Synthesis of Desoxydiplodialide D and Phoracantholide I from Dihydroresorcinol[1].

Jaswant Rai Mahajan* and Carlos Roberto da Silva

Departamento de Química, Universidade de Brasília, 70.910 Brasília, DF, Brasil.

Received: July 12, 1990

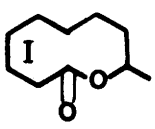
Um novo método para síntese de cetolactonas de 10-membros foi desenvolvido pela redução de 2-(3-oxobutil) dimedona (**13b**) à lactona viniloga **15b**, seguida de sua conversão na cloroidrina **10b** (Z = Cℓ) e expansão do anel para clorolactona **11b** (Z = Cℓ), cuja descloração (Zn,AcOH) rende o 3,3-dimetil-5-oxo-9-decanolídeo (**12b**). A mesma estratégia aplicada ao derivado de diidroresorcinol **13a** fornece o (±)-5-oxo-9-decanolídeo (**12a**; 3-desoxidiplodialídeo D). A dessulfurização do ditiocetal correspondente resulta no (±)-foracantolídeo I (**1**).

A novel route to 10-membered 5-oxolactones has been developed by reducing 2 - (3-oxobutil) dimedone (**13b**) to the bicyclic vinylogous lactone **15b**, followed by its conversion into the chlorohydrin **10b** (Z = Cℓ) and ring expansion to the chlorolactone **11b** (Z = Cℓ), which on dechlorination (Zn, AcOH) affords 3,3-dimethyl - 5-oxo-9-decanolide (**12b**). The same strategy when applied to the dihydroresorcinol derivative **13a** furnishes (±) -5-oxo-9-decanolide (**12a**; 3-desoxydiplodialide D). Desulfurization (Ra-Ni) of the corresponding dithioketal gives (±) - phoracantholide I (**1**).

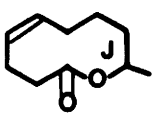
Key words: *5-oxo-decanolide, desoxydiplodialide D, phoracantholide I, dihydroresorcinol.*

Introduction

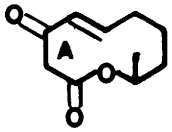
Phoracantholides I,J (**1,2**) and diplodialides A,B,C, and D (**3-6**), isolated respectively from the insect *Phorancantha synonyma*[2] and the fungus culture (*Diplodia pinea*)[3], have been the object of synthesis by several groups, including our own[4]. In 1981, we reported the synthesis of (±)-phoracantholide I (**1**) the deoxygenation of 6-oxo-9-decanolide[4a], while have been also developing alternative routes to the medium ring lactones by the ring-expansion of suitably substituted cycloalkane-1,3-diones[5]. Thus we reported the preparation of 6-acetoxi- and 6-acetamido-5-oxo-9-decanolides (**11a**: Z = OAc or NHAc) as promising precursors to the natural 10-membered lactones[5c]. However, we have been unable to eliminate the acetoxi or the acetamido group from these ketolactones, under a variety of conditions[6,7], probably due to the expected more stable quasi-equatorial conformation of these substituents. We envisaged to surmount this difficulty by changing the substituent (Z) to Br or Cℓ, which, apart from being better leaving groups, are also expected to undergo reductive elimination through the formation of the corresponding organo-metal halide. We hereby report the synthesis of the title compounds by a suitable adaptation of this strategy (Scheme).



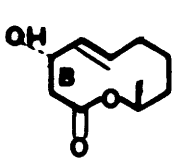
1



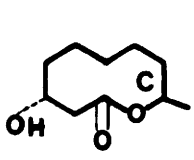
2



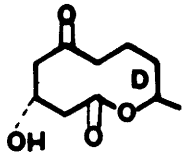
3



4



5



6

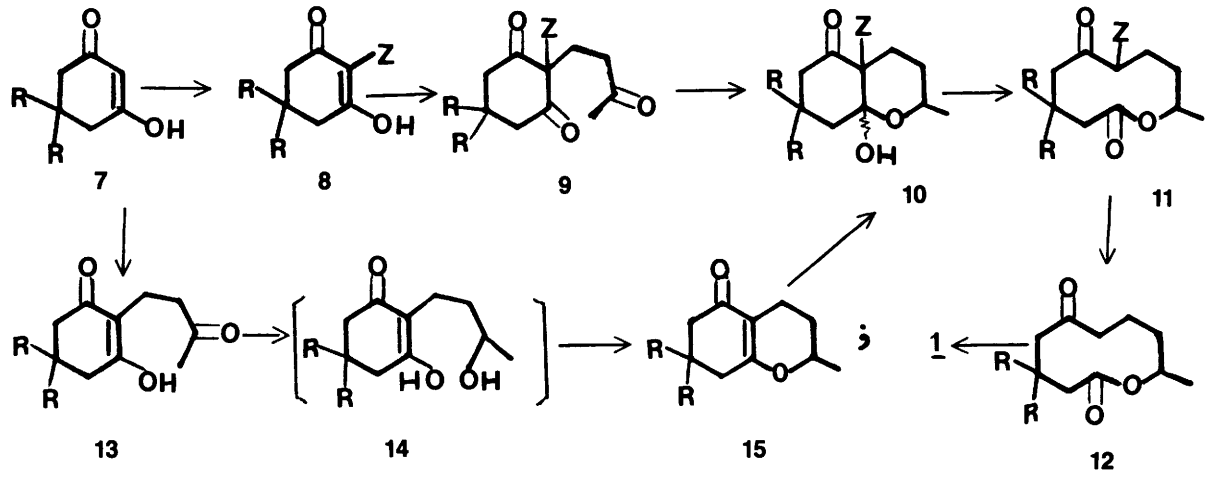
Experimental

Routine experimetal procedures and instruments for physical measurements, but for Nicolet 5ZDX-FT infrared spectrometer, have been indicated in our companion publication[4b]. 2-(3-Oxobutyl) cyclohexane-1,3-dione (**13a**) and its dimedone homolog **13b** were prepared according to the described methods[8].

Preparation of 2-bromo-2-(3-oxobutyl) dimedone (9b; Z=Br): to a solution of 2-(3-oxobutyl) dimedone **13b**; 210 mg, 1 mmoℓ) in ether (10 mℓ), containing pyridine (88 mg), was added a solution of bromine in $CC\ell_4$ (0.2M; 6mℓ). The reaction mixture was stirred at room temperature for 30 min, when it was filtered and the filtrate evaporated, affording a colorless solid (284 mg; 0.98 mmoℓ), m.p. 84-86°C; IR (KBr): ν = 1720, 1700 cm^{-1}.

^{1}HNMR ($CC\ell_4$): δ = 0.85 (s,3H,CH_3), 1.20 (s,3H,CH_3), 2.12 (s,3H,CH_3), 2.40 (s,4H,$2CH_2$), 2.20 and 3.37 (d each, J 15Hz, 4H, $2CH_2$).

Preparation of 2-chloro-2-(3-oxobutyl) dimedone (9b; Z=Cℓ): a mixture of **13b** (210 mg, 1 mmoℓ), N-Chlorosuccinimide (160 mg, 1.2 mmoℓ) and benzoyl peroxide (10 mg) in $CC\ell_4$ (10 mℓ) was refluxed for 2 h. The cooled reaction mixture was filtered and filtrate was washed



a: R = H b: R = CH_3 z: see text

SCHEME

with a saturated solution of sodium bicarbonate (5 mℓ) and brine (5 mℓ). Drying and evaporation gave a yellow solid (246 mg), which on recrystallization from aq. ethanol gave a colorless solid, m.p. 67-69°C; IR (KBr): ν = 1730, 1710 cm^{-1}.

^{1}HNMR ($CDC\ell_3$): δ 0.92 (s,3H,CH_3), 1.10 (s,3H,CH_3), 2.13 (s,3H,CH_3), 2.20-2.80 (m,4H,2CH_2), 2.50 and 3.10 (dd, J 15Hz, 4H, 2CH_2).

Preparation of vinylogous lactone **15b**: sodium borohydride (300 mg, 7.9 mmoℓ) was added to a stirred solution of **13b** (2.1 g, 10 mmoℓ) and sodium carbonate decahydrate (2.86g, 10 mmoℓ) in 95% ethanol (30 mℓ). After stirring at room temperature for 2 h, the reaction mixture was acidified with dilute hydrochloric acid and extracted with chloroform (30 mℓ). Organic extract was washed successively with brine, satd. solution of $NaHCO_3$ and brine. Drying and evaporation gave a colorless gum (1.95g), which on crystallization from n-hexane furnished a colorless solid (1.6 g; 82.5%), m.p. 56-59°C; IR (KBr): ν = 1644, 1616 cm^{-1}.

^{1}HNMR ($CC\ell_4$): δ = 1.03 and 1.07 (2s, 6H,2CH_3), 1.32 (d, J 6Hz, 3H, CH_3), 2.10 (s,2H, CH_2), 2.19 (s,2H,CH_2), 1.4-2.5 (m,4H,2CH_2), 3.8-4.2 (m, 1H, CH).

Preparation of bromohydrin **10b** *(Z = Br)*: a) a solution of 2-(3-oxobutyl) dimedone (**13b**; 420 mg, 2 mmoℓ) in 95% ethanol (6 mℓ), containing sodium carbonate decahydrate (572 mg, 2 mmoℓ), was treated with sodium borohydride (60mg, 1.6 mmoℓ) and stirred at room temperature for 2 h, when a solution of bromine in $CC\ell_4$ (0.2M) was added dropwise till the persistence of yellow coloration. Washing of the reaction mixture with brine (2x20mℓ) and usual work-up gave a yellowish gum (580mg); IR (neat): ν = 3450 (broad), 1720, 1080, 1060 cm^{-1}.

^{1}HNMR (CCl_4): δ = 1.08 (d,J 6Hz,CH_3), 1.10 (s,6H,2CH_3), 1.1-2.8 (m, 7H, 3.5CH_2), 3.20 (d,J 15Hz,1H, part A of AB system), 3.7 (s,OH), 4.0-4.4 (m,1H, CH).

b) aqueous solution of bromine (~0.18M) was added dropwise to a stirred solution of enol ether **15b** (97mg, 0.5 mmoℓ) in acetic acid (0.5mℓ), till there was persistent yellow coloration (3-3.5 mℓ). After stirring for 15 min, the reaction mixture was taken up in EtOAc (10 mℓ) and washed with brine, satd. solution of $NaHCO_3$ and brine. Drying and evaporation gave a colorless gum (146 mg; 100%), having IR and ^{1}HNMR almost identical with those of the above product.

Preparation of chlorohydrin **10b** *(Z = Cℓ)*: a) a solution of enol ether **15b** (1.94g, 10 mmoℓ) in acetic acid (10 mℓ) and ethyl acetate (50 mℓ) was treated with household sodium hypochlorite solution (Qboa; 120 mℓ). After stirring at room temperature for 30 min, excess of chlorine still persisted as revealed by its smell or blue coloration with starch-KI paper. Reaction mixture was washed with brine (2x20 mℓ), satd. solution of Na_2CO_3 (2x10 mℓ) and again brine (20 mℓ). Drying and evaporation furnished a colorless gum (2.47 g; 100% yield). IR (neat): ν = 3460 (broad), 1728, 1075, 1062 cm^{-1}.

^{1}HNMR ($CC\ell_4$): δ = 1.09 (s,6H,2CH_3), 1.11 (d, J 6Hz, 3H,CH_3), 1.2-2.6 (m,7H,3.5 CH_2), 3.05 (d,J 14Hz,1H, part A of AB system), 3.9-4.4 (m,2H,OH and CH).

b) sodium borohydride (60 mg, 1.6 mmoℓ) was added to a solution of 2-(3-oxobutyl) dimedone (**13b**; 420mg, 2 mmoℓ) in 95% ethanol (6 mℓ), containing sodium carbonate decahydrate (572 mg, 2 mmoℓ). After stirring at room temperature for 2 h, excess of chlorine (generated by the oxidation of hydrochloric acid with $KMnO_4$)[9] was passed into the reaction mixture. It was next extracted with chloroform (20 mℓ) and washed with satd. solution of sodium carbonate and brine. Usual work-up gave a pale-yellow gum (480mg), having IR and ^{1}HNMR spectra almost identical with those described above.

Lactonization of chlorohydrin **10b**(Z=Cℓ): a) a solution of chlorohydrin **10b**(Z=Cℓ; 2.47g, 10mmoℓ) in toluene (200mℓ), containing Dabco (336mg, 3mmoℓ), was refluxed with stirring for 12-14 h, till there was no more starting material (TLC). The cooled reaction mixture was washed successively with dilute hydrochloric acid (0.5N; 5×20mℓ), std. solution of sodium carbonate (3×10mℓ) and brine (3×10mℓ). Drying and evaporation furnished a brown oil (2.31g), which on short-path distillation (110-120°C/0.5 torr) afforded a colorless oil (2.22g; 90% Yield), having spectral data (see below) in accord with chlorolactone **11b**, (Z=Cℓ). Crystallization from petroleum ether gave colorless fine needles (177mg), m.p. 119-121°C; IR (Kbr): ν = 1728, 1717, 1232 cm^{-1}.

^{1}HNMR ($CC\ell_4$):δ= 1.17(s,3H,CH_3), 1.20 (d, J 6Hz, 3H, CH_3), 1.30 (s, 3H,CH_3), 1.4 - 2.6(m,8H,4CH_2), 4.2(dd,J 2.5 and 11.5Hz,1H,HCCℓ), 4.3 - 4.7(m,1H,HC - O).

Mother liquor had spectral characteristics almost identical with that of the crystalline product and on dechlorination it gave ketolactone **12b** (see below).

b) a solution of chlorohydrin **10b**(Z=Cℓ; 494 mg, 2 mmoℓ) in toluene (30 mℓ), containing sodium hydride (80% suspension; 15mg), was stirred and refluxed for 8h, when a fresh portion of NaH(16mg) was added and reflux continued for 12 h. A third portion of NaH(15mg) was added and reflux continued for further 8-10 h, till there was very little or no more starting material (TLC). The cooled reaction mixture was washed with brine (3×10 mℓ), dried and evaporated, obtaining a pale-brown gum (483 mg). Short-path distillation furnished a colorless thick liquid (424 mg), having TLC and spectral characteristics of chlorolactone **11b** (Z=Cℓ) described above. Crystallization from *n*-hexane afforded the solid chlorolactone (116 mg), m.p. 118-120°C.

Dechlorination of chlorolactone **11b**: a misture **11b**(1.23g, 5mmoℓ), acetic acid (7.5 mℓ) and zinc dust (1.3g, 20mmoℓ) was stirred at room temperature for 16-20 h, when most of zinc had reacted. The reaction mixture was taken up in ethyl acetate (30 mℓ) and washed with water (3×10 mℓ), stad. solution of sodium carbonate (2×10 mℓ) and brine. Drying and evaporation gave an yellowish oil, which was chromatographed over silica gel (20g). Elution with toluene-ethanol (98:2) furnished the desired ketolactone **12b** (578 mg, 2.72 mmoℓ; 54.4%), followed by the vinylogous lactone **15b** (266 mg, 1.37 mmoℓ; 27.4%), characterized by its m.p. and spectra (IR, ^{1}HNMR).

Ketolactone **12b** crystallized from petroleum ether as a colorless solid, m.p. 33-35°C; IR(neat) ν = 1742,1715, 1240,1228 cm^{-1}.

^{1}HNMR($CDC\ell_3$): δ = 1.13(s,3H,CH_3), 1.20(d,J 6Hz, 3H, CH_3),1.30(s,3H,CH_3), 1.4-2.9(m,1 OH,5CH_2), 4.4-4.8 (m,1H,CH).

Preparation of vinylogous lactone **15a**: 2-(3 oxobutyl) cyclohexane-1,3 dione(**13a**; 4.55g, 25 mmoℓ) was reduced with $NaBH_4$(760mg, 20mmℓ) and worked up exactly in the manner described for the dimedone homolog **13b**. Short-path distillation (110-120°C/0.5 torr) of the crude product furnished **15a** as a colorless oil (3.46g, 20.8 mmoℓ; 83.2% yield). IR(neat): ν = 1652, 1620 cm^{-1}.

^{1}HNMR($CC\ell_4$): δ = 1.33(d, J 6Hz,3H,CH_3), 1.4-2.5 (m,1 OH, 5CH_2), 3.8-4.2(m,1H,CH).

Preparation of chlorohydrin **10a**(Z=Cℓ): the above product (**15a**; 3.46g, 20.8 mmoℓ) dissolved in acetic acid (30mℓ) and ethyl acetate (210 mℓ), was treated with sodium hypoclorite solution (Qboa; 210mℓ) and elaborated in the manner described for the homologous compound **10b** (Z=Cℓ), obtaining a colorless oil (3.8g, 17.4 mmoℓ; 84% yeld). IR(neat): ν = 1733,1728,1078,1063 cm^{-1}.

^{1}HNMR($CC\ell_4$): δ = 1.08(d, J 6Hz,CH_3), 1.1 - 3.3 (m,1 OH,5CH_2), 3.80 (broad s,OH), 4.0-4.4(m,1H,CH).

Lactonizarion of chlorohydrin **10a** (Z=Cℓ): the above product (3.8g, 17.4 mmoℓ) dissolved in toluene (350 mℓ), containing Dabco (672 mg, 6 mmoℓ), was stirred and refluxed for 18h, when it was worked up as described for the homologous lactone **11b**. Short-path distillation (110-120°C/0.5 torr) of the crude product gave a colorless oil (3.61g, 16.5 mmoℓ; 95% yield), practically pure **11a** (TLC); IR(neat): ν = 1737,1708,1277,1230 cm^{-1}.

^{1}HNMR($CDC\ell_3$): δ = 1.18 (d,6Hz, CH_3), 1.3-3.4(m,1 OH, 5CH_2), 4.32 and 4.43 (dd, J 3Hz and 1 OHz,1H,HC-Cℓ), 4.4-4.9(m,1H,HC-O).

*Preparation of 5-keto-9-decanolode (desoxydiplodialide D; **12a**):* a) a mixture of chlorolactone **11a**(3.61g, 16.5 mmoℓ), acetic acid (25 mℓ) and zinc dust (4.3g) was stirred at room temperature for 18 h, when it was elaborated as described for the homologous ketolactone **12b**. The crude product (1.91g), a colorless oil, was chromatographed over silica gel (60g). Elution with toluene-ethanol (98:2) furnished pure **12a** (1.45g, 7.9 mmoℓ; 48% yield), as a colorless oil. IR(neat): ν = 1735,1708,1260,1220,1080 cm^{-1}.

^{1}HNMR(CCD_3): δ = 1.18(d, J 6Hz,CH_3), 1.25-3.00 (m,12H,6CH_2), 4.4-4.7(m,1H,CH).

The rest of the eluted material was enol ether **15a**, contaminated with ketolactone **12a**.

b) a mixture of chlorolactone **11a** (220mg, 1mmoℓ), acetic acid (1.5mℓ) and zinc dust (250 mg) was subjected to ultrasound[10] in a Thornton-Inpec (40kHz) apparatus for 50 min, when all of zinc had reacted. Usual work-up gave practically pure (TLC, IR, ^{1}HNMR) 5-keto-9-decanolide (180mg; 98% yield).

Conversion of 5-keto-9-decanolide (**12a**) *into phoracantholide I (9-decanolide;* **1***):*

I) Preparation of dithioketal - a solution of **12a** (690mg, 3.75 mmoℓ), ethanedithiol (0.38mℓ; 424mg, 4.5mmoℓ) and freshly distilled boron trifluoride etherate (0.62mℓ; 694mg, 4.9 mmoℓ) was stirred at room temperature for 23 h, when the execess of reagents was evaporated under reduced pressure. The residue was taken up in ethyl acetate (15mℓ) and washed with brine (10mℓ), satd. solution of sodium carbonate (2×5mℓ) and brine (10mℓ). Drying and evaporation furnished a colorless oil (816mg; 3.14 mmoℓ; 83.4% yield), which afforded a white solid from petroleum ether; m.p. 29-32°C; IR(neat): ν = 1728,1254 cm^{-1}.

^{1}HNMR($CDC\ell_3$): δ = 1.25(d, J 6Hz,CH_3), 1.0-2.7 (m,12H,6CH_2), 3.27 (s,4H,S-CH_2CH_2-S), 4.8-5.2 (m,1H,CH).

II) Desulfurization of the above thioketal (490mg,1.88 mmoℓ) was carried out by stirring it with a methanolic suspension of Ra-Ni (20mℓ) at room temperature for 21h. After filtering the solids, solvent was evaporated and the residue taken up in ethyl acetate (10mℓ). Washing with satd. solution of sodium carbonate and brine, followed by drying and evaporation gave a colorless oil (219mg), having the characteristic smell of phoracantholide I. Passage through a short column of silica gel (2g), eluted with n-hexane, furnished pure (TLC) 9-decanolide (153mg, 0.9 mmoℓ; 48% yield), having IR and ^{1}HNMR spectra superimposable on those of our earlier samples[4].

Results and Conclusions

Due to the known poor stability of dihydroresorcinol (**7a**), we decided to carry out the model studies with its much stabler 5,5-dimethyl homolog (dimedone; **7b**). 2-Bromodimedone (**8b**: Z = Br) was prepared[11], but we were unable to effect its addition to methyl vinyl ketone under various conditions[5,12], probably owing to its high acidity (pKa = 3.2)[13] and consequent poor nucleophilicity of its anion. We were able, however, to obtain the desired bromo compound **9b** (Z = Br) by brominating the known[8] 2-alkyldimedone **13b**. But on attempted reduction ($NaBH_4$, $NaBH_3CN$)[5b-d], the bromo compound **9b** (Z = Br) reverted to the alkyldimedone **13b**, probably by a nucleophilic attack on bromine, and its subsequent reduction product **15b**, in proportions dependent on the amount of hydride employed in the reaction. Reduction of the corresponding chloro compound **9b** (Zn=Cℓ) was also unsuccessful, affording the above by-products along with traces of the desired compound (TLC).

We next reduced ($NaBH_4$) the alkyldimedone **13b** and carried out, *in situ*, bromination or chlorination of the ex-

pected product **14b**, because on isolation it converts into the enol ether **15b** owing to its spontaneous dehydration. The desired halogenated product (**10b**: Z = Br or Cℓ) was obtained in 97-100% yield, but was always contaminated with some impurities, which were rather difficult to remove. Later on we discovered that the enol ether **15b** itself can be easily halogenated to afford the desired product (**10b**: Z = Br or Cℓ) in a quantitative yield and excellent purity (TLC, IR, NMR). However, no crystalline compound has been isolated, probably owing to the presence of several diastereoisomers.

Attempted lactonization of the bromo compound **10b** (Z = Br) was unsuccessful under a variety of basic, acidic or neutral conditions tried for this purpose: sodium hydride, potassium *t*-butoxide, triethylamine or pyridine, p-toluenesulfonic acid or *n*-tetrabutylammonium fluoride in benzene, toluene, tetrahydrofuran or dioxan[5]; in almost all cases there forms some ketolactone accompanied by enol ether **15b** and other unidentified components (TLC, IR, NMR).

The chloro compound **10b** (Z = Cℓ) underwent the expected ring-expansion with NaH in boiling toluene, but the reagent appeared to lose activity after 4-6h and further portion-wise additions (2-3) were necessary to obtain predominant conversion (TLC) into the desired lactone **11b** (Z = Cℓ). Consequently, we tried pyridine, 4-dimethylaminopyridine (DMAP), triethylamine and 1,4-diazabiciclo (2.2.2) octane (Dabco) for the above lactonization and found out that Dabco effected the desired isomerization in excellent yield (90-95%).

Owing to the presence of diastereoisomers, only a small portion of the chlorolactone **11b** (Z = Cℓ) was obtained as a crystalline solid. However, either the solid product or the mother liquor underwent dechlorination (Zn, AcOH) smoothly and furnished the ketolactone **12b**, along with some reversion to the enol ether **15b**. This reversion to **15b** is due obviously to the expected transannular[14] acylation of the organo-zinc intermediate **11b** (Z = ZnCℓ) and competes with its protonation to lactone **12b**.

Having dominated the entire route with the model compound (dimedone: **7b**), we repeated the same sequence with dihydroresorcinol (**7** → **13a** → **15a** → **10a** → **11a** → **12a**; Z= Cℓ) and finally obtained (±)-5-oxo-9-decanolide (**12a**: 3-desoxydiplodialide D). Desulfurization (Ra-Ni) of the corresponding dithioketal gave (±)-phoracantholide I (**1**), already synthesized in our and several other laboratories[4].

We are now examining the scope of our new methodology and its extension to the synthesis of other medium-ring and macrocyclic lactones.

Acknowledgement

C.R. Silva thanks CNPq for an M.Sc. scholarship.

References

1. a) C.R. Silva, *M. Sc. Thesis,* Chemistry Department, Brasília University, 1990;
   b) Abstract submitted to 4th Brazilian Meeting on Organic Synthesis (Teresópolis-RJ, September 2-6, 1990).
2. B.P. Moore and W.V.Brown, *Aust. J. Chem.* **29**, 1365-1374 (1976).
3. K. Wada and T. Ishida, *J. Chem. Soc. Perkin Trans.* **1**, 1154-1158 (1979).
4. a) J.R. Mahajan and H.C. Araújo, *Synthesis* 49-51 (1981);
   b) J.R. Mahajan, H.C. Araújo and I.S. Resck, *J. Braz. Chem. Soc.* **1**,13-16 (1990) and references cited therein.
5. a) J.R. Mahajan and H.C. Araújo, *Ciênc. Cult.* **32**, 893-903 (1980);
   b) J.R. Mahajan and I.S. Resck, *Synthesis* 998-999 (1980);
   c) J.R. Mahajan and M.B. Monteiro, *Ciênc. Cult.* **33** (7, supl.) 368 (1981);
   d) J.R. Mahajan, J.R. Botelho and I.S. Resck, *J. Braz. Chem. Soc.* **1**, 13-16 (1990);
   e) For a recent review of ring enlargement methods see: H. Stach and M. Hesse, *Tetrahedron* **44**, 1573-1590 (1988).
6. J.R. Mahajan, M.B. Monteiro, I.S. Resck and C.R. Silva, unpublished results.
7. H.O. House, *Modern Synthetic Reactions,* 2nd Edition (W.A. Benjamin, Menlo Park, Ca., 1972), pp. 158-162.
8. a) I.N. Nazarov and S.I. Zav'yalov, *Zhur. Obshchei Khim.* **23**, 1703-1712 (1953); *Chem. Abstr.* **48**: 13667h (1954);
   b) J.W. Ralls, W.C. Wildman, K.E. McCaleb and A.L. Wilds, *U.S.Pat.* 2.674.627; *Chem. Abstr.* **49**: 1813c (1955).
9. A.I. Vogel, *A Text-Book of Practical Organic Chemistry,* 3rd edition (Longmans, London, 1964), p. 183.
10. For a recent review on Ultrasound in Organic Synthesis see: R.F. Abdulla, *AldrichimicaActa* **21** (2), 31-42 (1988).
11. a) A.W. Fort, *J. Org. Chem.* **26**, 765-767(1961); b) J.R. Mahajan and C.R. Silva, *Ciênc. Cult.* **40** (7, supl.), 503 (1988).
12. E.D. Bergmann, D. Ginsburg and R. Pappo, *Org. React.* **10**, 179-555 (1959).
13. R.P. Bell and G.G. Davis, *J. Chem. Soc.* 353-361 (1965).
14. E.L. Eliel, *Stereochemistry of Carbon Compounds* (McGraw-Hill, New York, 1962), pp. 259-263.