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Research Article

A FACILE SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF (3-HYDROXY-2,4-DIMETHOXYPHENYL)(PHENYL) METHANONES BY FRIEDEL CRAFT'S ACYLATION IN THE PRESENCE OF PHOSPHOROUS PENTOXIDE AND METHANE SULFONIC ACID: EATON'S REAGENT

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ABSTRACT

In the present study, a series of (3-hydroxy-2,4-dimethoxyphenyl)(phenyl) methanones (4a-n), were synthesized by reacting 2, 6-dimethoxy phenol and chloroacetyl chloride by friedel craft's acylation using eaton's reagent. The chemical structures of the synthesized compounds were characterized by analytical and spectral (^{1}HNMR, ^{13}CNMR and HRMS) techniques. The title compounds were screened for qualitative (zone of inhibition) and quantitative antimicrobial activity (MIC) by agar well and microbroth dilution technique, respectively. Among the synthesized compounds in the series, the compounds 4k and 4j were found to exhibit significant antibacterial activity at lower concentration, against Gram positive bacteria such as staphylococcus aureus and Gram negative bacteria such as Salmonella typhimurium Escherichia coli, Vibrio typhimurium, Pseudomonas aeruginosa, Klebsiella pneumoniae and Bacillus subtilis. The other compounds displayed moderate antibacterial activity when compared to the standard positive controls Chloramphenicol.

Keywords: Friedel craft's acylation, eaton's reagent, antibacterial activity.

INTRODUCTION

The novelty of benzophenones forms the prominent position in organic chemistry and of at most practical and theoretical importance. The benzophenone analogues have been synthesized by adopting A. Ghinet et al[21] procedure. As a result, great deals of research activities are carried out in several laboratories. It is vast and expanding area of organic chemistry because of obvious applications of compounds in pharmacy, medicine, agriculture, plastic, polymer and other fields. Benzophenone analogues have displayed versatile biological activities such as anti-microbial, anit-cancer, anti-convulsant, anti-pyretic, anti-hypertensive, anti-diabetic, anti-inflammatory and analgesic by their polar feature of carbonyl group. Benzophenone is used as an ultraviolet (UV)-curing agent in sunglasses, and to prevent UV light from damaging scents and colors in products such as perfumes and soaps. Besides, benzophenones occur naturally in food such as Muscat grape and mango.

According to the Literature, Friedel-Crafts reaction is carried out using a protected methoxy-phenol and aromatic acids in PPA. However, this is a highly viscous medium which is difficult to stir and hydrolyze at the end of the reaction; then we decided to use Eaton's reagent (MeSo3H/ P2O5). In the prior as Eaton's reagent has been used in various reactions, showing its flexibility

depending on the reactant used. The present inventions provide an improved route for the acylation of protected methoxy phenol at ortho position; with respect to it with good quality and yield. It would be a significant contribution to the act to provide an improved process for the preparation of benzophenone and its analogues which would be scalable, cost effective and environment friendly. Typically the reaction of protected 2,6-dimethoxy phenol and aromatic acids in presence of Eaton's reagent results in the formation of an ester. As we protected the hydroxyl group by reacting it with chloroacetyl chloride followed by acylating the ring at meta position with respect to the hydroxyl group. This is because the dimethoxy group directs the incoming acyl group ortho with respect to it. The sodium acetate removing of the chloroacetyl protective group yielded metabolite. Through Friedel-Crafts reaction, we have developed a new synthesis of benzophenones which is currently the easiest method cited in the literature. Overall, these benzophenones exhibited interesting biological properties and have potential for further investigation as anticancer agents.

MATERIALS AND METHODS

All the solvents and reagents used were of AR grade and commercially available; used as such without further purification. All melting points were taken in open capillary tube and are uncorrected. The^{1} H NMR spectra were recorded on Shimadzu AMX 400-Bruker, 400 MHz spectrometer using $CDCl_3$ as a solvent and TMS as internal standard (chemical shift δ in ppm). The Elemental (C, H, N) analyses were obtained on Vario EL III Elementar. Slica gel column chromatography was performed using Merck Silica gel (100-200 mesh) and Merck made TLC plates were used for reaction monitoring. Mass spectra were recorded on LCMS Agilent 1100 series with MSD (ion trap) using 0.1% aqueous TFA in acetonitrile system on C18-BDS Column for 10 min duration.

GENERAL PROCEDURE FOR THE SYNTHESIS OF 2, 6-DIMETHOXYPHENYL 2-CHLOROACETATE

To a solution of 2,6-dimethoxy phenol and chloroacetyl chloride in tetrahydrofuran was added pyridine. The reaction mixture was stirred for 3h and the completion of the reaction was monitored through thin layer chromatography. The reaction mixture was concentrated and extracted with ethyl acetate, the organic layer then washed with water, sodium bicarbonate solution, brine solution, dries over sodium sulfate and concentrated with reduced pressure to get crude product. This crude product was recrystallized using methanol to obtain pure white crystalline solid 2,6-dimethoxyphenyl 2-chloroacetate (2).

GENERAL PROCEDURE FOR THE SYNTHESIS OF (3-HYDROXY-2, 4-DIMETHOXYPHENYL) (PHENYL) METHANONE ANALOGUES (4A-N)

To a solution of 2,6-dimethoxyphenyl 2-chloroacetate (2) and aromatic benzoic acids in Eaton's reagent (($MeSo_3H$/ P_2O_5) was refluxed for 4 h and the completion of the reaction was monitored through thin layer chromatography. The reaction mixture was cooled and diluted with dichloromethane and carefully poured into a beaker containing 10% $NaHCO_3$, allowed for stirring, the aqueous solution was extracted with CH_2Cl_2 and the combined organic layers were washed with water, brine solution, dried over sodium sulfate and concentrated under reduced pressure to produce a brownish oil as crude product. This crude product was purified by column chromatography on silica gel to afford 3-benzoyl-2,6-dimethoxyphenyl 2-chloroacetate(3a-n).

To a solution of 3-benzoyl-2, 6-dimethoxyphenyl 2-chloroacetate (3a-n) and sodium acetate in methanol was refluxed for 4h and the completion of the reaction was monitored through thin layer chromatography. The reaction mixture was concentrated and extracted with ethyl acetate, the organic layer then washed with water, brine solution, dried over sodium sulfate and concentrated with reduced pressure to get crude product. This crude product was recrystallized using methanol to obtain pure white crystalline solid (3-hydroxy-2,4-dimethoxyphenyl)(phenyl) methanone analogues (4a-n).

Table 1: Antimicrobial activity data of (3-hydroxy-2,4-dimethoxyphenyl)(phenyl)methanone analogues (4a-n) Zone of Inhibition in mm

Bacterial strains	B1	B2	B4	B7	B9	B10	B11	B14	+ve control Chloramphenicol
Staphylococcusaureus	12	12	16	15	16	-	18	14	23
Salmonella typhimurium	10	12	14	12	14	12	**17**	15	16
Escherichiacoli	-	12	-	-	15	**18**	15	13	15
Vibrio parahaemolyticus	-	-	-	-	-	-	-	-	20
Pseudomonas aeruginosa	-	-	-	-	-	-	-	-	15
Klebsiellpneumonae	-	-	-	-	-	-	-	8	20
Bacillus subtilis	-	-	-	-	-	12	15	11	20
Values are zones of inhibition in mm "-" – Not sensitive									

TYPICAL PROCEDURE FOR THE SYNTHESIS OF (3-HYDROXY-2, 4-DIMETHOXYPHENYL) (PHENYL) METHANONE (4A)

To a solution of (2) 2,6-dimethoxyphenyl 2-chloroacetate (2g, 0.8mmol) and benzoic acid (1.05g, 0.8mmol in Eaton's reagent (($MeSo_3H$/ P_2O_5) was refluxed for 4h and the completion of the reaction was monitored through thin layer chromatography. The reaction mixture was cooled and diluted with 20mL of dichloromethane and carefully poured into a beaker containing 20mL of 10% $NaHCO_3$ solution, allowed for stirring, the aqueous solution was extracted with 10mL of dichloromethane and the combined organic layers were washed with water, brine solution, dried over sodium sulfate and concentrated under reduced pressure to produce a brownish oil as crude product. This crude product was purified by column chromatography on silica gel 60:120 and petroleum ether: ethyl acetate as an eluent to afford 3-benzoyl-2,6-dimethoxyphenyl 2-chloroacetate(3a).

To a solution of (3a) 3-benzoyl-2,6-dimethoxyphenyl 2-chloroacetate (2g, 0.5mmol) and sodium acetate (4.5eq) in methanol was refluxed for 4 h and the completion of the reaction was monitored through thin layer chromatography. The reaction mixture was concentrated and extracted with 20mL of ethyl acetate, the organic layer then washed with 10mL of water, 10mL of brine solution, dried over sodium sulfate and concentrated with reduced pressure to get crude product. This crude product This crude product was purified by column chromatography on silica gel 60:120 and petroleum ether: ethyl acetate as an eluent to obtain pure white crystalline solid (3-hydroxy-2,4-dimethoxyphenyl)(phenyl) methanone analogues (4a) in 80% yield.

1HNMR (CDCl3) δppm: 3.84 (s, 6H), 5.80 (s, 1H, hydroxyl -H), 6.70 (d, 1H), 6.96 (d, 1H), 7.44 (m, 3H), 7.81 (d, 2H), MS: m/z= 259 (M+1). Anal. Calcd for C15H14O4: C, 69.76; H, 5.46; Found: C, 66.70; H, 5.40.

(3-hydroxy-2,4-dimethoxyphenyl)(4-methoxy phenyl)methanone (4b)

1HNMR (CDCl3) δppm: 3.83 (s, 9H), 5.75 (s, 1H, hydroxyl -H), 6.71 (d, 1H), 7.09 (d, 2H), 7.12 (t, 2H), 7.67 (d, 2H), MS: m/z= 289 (M+1). Anal. Calcd for C16H16O5: C, 66.66; H, 5.59; Found: C, 66.70; H, 5.40

(3-hydroxy-2,4-dimethoxyphenyl)(2-methoxy phenyl)methanone (4c)

1HNMR (CDCl3) δppm: 3.83 (s, 9H), 5.77 (s, 1H, hydroxyl -H), 6.70 (d, 1H), 7.09 (d, 1H), 6.85 (m, 3H), 7.34 (t, 1H), 7.54 (d, 1H), MS: m/z= 289 (M+1). Anal. Calcd for C16H16O5: C, 66.66; H, 5.59; Found: C, 66.60; H, 5.55.

(3,4-dimethoxyphenyl)(3-hydroxy-2,4-dimethoxyphenyl)methanone (4d)

1HNMR (CDCl3) δppm: 3.77 (s, 12H), 5.77 (s, 1H, hydroxyl -H), 6.70 (d, 1H), 6.84 (d, 1H), 6.91 (d, 1H), 7.32 (m, 1H), 7.54 (d, 1H) MS: m/z= 319 (M+1). Anal. Calcd for C17H18O6: C, 64.14; H, 5.70; Found: C, 64.60; H, 5.65.

(3-hydroxy-2,4-dimethoxyphenyl)(p-tolyl) methanone (4e)

1HNMR (CDCl3) δppm: 2.39 (s, 3H), 3.74 (s, 3H), 3.94 (s, 3H), 5.80 (s, 1H, hydroxyl -H), 6.70 (d, 1H), 6.94 (d, 1H), 7.32 d, 2H), 7.58 (d, 2H), MS: m/z= 273 (M+1). Anal. Calcd for C16H16O4: C, 70.57; H, 5.92; Found: C, 70.60; H, 5.65.

(3-hydroxy-2,4-dimethoxyphenyl)(o-tolyl) methanone (4f)

1HNMR (CDCl3) δppm: 2.39 (s,3H), 3.74 (s, 3H), 3.94 (s, 3H), 5.80 (s, 1H, hydroxyl -H), 6.80 (d, 1H), 6.92 (d, 1H), 7.32 (m, 3H), 7.58 (d, 1H), MS: m/z=

273 (M+1). Anal. Calcd for C16H16O4: C, 70.57; H, 5.92; Found: C, 70.60; H, 5.65.

(3-hydroxy-2,4-dimethoxyphenyl)(m-tolyl) methanone (4g)
1HNMR (CDCl3) δppm: 2.39 (s, 3H), 3.74 (s, 3H), 3.94 (s, 3H), 5.80 (s, 1H, hydroxyl -H), 6.70 (d, 1H), 6.94 (d, 1H), 7.32 (m, 3H), 7.58 (d, 1H), MS: m/z= 273 (M+1). Anal. Calcd for C16H16O4: C, 70.57; H, 5.92; Found: C, 70.60; H, 5.65.

(4-chlorophenyl)(3-hydroxy-2,4-dimethoxy phenyl)methanone (4h)
1HNMR (CDCl3) δppm: 3.98 (s, 6H), 5.60 (s, 1H, hydroxyl -H), 6.53 (d, 1H), 7.12 (d, 1H), 7.40 (d, 1H), 7.93 (d, 1H), MS: m/z= 293 (M+1), 295 (M+3). Anal. Calcd for C15H13ClO4: C, 61.55; H, 4.48; Found: C, 61.60; H, 4.65.

(2-chlorophenyl)(3-hydroxy-2,4-dimethoxy phenyl)methanone (4i)
1HNMR (CDCl3) δppm: 3.97 (s, 6H), 5.60 (s, 1H, hydroxyl -H), 6.51 (d, 1H), 7.12 (d, 1H), 7.42 (t, 1H), 7.56 (m, 3H), MS: m/z= 293 (M+1), 295 (M+3). Anal. Calcd for C15H13ClO4: C, 61.55; H, 4.48; Found: C, 61.60; H, 4.65.

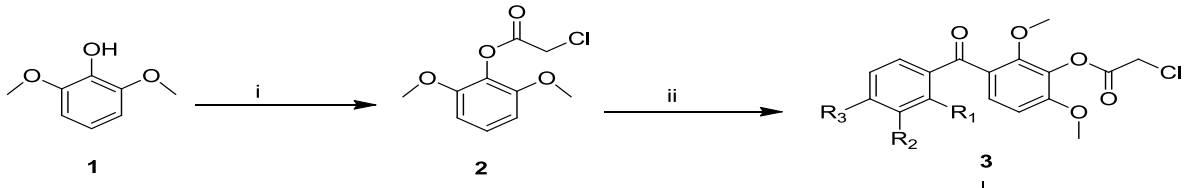
(3-chlorophenyl)(3-hydroxy-2,4-dimethoxy phenyl)methanone (4j)
1HNMR (CDCl3) δppm: 3.97 (s, 6H), 5.61 (s, 1H, hydroxyl -H), 6.51 (d, 1H), 7.13 (d, 1H), 7.43 (t, 1H), 7.54 (m, 3H), MS: m/z= 293 (M+1), 295 (M+3). Anal. Calcd for C15H13ClO4: C, 61.55; H, 4.48; Found: C, 61.60; H, 4.65.

(4-fluorophenyl)(3-hydroxy-2,4-dimethoxy phenyl)methanone (4k)
1HNMR (CDCl3) δppm: 3.97 (s, 6H), 5.60 (s, 1H, hydroxyl -H), 6.50 (d, 1H), 7.17 (m, 3H), 7.70 (t, 2H), MS: m/z= 277 (M+1). Anal. Calcd for C15H13ClO4: C, 61.55; H, 4.48; Found: C, 61.60; H, 4.65.

(4-bromophenyl)(3-hydroxy-2,4-dimethoxy phenyl)methanone (4l)
1HNMR (CDCl3) δppm: 3.90 (s, 6H), 5.65 (s, 1H, hydroxyl -H), 6.59 (d, 1H), 7.12 (m, 3H), 7.74 (t, 2H), MS: m/z= 337 (M+1), 339 (M+3). Anal. Calcd for C15H13BrO4: C, 53.43; H, 3.89; Found: C, 53.60; H, 3.65.

(3-hydroxy-2,4-dimethoxyphenyl)(4-hydroxy phenyl)methanone (4m)
1HNMR (CDCl3) δppm: 3.80 (s, 6H), 5.65 (s, 2H, hydroxyl -H), 6.50 (d, 1H), 6.80 (d, 2H) 7.13 (t, 2H), 7.65 (t, 2H), MS: m/z= 275 (M+1). Anal. Calcd for C15H14O5: C, 65.69; H, 5.15; Found: C, 65.60; H, 5.35.

(3-hydroxy-2,4-dimethoxyphenyl)(4-nitro phenyl)methanone (4n)
1HNMR (CDCl3) δppm: 3.97 (s, 6H), 5.60 (s, 1H, hydroxyl -H), 6.50 (d, 1H), 7.14 (d, 1H), 7.18 (t, 2H), 7.70 (t, 2H), MS: m/z= 304 (M+1). Anal. Calcd for C15H13NO6: C, 59.41; H, 4.32; N, 4.62; Found: C, 59.40; H, 4.35, N, 4.60



a: R_1=H,R_2=H,R_3=H
b: R_1=H,R_2=OMe,R_3=H
c: R_1=OMe,R_2=H,R_3=H
d: R_1=H,R_2=OMe,R_3=OMe
e: R_1=H,R_2=Me,R_3=H
f: R_1=Me,R_2=H,R_3=H
g: R_1=H,R_2=Me,R_3=H
h: R_1=H,R_2=H,R_3=Cl
i: R_1=Cl,R_2=H,R_3=H
j: R_1=H,R_2=Cl,R_3=H
k: R_1=H,R_2=H,R_3=F
l: R_1=H,R_2=H,R_3=Br
m:R_1=H,R_2=H,R_3=OH
n: R_1=H,R_2=H,R_3=NO_2

Scheme 1 :Reagents and conditions; (i) chloroacetyl chloride, pyridine, THF, 2h; (ii) Eaton's reagent, aromatic acids, 4h; (iii) Sodium acetate(4.5eq), methanol.

ANTIBACTERIAL ACTIVITY BY WELL DIFFUSION METHOD

The antibacterial activity of the synthesized benzophenones 4a-n was investigated by following the well diffusion method of Odeyemi and Fagbohun, 2005. Sterile solidified nutrient agar plates were prepared and inoculated with different test bacterial strain by spread plate method. 6mm wells were made in the nutrient agar plates and were filled with the predetermined concentration of different test samples (10 µg). The loaded plates were then kept for incubation at 370C for 24 hrs. Antibacterial activity of all the synthesized compounds 4a-n was evaluated by measuring the zone of inhibition against the test microorganisms. Ethanol was used as negative control and 10 µg chloramphenicol was used as a positive control. After incubation, the inhibition zone formed around the wells was measured in millimeter. The study was performed in triplicate.

RESULTS AND DISCUSSION

The desired compounds 4a-n was synthesized as outlined in the scheme-1. Compounds 4a-n was synthesized by reacting 2 in presence of eaton's reagent. The present inventions provide an improved route for the formylation of aromatic compounds. These inventions disclose the use of Eaton's reagents with specific content of phosphorous pentoxide in methane sulfonic acid for selective formylation at ortho position of Benzophenone with good quality and yield. Methanesulfonic acid is Bronsted acid that is used as catalyst and solvent for condensation or rearrangements reactions. It is used as catalyst in the Fries rearrangement of Phenolic esters was already known. Addition of P_2O_5 increased the solubility of organic compounds in MSA that has been used extensively in organic synthesis.

Eaton's reagent was prepared from P_2O_5 and CH_3SO_3H MSA (with ratio P_2O_5: MSA 1:10) the mixture was heated at 40°C under N_2 atmosphere until complete homogeneity. In the prior as Eaton's reagent has been used in various reactions, showing its flexibility depending on the reactant used. Consequently, it would be a significant contribution to the act to provide an improved process for the preparation of benzophenone and its analogues, which would be scalable, cost effective and environment friendly.

The present approach offers several advantages such as shorter reaction time, cleaner reaction, good yields, inexpensive reagents and mild reaction conditions

The structures of the desired compounds were determined on the basis of ^{1}HNMR, ^{13}CNMR and mass spectroscopy. The spectral data are mentioned above, which confirms the structure of synthesized compounds.

In vitro antibacterial activity data of 2,6-dimethoxy benzophenones (4a-n) against tested organisms displayed the varying antibacterial activity against used test cultures. All the test sample of 4a-n series was active against *Staphylococcus aureus* except 4j. 4k was stronger when compared to the other sample of the series. Sample 4a, 4b, 4d, 4g, 4i, 4j – showed the bacteriostatic activity, whereas 4k and 4n showed the strong bacterialcidal activity against *Salmonella typhimurium*, 4k was more potent than positive control used. In case of *Escherichia coli,* only 4b, 4i, 4j, 4k and 4n were active and 4j was stronger than the positive control used. Whereas, *Vibrio parahaemolyticus, Pseudomonas aeruginosa* and *Klebsiella pneumonae* showed the resistance against used test sample of 4a-n series. But, Bacillus subtilis was susceptible to sample 4j, 4k and 4n. Overall among the 4a-n series sample tested for their antibacterial activity against different bacterial strains, 4k was potent and followed by 4j, 4i and 4n. And the present work concludes that sample 4k and 4j can be used to replace the positive control against respective test cultures

CONCLUSIONS

In conclusion, we have reported a facile route for the rapid synthesis of benzophenones (4a-n) using eaton's reagent. The molecular frame work has shown broad spectrum antibacterial activity which is substantiated by the presence of hydroxyl, carbonyl group and electronegative atoms, among the synthesized compounds (4a-n), compounds 4k and 4j bearing electronegative atoms respectively in the molecular frame work have exhibited potent antibacterial activity, when compared to the standard positive controls.

REFERENCES

1. Henry GE, Jacobs H, Carrington CMS, McLean S and Reynolds WF. Tetrahedron. 1999;55:1581.
2. Vidya R, Eggen M, Georg GI and Himes RH. Bioorg Med Chem Lett. 2000;13:757.
3. Wyatt PG, Bethell RC, Cammack N et al. J Med Chem. 1995;38:1657.
4. Gustafson KR, Blunt JW, Munro MHG, Fuller RW, Mckee TC, Cardellina II JH,

McMahon JB, Cragg GM and Boyd MR. Tetrahedron. 1992;48:10093.
5. Palomer A, Pascual J, Cabre M, Borras L, Gonzalez G, Aparici M, Carabaza A, Cabre F, Garcia ML and Mauleon D. Bioorg Med Chem Lett. 2002;12:533.
6. Burns DT, Tungkananuruk N and Thuwasin S. Anal Chim Acta. 2000;419:41.
7. Kadry AM, Okereke CS and Abdel-Rahman MS. Toxicol Lett. 1995;80:61.
8. White LS. J Mem Sci. 2002;205:191.
9. Shaukath Ara Khanum, Sheena Shashikanth and Sudha BS. Heterochem. 2004;15:37.
10. Fulop F, Bernath G and Pihlaja K. Adv Heterocycl Chem. 1998;41:6551.
11. Du Y, Ma C, Kwok WM, Xue J and Philips DL. J Org Chem. 2007;72:7149.
12. Srivastava SK, Srivastava SI and Srivastava SD. Indian J Chem. 2000;39B:464.
13. Sahin G, Palaska E, Ekizoglu M and Ozalp M. IL Farmaco. 2002;57:539.
14. Falaska F, Sahin G, Kelicon P, Durllu NT and Attinok G. IL Framaco. 2002;57:101.
15. Gomez –Gallego M, Mancheno MJ and Sierre MA. Tetrahedron. 2000;56:5743.
16. The organic chemistry of β-lactams. George GI. Ed., VCH Publishers: New York, 1993; De Kimpe, N. in "Azetidines, Azetines and Azetes in Comprehensive Heterocyclic Chemistry II, a review of the literature of 1982-1995, IB." Pergamon: Oxford, 1996.
17. Nakagava Y, Suzuki T and Tayama S. Toxicolo. 2000;156:27.
18. Rieger MM. Cosmetics and Toiletries. 1997;74:51.
19. Kimbrough DR. J Chem Educ. 1997;74:51.
20. Rajendra CS. Chem Abstr. 2000;133:345697.
21. Qianghua W and Baojum Q. J App Polym Sci. 2002;85:1581.
22. Eaton PE, Carlson GR and Lee JT. J Org Chem. 1973;38:4071.
23. Boger DL. J Org Chem. 1978;43:2296.
24. Ghinet A et al. Bioorg Med Chem. 2011;19:6042–6054.
25. Kulkarni. Orient J Chem. 2015;31(1):447-451.
26. J Org. Chem. 1997;62(11):3553.
27. J Org Chem. 1973;38(23):4072.
28. Pettit GR, Toki B, Herald DL, Verdier-Pinard P, Boyd MR, Hamel E and Pettit RK. J Med Chem. 1998;41:1688.
29. Wu M, Ji Q, Yang C and Xie Y. OPPI Briefs. 2005;37:272.
30. Rigby JH, Kotnis A and Kramer J. J Org Chem. 1990;55:5078
31. Perkin WH. Jr and Weizmann C. J Chem Soc. 1906;89:1649.
32. Aichaoui H, Lesieur D and Hénichart JP. J Heterocycl Chem. 1992;29:171.
33. Aichaoui H, Poupaert JH, Lesieur D and Hénichart JP. Tetrahedron. 1991;47:6649.
34. Cf. PE. Eaton and Muller RH. J Amer Chem Soc. 1872;94:1014.
35. Groves JK. Chem SOCR. ev. 1972;1:73.
36. Eaton PE, Cooper GF, Johnson RC and Muller RH. J Org Chem. 1972;87:1947.
37. Organic Preparations and Procedures International. 2009;41:229–236.