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New Oxidative Aromatization of α,β-Unsaturated Cyclohexenones with Iodine-Cerium(IV) Ammonium Nitrate in Alcohol

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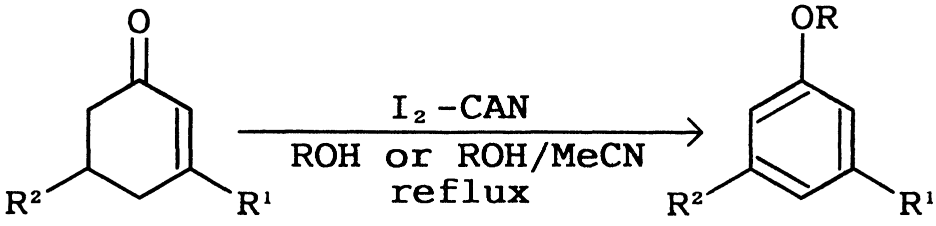
The reaction of 2-cyclohexen-1-one derivatives with iodine-cerium(IV) ammonium nitrate in alcohols (methanol, ethanol, 1-propanol, 2-propanol, and 1-butanol) under refluxing, gave the corresponding alkyl phenyl ethers in good yields. In the case of diol (ethylene glycol, 1,3-propanediol, and 1,4-butanediol), phenoxyalkanol derivatives were obtained. The present method was also applicable to oxidative rearrangement of isophorone.

The oxidative aromatization of α,β-unsaturated cyclohexenones to ethers are usually resulted by one of the following methods: the reaction of isophorone with oleum and acetic anhydride;[1] the dehydrogenation of 2-cyclohexen-1-one parts in polycyclic compounds using palladium[2] and *N*-bromosuccinimide;[3] the reaction of 5-(4-chlorophenyl)-3-methyl-2-cyclohexen-1-one with iodine in methanol;[4] the reaction of 2-cyclohexen-1-one with copper(II) bromide and lithium bromide;[5] or the reaction of 2-cyclohexen-1-one with $VO(OR)Cl_2$, or $VO(OEt)Cl_2$-AgOTf in alcohol.[6]

We have been investigating a novel iodination method using iodine-copper(II) acetate.[7] These procedures suffer some deficiencies. The most serious of these is the loss of iodine from the reaction as copper(I) iodide. In a previous paper,[8] we reported a novel α-iodination of



1: $R^1 = R^2 = H$
2: $R^1 = Me, R^2 = H$
3: $R^1 = R^2 = Me$

5,6,7
a: R=Me
b: R=Et
c: R=n-Pr
d: R=i-Pr
e: R=n-Bu
f: $R=CH_2CH_2OH$
g: $R=CH_2CH_2CH_2OH$
h: $R=CH_2(CH_2)_2CH_2OH$

ketones in acetic acid or methanol; and a new alkoxyiodination and nitratoiodination of olefins using iodine-cerium(IV) ammonium nitrate (CAN). Now in this paper, we would like to report that the reaction of α,β-unsaturated cyclohexenones with iodine-CAN in alcohol gave the corresponding alkyl phenyl ethers in good yields. A mixture of 2-cyclohexen-1-one (1)(490 mg), iodine (648 mg), CAN (1.398 g), and 1-propanol (20 ml) was stirred under refluxing for 8 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed

Table 1. Reaction of 2-Cyclohexen-1-one Derivatives with Iodine-Cerium(IV) Ammonium Nitrate in Alcohol or Diol/Acetonitrile[a)] under Refluxing

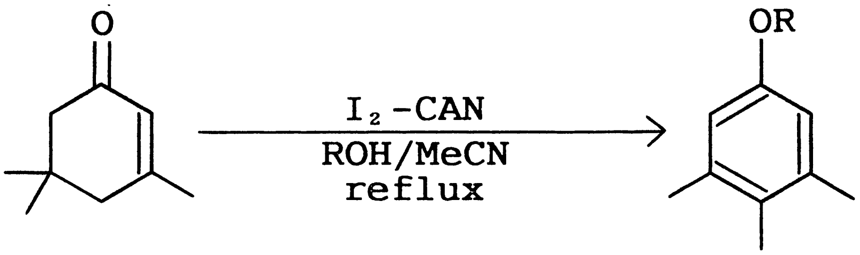
Run	Substrate	Alcohol[b)]	Time/h	Product	Yield/%[c)]
1	1	MeOH	7	5a	43[d)]
2	1	EtOH	7	5b	60[d)]
3	1	*n*-PrOH	8	5c	81
4	1	*i*-PrOH	10	5d	73
5	1	*n*-BuOH	10	5e	82
6	1	EG	10	5f	70
7	1	1,3-PD	10	5g	78
8	1	1,4-BD	10	5h	70
9	2	MeOH	7	6a	55[d)]
10	2	EtOH	7	6b	65[d)]
11	2	*n*-PrOH	7	6c	95
12	2	*i*-PrOH	10	6d	71
13	2	*n*-BuOH	10	6e	74
14	2	EG	10	6f	84
15	2	1,3-PD	10	6g	86
16	2	1,4-BD	10	6h	80
17	3	MeOH	7	7a	54[d)]
18	3	EtOH	7	7b	77[d)]
19	3	*n*-PrOH	10	7c	79
20	3	*i*-PrOH	10	7d	58
21	3	*n*-BuOH	10	7e	70
22	3	EG	10	7f	78
23	3	1,3-PD	10	7g	91
24	3	1,4-BD	10	7h	78

a)Substrate (5.10 mmol), I_2 (2.55 mmol), CAN (2.55 mmol), and Alcohol (20 ml); or Diol (0.153 mol) and Acetonitrile (20 ml). b)PD:Propanediol. BD: Butanediol. c)Isolated yield. d)Yields were determined by GLC.

with water, dried, and concentrated. The resulting oil was chromatographed on silica gel. Elution with hexane gave propoxybenzene (5c) as oil, bp 79 °C /15 mmHg (lit,[9] bp 94 °C /25 mmHg). These results are summarized in Table 1.

As can be seen in the Table 1, the present aromatization appears more efficient than the method described heretofore and the reaction provides a new simple method for the preparation of phenoxy alkanol derivatives.

In the case of isophorone (4), it was found that the oxidative rearrangement with 1,2-migration of the C_5-methyl group occurs. Therefore, this reaction provides a new simple method for the preparation of 5-alkoxy-1,2,3-trimethylbenzene derivatives. The results are summarized in Table 2.



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8a:R=Me
8b:R=Et
8c:R=n-Pr
8d:R=i-Pr
8e:R=n-Bu
8f:R=CH_2CH_2OH
8g:R=$CH_2CH_2CH_2OH$
8h:R=$CH_2(CH_2)_2CH_2OH$

Table 2. Reaction of Isophorone (4) with Iodine-Cerium(IV) Ammonium Nitrate in Alcohol or Diol/Acetonitrile[a] under Refluxing

Run	Alcohol[b]	Time/h	Product	Yield/%[c]
1	MeOH	8.5	8a	82
2	EtOH	22	8b	89
3	*n*-PrOH	25	8c	66
4	*i*-PrOH	20	8d	45
5	*n*-BuOH	18	8e	90
6	EG	10	8f	85
7	1,3-PD	10	8g	80
8	1,4-BD	10	8h	86

a)Substrate (5.10 mmol), I_2 (2.55 mmol), CAN (2.55 mmol), and Alcohol (20 ml); or Diol (0.153 mol) and Acetonitrile (20 ml). b)EG:Ethylene glycol. PD:Propanediol. BD:Butanediol. c)Isolated yield.

Moreover, in order to clarify the effects of other cerium salts, the reaction with cerium(IV) ammonium sulfate dihydrate (CAS), cerium(IV) sulfate tetrahydrate (CS), or cerium(III) ammonium nitrate tetrahydrate [(CAN(III)] was carried out in a similar manner to the procedure mentioned above, and the results are presented in Table 3.

From these results, it was found that the observed reactivity order for these various cerium salts [CAN(IV) 〉 CS〉 CAN(III)〉 CAS] indicates.

Table 3. Reaction of 2-Cyclohexen-1-one (1) with Iodine-Cerium Salt in 1-Butanol[a)]

Run	Cerium salt	Isolated yield/%
1	CAN	82
2	CAS	51
3	CS	69
4	CAN(III)	56

a)A mixture of 2-cyclohexen-1-one (1, 5.10 mmol), iodine (2.55 mmol), cerium salt (2.55 mmol), and 1-butanol (20 ml) was stirred under reflux for 10 h affording butyl phenyl ether (5e).

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