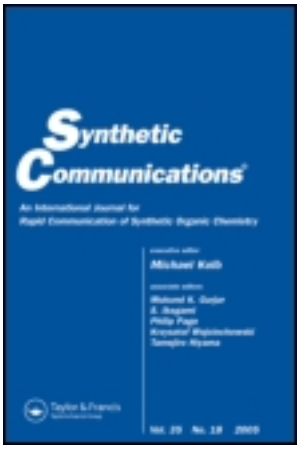


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

One-Pot Synthesis of 3-Phenacylphthalides

Madhusudan V. Paradkar [a], Suhas Y. Gadre [a], Twarita A. Pujari [a], Priti P. Khandekar [a] & Virendra B. Kumbhar [a]

[a] Department of Chemistry, Post Graduate & Research Center, A.G. College, Karve Road, Pune, 411 004, India

Version of record first published: 28 Jul 2007

To cite this article: Madhusudan V. Paradkar, Suhas Y. Gadre, Twarita A. Pujari, Priti P. Khandekar & Virendra B. Kumbhar (2005): One-Pot Synthesis of 3-Phenacylphthalides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:3, 471-474

To link to this article: http://dx.doi.org/10.1081/SCC-200048976

Synthetic Communications®, 35: 471–474, 2005

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1081/SCC-200048976

Taylor & Francis
Taylor & Francis Group

One-Pot Synthesis of 3-Phenacylphthalides

Madhusudan V. Paradkar, Suhas Y. Gadre, Twarita A. Pujari, Priti P. Khandekar, and Virendra B. Kumbhar
Department of Chemistry, Post Graduate & Research Center, A.G. College, Pune, India

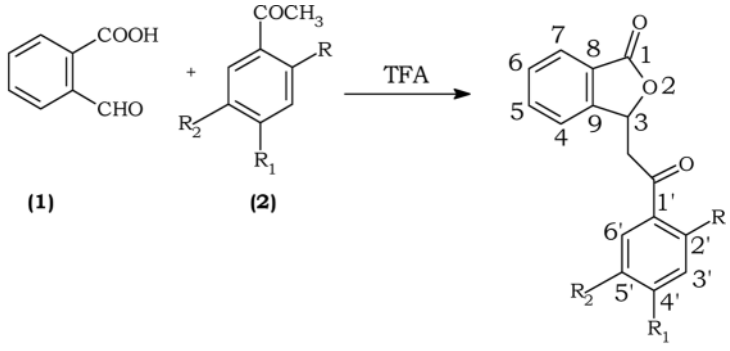
Abstract: Acid catalyzed condensation of phthalaldehydic acid (**1**) with aromatic methyl ketones (**2**) providing 3-phenacylphthalides (**3**) is described.

Keywords: One-pot synthesis, 3-phenacylphthalides, phthalaldehydic acid

3-aryl phthalides are widely accepted synthons for the elaboration to polycyclic compounds. 3-phenacylphthalides, i.e., 3-[2-Oxo-2-phenyl-ethyl 3H isobenzofuran 1-one], and its derivatives are used as softening agents.[1] These phthalides are easily converted into a) 3-phenacylidene phthalides, known for their plant growth regulatory activity[2,3] b) 3-alkylidene phthalides, known for their biological importance,[4] and c) 3-styryl phthalides which are used as color formers for heat and pressure-sensitive recording materials.[5] The literature survey revealed that 3-phenacylphthalides are synthesized by reacting 2-bromo benzaldehyde with 1,3 dicarbonyl compounds under catalytic[6] conditions in the presence of alkali.[2,7] The method to obtain 3-phenacylphthalides in one step was not reported yet. Recently we reported that the reaction of phthalaldehydic acid with various aromatic methyl ethers in the presence of TFA provided 3-aryl phthalides in good yields.[8] This observation led us to explore the reaction of phthaladehydic acid (**1**) with acetophenone which gave 3-phenacylphthalide (**3a**) in 69% yield. Substituted acetophenones (**2b**–**2f**) and phthaladehydic acid gave

Received in India September 25, 2004
Address correspondence to Suhas Y. Gadre, Department of Chemistry, Post Graduate & Research Center, A.G. College, Karve Road, Pune 411 004, India. E-mail: syg46@rediffmail.com

products (**3b–3f**) which were fully characterized by ^{1}H NMR, ^{13}C NMR, IR and elemental analysis.



(1) (2) (3)

a R=R_1=R_2=H d R=H, R_1=Cl, R_2=H

b R=H, R_1=CH_3, R_2=H e R=H, R_1=NO_2, R_2=H

c R=H, R_1=OCH_3, R_2=H f R=OH, R_1=H, R_2=CH_3

EXPERIMENTAL

General Procedure for the Synthesis of 3-Phenacylphthalides

A solution of phthalaldehydic acid (**1**) (3.3 mmol), aromatic methyl ketones (**2a–2f**) (3.3 mmol), in trifluoroacetic acid (13 mmol) was refluxed and monitored by TLC. The reaction mixture was cooled and was poured over crushed ice. The solid was filtered and recrystallized using hexane: ethyl acetate (80:20).

3-Phenacylphthalide (3a): 69% yield; M.P. 145°C;[9] IR (KBr); 1772, 1679 cm^{-1}, ^{1}H NMR ($CDCl_3$, 300 MHz). data δ 3.4 (dd, J = 17.3 Hz, 7.3 Hz, 1H), 3.8 (dd, J = 17.6 Hz, 5.57 Hz, 1H), 6.19 (t, J = 6.7 Hz, 1H), 7.4–7.8 (m, 6H), 7.9 (m, 3H). ^{13}C NMR (DMSO-d_6, 200 MHz); data 43.61 (-CH_2), 78.00 (C_3), 123.74–137.0 (C_4–C_9, $C_{1'}$–$C_{6'}$), 170.71 (lactone carbonyl), 197.30 (-CO-). Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.12; H, 4.76. Found: C, 76.02; H, 4.70.

3-(4-Methyl phenacyl)phthalide (3b) 68% yield; M.P. 149°C; IR (KBr); 1762, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz); data δ 2.5 (s, 3H), 3.4 (dd, J = 17.6 Hz, 7.61 Hz, 1H), 3.8 (dd, J = 17.6 Hz, 5.6 Hz, 1H), 6.22 (t, J = 6.7 Hz, 1H), 7.25–7.35 (m, 2H), 7.5–7.8 (m, 3H), 7.9 (m, 3H). ^{13}C NMR (DMSO-d_6, 200 MHz); data 22.0 (-CH_3), 43.31 (-CH_2), 78.17 (C_3), 123.73–135.27 (C_4–C_9, $C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{5'}$, and $C_{6'}$), 145.10 ($C_{4'}$), 170.85 (lactone carbonyl), 196.83 (-CO-). Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.69; H, 5.2. Found: C, 76.60; H, 5.13.

3-(4-Methoxy phenacyl)phthalide (3c): 81% yield; M.P. 120°C[3]; IR (KBr); 1760, 1666 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz); data δ 3.35 (dd, J = 17.6 Hz, 7.6 Hz, 1H), 3.75 (dd, J = 17.6 Hz, 5.6 Hz, 1H), 3.83 (s, 3H), 6.18 (t, J = 5.6 Hz, 1H), 6.95 (d, 2 H), 7.65 (m, 3H), 7.95 (m, 3H). ^{13}C NMR ($CDCl_3$, 200 MHz); data 43.61 (-CH_2), 55.96 (-OCH_3), 77.84 (C_3), 114.35 ($C_{3'}$, $C_{5'}$), 123.35–134.69 (C_4–C_9, $C_{1'}$, $C_{2'}$, and $C_{6'}$), 164.44 ($C_{4'}$), 170.65 (lactone carbonyl), 194.82 (-CO-). Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.34; H, 4.96. Found: C, 72.14; H, 4.88.

3-(4-Chlorophenacyl)phthalide (3d): 77% yield; M.P. 146°C; IR (KBr); 1751, 1681 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) data δ 3.38 (dd, J = 17.6 Hz, 7.0 Hz, 1H), 3.76 (dd, J = 17.6 Hz, 5.86 Hz,1H), 6.16 (t, J = 6.5 Hz, 1H), 7.44–7.72 (m, 5H), 7.88–7.96 (m, 3H).^{13}C NMR (DMSO-d_6, 200 MHz); data 43.67 (-CH_2), 77.88 (C_3), 123.75–139.50 (C_4–C_9 and $C_{1'}$–$C_{6'}$), 170.65 (lactone carbonyl), 196.36 (-CO-). Anal. Calcd. for $C_{16}H_{11}O_3Cl$: C, 67.01; H, 3.83. Found: C, 66.97; H, 3.78.

3-(4-Nitrophenacyl)phthalide (3e): 86% yield; M.P. 210°C; IR (KBr); 1747, 1689 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz); data δ 3.46 (dd, J = 17.6 Hz, 6.4 Hz, 1H), 3.78 (dd, J = 17.6 Hz, 6.5 Hz, 1H), 6.17 (t, J = 6.5 Hz, 1H), 7.55–7.72 (m, 3H), 8.10 (m, 3H) 8.40 (d, J = 8 Hz, 2H). ^{13}C NMR (DMSO-d_6, 200 MHz); data 44.20 (-CH_2), 77.68 (C_3), 123.76–135.25 (C_4–C_9, $C_{2'}$, $C_{3'}$, $C_{5'}$, and $C_{6'}$), 141.51 ($C_{1'}$), 151.62 ($C_{4'}$) 170.62 (lactone carbonyl), 196.66 (-CO-). Anal. Calcd. for $C_{16}H_{11}NO_5$: C, 64.65; H, 3.7. Found: C, 64.58; H, 3.68.

3-(2-Hydroxy-5-methylphenacylphthalide (3f): 56% yield; M.P. 132–135°C; IR (KBr); 1755.1 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz); data δ 2.3 (s, 3H), 3.48 (dd, J = 17.6 Hz, 6.7 Hz, 1H), 3.82 (dd, J = 17.6 Hz, 6.1 Hz, 1H), 6.21 (t, 6.7 Hz, 1 Hz, 1H), 7.45–7.80 (m, 5H), 8 (d, J = 7.9 Hz, 2H), 12 (s, 1H). ^{13}C NMR (DMSO-d_6, 200 MHz); data s20.73 (-CH_3), 45.11 (-CH_2), 77.78 (C_3), 118.38–137.7 (C_4–C_9, $C_{1'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, and $C_{6'}$), 159.17 ($C_{2'}$), 170.63 (lactone carbonyl), 201.92 (-CO-). Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.34; H, 4.96. Found: C, 72.28; H, 4.90.

ACKNOWLEDGMENT

We are thankful to Dr. A. S. Inamdar, principal, and Dr. H. G. Damle, head, Department of Chemistry, Abasaheb Garware College, Pune, for providing the necessary facilities. We are also thankful to the Department of Chemistry, University of Pune, for providing spectral and elemental analyses.

REFERENCES

1. Haber, R. G.; Ebnother, A.; Schmid, H. Die Synthese Von (±) Eleutherol. Inhaltsstoffe aus Eleuthrine bulbosa (Mill) Urb.VIII). *Helv. Chim. Acta* **1956**, *39*, 1529.

2. Bousquet, E. W.; Moran, M. D.; Harmon, J.; Johnson, A. L.; Summers, J. C. Synthesis of 3,3a-dihydro-8H-Pyrazolo[5,1-a] isoindol-8-ones and 8H-pyrazolo [5,1-a] isoindol-8-ones. *J. Org. Chem.* **1975**, *40*, 2208.
3. Houbin, J. A.; Dayawan, M. W. Use of substituted 3-phenacylidenephthalides as corn plant growth regulants. U.S. Patent, 4,255,181, March 10, 1981(Monsanta Co.).
4. Mali, R. S.; Patil, S. R.; Kulkarni, B. K.; Yeola, S. M. A useful synthesis of naturally occurring 3-alkylidenephthalides. *Indian J. Chem.* **1990**, *29B*, 319.
5. Mali, R. S.; Massey, A. P. Convenient Synthesis of 3-stryrilphthalides. *Syn. Comm.* **1997**, *27* (6), 1049.
6. Lee, D. Y.; Cho, C. S.; Jiang, L. H.; Wu, X.; Shim, S. C.; Oh, D. H. Palladium-Catalysed synthesis of 3-alkyphthalides via carbonylative cyclization of o-bromo-benzaldehyde with 1,3-dicarbonyl compounds. *Syn. Comm.* **1997**, *27* (19), 3449–3455.
7. Chatterjea, J. N.; Bhakta, S. C.; Chattopadhyay, A. K. Napthoisocoumarins and related compounds. *J. Indian Chem. Soc.* **1974**, *LI*, 757.
8. Paradkar, M. V.; Ranade, A. A.; Joseph, A. R.; Kulkarni, M. S.; Godbole, H. M. Efficient synthesis of 3-arylphthalides. *J. Chem. Research (S)* **1998**, 332.
9. Geigy, J. R. 5,6,7,12-Tetrahydrodibenzo [a,d] Cycloocten-12-one. *Swiss 407, 101. Chem. Abstr.* **1967**, *66*, 10791 mA-G (by W. Schindler and Honsblattner).