[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

REACTIONS OF ATOMS AND FREE RADICALS IN SOLUTION. XXXI. REACTIONS OF FREE BENZOYL RADICALS WITH AZO COMPOUNDS (PRELIMINARY PAPER)

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Until fairly recently it was assumed by some investigators that short-lived free radicals are extremely reactive. That is, they were supposed to interact at first collision (without activation energy) with any available co-reactant. The fallacy of this assumption did much to retard early progress in the free-radical field, and befuddle interpretations of experimental results.

It is now well established that in solution short-lived free radicals may react in different ways. (A) They may attack the solvent, either by adding to it or by abstracting from it a univalent atom (hydrogen or halogen) or a monovalent group. (B) They may donate to the solvent or some component of the reaction system (which may be another free radical) a hydrogen or a halogen atom. When such an exchange takes place between two like free radicals, the reaction is usually called a disproportionation. (C) They may combine with other free radicals including those of their own kind.

There are, naturally, some structural limitations on the behavior of certain free radicals. Such free radicals as methyl or phenyl would scarcely be expected to disproportionate or to donate hydrogen atoms to potential hydrogen acceptors. Structural limitations aside, however, is there not some criterion by which one might predict the probable behavior of a given free radical in a given reaction medium?

At present it would appear that the most useful of such criteria is the "relative reactivity" of the free radical in question—that is, its ability to abstract a hydrogen or a halogen atom from a potential hydrogen or halogen donor. There is already a good deal of qualitative data bearing upon this criterion, of which the scope and applicability might be indefinitely extended.[1]

Free radicals as oxidants and reductants. By the use of the criterion just outlined, it may be shown that short-lived free radicals differ tremendously in their "relative reactivities"; moreover, by the same criterion they may be arranged

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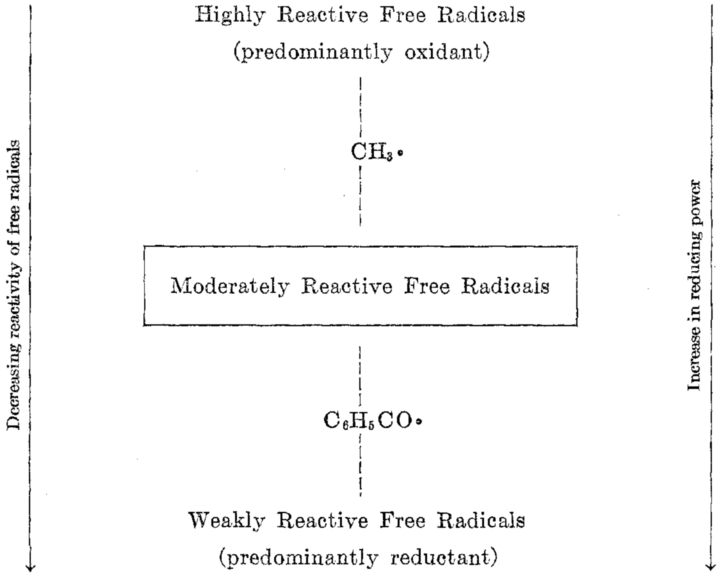
[1] Potential hydrogen or halogen donors differ greatly in their vulnerability to free radical attack. In general it may be said that, with respect to abstraction by a free radical, a tertiary hydrogen atom in a hydrocarbon is more vulnerable than a secondary hydrogen atom, and this in turn is more labile than a primary hydrogen atom. However, in substituted hydrocarbons, the relative labilities of the hydrogen atoms are determined both by the numbers and by the nature of the substituents present. For example, with respect to attack by a free methyl radical, a secondary hydrogen atom in a chloromethyl group ($AlkCH_2Cl$) is more labile than a secondary hydrogen atomn i a normal alkane ($AlkCH_2Alk'$). It can also be demonstrated that in the presence of suitable substituents a secondary hydrogen atom may be more labile than a tertiary hydrogen atom [see Kharasch and Büchi, *J. Am. Chem. Soc.*, **73**, 632 (1951)].

in an ordered series. To avoid unnecessary complications, and perhaps confusing refinements, we shall give here merely the skeleton of such a series, and shall compare the properties of certain radicals which fall, not near the extremes of the series, but still well beyond the limits of the intermediate group, namely the "moderately reactive" free radicals. (Table I)

The free methyl radical is so highly reactive in the sense specified that in most reaction systems it is an excellent oxidant (oxidant and reductant are relative terms, and are here used with all due reservations) and abstracts a hydrogen or halogen atom from the donor molecule. By the criterion here adopted, the free methyl radical is more reactive (and a better oxidant) than the free propyl radical.[2] It is also reasonable to assume that benzaldehyde when treated with sufficiently reactive free radicals should give the free benzoyl radical which would be of very low reactivity. The question then arises whether such a radical, since it is so weak an oxidant in the sense already defined, might not, in the presence of a suitable co-reactant, be made to serve as a reductant. The co-reactants selected for this study were benzaldehyde and azobenzene and benzaldehyde and α,α'-azodiisobutyronitrile. The nitrogen-to-nitrogen double bond, in both of these cases, was cleaved, with the formation, respectively, of benzanilide and α,α-dimethylhippuronitrile.

TABLE I



Reaction of benzaldehyde, azobenzene, and tert-butyl peroxide. No reaction takes place when freshly distilled benzaldehyde (free of peroxides) and azobenzene are heated for 6–8 hours at 145° in a flask from which the air is displaced by

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[2] Free methyl radicals react with trimethylacetic acid to give 75% of tetramethyladipic acid, but only 3% of this acid is formed when free propyl radicals are used (unpublished work). On the other hand, cumene reacts with free propyl radicals to give 75% of bi-α-cumyl and with free methyl radicals nearly 100% of the calculated amount of bi-α-cumyl.

nitrogen gas.[3] Almost all the azobenzene is recovered unchanged. However, when azobenzene (0.1 mole) dissolved in benzaldehyde (70 ml.) is heated to 135–140° (in a flask in which air has been displaced by nitrogen gas) and *tert*-butyl peroxide (0.05 mole) dissolved in benzaldehyde (36 ml.) is added to the mixture over a period of seven hours, all the azobenzene is consumed. Benzanilide (29%), monobenzoylhydrazobenzene (15%) (on the basis of azobenzene used), and an unidentified oil (6.2 g.) are formed.

In the experiment just cited, a tenfold excess of benzaldehyde was used with stoichiometric amounts of azobenzene and *tert*-butyl peroxide. From an inspection of the total yield and the nature of the reaction products, it appears reasonable to assume that the reaction in question is a free-radical chain reaction, and should, therefore, proceed to completion even when *tert*-butyl peroxide is present in small amount only. This was found to be the case. The yield of monobenzoylhydrazobenzene, when only five mole-% of peroxide was used, was 80% on the basis of the azobenzene consumed. The amount of benzanilide formed in the reaction (if any) was very small.

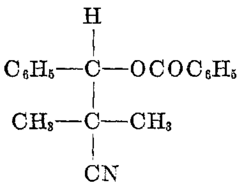
The chain reaction whereby monobenzoylhydrazobenzene is formed from benzaldehyde and azobenzene may be formulated as follows:[4]

1. $[(CH_3)_3CO]_2 \xrightarrow{\Delta} 2\ (CH_3)_3CO\cdot$
2. $C_6H_5CHO + (CH_3)_3CO\cdot \rightarrow C_6H_5C(=O)\cdot + (CH_3)_3COH$
3. $C_6H_5N=NC_6H_5 + C_6H_5C(=O)\cdot \rightarrow C_6H_5[C_6H_5(C_6H_5CO)N]N\cdot(\mathbf{A})$
4. $\mathbf{A} + C_6H_5CHO \rightarrow (C_6H_5)(C_6H_5CO)N-NHC_6H_5 + C_6H_5C(=O)\cdot$

Much less certain, however, is the mechanism whereby benzanilide is formed in this reaction. Experiments different from those here recorded are needed for confident selection among the various conceivable reaction schemes, and work along these lines is now underway.

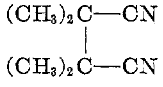
Reaction of α,α′-azodiisobutyronitrile with benzaldehyde. α,α′-Azodiisobutyronitrile, dissolved in benzaldehyde, was slowly added to benzaldehyde maintained at 90–100°. From the reaction mixture the following products were isolated:[5]

Compound **A**



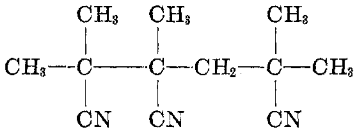
$C_6H_5-CH(OCOC_6H_5)-C(CH_3)_2-CN$

Compound **B**



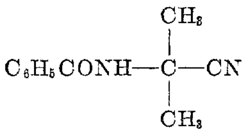
$(CH_3)_2C(CN)-C(CH_3)_2CN$

Compound **C**



$CH_3-C(CH_3)(CN)-C(CH_3)(CN)-CH_2-C(CH_3)(CN)-CH_3$

Compound **D**



$C_6H_5CONH-C(CH_3)_2-CN$

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[3] The unusual reactions which azobenzene undergoes when heated with many reagents will be discussed in a later publication.

[4] The chain-terminating steps of this reaction are as yet unknown. It is believed that

The formation of tetramethylsuccinonitrile (Compound **B**) and 2,3,5-trimethyl-2,3,5-tricyanohexane (Compound **C**) in the decomposition of α,α'-diisobutyronitrile in solvents has been noted by others (1). The formation of Compound **A** is readily accounted for on the following basis:

1. $[\mathrm{NC(CH_3)_2CN{=}}]_2 \xrightarrow{\Delta} 2\,\mathrm{NC(CH_3)_2C\cdot} + \mathrm{N_2}$
2. $\mathrm{NC(CH_3)_2C\cdot} + \mathrm{C_6H_5CHO} \rightarrow \mathrm{NC(CH_3)_2CH} + \mathrm{C_6H_5C({=}O)\cdot}$
3. $\mathrm{C_6H_5C({=}O)\cdot} + \mathrm{C_6H_5CHO} \rightarrow \mathrm{C_6H_5(C_6H_5CO_2)CH\cdot}$
4. $\mathrm{C_6H_5(C_6H_5CO_2)CH\cdot} + \mathrm{NC(CH_3)_2C\cdot} \rightarrow \text{Compound } \mathbf{A}$
5. $\mathrm{C_6H_5(C_6H_5CO_2)CH\cdot} + [\mathrm{NC(CH_3)_2CN{=}}]_2 \rightarrow \text{Compound } \mathbf{A} + \mathrm{N_2} + \mathrm{NC(CH_3)_2C\cdot}$

However, in the case of Compound **D**, the free benzoyl radical, formed as in 2 above, must add to the α,α'-azodiisobutyronitrile molecule.

6. $[\mathrm{NC(CH_3)_2CN{=}}]_2 + \mathrm{C_6H_5C({=}O)\cdot} \rightarrow \mathrm{NC(CH_3)_2C[NC(CH_3)_2C(C_6H_5CO)N]N\cdot}$ **(E)**

As in the analogous formation of benzanilide from azobenzene and free benzoyl radical, the precise mechanism whereby the intermediate **E** is transformed to α α'-dimethylhippuronitrile is as yet unknown, although several plausible reaction schemes might be proposed.

It is most striking that no hydrobenzoin dibenzoate is formed when benzaldehyde (10 moles) is heated with *tert*-butyl peroxide in the presence of azobenzene (1 mole). This implies that the rate of addition of free benzoyl radicals to the nitrogen-to-nitrogen double bond in azobenzene is many times faster than the addition to the carbon-to-oxygen double bond in benzaldehyde. Note also that little or no hydrobenzoin dibenzoate is formed when α,α'-diisobutyronitrile is decomposed in the presence of a large excess of benzaldehyde.

EXPERIMENTAL PART

(*a*) Azobenzene (2.6 g.) dissolved in freshly distilled peroxide-free benzaldehyde (16 ml.) was heated for seven hours at 145° in a nitrogen atmosphere. At the end of that time, the benzaldehyde was removed under reduced pressure. The residue was practically pure azobenzene.

(*b*) Azobenzene (18.2 g.) dissolved in freshly distilled benzaldehyde (70 ml.) was placed in a three-necked flask, provided with a stirrer, dropping-funnel, and condenser. The air in the apparatus was displaced by nitrogen gas. The whole was heated to 135–140°, and *tert*-butyl peroxide (7.3 g.), dissolved in 36 ml. of benzaldehyde, was added slowly over a period of six hours. The gas (390 cc.) liberated in the reaction was collected over water.

The cooled reaction mixture was steam-distilled to remove unchanged benzaldehyde, and the residue was extracted several times with hot water. From the water extract benzoic acid (0.6 g.) was obtained. The residue was dissolved in ether, and the solution was dried with sodium sulfate. The drying agent was collected, and the ether removed from the filtrate. A colored viscous oil (32 g.) remained.

A quantity of this oil (6.2 g.) was chromatogrammed on alumina (150 g.). The column diameter was 2.4 cm. and the height 21 cm.

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identification of the components of the oil formed in the reaction would prove helpful in this connection. This study is now underway.

[5] A large quantity of the α,α'-azodiisobutyronitrile decomposed into nitrogen, $\mathrm{(CH_3)_2CHCN}$, and $\mathrm{NC(CH_3)C{=}CH_2}$. These products, however, were not isolated because they have no direct bearing on the reaction in question.

A mixture of benzene and ether (9:1) eluted benzanilide (2.2 g.), and an oil. The oil was chromatogrammed again on alumina. A mixture of ether and chloroform (9:1) eluted monobenzoylhydrazobenzene (2.8 g.). An oil (1.2 g.) was the intermediate fraction in the chromagram. The identities of the benzanilide and the monobenzoylhydrazobenzene were established by conventional methods.

These data indicate that 29% of benzanilide and 50.4% of monobenzoylhydrazobenzene, on the basis of the azobenzene used, are formed in the reaction. The identity of the oil has not been established as yet.

(*c*) In another experiment, the conditions were the same as described in (*b*), except that only five mole-% of *tert*-butyl peroxide, on the basis of the azobenzene, was used.

The decomposition of α,α′-azodiisobutyronitrile in benzaldehyde. There were small variations in the yields of the various reaction products with variations in the temperature of decomposition. The most satisfactory yields were obtained at temperatures of 90–110°. Only the results of two typical experiments at 110° and 90° are here recorded.

(*a*) *Decomposition of α,α′-azodiisobutyronitrile in benzaldehyde at 110°.* Freshly distilled benzaldehyde (80 ml.) was placed in a three-necked flask fitted with a stirrer, reflux condenser, and a dropping-funnel. The air in the apparatus was displaced by nitrogen gas. The whole was then heated and maintained at 110°. A solution of α,α′-azodiisobutyronitrile (30 g.) in benzaldehyde (340 ml.) was then added gradually over a period of nine hours.

The reaction mixture was steam-distilled. The first distillate was benzaldehyde, followed by tetramethylsuccinonitrile. The latter partly separated from the water. This solid (m.p. 163–164°) was collected (3.1 g.). Extraction of the aqueous distillate yielded an additional quantity (1.2 g.) of tetramethylsuccinonitrile. From the benzaldehyde, upon distillation at reduced pressure, more tetramethylsuccinonitrile (6.6 g.) was obtained. The total yield of this material was 10.9 g. (36% on the basis of the azo compound used).

To the material remaining in the flask of the steam-distillation apparatus sufficient water was added to make the total volume 1000 ml. The whole was heated to boiling, and the water was decanted. From the water solution α,α-dimethylhippuronitrile (1.5 g.) separated upon cooling. The oil (7.4 g.) remaining in the flask was chromatogrammed on alumina (120 g.). Benzene eluted crystalline Compound **A** (3.2 g.) which melted at 123–124°. A mixture of ether and methanol (9:1) eluted a further crop (1.3 g.) of α,α-dimethylhippuronitrile. The remaining oil (2.9 g.) was not further investigated although it was known to contain some of Compound **C**.

(*b*) *Decomposition of α,α′-azodiisobutyronitrile in benzaldehyde at 90°.* α,α′-Azodiisobutyronitrile (30 g.) dissolved in 250 ml. of freshly distilled benzaldehyde was slowly added over a period of 7½ hours to benzaldehyde maintained at 90°. The reaction mixture was worked up in the manner described in the previous experiment. The following products were isolated: (a) tetramethylsuccinonitrile (12 g.); (b) α,α-dimethylhippuronitrile (2.4 g.); (c) Compound **A** (0.5 g.); (d) Compound **C** (2.1 g.); (e) unidentified oil.

Identification of α,α-dimethylhippuronitrile. The α,α-dimethylhippuronitrile obtained in this study melted at 168°. The melting point recorded in the literature is 168.5°.

Anal. Calc'd for $C_{11}H_{12}N_2O$: C, 70.2; H, 6.43; N, 14.87.
Found: C, 70.1; H, 6.2; N, 14.78.

The *α,α-dimethylhippuric acid* prepared from this material melted at 199–200°. The literature reports 198° as the melting point of the acid. The *methyl ester* of the acid prepared by us melted at 122°. The literature reports 124° as the melting point of the ester.

Identification of compound **A**. Neither Compound **A** (presumably 2,2-dimethyl-3-benzoxy-3-phenylpropionitrile) nor its degradation product are known compounds. However, there is little doubt that Compound **A** must be $C_6H_5(OCOC_6H_5)CHC(CH_3)_2CN$.

Anal. Calc'd for $C_{18}H_{17}NO_2$: C, 77.50; H, 6.14; N, 5.02.
Found: C, 77.61; H, 6.52; N, 5.3.

Compound **A** (0.2 g.) was heated with a one % solution of sodium hydroxide in methanol.

By working-up the reaction mixture benzoic acid (*ca.* 0.09 g.) and a neutral fraction (*ca.* 0.12 g.) were obtained. The neutral fraction crystallized upon standing. For analyses it was crystallized from a mixture of chloroform and ligroïn. It melted sharply at 67–68°. The compound is presumably $C_6H_5CH(OH)C(CH_3)_2CN$ (2,2-dimethyl-3-hydroxy-3-phenylpropionitrile), formed by hydrolysis of Compound **A**.

Anal. Calc'd for $C_{11}H_{13}NO$: C, 75.4; H, 7.48; N, 8.0.
Found: C, 75.35; H, 7.39; N, 7.85.

Identification of compound **C**. The melting point of this compound is the same as that given by Waters and Bickel (1) for 2,3,5-trimethyl-2,3,5-tricyanohexane.

Anal. Calc'd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67.
Found: C, 70.55; H, 8.32; N, 20.11.

Upon hydrolysis with a concentrated solution of potassium hydroxide in ethylene glycol, ammonia was evolved. The acid (m.p. 212°) obtained was *trimethyl(2-carboxyisobutyl)succinonitrile*. The melting point recorded for this acid by Waters and Bickel is 212°.

Anal. Calc'd for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81.
Found: C, 59.53; H, 7.63; N, 5.56.

Photochemically induced reaction of α,α'-azodiisobutyronitrile with benzaldehyde. α,α'-Azodiisobutyronitrile (10 g.) dissolved in benzaldehyde (100 ml.) was internally illuminated for five hours with a neon-type quartz coil containing mercury vapor.[6] The reaction mixture was worked up as described previously. A total of 6.5 g. of material was obtained. This consisted of tetramethylsuccinic acid (2.4 g.), α,α-dimethylhippuronitrile (0.5 g.), and an oil (3.6 g.) which was not further investigated.

SUMMARY

1. The following products were isolated when α,α'-azodiisobutyronitrile was decomposed in benzaldehyde at 110°: 2,3,5-trimethyl-2,3,5-tricyanohexane, α,α'-dimethylhippuronitrile, 2,2-dimethyl-3-benzoxy-3-phenylpropionitrile, and tetramethylsuccinonitrile.

2. No reaction takes place when benzaldehyde and azobenzene are heated at 140° in the absence of oxygen or peroxidic materials.

3. In the presence of a small quantity of *tert*-butyl peroxide, benzaldehyde and azobenzene react at 140° to give monobenzoylhydrazobenzene as the major reaction product.

4. Benzaldehyde reacts with azobenzene, at 140° in the presence of half-molar quantities of *tert*-butyl peroxide (on the basis of the azobenzene), to give monobenzoylhydrazobenzene and benzanilide.

5. Some properties of free benzoyl radicals are discussed.

CHICAGO 37, ILLINOIS

REFERENCES

(1) For references see WATERS AND BICKEL, *Rec. trav. chim.*, **69**, 1490 (1950).

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[6] For a description of the apparatus, see Kharasch and Friedlander, *J. Org. Chem.*, **14**, 245 (1949).