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THERMAL HIGH YIELD AROMATIC ARYLATION WITH α-AZOHYDROPEROXIDE (PART 1). A NOVEL FREE RADICAL AROMATIC ARYLATION REACTION

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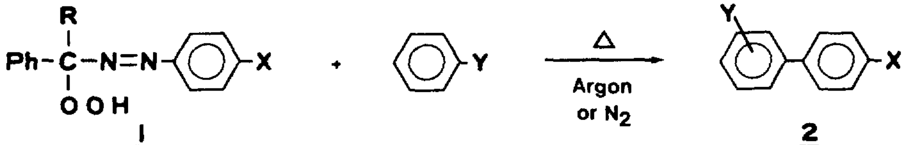
Abstract: Heating α-azohydroperoxide (1) (ca. 10^{-3} M) in benzene under reflux with bubbling inert gas for 20 - 23 hours affords biphenyls (2) in high yields (70 - 90%). A mechanism involving an induced decomposition radical chain reaction is suggested.

Free radical aromatic arylation has been an important topic both from the mechanistic and synthetic points of view since the discovery of Gomberg's aromatic arylation reaction.[1,2] Although some metal assisted and/or photochemical aromatic arylation give high yields of biaryls,[3,4] the free radical arylation generally gives low or moderate yields of arylated aromatics. We now report a new thermal free radical high yield aromatic arylation with α-azohydroperoxide (1). The reaction found in this study is of importance not only from the synthetic but also from the mechanistic point of view.

α-Azohydroperoxide (1) was prepared by autoxidation of hydrazone in high yields.[5-7] When a benzene solution of 1 (ca. 10^{-3} M) was heated under reflux with bubbling argon or nitrogen gas until 1 decomposed completely (20 - 23 hours), biphenyls (2) were formed in high yields (70 - 90%) (Table 1, No. 1 - 8) accompanied by benzaldehyde and phenol (Scheme 1). It is important to note the following. The monitoring of the reaction by HPLC indicated that both the decomposition of 1 and biaryl formation took place slowly, completing the reaction in 20 - 23 hours. For example, 8 hours heating gave merely moderate yields of 2 accompanied by the recovered 1. In order to obtain reproducible results, it is recommended to use an oil bath (bath temperature 90°C) rather than a mantle heater, and to bubble gently inert gas through the solution rather than to use a gas balloon.

The mechanism of this novel thermal arylation with 1 is quite interesting.

Scheme 1.



1

2
(70 ~ 90%)
Y=H

a:R=H;X=Br, b:R=H;X=CH_3, c:R=H;X=OCH_3
d:R=H;X=Cl, e:R=H;X=H, f:R=CH_3;X=Br

Table 1. Yields of biphenyls (2) in the arylation of benzene with α-azohydroperoxide (1).

No.	1	Condition (Concentration)		Biphenyls (2) X	Yields[a)] (%)	Time (Hours)
1	1a	Δ	(10^{-2} M)	Br	71%	23
2	1a	Δ	(10^{-3} M)	Br	78%	23
3	1a	Δ	(10^{-4} M)	Br	80%	23
4	1b	Δ	(10^{-3} M)	CH_3	77%	22
5	1c	Δ	(10^{-3} M)	OCH_3	90%	23
6	1d	Δ	(10^{-3} M)	Cl	70%	23
7	1e	Δ	(10^{-3} M)	H	88%	23
8	1f	Δ	(10^{-3} M)	Br	76%	20
9	1f	hν	(10^{-3} M)	Br	45%	3
10	1a	hν	(10^{-2} M)	Br	48%	8
11	1e	hν	(10^{-3} M)	H	34%	24

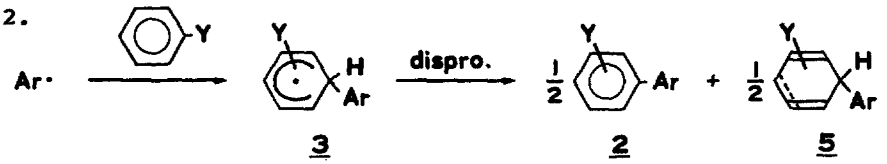
Δ : Thermal reaction at the reflux temperature.
hν: Photolysis (>280 nm).
a) Yield is based on 1. The amount of biphenyls was determined by HPLC and GLC, and/or by the TLC isolation.

The following observations provide some insights into the reaction. In the presence of nitrosobenzene (10 times to 1a) the arylation of benzene with 1a was hampered reducing the yield of biphenyls (2a) to 51%. Similarly, bromoform (5 times) reduced the yield of biphenyls to 27%. The ortho:meta:para isomer ratio of bromobiphenyls obtained by the thermal reaction of 1e with bromobenzene was found to be 60:23:17, indicating that the thermal aromatic arylation with 1 involves the free radical reaction.

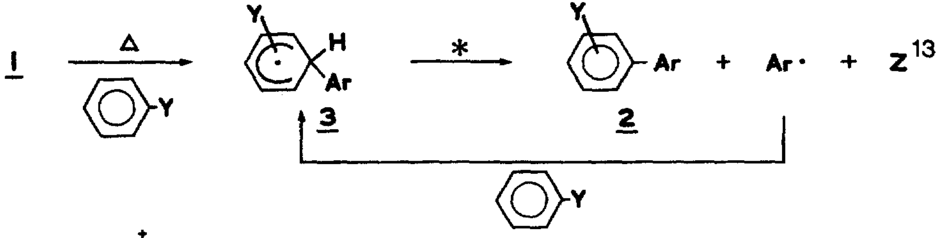
However, the high yield arylation reaction with 1 is not simply a usual free radical arylation via the disproportionation of the cyclohexadienyl radical intermediate (3) which is formed by the attack of aryl radical onto aromatics. This is because the disproportionation of cyclohexadienyl radicals (3) usually gives biphenyls and dihydrobiphenyls (5) in the 1:1 ratio in addition to the dimer of 3, rendering the yield of biaryl less than 50% (Scheme 2).[8,9] In fact, as reported in the literature, we observed only a moderate yield of biphenyl (2e) in the thermal reaction of dibenzoyl peroxide with benzene under the same conditions used for the reaction with 1.

Similarly, the high yield in the biaryl formation by 1 is not in consequence of the oxidation of the dihydrobiphenyls (5), the disproportionation product from 3, to 2. This is because 5 was not identified in the reaction mixture. In addition, the oxidation of the reaction mixture which was obtained after 22 hours of heating 1 in benzene, with molecular oxygen (bubbling through) or quinones at the reflux temperature did not increase the yield of 2.

Scheme 2.



Scheme 3.



$* = 1$, $\mathrm{Ar\overset{+}{N}{\equiv}N}$, or others $\qquad$ $(\mathrm{Ar{=}p\text{-}X\text{-}C_6H_4\text{-}})$

The time dependent study also has indicated that there is no preceding compound to 2.

All of these observations demonstrate that the high yield arylation with 1 is the result of a new reaction involving the efficient oxidation of the cyclohexadienyl radicals (3) by some oxidants.[8,9] Several possible mechanisms can be assumed. For example, free hydroxyl radical which is considered to be generated from 1 together with aryl radical by heating,[6,10] can be a possible oxidant for 3; the oxidation of 3 with hydroxyl radical could give the high yield of biphenyls. To test this, we compared photo reactions. Photolysis of 1 (10^{-3} M) in benzene with a high pressure mercury lamp through a Pyrex filter, by which both free hydroxyl and aryl radicals are generated simultaneously and

$$1 \xrightarrow{h\nu} \mathrm{Ar\cdot} + \mathrm{\cdot OH} + \mathrm{PhCOR} + \mathrm{N_2}$$

efficiently,[6] gave merely low or moderate yields of biphenyls (2) (Table 1, No. 9 - 11).[11] In this reaction phenol which is a product of the reaction of hydroxyl radical with benzene, was formed in 10 - 20% yield as reported in the previous paper.[6] These our observations indicate that hydroxyl radical generated freely from 1 reacts rapidly and efficiently with solvent benzene to give hydroxylated compounds prior to acting as the oxidant for 3.[12] This does not support the possibility of free hydroxyl radical as the oxidant for 3.

On the other hand, the high yield arylation is explainable by the radical chain mechanism involving an electron transfer oxidation of 3, in which the induced decomposition of 1, arenediazonium ions,[7] or other species (* in Scheme 3)[13] that are supposed to be generated from 1 by heating, by cyclohexadienyl radical (3) is included. The induced decomposition of α-azohydroperoxide and/or arenediazonium ions in the radical chain reactions has recently been reported.[14,15] Therefore, we consider that the induced decomposition radical chain mechanism involving the oxidation of 3 explains most reasonably the observed high yield arylation with 1 (Scheme 3). However, the details of this mechanism must be elucidated by further studies in progress. We shall report the mechanism of this novel reaction in our forthcoming paper.

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