



RESEARCH ARTICLE

Synthesis and Characterization of Novel 3-Substituted 2,4-Pentane Diones

Bhatt ND^{*1}, Nimavat K²

^{*1}*Research Schlolar, JJT University, Jhunjhunu-333001, Rajasthan, India.*

¹*Govt. Science College, Gandhinagar, Gujarat, India.*

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ABSTRACT

The synthesis of novel 3-substituted 2,4-pentane diones **2(a-g)** were achieved by the reaction of 2-(2,4-dioxopentan-3-yl)benzoic acid (**1**) with various Alcohols using Dry HCl gas as a catalyst. The formations of products have been confirmed on the basis of spectral characterized by ¹H NMR and Elemental analysis.

KEYWORDS

3-substituted 2,4-pentane diones, Alkyl 2-(2,4-dioxopentan-3-yl)benzoate.

INTRODUCTION

Acetylacetone is an organic compound that famously exists in two tautomeric forms that rapidly interconvert. The less stable tautomer is a diketone formally named pentane-2,4-dione. The more common tautomer is the enol form. The pair of tautomers rapidly interconverts and is treated as a single compound in most applications. It is a colourless liquid that is a precursor to acetylacetonate (acac), a common bidentate ligand. It is also a building block for the synthesis of heterocyclic compounds. 1,3-Disubstituted propane-1,3-diones are classic examples of precursors for the synthesis of mesogenic heterocycles or metallomesogenic derivatives. Mesogenic pyrazoles and isoxazoles obtained via beta-diketones have been described previously in the literature^{1,2} and beta-diketones have been widely used as organic ligands in mesogenic

co-ordination complexes of some transition metals such as Cu(II), Tl (I), Cr(III), V(IV), and Pd-(II).

The reaction of acetylacetone with aryl halides has been known only in cases of aryl halides substituted with a carboxy group in the ortho-position in the presence of Cu(II) derived from disproportionation of Cu(I). In such a case, it was presumed that a carboxylate anion would be concerned in reaction. Some preparations of arylacetones have been reported³⁻⁶

In the course of our research program involving the synthesis of novel molecules, we wished to use different beta-diketone derivatives as synthetic intermediates. An investigation of a new efficient synthetic molecule of arylacetones gives us interesting useful intermediates for drug synthesis of central nervous agents.

In this paper, we wish to report an efficient, synthesis of esters of 3-substituted arylacetones from the reaction of aryl halides with acetylacetone then its esterification. (Scheme 1)

***Address for Correspondence:**

Bhatt Nilay D.
Research Schlolar,
JJT University, Jhunjhunu-333001,
Rajasthan, India.
E-Mail Id: nilay1381@gmail.com

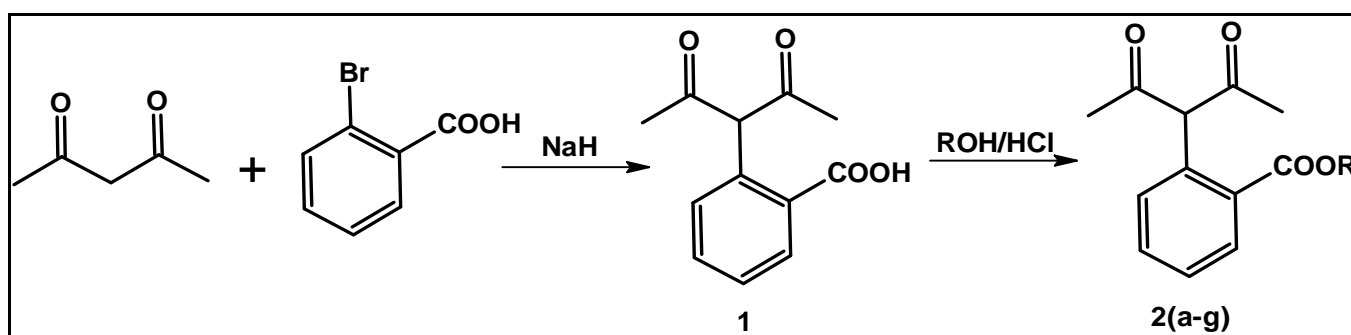
MATERIALS AND METHODS

All chemicals were purchased from commercial suppliers and used without further purification. Melting points were determined using a Veeco microprocessor based melting point and are uncorrected. MS and MS/MS spectra samples were recorded on Waters LCMS-Q-TOF instrument in only positive ion detection mode. ^1H and ^{13}C NMR-spectra were recorded either in CDCl_3 on a Bruker Avance II 500 (500MHz) spectrometer and chemical shifts are reported in ppm. IR spectra recorded on Perkin Elmer spectrometer as a KBr pellet.

filtered using Celite bed. Excess of acetyl acetone was extracted using Ether. Remaining aqueous layer was acidified using concentrated hydrochloric acid solution. Part of the oily residue slowly gets crystallized to get crude 2-(2,4-dioxopentan-3-yl)benzoic acid as light brown coloured solid. Recrystallization from MeOH:Water gave 17.0gm of pure compound. M.P: $141-42^\circ\text{C}$, Yield: 62%.⁷

General procedure for the preparation of Alkyl 2-(2,4-dioxopentan-3-yl)benzoate

A mixture consisting of 5.0gm (0.022 mole) 2-(2,4-dioxopentan-3-yl)benzoic acid in 50ml



Scheme 1: The synthetic route to the target compounds 2a-g.

Experimental

Melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used were laboratory grade. ^1H NMR spectra were recorded on a Bruker 300MHz spectrometer using TMS as an internal standard in CDCl_3 and DMSO-d_6 . Elemental analysis was performed on a Perkin Elmer 2400 Series II instrument.

Procedure for the preparation of 2-(2,4-dioxopentan-3-yl)benzoic acid

A mixture consisting of 25gm (0.12mole) 2-bromo benzoic acid, 1.0gm (4% w/w) of Copper (I) Iodide, and 150ml of acetylacetone was vigorously stirred while being treated with 12.43gm (0.31mole) of Sodium hydride (60% in Paraffin oil). The Solid was added in such a manner that the temperature of reaction mixture maintained between $50-55^\circ\text{C}$. Heated the reaction mixture at $80-85^\circ\text{C}$ for 5hrs. After cooling, the reaction mixture was quenched in 500ml Water. Some insoluble suspension was

(5 Vol) of alcohol was saturated with Dry HCl gas and refluxed for 6.0 hrs. Reaction progress was monitored on TLC. Hexane: Ethylacetate (80:20). After completion of reaction solvent was completely evaporated under reduced pressure to get crude Alkyl 2-(2,4-dioxopentan-3-yl) benzoate. Recrystallization from Ethyl acetate:Hexane gave pure compound.

Analytical Data

Methyl 2-(2,4-dioxopentan-3-yl)benzoate:(2a)

Mol. Wt: 234.24; Yield 89 % R_f 0.80; ^1H NMR (δ ppm): 2.08 (s,6H,Di-Methyl), 3.83 (s,3H,-OCH₃), 5.51 (s,1H,-CH-), 7.05-7.96 (m,4H,Aromatic); Elemental analysis for $\text{C}_{13}\text{H}_{14}\text{O}_4$; Calculated: C, 66.66; H, 6.02; O,27.32 Found: C, 66.39; H, 6.30; O,27.26

Ethyl 2-(2,4-dioxopentan-3-yl)benzoate:(2b)

Mol. Wt: 248.27; Yield 87 % R_f 0.80; ^1H NMR (δ ppm): 1.32 (t,3H,-CH₃), 2.09 (s,6H,Di-Methyl), 4.36 (q,2H,-OCH₂), 5.48 (s,1H,-CH-), 7.15-8.03 (m,4H,Aromatic); Elemental analysis

for C₁₄H₁₆O₄; Calculated: C, 67.73; H, 6.50; O, 25.78 Found: C, 67.31; H, 6.33; O, 25.56

Propyl 2-(2,4-dioxopentan-3-yl)benzoate:(2c)
Mol. Wt: 262.30; Yield 80 % R_f 0.80 ; ¹H NMR (δppm): 1.05 (t, 3H, -CH₃), 1.73 (m, 2H, -CH₂-), 2.10 (s, 6H, Di-Methyl), 4.27 (t, 2H, -OCH₂), 5.49 (s, 1H, -CH-), 7.13-8.07 (m, 4H, Aromatic); Elemental analysis for C₁₅H₁₈O₄; Calculated: C, 68.68; H, 6.92; O, 24.40 Found: C, 68.43; H, 6.64; O, 24.53

Isopropyl 2-(2,4-dioxopentan-3-yl)benzoate:(2d) Mol. Wt: 262.30; Yield 83 % R_f 0.80 ; ¹H NMR (δppm): 1.15 (d, 6H, -(CH₃)₂), 3.96 (m, 1H, -O-CH-), 2.12 (s, 6H, Di-Methyl), 5.46 (s, 1H, -CH-), 7.16-8.17 (m, 4H, Aromatic); Elemental analysis for C₁₅H₁₈O₄; Calculated: C, 68.68; H, 6.92; O, 24.40 Found: C, 68.36; H, 6.77; O, 24.29

Butyl 2-(2,4-dioxopentan-3-yl)benzoate:(2e)
Mol. Wt: 276.32; Yield 75 % R_f 0.80 ¹H NMR (δppm): 0.9 (t, 3H, -CH₃), 1.51 (m, 2H, -CH₂-CH₃), 2.11 (s, 6H, Di-Methyl), 4.20 (t, 2H, -OCH₂), 5.49 (s, 1H, -CH-), 7.18-8.21 (m, 4H, Aromatic); Elemental analysis for C₁₆H₂₀O₄; Calculated: C, 69.54; H, 7.30; O, 23.16 Found: C, 69.65; H, 7.38; O, 23.09

Tert-butyl 2-(2,4-dioxopentan-3-yl)benzoate:(2f) Mol. Wt: 276.32; Yield 79 % R_f 0.80 ; ¹H NMR (δppm): 1.49 (s, 9H, -(CH₃)₃), 2.12 (s, 6H, Di-Methyl), 5.46 (s, 1H, -CH-), 7.11-8.13 (m, 4H, Aromatic); Elemental analysis for C₁₆H₂₀O₄; Calculated: C, 69.54; H, 7.30; O, 23.16 Found: C, 69.76; H, 7.28; O, 23.19

Iso-butyl 2-(2,4-dioxopentan-3-yl)benzoate:(2g) Mol. Wt: 276.32; Yield 78 % R_f 0.80; ¹H NMR (δppm): 0.99 (d, 6H, -(CH₃)₂), 2.12 (s, 6H, Di-Methyl), 2.37 (m, 1H, -CH-(CH₃)₂), 3.92 (d, 2H, -O-CH₂), 5.49 (s, 1H, -CH-), 7.19-8.21 (m, 4H, Aromatic); Elemental analysis for C₁₆H₂₀O₄; Calculated: C, 69.54; H, 7.30; O, 23.16 Found: C, 69.71; H, 7.42; O, 23.33

RESULTS AND DISCUSSION

The different Alkyl 2-(2,4-dioxopentan-3-yl)benzoate were synthesized by the esterification of 2-(2,4-dioxopentan-3-yl)benzoic acid in presence of dry HCl gas with

various alcohols. The purity of compounds was analyzed by TLC. The structures of the synthesized compounds **2a-g** were confirmed on the basis of spectral and elemental analysis. In ¹H NMR spectrum the appearance of signal at δ 2.10 (s, 6H, Di-Methyl), 5.5 (s, 1H, -CH-), 7.0-8.2 (m, 4H, Ar-H) along with respective peaks of alkyl protons in the region of 0.9-3.0 ppm confirms the presence of ester group on aromatic ring attached to 2,4-pentane dione.

CONCLUSION

Thus a series of novel Alkyl 2-(2,4-dioxopentan-3-yl)benzoate derivatives were designed and synthesized, and their structures were confirmed by ¹H NMR and elemental analysis. The modification of the active methylene group of 2,4-pentane dione offers a promising and useful intermediate for the formation of new chemical entities.

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