SYNTHESIS OF THIOPHENOACETYL-1,4-BENZOQUINONES

P. Khatri[a], Ignatious Abraham[a], P. Pardasani[a] R.T. Pardasani[a]*, and T. Mukherjee[b]
[a] Department of Chemistry, University of Rajasthan, Jaipur – 302004, India
[b] Chemistry Division, Bhabha Atomic Research Centre, Mumbai – 400085, India
Email: pardasanirt@satyam.net.in

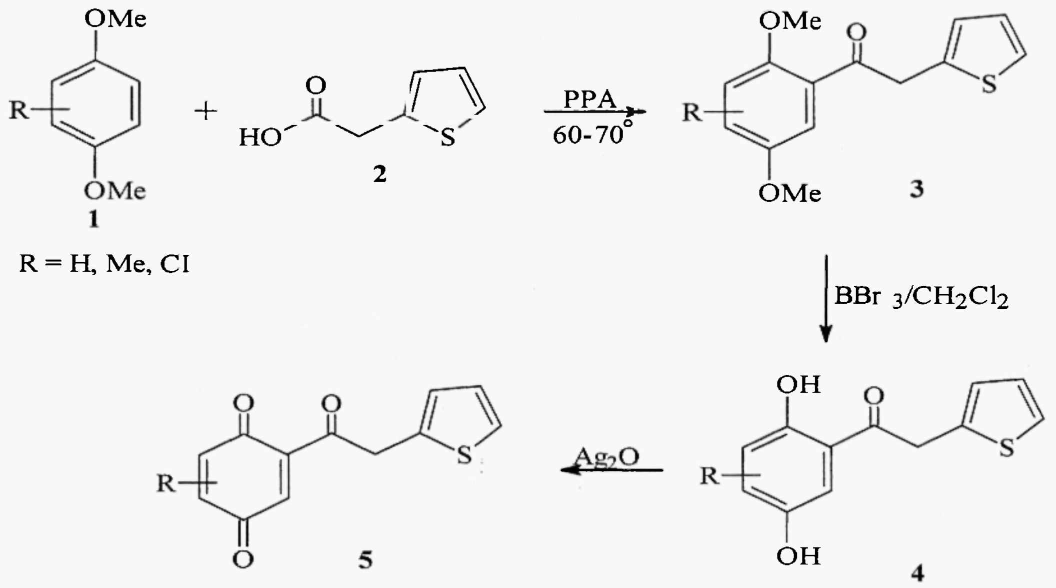
Abstract : A convenient three step synthesis of 2-(2`-thiophenoacetyl)-1,4-benzoquinone and derivatives *via* readily available starting materials is described. The synthesized quinones have been characterized by spectral data.

Introduction

Quinones are known for their medicinal properties (1-3) and work as good dienophiles in Diels-Alder cycloaddition reactions (4). Quinones can form the foundation upon which new molecules of natural interest can be constructed, for example, maturinone and derivatives are important class of heterocyclic quinones. Besides a considerable interest has been evoked in understanding the radiolytic behavior of these quinone systems because they are known to act as very efficient electron accepting agents (5). A sufficient amount of research has gone into elucidating the molecular mechanics of action of quinone based antitumour drugs (6). The quinone ring as well as carbonyl group are much prone to reduction with an electron. We have examined (7) pulse radiolytic behaviour of a few quinones but work on the effect of chain lengthening in the carbonyl moiety of quinone has remained unexplored. Keeping these observations in mind and in pursuit of our interest on quinone studies and [3+2] cycloaddition reactions (8-10), a number of thiophenoacetyl-1,4-benzoquinones have been synthesized. These quinones may act as good precursors for photochemical [3+2] cycloaddition reactions leading to maturinone analogues as well as flash photolytic studies.

Results and Discussions

Our approach towards the synthesis of quinones employ three steps to secure the target molecules from readily available precursors :



Condensation between an appropriate thiophene-2/3-acetic acid **2** with a suitable 1,4-dimethoxybenzene derivative **1** in the presence of polyphosphoric acid at 60-70° under stiring for 6-7 hrs afforded dimethoxyketones **3** in 65-71% yield. Their IR spectra exhibited a strong band in the region 1690-1660cm^{-1} due to υC=O. In the PMR spectra, the methoxy protons appeared as two separate sharp singlets at δ3.72-3.90; the methylene protons appeared as singlet at δ4.07-4.30, aromatic 3-, 4- and 6-H at δ 7.1-7.4 and heteroprotons 2'-, 3'-,4'- and 5-'H at δ 7.4-8.0 ppm, a singlet at δ 2.1-2.2 was assigned to methyl protons.

Dimethylation of ketones **3** was carried out by stirring their solution in dichloromethane with an excess of boron tribromide at 0^0 C for 5-7 hrs. The hydroquinones **4** were obtained as yellow-orange crystals in 60-89% yield. The formation of hydroquinones was easily ascertained by disappearance of methoxy singlets in PMR and appearance of a broad singlet at δ 11.1-12.5 ppm for hydrogen bond OH as well as appearance of a medium band in IR around 3350-3330 cm^{-1} due to υOH.

The quinones **5** were prepared by the oxidation of the corresponding hydroquinones **4** using 5-8 fold excess of silver oxide at room temperature in benzene in 55-82% yield. The absence of broad peaks in the region 3350-3330 cm^{-1} in the IR spectra of these quinones shows the disappearance of hydroxyl group whereas the quinonoid carboxyl stretching bands appeared at 1690-1650 cm^{-1}. In the PMR spectra, the hydroxy signals in the range of δ 11.1-12.5 ppm were absent and the quinonoid protons appeared at δ 6.75-7.15 either as multiplet or as broad singlet with some fine structure. The hetero protons appeared in the range δ 7.5-8.0 ppm. In the mass spectrum of thiophenoacetyl-1,4-benzoquinone, the base peak appeared at m/z 125 due to α-cleavage (route-a, Figure-1). An intense peak at m/z 150 was noticed due to elimination of $C_4H_2O_2$ fragment (route-b). A prominent peak at m/z 204 was due to loss of CO moiety from the molecular ion peak (route-c). A peak corresponding to m/z 206 appeared due to cleavage-d. Besides, all usual fragments appeared at their appropriate m/z values. In addition all the compounds showed satisfactory elemental analysis. The characteristic data are given in Table-1.

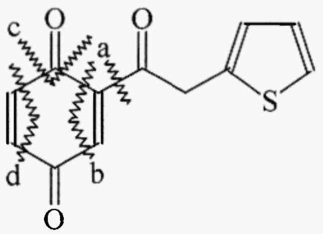
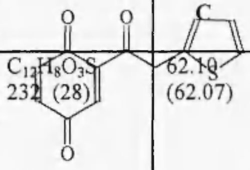
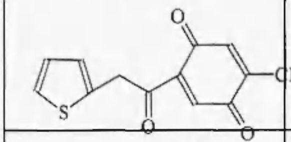
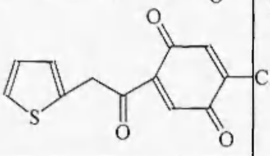
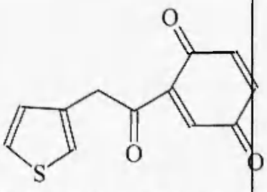
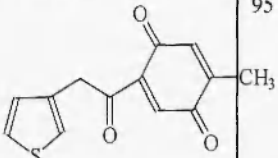
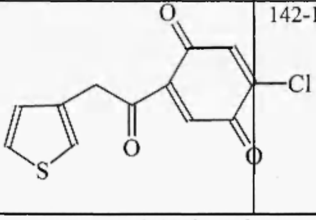


Figure-1 : Mass fragmentation pattern of thiophenoacetyl-1,4-benzoquinone

Experimental

The uncorrected melting points were taken in open glass capillaries. The IR spectra were recorded on a Nicolet Magna IR Spectrometer Model 550 in KBr pellets and band positions are reported in wave numbers (cm^{-1}). The ^{1}H NMR spectra have been recorded on a Bruker 300 MHz in $CDCl_3$ using tetramethylsilane as an internal standard. The chemical shifts are given in δ ppm values. Mass spectra were recorded on a Varian Met 711 mass spectrometer. Elemental analyses were performed on a Perkin Elmer Series C, H, N, S Analyzer 2400. Column chromatography was performed on silica gel 60 (Merck).

Table-1 : Characterization data for thiophenoacetyl-1,4-benzoquinones 5

Compound	M.P.^{0}C	% yield	Molecular ion	**Analysis: Found/Cald.**		PMR (δ, ppm)
				C	**H**	
	97-98	74	 $C_{12}H_8O_3S$ 232 (28)	62.10 (62.07)	3.42 (3.45)	4.3 (s, CH_2),7.04(bs, H-3+5+6), 7.15(dd,J_1=4.0Hz,J_2=1.542, H-4'),7.4(d,J=4.0Hz, H-5'),7.82(d,J=1.5Hz, H-3')
	107	81	$C_{13}H_{10}O_3S$ 246 (31)	63.34 (63.41)	4.03 (4.06)	2.1(d, J=1.6Hz, 5-CH_3), 4.17(s, CH_2) 6.82(q, J=1.6Hz, H-6), 7.0(s, H-3), 7.3 (m, H-4'), 7.54 (dd,J_1=3.7 Hz, J_2=1.5Hz, H-5'),7.9 (d,J=1.7 Hz, H-2')
	137-138	57	$C_{12}H_7ClO_3S$ 266.5 (14)	54.09 (54.03)	2.59 (2.63)	4.07 (s, CH_2), 6.9 (s, H-3), 7.1(s,H-6),7.4 (m, H-4'+5'), 7.94 (d,J=1.5Hz, H-3')
	114	63	$C_{12}H_8O_3S$ 232 (26)	62.02 (62.07)	3.40 (3.47)	4.25 (s,CH_2), 7.0(s with fine structure, H -3+5+6), 7.5(m, H-4'+5'), 7.8(d, J=1.5Hz, H-2')
	95	69	$C_{13}H_{10}O_3S$ 246 (36)	63.38 (63.41)	4.00 (4.06)	2.2 (d,J=1.7Hz, 5-CH_3), 4.03(s, CH_2), 6.75 (q, J=1.7Hz, H-6), 6.98(s, H-3), 7.4 (m, H-4'+5'), 7.96 (d, J=1.5Hz, H-2')
	142-143	55	$C_{12}H_7ClO_3S$ 266.5 (12)	54.08 (54.03)	2.60 (2.63)	4.1 (s, CH_2), 6.97 (s, H-3), 7.15 (s, H-6), 7.52 (m, H-4'+5'), 8.0 (d, J=1.5 Hz, H-2')

* Values in parentheses denote relative intensitie

In summary, a convenient and high yielding synthesis of thiophenoacetyl–1,4-benzoquinones has been accomplished from readily available starting materials and their application to the cycloaddition and pulse radioilytic studies is currently under progress.

The following procedure is representative. A mixture of an appropriate acid **2** (0.011 mol), suitable dmethoxybenzene derivative **1** (0.01 mol) and polyphosphoric acid (25 ml) was heated at 70-80^0 C with vigorous mechanical stirring on an oil bath for 6-7 hrs. The colour of the reaction mixture gradually changed from yellow to red. The reaction mixture was then poured into 250 ml of hot water with continuous stirring and then allowed to cool. It was extracted with diethyl ether (4x25 ml), and then the ether layer was washed with sodium bicarbonate solution (2x25 ml) to remove excess of acid and finally with water (2x25 ml) and then dried over anhydrous sodium sulfate. Filtration and evaporation of the solvent afforded the dimethoxyketones **3** which were purified by column chromatography using petroleum ether-chloroform (5:1) as eluent.

To a solution of the ketone **3** (0.01 mol) in dry methylene chloride (10 ml) at 0^0 C was added dropwise a solution of boron tribromide (0.03 mol) in dry methylene chloride (15 ml). The resultant red solution was stirred for 5-7 hrs. and further decomposed with cold water (25 ml). After separating aqueous layer, the organic layer was washed with water (3x25 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give **4** as yellow orange crystalline solids in 60-89% yield.

A mixture of hydroquinone **4** (0.005 mol), silver oxide (0.02-0.04 mol), anhydrous sodium sulfate (1.7 gm) in dry benzene (25 ml) was shaken at room temp. for 6 hrs under aluminium foil cover. The products **5** in benzene were filtered through celite, concentrated and crystallised from pet.ether-chloroform as yellow orange crystalline solids, yield 55-82%.

Acknowledgements

The authors are thankful to the BRNS, Department of Atomic Energy, Mumbai for financial support.

References

1. K. Kobayashi, H.Shimizu, A.Sasaki and H.Suginome, J.Org.Chem., **58**, 4614 (1993).
2. S.Patai and Z.Rppoport (Eds.) l; The Chemistry of Functional Groups. The Chesmistry of Quinonoid Compounds, John-Wiley and Sons, New York, **Vol.2**,1988.
3. R.H.Thomson, Naturally Occurring Quinones, Chapman and Hall, London, **Vol.3**,1987.
4. W.Carruthers, Cycloaddition Reations in Organic Synthesis, Pergamon, Oxford,1990.
5. T.Mukherjee, Physical and Theoretical Chemistry, Elsevier Science, **87**, pp 287-317(2001).
6. T.Itoh, Chem. Rev., **95**, 235 (1995).
7. M.C.Rath, T.Mukherjee, R.Ghosh, S.Muktawat, P.Pardasani, and R.T.Pardasani, Res.Chem.Intermed. **27**, 379 (2001).
8. R.T.Pardasani, P.Pardasani, M.M.Agarwal and G.Mathur, Indian J.Chem., **40B**, 518 (2001).
9. R.T. Pardasani, P. Pardasani, V. Chaturvedi, S.K. Yadav, A. Saxena and I. Sharma Heteroatom Chem., **14**, 36 (2003); R.T. Pardasani, P. Pardasani, D. Sherry and V. Chaturvedi, Synth. Commun, **32**, 435, (2002).
10. R.T. Pardasani, P. Pardasani, Abhinandan Jain and S. Kohli, P, S and Si and the Related Elements, **179,** 1569, (2004); R.T. Pardasani, P. Pardasani, B. Gupta, A.V. Londhe and S. Kohli, Indian J. Chem. **44B**, 1252 (2005).

Received on January 20, 2006