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AIR OXIDATION OF REISSERT COMPOUNDS

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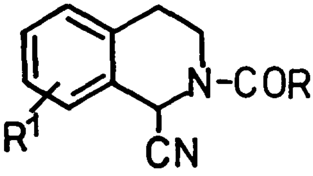
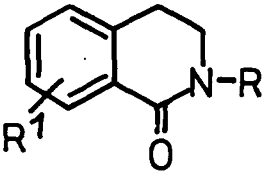
In the course of our investigations on dihydroisoquinoline Reissert compounds /1/[1,2] we noticed that in various reactions significant amounts of side products of dihydroisocarbostiril structure /2/ are formed.


1

a, $R=C_6H_5$, $R^1=H$
b, $R=OC_2H_5$, $R^1=H$
c, $R=C_6H_5$, $R^1=6,7-OCH_2O-$
d, $R=OC_2H_5$, $R^1=6,7-OCH_2O-$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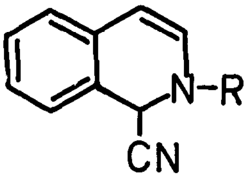
a, $R=R^1=H$
b, $R=H$, $R^1=6,7-OCH_2O-$
c, $R=COC_6H_5$, $R^1=6,7-OCH_2O-$
d, $R=CH_3$, $R^1=6,7-OCH_2O-$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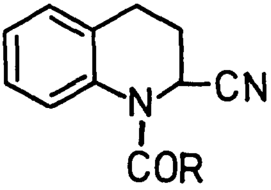
a, $R=COC_6H_5$
b, $R=COOC_2H_5$
c, $R=SO_2C_6H_5$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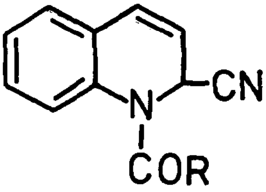
a, $R=C_6H_5$
b, $R=OC_2H_5$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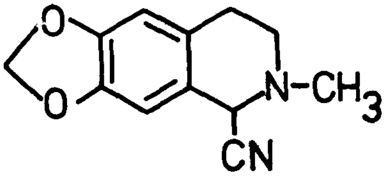
a, $R=C_6H_5$
b, $R=OC_2H_5$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At first, we considered the formation of the carbonyl derivatives /2/ as resulting from an internal red-ox process /preceded substitution of CN by OH/ rather than from autoxidation. Further investigations revealed, however, that the by-products were found only in experiments carried out in the presence of air but not under an atmosphere of argon. We also established that compounds /2/ appeared in reactions in which Reissert anions were generated, i.e., under conditions in which strong bases, for example sodium hydride or concentrated aqueous sodium hydroxide, were present in the reaction medium.

As far as we know, no accounts of reactions of Reissert compounds with oxygen /from air and other oxidizing agents/ have been reported, although base catalysed autoxidations of carbanions are well known[3].

In this paper we wish to present our results of air oxidation of various Reissert compounds and their analogs /1-6/ carried out in a catalytic two-phase system[4] in which concentrated aqueous sodium hydroxide in the presence of triethylbenzylammonium chloride /TEBA/ was used for the generation of carbanions. We studied Reissert compounds belonging not only to the dihydro series /1,4,6/ but also to the normal one /3,5/. Analogs possessing different N-substituents, such as N-ethoxycarbonyl, N-phenylsulfonyl and N-methyl in addition to the benzoyl derivatives, were investigated.

In a standard procedure, air was bubbled into a well stirred two-phase system consisting of the Reissert derivative /1mmol/ in benzene /12ml/, 50% aqueous sodium hydroxide /2ml/ and TEBA /30mg/. After 5 hours /or 1,5 hour in the case of compounds 3/ the organic phase was separated and washed with water, then with dilute hydrochloric acid, again with water and dried. The solvent was evaporated and the residue was crystallized from a suitable solvent. Products were identified by their melting points, IR and mass spectra as well as by thin layer chromatography.

The results of oxidation experiments are summarized in Table 1.

Dihydroisoquinoline derivatives /1,6/ were easily oxidized in good yields to the corresponding oxo compounds 2. On the other hand, dihydroquinoline Reissert analogs /4/ remained unchanged under the reaction conditions described above. This parallels our earlier observation[5], namely, that dihydroquinoline derivatives do not form anions in the two-phase catalytic system. It also suggests that the autoxidation involves the formation of anions in its initial step.

The action of oxygen on normal Reissert compounds /3 and 5/ resulted in isoquinaldonitrile and quinaldonitrile, respectively; the latter being accompanied by large amounts of polymeric material. The formation of isoquinaldonitrile from various modified isoquinoline Reissert derivatives /e.g. N-alkoxycarbonyl, N-alkylsulfonyl or N-arylsulfonyl/, under the action of bases /e.g. sodium hydride, phenyllithium or 5% aqueous sodium hydroxide/ have been reported earlier[6,7], but not in terms of an oxidation process.

It was of interest to find whether the oxygen is needed for this transformation. Therefore two Reissert compounds 3b and 3c were treated with bases /sodium hydride in dimethylformamide or 50% aqueous sodium hydroxide in the two-phase catalytic system/ under an argon atmosphere. In the case of 2-ethoxycarbonyl-1,2-dihydroisoquinaldonitrile /3b/ under both reaction conditions, starting material was recovered unchanged /ca. 85%/. This demonstrates that the formation of isoquinaldonitrile as well as quinaldonitrile from N-acyl Reissert compounds is an oxidation process. Additional support for this state-

Table 1

Reissert compounds and their oxidation products

Reissert compound	Oxidation product	Yield %
Dihydro-Reissert compounds[a]		
2-Benzoyl-1,2,3,4-tetrahydroisoquinaldonitrile /1a/	Dihydroisocarbostyril /2a/	75
2-Ethoxycarbonyl-1,2,3,4-tetrahydroisoquinaldonitrile /1b/	Dihydroisocarbostyril /2a/	68
2-Benzoyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinaldonitrile /1c/	6,7-Methylenedioxydihydroisocarbostyril /2b/	80
	2-Benzoyl-6,7-methylenedioxydihydroisocarbostyril /2c/[b]	64
2-Ethoxycarbonyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinaldonitrile /1d/	6,7-Methylenedioxydihydroisocarbostyril /2b/[c]	37
1-Benzoyl-1,2,3,4-tetrahydroquinaldonitrile /4a/	Starting material	76
1-Ethoxycarbonyl-1,2,3,4-tetrahydroquinaldonitrile /4b/	Starting material	87
2-Methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinaldonitrile /6/	2-Methyl-6,7-methylenedioxydihydroisocarbostyril /2d/	92
Reissert compounds[a]		
2-Benzoyl-1,2-dihydroisoquinaldonitrile /3a/	Isoquinaldonitrile	90
2-Ethoxycarbonyl-1,2-dihydroisoquinaldonitrile /3b/	Isoquinaldonitrile	90
2-Benzenesulfonyl-1,2-dihydroisoquinaldonitrile /3c/	Isoquinaldonitrile	83
1-Benzoyl-1,2-dihydroquinaldonitrile /5a/	Quinaldonitrile[d]	45
1-Ethoxycarbonyl-1,2-dihydroquinaldonitrile /5b/	Quinaldonitrile[d]	45

[a] Prepared from appropriate isoquinoline or quinoline derivatives according to the known procedure[12,13]. [b] Reaction carried out for 30 min. [c] Obtained as a side product in reaction of 1d with benzaldehyde, conducted in the air[1]. [d] Large amounts of unsoluble polymers were precipitated.

ment was gained from the fact that benzoic acid /in ca. 90% and 65% of yield, respectively/ was isolated in addition to the nitrile in reaction of compounds 3a and 5a with air oxygen in the two-phase catalytic method. On the other hand, 2-benzenesulfonyl-1,2-dihydroisoquinaldonitrile /3c/ was always converted into isoquinaldonitrile and sodium benzenesulfinate in high yields, irrespective of the type of base and atmosphere /air or argon/ used in the reaction. This is consistent with an earlier assumption[7] of an internal red-ox process.

It is evident from the results presented in this paper, that Reissert compounds /with the exception of dihydroquinoline derivatives/ tend to undergo autoxidation in basic solutions in the presence of air.

Dihydroisoquinoline Reissert derivatives /1,6/, independently of the nature of the N-substituent, undergo oxidative decyanation resulting in derivatives of dihydroisocarbostyril /2/. At this point they resemble secondary arylacetonitriles, which give ketones when exposed to oxygen in basic solutions[8–11]. A peroxidic intermediate arising from the interaction of the base-induced carbanion with molecular oxygen, is postulated in this process. Recently, α-cyanohydroperoxides and their acyl derivatives were isolated and characterized, when the reaction of secondary acetonitriles with oxygen was quenched with hydrochloric acid or acyl halide, respectively[10]. In the course of further reaction these unstable peroxy intermediates decompose to carbonyl derivatives and cyanate[9] or isocyanate[11] ions.

We were able to isolate 2-benzoyl-6,7-methylenedioxy-3,4-dihydroisocarbostiril /2c/ when the oxidation of 2-benzoyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinaldonitrile /1c/ was stopped after 30 mins. This indicates that in the case of dihydro-Reissert compounds the oxidation step is followed by hydrolysis of the acyl group.

The autoxidation of normal Reissert compounds is also likely to proceed via peroxy intermediates.

No attempts have been made to isolate the peroxy intermediate in the case of Reissert derivatives as yet, but further investigations are in progress.

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