, and air-dried. It was separated into three fractions by successive extractions (Soxhlet) with light petroleum (b. p. 40—60°), light petroleum (b. p. 60—80°), and chloroform. The first fraction was separated by fractional sublimation into biphenyl (2·4 g., 13·5%), biphenyl-2-carboxamide (1·1 g., 5%), and fluorenimine (9·4 g., 47·5%). The second fraction consisted of fluorenone azine (0·86 g., 4·5%), m. p. 267—268° after crystallisation from benzene, and a trace of fluorenimine. The third fraction was phenanthridone (3·8 g., 17·5%). The minute residue in the Soxhlet thimble was inorganic and presumably derived from the ferric nitrate used to prepare the sodamide. The products isolated account for 88% of the fluorenone used and no evidence was obtained for the presence of others in this or similar reactions.

(c) *t-Butylamine.* Fluorenone (3·6 g.), sodamide (from sodium, 1 g.), and t-butylamine (purified by distillation from sodium, 75 ml.) were boiled for 18 hr. and the t-butylamine was then removed by distillation. Water (130 ml.) was added to the residue and the resulting solid was collected, washed with water, and air-dried. It was separated as described above into biphenyl (0·81 g., 20%), m. p. 72°, *N*-t-butylbiphenyl-2-carboxamide (1·3 g., 27%), m. p. 111°, and phenanthridone (0·94 g., 25·5%), m. p. 291—292°. When a similar reaction was stopped after 2 hr. biphenyl-2-carboxamide (0·58 g., 15·2%), m. p. 177°, was one of the products.

*The Action of Alkali-metal Amides on Biphenyl-*2*-carboxamides.*—Biphenyl-2-carboxamide (0·20 g.), potassamide (from potassium, 0·87 g.), and t-butylamine (80 ml.) were warmed at 40° until effervescence stopped (about ½ hr.); in one experiment the evolved gas was collected and shown to contain hydrogen by mass spectrometry. The other products were found to be biphenyl (53%) and phenanthridone (40%). When sodamide was used the reaction required boiling for 24 hr., giving biphenyl (21%) and phenanthridone (19%), but with lithium amide no reaction occurred even during 3 days. From similar reactions the mono- and the di-amide of diphenic acid, and the methylamide and t-butylamide of biphenyl-2-carboxylic acid were recovered unchanged, even after prolonged boiling with potassamide in t-butylamine; 2,4,6-triphenylbenzamide gave 1,3,5-triphenylbenzene (77%) and no 5,7-diphenylphenanthridone.

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