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# PYRIDINE ASSISTED OXIDATIONS OF ALCOHOLS TO CARBONYL COMPOUNDS BY MEANS OF 3-CARBOXYPYRIDINIUM DICHROMATE (NDC) REAGENT[1].

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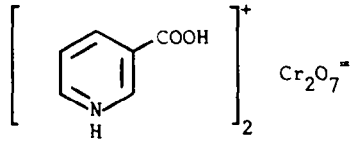
**Abstract** - 3-Carboxypyridinium dichromate (NDC), readly prepared from nicotinic acid and chromium trioxide, is an efficient reagent for the oxidation of alcohols into carbonyl compounds in the presence of pyridine. The optimum molar ratio substrate:reagent:pyridine to ensure complete oxidation of starting material in a short reaction time was found 1:2.5:20 respectively. A brief comparison between this reagent and pyridinium dichromate (PDC) is made. In contrast to the PDC reagent, NDC allows selective oxidation between benzylic alcohols and aliphatic alcohols. The NDC-pyridine system has been successfully extended to the oxidation of N-(2-hidroxy-2-phenyl or 2-methylethyl)-ß-lactams into their corresponding carbonyl compounds as N-H azetidin-2-one precursors. In contrast, primary N-(2-hydroxyethyl)-ß-lactams upon treatment with this reagent system afforded N-formylazetidin-2-ones. The influence of pyridine in oxidations by means of NDC is further shown in the conversion of hydroquinones into quinones. Another interesting feature associated with the use of this reagent is the ease of purification of the final products.

Oxidation is an esential operation in organic synthesis and several reagents have been developed for a wide variety of transformations[2]. Among the reagents available for the oxidation of organic compounds, the chromium (VI) derivatives have received great attention in the past years[3]. After having developed methods for oxidation reactions with trimethylsilyl chlorochromate[4], chromium trioxide-crown ether[5], and pyridinium dichromate-chlorotrimethylsilane[6], we turned our attention to onium-Cr(VI) reagents.

Recently we have preliminary reported[7a] a new chromium(VI) reagent, 3-carboxypyridinium dichromate 1 (NDC)† for oxidation of a wide variety of organic substrates, including hydroxy sugars[7b]. In this paper we report the detailed accounts on the oxidation of alcohols to carbonyl compounds by means of this cheap reagent.

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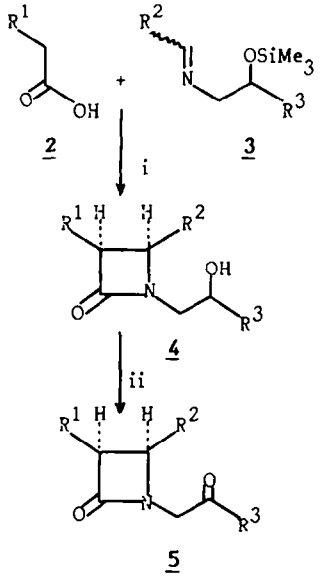
†According IUPAC nomenclature the correct name of this reagent is 3-carboxypyridinium dichromate instead of nicotinium dichromate named in our previous works. In this paper we maintain the abreviature NDC to indicate that the reagent proceeds from nicotinic acid.

## RESULTS AND DISCUSSION

Although many useful procedures for the oxidation of alcohols to the corresponding carbonyl compounds have been reported[2,3], the general problem cannot be considered definitely settled. The chief drawbacks of the procedures involving Cr (VI) reagents were the long reaction times, the relative difficulty in the preparation of reagents, variable or poor selectivity and the working-up of the reaction mixture. In the course of a variety of projects being carried out in our laboratory, and in connection with several projected problems, we needed an efficient mild method for the oxidation of a variety of alcohols into carbonyl compounds, which would permit the preparation of N-benzoylmethyl-ß-lactams as N-H azetidin-2-one precursors[6] (Scheme 1). It is well known that pyridinium dichromate[8] (PDC) and pyridinium chlorochromate[9] (PCC) allow mild and large scale oxidation of a wide range of alcohols to carbonyl compounds in methylene chloride at room temperature. Unfortunately, in the case of N-(2-hydroxyethyl)-ß-lactams these conditions lead to a very long and incomplete reaction and in some cases undesired products were obtained[7]. Examining the synthetic utility of NDC reagent, we have found that the addition of pyridine in the reaction media is exceeding effective in the conversion of alcohols into the corresponding carbonyl compounds.




a: $R^1$= $C_6H_5O$; $R^2$= $C_6H_5$; $R^3$= $C_6H_5$
b: $R^1$= $C_6H_5O$; $R^2$= $C_6H_5$; $R^3$= $CH_3$
c: $R^1$= $C_6H_5O$; $R^2$= 4-$CH_3OC_6H_4$; $R^3$= $C_6H_5$
d: $R^1$= $C_6H_5O$; $R^2$= 4-$CH_3OC_6H_4$; $R^3$= $CH_3$
e: $R^1$= $C_6H_5O$; $R^2$= 4-$NO_2C_6H_4$; $R^3$= $C_6H_5$
f: $R^1$= Pht ; $R^2$= $C_6H_5$; $R^3$= $C_6H_5$
g: $R^1$= Pht ; $R^2$= 2-furyl ; $R^3$= $C_6H_5$
h: $R^1$= Pht ; $R^2$= 4-$CH_3OC_6H_4$; $R^3$= $C_6H_5$
i: $R^1$= $C_6H_5OCH_2CONH$; $R^2$= $C_6H_5$; $R^3$= $C_6H_5$
j: $R^1$= $C_6H_5OCH_2CONH$; $R^2$=4-$CH_3OC_6H_4$; $R^3$= $C_6H_5$

**Scheme 1.** Reagents and Conditions : i , $PhO(PO)Cl_2$,$NEt_3$, $Cl_2CH_2$, r.t.,ref.10; ii , NDC(2.5 equiv.), pyridine (20 equiv.), $Cl_2CH_2$, r.t.

First, the oxidation reaction was examined between some benzylic alcohols and NDC alone in a molar ratio 1:2.5 respectively using methylene chloride as solvent, and the results are represented in Figure 1. The progress of NDC oxidation of these alcohols was monitored taking samples periodically and analyzing them inmediately by NMR (integrating the aldehydic proton and the methylene group in the remaining benzyl alcohol). As revealed in Figure 1, the oxidation is dependent of the substituent attached in the aromatic ring. Thus, while oxidation of 4-methoxybenzyl alcohol gives anisaldehyde in 90% of conversion after 8 h at room temperature, oxidation of 4-nitrobenzyl alcohol requires 32 h to achieve the same conversion. Under these conditions 3-phenylpropanol upon treatment with NDC yielded the corresponding aldehyde in 50% at most and the oxidation was extremely slow. In contrast, as shown in Table 1, when the oxidation of these alcohols was carried out in the presence of pyridine (molar ratio substrate:reagent:pyridine, 1:2:4 respectively) the

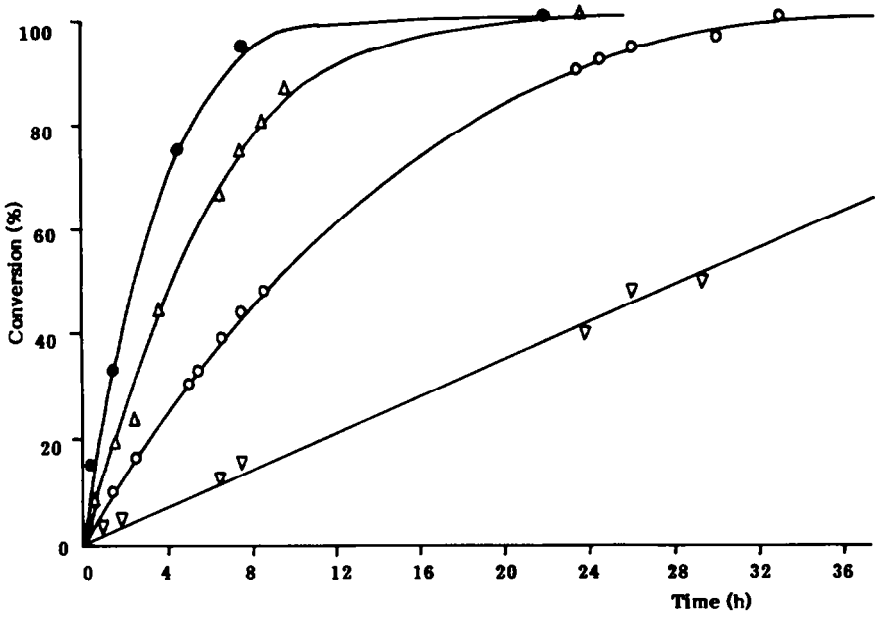



**Figure 1. Oxidation of 4-methoxybenzyl alcohol (●),benzyl alcohol (Δ), 4-nitrobenzyl alcohol (○) and 3-phenylpropanol (▽) by means of nicotinium dichromate in methylene chloride at room temperature.**

reaction proceeded rapidly and smoothly in methylene chloride at room temperature. Since in the absence of pyridine oxidation of 3-phenylpropanol proved to be remarkably slow, we examined the utility of NDC in selective oxidation of alcohols. Thus, when an equimolar mixture of p-nitrobenzyl alcohol and 3-phenylpropanol was subjected to oxidation by means of fourfold excess of NDC in methylene chloride for 30 h at room temperature, selectively afforded p-nitrobenzaldehyde in 80% isolated yield. Less than 40% of the corresponding 3-phenylpropanal was formed under these conditions. In contrast, under normal reaction conditions pyridinium dichromate (4 equiv,24 h) afforded the corresponding aldehydes without

Table 1. Oxidation of alcohols by NDC[a]

| Alcohol | cosolvent | time | Yield%[c,d] |
|---|---|---|---|
| $C_6H_5CH_2OH$ | none | 24h | 80 |
| | pyridine[b] | 25m | 85 |
| $4\text{-}CH_3OC_6H_4CH_2OH$ | none | 8h | 90 |
| | pyridine[b] | 25m | 85 |
| $4\text{-}NO_2C_6H_4CH_2OH$ | none | 30h | 82 |
| | pyridine | 30m | 80 |
| $Ph_2CHOH$ | pyridine | 30m | 90 |
| $C_6H_5CH_2CH_2CH_2OH$ | none | 30h | 45 |
| | pyridine | 2h | 70 |

[a]All reactions were carried out at room temperature with the respective alcohol,NDC and pyridine in methylene chloride, in a molar ratio 1:2:4 respectively. [b]Oxidation was carried out at 0°C. [c]Yield of pure isolated product,the purity of the liquid products was found to be ≥98% by GLC analysis. [d]Melting points and boiling points were in agreement with the literature values, Rappoport,ZVI.Handbook of Tables for Organic Compounds Identification,3rd ed.,CRC Press,Cleveland (1977).

any noticeable amount of the respective starting alcohols as determined by NMR and TLC analysis of the crude mixture. In a similar manner, when the oxidation of an equimolar mixture of 4-methoxybenzyl alcohol and 3-phenylpropanol was treated with 2.5 fold excess of NDC at room temperature for 4 h, anisaldehyde was formed in 85% isolated yield (100% of conversion) and less than 20% of 3-phenylpropanal was detected by GLC analysis as was expected by the results in Figure 1. When this selective oxidation was tested in benzene in place of methylene chloride as solvent the selectivity was notably enhanced. Thus, treatment of this equimolar mixture of alcohols for 2.5 h at room temperature, anisaldehyde was quantitatively formed and less than 5% of 3-phenylpropanal was formed under these conditions. When NDC in combination with pyridine was tested for these oxidations a poor degree of selectivity was obtained.

Table 2. Oxidation of alcohols by NDC and PDC under different concentrations of pyridine[a]

| Substrate | Pyridine[b] | oxidations from NDC | | oxidations from PDC | |
|---|---|---|---|---|---|
| | | time | conversion,%[d] | time | conversion,%[c] |
| cyclohexanol | none | 7 h | 44 | 4 h | 72 |
| | none | 20 h | 100 | 20 h | 100 |
| | 5 | 60 min | 100(80) | 4.5h | 76 |
| | 7.5 | 30 min | 100(80) | | |
| | 10 | 15 min | 99 | | |
| | 20 | 15 min | 100(85) | 4 h | 81 |
| menthol | none | 10 h | 100 | | |
| | 5 | 2 h | 100(85) | | |
| | 10 | 15 min | 86 | | |
| | 20 | 15 min | 100(91) | | |
| benzoin | 5 | 5 h | 100(72) | | |
| | 20 | 35 min | 100(70) | 35min | 20 |

[a]All reactions were carried out at room temperature in methylene chloride with the respective alcohol and NDC or PDC in a molar ratio 1:2.5 respectively. [b]Molar ratio with respect to the substrate. [c]Conversion determined by GLC. [d]The number in parentheses indicate isolated yields of the respective carbonyl compound by kugelrhör distillation.

To observe the influence of pyridine, the oxidation of some structurally different hydroxyl compounds was examined under various pyridine molar ratios. The results are gathered in Table 2. For example, under similar conditions to those used in the oxidation of benzylic alcohols, secondary aliphatic alcohols such as cyclohexanol and menthol afforded good yields of the expected carbonyl compounds in relatively short reaction times. Under these conditions oxidation of benzoin was found more slow and the best results for the oxidation of these hydroxyl compounds were obtained by using 20-fold excess of pyridine. It is worthy of note that under these conditions PDC reagent was found less efficient than NDC reagent for carry out these oxidations. For example, when both cyclohexanol and benzoin were treated with PDC reagent in the absence of pyridine or using pyridine as cosolvent, the respective reaction times were similar. Also, it should be noted that,whereas NDC alone shows a similar behaviour than PDC in these oxidations, the use of pyridine as cosolvent remarkably increased the oxidation rate of these alcohols by means of NDC. Of the solvents examined as substitutes of methylene chloride, benzene remains the best, acetone, acetonitrile, N,N-dimethylformamide, and pyridine alone proved unsuitable substitutes. Although color changes were observed, low yields of the cyclohexanone and

4-nitrobenzaldehyde were obtained and the work-up was complicated in each case.

In order to stablish the optimum molar ratio of substrate:reagent:pyridine in the oxidation of alcohols to carbonyl compounds, we have tested the method with four representative aliphatic alcohols such as cyclohexanol, 3-phenylpropanol, phenethyl alcohol and geraniol. The results are listed in Table 3. As expected, the reaction rate increased when the molar ratio of Cr(VI) to alcohol was increased, and very fast reactions could be obtained by using a molar ratio of alcohol:NDC:pyridine 1:2.5:20 respectively. Under these conditions oxidation of geraniol afforded geranial in 97% conversion with no more than 3% of neral. It should be noted that the oxidation of phenethyl alcohol yielded phenylacetaldehyde together with products of over oxidation, such as benzaldehyde. In fact, when pure phenylacetaldehyde was subjected to treatment with NDC under the same conditions to those used in the oxidation of phenethyl alcohol, benzaldehyde was slowly formed. In the absence of pyridine the starting phenylacetaldehyde was recorvered unchanged.

Table 3. Oxidation of alcohols by NDC-pyridine system under different molar ratios[a]

| Substrate | molar ratio NDC:Pyridine | time,min | conversion,%[b,c] |
|---|---|---|---|
| cyclohexanol | 1.5:20 | 15 | 75 |
| | 1.5:20 | 30 | 85 |
| | 2.0:20 | 30 | 87 |
| | 2.0:20 | 60 | 100(80) |
| | 2.0:30 | 15 | 88 |
| | 2.0:30 | 30 | 90 |
| | 2.0:30 | 60 | 100(85) |
| | 2.5:20 | 15 | 94 |
| | 2.5:30 | 15 | 93 |
| | 2.5:40 | 15 | 94 |
| 3-phenylpropanol | 2.0:20 | 15 | 86 |
| | 2.0:20 | 45 | 94 |
| | 2.5:20 | 15 | 100(80) |
| phenethyl alcohol | 2.5:20 | 15 | 100[d] |
| geraniol | 2.5:20 | 15 | 97(70) |

[a]Reaction with 5 mmol of alcohol in 20 ml of benzene at room temperature. [b]Ratio determined by GLC. [c]The number in parentheses indicate isolated yields. [d]45% of PhCHO, 31% of $PhCH_2CHO$ and 24% of other products.

The study of the reactivity of our reagent system led us to three interesting observations. First, while pyridine assisted oxidations of alcohols by means of NDC reagent in methylene chloride or benzene, the addition of pyridine in the reaction media when PDC was the reagent of choice did not alter the oxidation rate; second, the use of NDC without pyridine could permit selective oxidations between benzylic alcohols and aliphatic alcohols and finally, in these oxidations by means of NDC or PDC-pyridine system the work-up was more clean than by using PDC, thus filtration of chromium ions through a pad of silica gel and extensive washing of the mixture with water, followed by 6N HCl

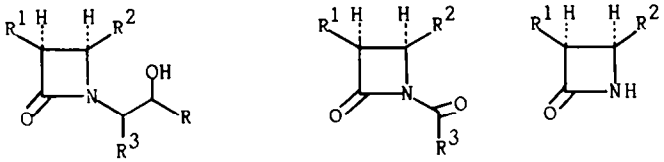
aq. and $NaHCO_3$ aq., resulted in the complete removal of chromium by products and fairly pure products were obtained. These findings led us to explore the scope and limitations of NDC reagent together with pyridine in the oxidation of the N-(2-hydroxyethyl) ß-lactams depicted in Scheme 1.

The reaction was generally performed by addition of the corresponding alcohols to the suspension of NDC reagent and pyridine (molar ratio 1:2.5:20 respectively) in methylene chloride at room temperature. The results are summarized in Table 4 and illustrate the efficiency, the applicability and the scope of the present method. Conversion of secondary hydroxyl compounds into ketones, usually proceeds completely at room temperature within 15–30 min. When the molar ratio of reagent:pyridine was decreased from 2.5:20 to 2.5:5 the oxidation rate decreased notably as was expected by the above observations. The use of pyridinium dichromate (PDC) instead of our reagent system, caused oxidation of these N-(2'-hydroxyethyl) ß-lactams, but, however the reactions times are quite long and products of over oxidation were detected and characterized by TLC and NMR analysis of the crude products.

Table 4. Oxidation of N-(2 -hydroxyethyl-2 -phenyl or methyl) ß-lactams 4[a,b]

| | Product 5 | | | Pyr[c] | time | Yield,% | mp,°C |
|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | | | | |
| a | PhO | Ph | Ph | 20 | 30min | 90 | 165-167 |
| | | | | 5 | 3h | 88 | |
| | | | | - | 24h | 60[d] | |
| b | PhO | Ph | $CH_3$ | 20 | 30min | 85 | 129-130 |
| | | | | 5 | 5h | 88 | |
| c | PhO | 4-$CH_3OC_6H_4$ | Ph | 20 | 30min | 96 | 97-99 |
| | | | | 5 | 3h | 95 | |
| | | | | - | 30h | 60[d] | |
| d | PhO | 4-$CH_3OC_6H_4$ | $CH_3$ | 20 | 30min | 80 | syrup |
| | | | | 5 | 7h | 83 | |
| e | PhO | 4-$NO_2C_6H_4$ | Ph | 5 | 3h | 80 | 169-170 |
| | | | | - | 24h | 66[d] | |
| f | Pht | Ph | Ph | 20 | 30min | 95 | 230-231 |
| g | Pht |  | Ph | 20 | 30min | 85 | 215-217 |
| h | Pht | 4-$CH_3OC_6H_4$ | Ph | 20 | 30min | 91 | 156-158 |
| | | | | 5 | 5h | 70 | |
| i | $PhOCH_2CONH$ | Ph | Ph | 5 | 3h | 75 | 178-180 |
| j | $PhOCH_2CONH$ | 4-$CH_3OC_6H_4$ | Ph | 20 | 30min | 85 | |

[a]These ß-lactams were prepared by the method reported in ref.10. Pht: Phthalimido group. [b]All reactions were carried out at room temperature with the respective N-(2-hydroxyethyl)-ß-lactam and NDC in a molar ratio 1:2.5 respectively. [c]Molar ratio of pyridine with respect to the substrate. [d]From PDC reagent without pyridine.



6 R = H ; $R^3$ = H 9 $R^3$ = H 11

7 R = H ; $R^3$ = $COOCH_3$ 10 $R^3$ = $COOCH_3$

8 R= $CH_3$; $R^3$ = $COOCH_3$

a $R^1$ = Pht ; $R^2$ = Ph

b $R^1$ = $C_6H_5O$ ; $R^2$ = 4-$CH_3OC_6H_4$

c $R^1$ = Pht ; $R^2$ = CH=CHPh

d $R^1$ = $CH_3O$ ; $R^2$ = 4-$CH_3OC_6H_4$

-Figure 2-

Furthermore, we have found that, under similar conditions to those used for NDC oxidation of the secondary hydroxyl group in ß-lactams, the reaction between NDC--pyridine system and primary N-(2 -hydroxyethyl) ß-lactams 4 can take a different course to produce N-formyl compounds 9 (Figure 2). Manhas and coworkers[11] have reported that oxidation of ß-lactams 7 and 8 by Jones' reagent afforded N-unsubstituted ß-lactams 11. Now, we have found that this degradative oxidation process can be controlled by the use of NDC reagent in combination with pyridine. First, the reaction was carried out in methylene chloride at room temperature. When N-(2 -hydroxyethyl)-4-phenyl-3-phthalimidoyl-azetidin-2-one 6a was treated with 3.0 equiv of NDC and 6.0 equiv of pyridine in methylene chloride at room temperature for 7 h, 1-formyl-4-phenyl-3-phthalimidoylazetidin-2--one 9a was obtained in 5% yield after purification by column chromatography on silica gel (eluent AcOEt/hexane). The starting hydroxy ß-lactam 6a also was recovered along with other products which were not investigated. However, the yield of the isolated product 9a was increased when benzene was the solvent of choice and the reaction was performed under reflux conditions. Thus the ß-lactams 6 and 7 upon treatment with NDC--pyridine in refluxing benzene for 30 min yielded the corresponding ß-lactams 9 and 10 in yields between in the range 30-55%. Some experimental results are reported in Table 5 and illustrate the applicability and the scope of the present method. Although, PDC and PCC reagents together with pyridine were in fact satisfactory for carry out this new oxidative carbon-carbon bond cleavage, NDC reagent alloved more easy work-up. It is worthy of note that these N-formyl azetidin-2-ones 9 and specially the N-oxalamido derivative 10 can be regarded as model compounds for a potential synthesis of penems[12] and for the preparation of N-unsubstituted azetidin-2-ones[13]. The results obtained indicate that compounds involving electron with-drawing groups at the ß-position respect to the hydroxyl group are capable to undergo an over oxidation process similarly to the C-C bond fragmentation of phenethyl alcohol.

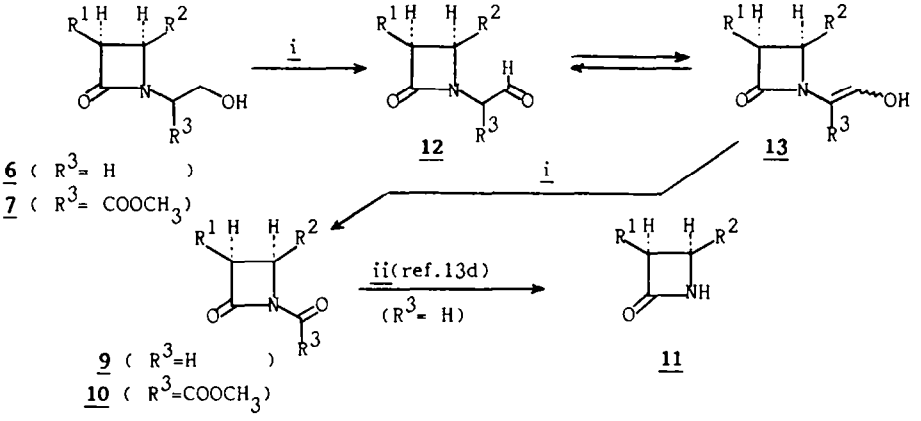
In order to explain this novel transformation, a possible reaction pathway, scheme 2, could involve initial oxidation of the primary hydroxyl group in 6 and 7 to give the aldehyde 12 followed by oxidative cleavage of the C-C double bond in 13. From this assumption it seems to be clear that the presence of a tertiary organic base such as

Table 5. Oxidation of N-(2 -hydroxyethyl) ß-lactams 6 and 7

| Product[a] | $R^1$ | $R^2$ | Reagent[c] | time(min) | Yield,%[e] | mp,°C |
|---|---|---|---|---|---|---|
| **9a** | Pht[b] | $C_6H_5$ | PDC | 40 | 30 | 190-192 |
| | | | PCC | 30 | 35 | |
| | | | NDC | 30 | 45 | |
| **9b** | PhO | 4-$CH_3OC_6H_4$ | PDC | 60 | 30 | 134-135 |
| | | | NDC[d] | 70 | 55 | |
| **9c** | Pht | CH=CHPh | PDC | 60 | 40 | 108-110 |
| | | | NDC[d] | 70 | 40 | |
| **9d** | $CH_3O$ | 4-$CH_3OC_6H_4$ | PDC | 70 | 30 | 109-110 |
| | | | NDC | 20 | 30 | |
| **10a** | Pht | $C_6H_5$ | NDC[d] | 90 | 35 | 205-206 |

[a] All compounds present cis-configuration at $C_3$-$C_4$, determined by nmr spectroscopy; [b] Pht: Phthalimido group; [c] molar ratio substrate:reagent:pyridine 1:5:10; [d] molar ratio ,1:3:6; [e] isolated yields after recrystallization from hexane/methylene chloride, yields not optimized.

pyridine should favour the formation of the enol 13. Indeed, as the results in Table 5 confirm, the choice of pyridine as cosolvent remarkably increased the yields of oxidized products. The use of triethylamine in place of pyridine did not lead to the expected formyl compounds and side reactions predominated.




**Scheme 2.** Reagents and conditions : i, PDC,NDC or PCC (3.0-5.0 equiv.),pyridine (6.0-10.0 equiv.),80°C; ii, MeOH,$NEt_3$(cat.)

The influence of pyridine in oxidation reactions by means of NDC is further shown in the conversion of hydroquinones into quinones. Thus, we have found that hydroquinones upon treatment with NDC and pyridine, in 1:3:6 molar ratio respectively, afforded the corresponding quinones in excellent yields. The progress of the reaction can be followed by TLC analysis and the reaction was found to be complete in 15-30 min in all the cases tested. After work-up, the isolated crude products are almost pure as judged by their physical properties. As can be seen from the results listed in Table 6, oxidation

of hydroquinones by means of NDC reagent together with pyridine is more rapid than oxidation by means of PDC reagent. Also, it should be noted that addition of pyridine in the latter case did not alter the oxidation rate. Furthermore, NDC alone was found unsuitable for carrying out this transformation. As shown in the Table the oxidation rate was enhanced when the amount of pyridine was increased. However yields often became poor except for the more substituted hydroquinones. The synthetic utility of this procedure is shown by the conversion of trimethyl-p-hydroquinone to the corresponding p-benzoquinone, which is a key intermediate in the synthesis of tocopherol[14]. Our procedure would appear to be an attractive alternative to other methods developed for oxidation of hydroquinones into quinones[15].

Table 6. Oxidation of 1,4-hydroquinones by NDC and PDC under different concentrations of pyridine[a].

| Substrate | Pyridine[b] | oxidation from NDC | | oxidation from PDC | |
|---|---|---|---|---|---|
| | | time | Yield,%[c,d] | time | Yield,%[c,d] |
| hydroquinone | none | 48 h | —[b] | 1 h | 80 |
| | 6 | 30 min | 80 | 3 h | 80 |
| | 10 | 5 min | 75 | | |
| methylhydroquinone | none | —— | — | 1.5 h | 87 |
| | 6 | 15 min | 85 | 3 h | 87 |
| | 10 | 5 min | 60 | | |
| | 20 | 5 min | 54 | | |
| 2,5-Di-tert-buthylhydroquinone | 6 | 10 min | 99 | | |
| | 20 | 5 min | 90 | | |
| trimethylhydroquinone | none | —— | — | 1.5 h | 100 |
| | 6 | 20 min | 100 | 1.5 h | 100 |
| | 20 | 5 min | 100 | | |
| chlorohydroquinone | none | —— | — | 2 h | 80 |
| | 2 | 30 min | 75 | | |
| | 6 | 10 min | 42 | | |
| | 10 | 5 min | 10 | | |
| methoxyhydroquinone | none | —— | — | 2 h | 100 |
| | 2 | 4 h | 70 | | |
| | 4 | 2 h | 50 | | |
| | 10 | 10 min | 35 | | |

[a]All reactions were carried out at room temperature in methylene chloride with the respective hydroquinone and NDC or PDC in a molar ratio 1:3 respectively. [b]Not determined the starting product was detected by TLC. [c]Yield of isolated pure quinones. [d]Physical properties were in agreement with those reported for autentic samples (from Aldrich).

Although the causes of differences between NDC reagent and PDC reagent when pyridine was used as cosolvent are not clear at present, their could be atributed to the carboxyl moiety in NDC reagent. Furthermore, the ready and cheap preparation of 3-carboxypyridinium dichromate, its selectivity, the ease of using and the simplicity in working-up, this reagent may prove to be a useful alternative to other reagents in oxidation reactions and may be readly extended to further applications.

## EXPERIMENTAL

Melting points were determined on a Büchi SMP-20 melting point apparatus and are uncorrected. Proton NMR spectra were measured on a Varian EM-360 Espectrometer and are reported in parts per million downfield from internal tetramethylsilane. The couplings (J) are in hertz (Hz). The infrared (IR) spectra were determined on a Shimadzu IR-435 spectrometer and are reported in reciprocal centimeters ($cm^{-1}$). CHN analysis was provided by Organic Chemistry Department of Colegio Universitario de Alava (Spain). All the starting materials used in this work were either commercially available in generally 98% or higher purity and used without further purification or prepared by literature procedures. The N-(2-hydroxyethyl)ß-lactams 4 and 6 were prepared by our procedure[10]. All the synthetic ß-lactams are racemic mixtures.

### 3-Carboxypyridinium dichromate (NDC)[7] 1

Chromium trioxide (48 g, 480 mmol) was disolved in water (48 ml) and then nicotinic acid (29.52 g, 240 mmol) was added at 0-5°C (ice-water bath) with mechanical stirring. After 15 min, acetone (100 ml) was added at 0-5°C to the resulting red-orange suspension and the mixture was stirred at 0-5°C for 15 min. The product was filtered off and washed under stirring with acetone (4 x 200 ml) and then with methylene chloride (100 ml) affording 3-carboxypyridinium dichromate 47 g (85%) as orange-yelow solid m.p. 215-217°C (d); IR (KBr) $cm^{-1}$: 1660, 960, 910, 840, 750, 730.

### General method for the oxidation of alcohols

To a suspension of NDC (2.32 g, 5 mmol) in methylene chloride (15 ml), pyridine (3.2 ml, 40 mmol) and the hydroxyl compound (2.0 mmol) were added and the resulting mixture was stirred at room temperature for a certain time. (The oxidation can be monitored by tlc analysis : Silica gel plates; eluent: AcOEt/hexane 1:1). then the reaction mixture was filtered off through a pad of silica gel 70-230 mesh and washed with water (15 ml), 6N HCl (15 ml) and $NaHCO_3$ sat. (15 ml). The organic layer was separated and dried with sodium sulphate. Evaporation of the solvent gave a fairly pure carbonyl compound which was crystallized or distilled.

**cis-1-Benzoylmethyl-3-phenoxy-4-phenylazetidin-2-one** 5a : IR(nujol), ν $cm^{-1}$: 1760, 1690 (C=O). $^1$H-NMR($CDCl_3$, δ ppm): 8.16-6.81 (m,15H,arom.); 5.72(d,J=5 Hz,1H,CH); 5.36(d,J=5 Hz,1H,CH); 5.3(d,J=-18 Hz,1H,NCHCO); 4.36(d,J=-18 Hz,1H,NCHCO). $C_{23}H_{19}NO_3$ Requires C, 77.28; H, 5.36; N, 3.92. Found C, 77.48; H, 5.16; N, 3.78%.

**cis-1-Acetonyl-3-phenoxy-4-phenylazetidin-2-one** 5b: IR(nujol, ν $cm^{-1}$): 1765, 1718(C=O). $^1$H-NMR($CDCl_3$, δ ppm): 6.69-7.52(m,10H,arom.); 5.50(d,J=5Hz,1H,CH); 5.21(d,J=5Hz,1H,CH); 4.49(d,J=-18Hz,1H,CH); 3.52(d,J=-18Hz,1H,CH); 2.03(s,3H,$CH_3$). $C_{18}H_{17}NO_3$ requires C, 73.19; H, 5.81; N, 4.74. Found C, 73.20; H, 5.81; N, 4.73.

**cis-1-Benzoylmethyl-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one** 5c : IR(nujol,ν $cm^{-1}$) : 1790, 1720(C=O). $^1$H-NMR($CDCl_3$, δ ppm): 7.66-6.50(m,14H,arom.); 5.43(d,J=5Hz,1H,CH); 5.09(d,J=5Hz,1H,CH); 4.92(d,J=-18Hz,1H,NCHCO); 3.96(d,J=-18Hz,1H,NCHCO); 3.58(s,3H,$OCH_3$). $C_{24}H_{21}NO_4$ requires C, 74.39; H, 5.47; N, 3.62. Found C, 74.27; H, 5.69; N, 3.70.

**cis-1-Acetonyl-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one** 5d : $^1$H-NMR($CDCl_3$, δ ppm): 7.28-6.62(m,9H,arom.); 5.50(d,J=5Hz,1H,CH); 5.12(d,J=5Hz,1H,CH); 4.48(d,J=-19Hz,1H,NCHCO); 3.67(s,3H,$OCH_3$); 3.53(d,J=-19Hz,1H,NCHCO); 2.03(s,3H,$CH_3$).

**cis-1-Benzoylmethyl-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one** 5e : IR($CHCl_3$, ν $cm^{-1}$): 1800, 1720(C=O). $^1$H-NMR($CDCl_3$, δ ppm): 8.13-6.48(m,14H,arom.); 5.60(d,J=5Hz,1H,CH); 5.30(d,J=5Hz,1H,CH); 5.09(d,J=-18Hz,1H,NCHCO); 4.12(d,J=-18Hz,1H,NCHCO). $C_{23}H_{18}N_2O_5$ requires C, 68.64; H, 4.52; N, 6.96. Found C, 69.11; H, 4.07; N, 7.30.

**cis-1-Benzoylmethyl-4-phenyl-3-phthalimidoylazetidin-2-one** 5f : IR(KBr,ν $cm^{-1}$): 1782, 1718 (C=O). $^1$H-NMR($CDCl_3$, δ ppm): 8.01-6.95(m,14H,arom.); 5.75(d,J=5Hz,1H,CH); 5.40(d,J=5Hz,1H,CH); 5.35(d,J=-18Hz,1H,NCHCO); 4.40(d,J=-18Hz,1H,NCHCO). $C_{25}H_{18}N_2O_4$ requires C, 73.15; H, 4.43; N, 6.83. Found C, 73.28; H, 4.53; N, 7.07.

**cis-1-Benzoylmethyl-4-(2-furyl)-3-phthalimidoylazetidin-2-one** 5g : IR(KBr, ν $cm^{-1}$): 1762, 1718(C=O). $^1$H-NMR($CDCl_3$, δ ppm): 8.06-7.26(m,9H,arom.); 6.45-6.15(m,3H,furyl); 5.75(d, J=5Hz,1H,CH); 5.45(d,J=5Hz,1H,CH); 5.25(d,J=-18Hz,1H,NCHCO); 4.40(d,J=-18Hz,1H,NCHCO). $C_{23}H_{16}N_2O_5$ requires C,68.99; H, 4.03; N, 6.99. Found C, 68.88; H, 4.12; N, 7.13.

**cis-1-Benzoylmethyl-4-(4-methoxyphenyl)-3-phthalimidoylazetidin-2-one 5h:** IR(nujol, $\nu$ $cm^{-1}$): 1760, 1700(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 8.03-6.67(m,13H,arom.); 5.74(d,J=5Hz,1H,CH); 5.36(d,J=-18Hz,1H,NCHCO); 5.33(d,J=5Hz,1H,CH); 4.36(d,J=-18Hz,1H,NCHCO); 3.85(s,3H,$OCH_3$). $C_{26}H_{20}N_2O_5$ requires C, 70.89; H, 4.59; N, 6.36. Found C, 71.01; H, 4.70; N, 6.42.

**cis-1-Benzoylmethyl-3-phenoxyacetamido-4-phenylazetidin-2-one 5i :** IR($CHCl_3$, $\nu$ $cm^{-1}$): 1770, 1700(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 7.78-6.42(m,16H,arom.,NH); 5.75(dd,J=5Hz,J'=8Hz,1H,CH); 5.31(d,J=5Hz,1H,CH); 5.15(d,J=-18Hz,1H,NCHCO); 4.22(d,J=-18Hz,1H,NCHCO); 4.22(d,J=-14Hz, 1H,OCHCO); 4.01(d,J=-14Hz,1H,OCHCO). $C_{25}H_{22}N_2O_4$ requires C, 72.44; H, 5.36; N, 6.76. Found C, 72.40; H, 5.52; N, 6.87.

**cis-1-Benzoylmethyl-4-(4-methoxyphenyl)-3-phenoxyacetamidoazetidin-2-one 5j :** IR(KBr, $\nu$ $cm^{-1}$): 1770, 1700(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 7.91-6.52(m,15H,arom.,NH); 5.75(dd,J=5Hz, J'=10Hz,1H,CH); 5.29(d,J=5Hz,1H,CH); 5.14(d,J=-20Hz,1H,NCHCO); 4.38(d,J=-17Hz,1H,OCHCO); 4.22(d,J=-20Hz,1H,NCHCO); 4.08(d,J=-17Hz,1H,OCHCO); 3.70(s,3H,$OCH_3$). $C_{26}H_{24}N_2O_5$ requires C, 70.25; H, 5.45; N, 6.30. Found C, 70.30; H, 5.39; N, 6.32.

**N-Formylß-lactams 9. General procedure.**

To a suspension of PDC (9.4g,25mmol), NDC (11.6g,25mmol) or PCC (5.3g,25mmol) in benzene (25ml), pyridine (4ml, 50mmol) and the N-(2-hydroxyethyl)ß-lactam **6** (5mmol) were consecutively added. The reaction mixture was refluxed for a certain time, see Table V, and then cooled at room temperature and filtered off through a pad of silica gel 70-230 mesh and washed with methylene chloride. The combined organic solvents were washed with 6N HCl (2 x 30ml) and then with 5% $NaHCO_3$ aq. (2 x 30ml). The organic layer was dried with $MgSO_4$ and the solvent was evaporated under reduced pressure to give the corresponding crude N-formylß-lactam **9** which was purified by column chromatography, silica gel 70-230 mesh, eluent AcOEt:$CH_2Cl_2$ 1:4 (v/v).

**N-Formyl-4-phenyl-3-phthalimidoylazetidin-2-one 9a :** IR(KBr, $\nu$ $cm^{-1}$): 1805, 1775, 1715, 1700(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 9.22(s,1H,CHO); 7.67(m,4H,arom.); 7.15(s,5H,arom.); 5.75(d,J=6Hz,1H,CH); 5.53(d,J=6Hz,1H,CH). $C_{18}H_{12}N_2O_4$ requires C, 67.49; H, 3.78; N, 8.75. Found C, 67.12; H, 3.81; N, 8.71.

**N-Formyl-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one 9b :** IR(KBr, $\nu$ $cm^{-1}$): 1790, 1760 (C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 9.02(s,1H,CHO); 7.32-6.72(m,9H,arom.); 5.55(d,J=6Hz,1H,CH); 5.37(d,J=6Hz,1H,CH); 3.77(s,3H,$OCH_3$). $C_{17}H_{15}NO_4$ requires C, 68.67; H, 5.10; N, 4.71. Found C, 68.76; H, 5.14; N, 4.75.

**N-Formyl-3-phthalimidoyl-4-styrylazetidin-2-one 9c :** IR(KBr, $\nu$ $cm^{-1}$): 1805, 1775, 1717, 1685(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 8.78(s,1H,CHO); 7.56(m,4H,arom.); 7.20(m,5H,arom.); 6.53(d,J=16Hz,1H,CH); 5.93(dd,J=8Hz,J'=16Hz,1H,CH); 5.51(d,J=16Hz,1H,CH); 4.91(d,J=16Hz,1H, CH). $C_{20}H_{14}N_2O_4$ requires C, 69.35; H, 4.08; N, 8.09. Found C, 69.25; H, 4.21; N, 8.22.

**N-Formyl-3-methoxy-4-(4-methoxyphenyl)azetidin-2-one 9d :** IR(KBr, $\nu$ $cm^{-1}$): 1800, 1690 (C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 8.77(s,1H,CHO); 6.92(m,4H,arom.); 5.05(d,J=6Hz,1H,CH); 4.65(d,J=6Hz,1H,CH); 3.67(s,3H,$CH_3$). $C_{12}H_{13}NO_4$ requires C, 61.26; H, 5.58; N, 5.96. Found C, 61.16; H, 5.79; N, 6.00.

**N-Methoxalyl-4-phenyl-3-phthalimidoylazetidin-2-one 10a :** IR(KBr, $\nu$ $cm^{-1}$): 1817, 1779, 1755,1722(C=O). $^1$H-NMR($CDCl_3$, $\delta$ ppm): 7.52(m,4H,arom.); 7.02(m,5H,arom.); 5.63(d,J=7Hz,1H, CH); 5.50(d,J=7Hz,1H,CH); 3.89(s,3H,$OCH_3$). $C_{20}H_{14}N_2O_6$ requires C, 63.48; H, 3.74; N, 7.41. Found C, 63.69; H, 3.64; N, 7.26.

**General procedure for the oxidation of hydroquinones.**

To a solution of the hydroquinone (5mmol) and pyridine (2.4ml, 30mmol) in methylene chloride (20ml), 3-carboxypyridinium dichromate (6.96g, 15mmol) was added at room temperature. The reaction mixture was stirred for 15 min and then was filtered off through a pad of silica gel 70-230 mesh and washed with methylene chloride (4 x 50ml). The organic layer was washed with water (30ml), 6N HCl (2 x 50ml) and finally with $NaHCO_3$ sat.(2 x 40ml). The organic layer was dried and the solvent was evaporated under reduced pressure to give the corresponding fairly pure quinone.

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