MANGANESE(III) ACETATE AND CERIUM(IV) AMMONIUM NITRATE MEDIATED OXIDATIVE RADICAL ADDITIONS OF β-DIKETONES AND β-KETOESTERS TO LIMONENE: CHEMO AND REGIOSPECIFIC PREPARATION OF 2,3-DIHYDROFURANS

Marcio C.S. de Mattos*[a], Soraia P.L. de Souza[a] and Simone M. Elias[b]

[a]*Instituto de Química, Departamento de Química Orgânica,*
Universidade Federal do Rio de Janeiro, Caixa Postal 68545,
21945-970, Rio de Janeiro, Brazil

[b]*Instituto de Quimica, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil*

Abstract: $Mn(OAc)_3 \cdot 2H_2O$ mediated oxidative radical addition of β-diketones (acetylacetone, benzoylacetone, 1,3-cyclohexanodione) and β-ketoesters (ethyl acetoacetate, ethyl benzoylacetate) to limonene produced chemo- and regiospecificaly 2,3-dihydrofurans as a *ca.* 1:1 mixture of diastereoisomers in 72-86% isolated yields. On the other hand, the reactions mediated by CAN produced the same products in lower yields (29-35%).

Introduction

The addition of organic free radicals to alkenes is a powerful methodology for construction of C-C bonds (1) and among them the so-called "oxidative free radical addition" mediated by transition metal salts has enormously increased in the last 30 years (2). Examples of the synthetic utility of this methodology are the preparation of δ-butyrolactones and 2,3-dihydrofunas by the reactions of alkenes with carboxylic acids and β-dicarbonyl compounds, respectively (3).

We reported (4) the chemo- and regiospecific formation of the natural product norbisabolide (2, $R_1 = R_2 = H$) and related δ-butyrolactones in good yields by the oxidative radical addition of carboxylic acids to limonene 1 mediated by CAN [cerium(IV) ammonium nitrate]. On the other hand, a group from India (5) published a similar reaction using β-diketones (dimedone or acetylacetone), producing the 2,3-dihydrofurans 3 in moderate yield (Scheme 1). Recently (6) we investigated the addition of ethyl acetoacetate to limonene and the results were disappointing with Ce(IV), Fe(III), Co(II), and Cu(II), but good when $Mn(OAc)_3 \cdot 2H_2O$ was employed.

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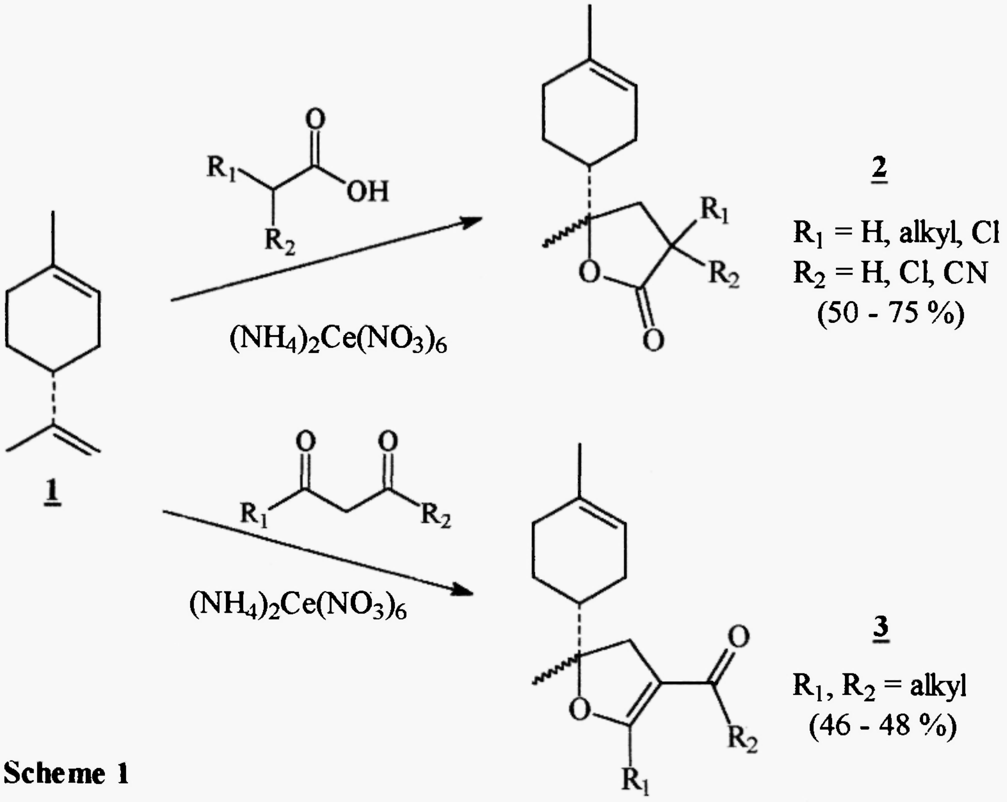
* to whom correspondence should be addressed. *E-mail:* mmattos@iq.ufrj.br



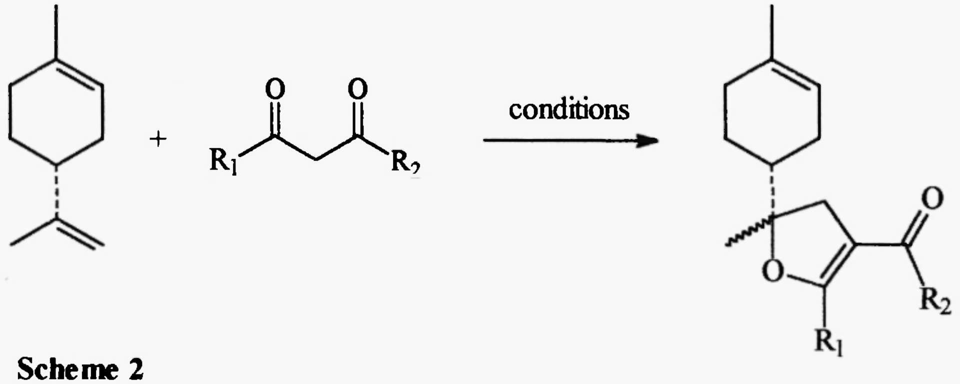
Scheme 1

Continuing our interest in chemo- and regiospecific reactions of limonene (4, 6, 7), we describe here our results on the preparation of 2,3-dihydrofurans by reaction of limonene with diverse β-diketones and β-ketoesters mediated by CAN and by $Mn(OAc)_3•2H_2O$.

Results

The reactions were performed stirring limonene (10 mmol) with the β-dicarbonyl compounds (10 mmol) in the presence of CAN (20 mmol) to produce the corresponding 2,3-dihydrofurans in 29-35% isolated yield as a *ca.* 1:1 mixture of diastereoisomers (8) - determined by high resolution gas chromatography. As the yields were low, we revisited the reaction using $Mn(OAc)_3•2H_2O$ in the place of CAN and obtained the same products but in higher isolated yields (72-86%) - Scheme 2 and Table 1 summarize the results.

In summary, in contrast with the literature information (3a, 5, 9), in our hands, $Mn(OAc)_3•2H_2O$ was better than CAN to mediate the oxidative radical addition of β-dicarbonyl compounds to limonene. Furthermore the utilization of the Mn(III) salt is also very convenient because it is a superior reagent in terms of atom economy (10) (its molecular weigh is *ca.* half of the CAN to produce the same effect, *ie.*, one electron transferring).



Scheme 2

R_1	R_2	conditions	Yield (%)[a]
Me	Me	CAN / MeOH / 5°C / 90 min	29
Me	Me	$Mn(OAc)_3 \cdot 2H_2O$ / HOAc / 70°C / 90 min	86
Me	Ph	CAN / MeOH / 5°C / 90 min	35
Me	Ph	$Mn(OAc)_3 \cdot 2H_2O$ / HOAc / 70°C / 90 min	80
$-(CH_2)_3-$		$Mn(OAc)_3 \cdot 2H_2O$ / HOAc / 70°C / 120 min	86
Mc	OEt	CAN / McOH / 5°C / 20 min	35
Me	OEt	$Mn(OAc)_3 \cdot 2H_2O$ / HOAc / 70°C / 90 nun	72
Ph	OEt	$Mn(OAc)_3 \cdot 2H_2O$ / HOAc / 70°C / 90 min	76

[a] isolated yield.

Table 1. Yields of 2,3-dihydrofurans from the reaction of limonene and diverse β-dicarbonyl compounds mediated by CAN and by $Mn(OAc)_3 \cdot 2H_2O$.

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(8) Selected analytical data. ***(1'R,5RS)-3-ucetyl-2,5-dimethyl-5-(4'-methylcyclohex-3'-enyl)-4,5-dihydrofuran*** (mixture of diastereoisomers): **^{1}H NMR** (200 MHz, $CDCl_3$): δ 5.20 (brs, 1H, olefinic), 2.90-2.32 (m, 3H), 2.15 (s, 6H), 1.90-1.70 (m, 6H), 1.60 (s, 3H), 1.22 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 193.8 (C=O), 166.0 (q), 132.5 (q), 120.2 (CH), 112.4 (q), 91.0, 90.7 (q), 42.5, 42.3 (CH), 39.2, 39.0 (CH_2), 30.3, 30.1 (CH_2), 29.1 (CH_2), 26.0, 25.4 (CH_3), 24.0, 23.8 (CH_3), 23.0 (CH_3), 15.0 (CH_3) ppm. **MS** (70 eV, electron impact): m/z 234, 216, 191, 173, 151, 134 (100%), 119, 93, 79. ***(1'R,2RS)-2-methyl-2-(4'-methylcyclohex-3'-enyl)-2,3,5,6,7-pentahydrobenzo[1,2-b]furan-4-one*** (mixture of diastereoisomers): **^{1}H NMR** (200 MHz, $CDCl_3$): δ 5.30 (brs, 1H, olefinic), 2.60-2.30 (m, 4H), 2.20 (s, 3H), 2.10 (s, 2H), 1.95-1.64 (m, 6H), 1.50 (s, 3H), 1.30 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): 195.1 (C=O), 175.2 (q), 133.9 (q), 120.0 (CH), 111.2 (q), 95.1, 94.9 (q), 42.7, 42.5 (CH), 38.1 (CH_2), 34.6 (CH_2), 34.0 (CH_2), 33.5 (CH_2), 29.9 (CH_2), 28.3, 28.1 (CH_2), 25.9, 25.6 (CH_2), 24.0, 23.7 (CH_3), 22.2 (CH_3) ppm **MS** (70 eV, electron impact): m/z 246, 228, 217, 163, 151, 134, 121 (100%), 119, 93, 79. ***(1'R,5RS)-3-carboethoxy-2,5-dimethyl-5-(4'-methylcyclohex-3'-enyl)-4,5-dihydrofuran*** (mixture of diastereoisomers): **^{1}H NMR** (200 MHz, $CDCl_3$): δ 5.38 (brs, 1H, olefinic), 4.16 (q, 2H), 2.82 (d, 1H), 2.46 (dd, 1H), 2.17 (s, 3H), 1.98-1,73 (m, 7H), 1.65 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.2, 167.0 (C=O), 166.8 (q), 134.3, 134.1 (q), 120.3, 120.2 (CH), 101.2 (q), 90.8, 90.6 (q), 59.5 (CH_2), 43.3, 43.2 (CH), 39.2, 38.5 (CH_2), 30.7, 30.6 (CH_2), 29.9 (CH_2), 24.9, 24.5 (CH_3), 23.7 (CH_3), 14.7, 14.5 (CH_3) ppm. **MS** (70 eV, electron impact): m/z 264, 246, 219, 191, 172, 157, 134 (100 %), 119, 97, 79.

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