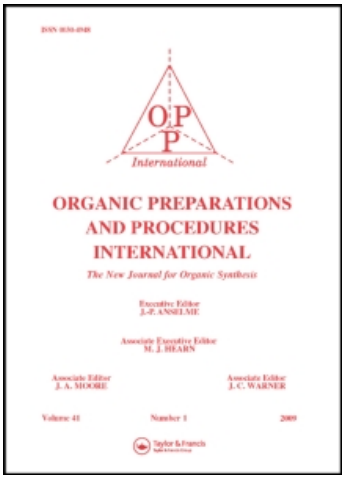

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

Thermal and Photochemical Approaches to the Synthesis of *vic*-Tricarbonyl Compounds from 4-Hydroxyquinolin-2(1*H*)-ones

Jia-Hai Ye[a]; Zhichun Qin[a]; Bin Zhou[a]; Wenchao Zhang[a]; Guirong Tian[a]; Lei Yuan[a]; Jian-Hua Xu[b]
[a] Department of Applied Chemistry, Nanjing University of Science and Technology, Nanjing, P. R. China [b] Department of Chemistry, Nanjing University, Nanjing, P. R. China

To cite this Article Ye, Jia-Hai , Qin, Zhichun , Zhou, Bin , Zhang, Wenchao , Tian, Guirong , Yuan, Lei and Xu, Jian-Hua(2009) 'Thermal and Photochemical Approaches to the Synthesis of *vic*-Tricarbonyl Compounds from 4-Hydroxyquinolin-2(1*H*)-ones', Organic Preparations and Procedures International, 41: 1, 83 — 87
To link to this Article: DOI: 10.1080/00304940802711085
URL: http://dx.doi.org/10.1080/00304940802711085

Organic Preparations and Procedures International, 41:83–87, 2009

ISSN: 0030-4948 print
DOI: 10.1080/00304940802711085

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Thermal and Photochemical Approaches to the Synthesis of *vic*-Tricarbonyl Compounds from 4-Hydroxyquinolin-2(1*H*)-ones

Jia-Hai Ye,[1] Zhichun Qin,[1] Bin Zhou,[1]
Wenchao Zhang,[1] Guirong Tian,[1] Lei Yuan,[1] and Jian-Hua Xu[2]

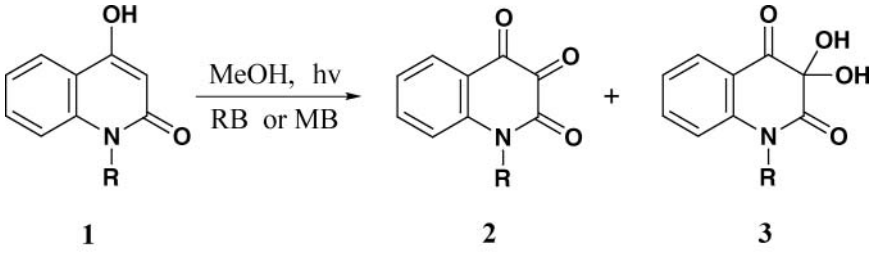
[1]Department of Applied Chemistry, Nanjing University of Science and Technology, Nanjing, P. R. China
[2]Department of Chemistry, Nanjing University, Nanjing, P. R. China

vic-Tricarbonyl compounds are important both as interesting synthetic intermediates and as biologically active compounds.[1–6] As a result, the investigation of synthetic methodology of vicinal triketones remains of current research interest. However, the preparation of *vic*-tricarbonyl compounds from 1,3-dicarbonyl compounds usually requires their initial transformation to an active precursor such as the keto-phosphorane or enamine, which is then readily oxidized to the tricarbonyls either thermally (*e.g.* by ozone) or photochemically.[7–12] Hypervalent iodine (V and III) compounds have also been used as alternative oxidants but the explosive character is a drawback for hypervalent iodine (V) and the employment of the ozone as the co-oxidant restricts practical application of hypervalent iodine (III).[13–14] Two decades ago, Wasserman *et al*. described the dye-sensitized photooxidation of cyclic enolic 1,3-dicarbonyl compound with singlet oxygen. However, for heterocyclic 1,3-dicarbonyl compounds, such as 4-hydroxycoumarin, none of the corresponding trione was obtained under this dye-sensitized reaction condition.[15] Shortly thereafter, Wamhoff *et al*. reported the synthesis of quinolinetriones from the singlet oxygen photolysis of dihalo-4-hydroxyquinolin-2(1*H*)-one.[16] With the goal of expanding the scope of an efficient route to *vic*-tricarbonyl compounds, we now report the convenient synthetic methods of *vic*-heterocyclic tricarbonyl compounds directly from enolic dicarbonyl compounds through photochemical and thermal approaches without the co-oxidant.

In the context of our research interest in the photochemistry of quinoline and isoquinoine derivatives,[17–18] the synthesis of *vic*-tricarbonyls was achieved from the reaction of 4-hydroxyquinolin-2(1*H*)-ones with singlet oxygen using methylene blue

Submitted November 1, 2007.
Address correspondence to Jia-Hai Ye, Department of Applied Chemistry, Nanjing University of Science and Technology, Nanjing 210094, P. R. China. E-mail: yejiahai@mail.njust.edu.cn

(MB) or rose bengal (RB) as the sensitizers. Irradiation of a solution of **1a** (0.05 mol L^{-1}) and the sensitizer RB (5×10^{-4} mol L^{-1}) in 20 ml methanol under oxygen atmosphere at room temperature with light of wavelength $>$ 500 nm resulted in smooth consumption of the starting material and gave the quinolin-2,3,4-trione **2a** (12%) and its hydrate **3a** (72%) as the products (*Scheme 1*). The RB sensitized photooxygenation of **1b** under

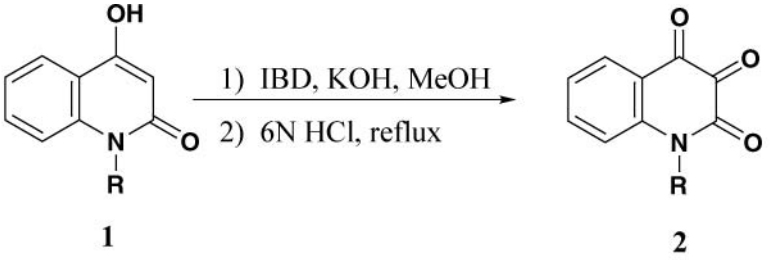


a) R = Me, b) R = Et, c) R = Ph

Scheme 1

similar conditions gave the corresponding triketone **2b** and its hydrate **3b** in 98% total yield. But only the corresponding triketone was obtained in the photooxygenation of **1c**. Photooxygenation of **1a**-**1c** in methanol with Methylene Blue (MB) as the sensitizer gave results similar to that with RB as a sensitizer but in slightly lower total yields (*Table 1*).

In addition to the dye-sensitized photooxidation of **1**, we next focused our interest on the thermal oxidation of **1**. After many usual oxidants were tested, inexpensive commercially available $PhI(OAc)_2$ (iodobenzene diacetate, IBD), was found to be an effective reagent for the oxidation of 4-hydroxyquinolin-2(1*H*)-ones. 4-Hydroquinolin-2-ones **1** was oxidized by IBD (1.5 equiv.) in the presence of base, followed by the hydrolysis using 6N HCl as the catalyst under reflux to afford the expected triketones **2** in moderate overall yield (*Scheme 2*). It should be noted that when the substitutent on nitrogen was Ph, the fully hydrated vicinal tricarbonyl compound (**2c**·$3H_2O$) was obtained.



a) R = Me (yield:61%), b) R = Et (yield:58%), c) R = Ph (yield:52%)

Scheme 2

In conclusion, the new efficient synthetic routes of vicinal heterocyclic tricarbonyl compounds from 4-hydroxyquinolin-2(1*H*)-ones through thermal and photochemical approaches were conveniently achieved.

Table 1
Dye-sensitized photooxygenation of **1**

Substrate	Sensitizer	Irradiation time (h)	Products and Yields (%)
1a	RB	26	2a (12), 3a (72)
1b	RB	21	2b (10), 3b (88)
1c	RB	42	2c (75)
1a	MB	42	2a (11), 3a (65)
1b	MB	38	2b (9), 3b (72)
1c	MB	35	2c (64)

Experimental Section

All commercial available reagents used were AR grade. MeOH and THF were distilled according to the standard method prior to use. Mps were measured on a YANACO microscopic melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Bruker 300 spectrometer in $CDCl_3$ with $SiMe_4$ as an internal standard. *J* values are given in Hz. IR spectra were taken on a Nicolet 5DXFT-IR spectrometer. Mass spectra were recorded on a VG ZAB-HS spectrometer. Elemental analyses were obtained using a Perkin-Elmer-240C analyzer.

General Procedure for the Preparation of 2 and 3.

(a) Photochemical Reaction. All the photolyses were carried out with light of wavelength longer than 300 nm from a 500 W medium-pressure mercury lamp in a cooled glass water-jacketed vessel. Solutions of 4-hydroquinolin-2-ones **1** (3 mmol) and RM or MB (0.03 mmol) in 100 ml methanol were placed in several glass tubes (20 ml each) and irradiated around the light source under constant dry oxygen bubbling. The course of reaction was monitored by TLC. At the end of the reaction, the solvent was removed and the residue was subjected to silica gel column chromatography with ethyl acetate and petroleum (b.p. 60–90°C) as eluent for gradient elution to afford the products **2** and **3**.

(b) Thermal Reaction. A mixture of IBD (3 mmol), KOH 6 mmol) and 4-hydroquinolin-2-ones **1** (2 mmol) was stirred in MeOH (15 ml) at 0°C, then for 12 h at room temperature. After the reaction was stopped, the solvent was removed *in vacuo* and water was added and the product was extracted with ethyl acetate (3×8 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and evaporated to give the crude compound. This crude compound was dissolved in 10 mL THF and 2 mL 6N HCl was added. The mixture was heated at 80°C for 2 h. Then the solvent was removed *in vacuo* and water was added and the product was extracted with ethyl acetate (3×10mL). The combined organic layer was dried over anhydrous $MgSO_4$ and evaporated to give crude product which was purified by column chromatography on silica gel with ethyl acetate and petroleum (bp 60–90°C) as eluent for gradient elution to give the product **2.**

N-Methylquinoline-2,3,4-trione (2a), mp. 125–127°C; IR: 3050, 2830, 1720, 1605, 1462, 1360, 1312, 1105, 1085, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.30 (3H, s, CH_3), 7.00–7.94 (4H, m, ArH); Mass Spec. m/z(EI): 161 (M-C = O, 33), 146 (19), 133(23), 104(100), 90(23), 77(33).

Anal. Calcd for $C_{10}H_7NO_3$: C, 63.49; H, 3.73; N, 7.40

Found: C, 63.63; H, 4.01; N, 7.41

N-Methyl-3,3-dihydroxyquinoline-2,3,4-trione (3a), mp. 82–84°C (decomposed); IR: 3340, 3100, 1708, 1640, 1600, 1472, 1385, 1295, 1100, 1025, 998, 770 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.35 (2H, br, 2OH), 3.48 (3H, s CH_3),7.25–8.33 (4H, m, ArH); Mass Spec. m/z(EI): 175 (M-H_2O, 14), 147 (14), 131 (48), 119 (100), 104 (89), 90 (72), 77 (83).

Anal. Calcd for $C_{10}H_9NO_4$: C, 57.97; H, 4.38; N, 6.76

Found: C, 57.99; H, 4.65; N, 6.47

N-Ethylquinoline-2,3,4-trione (2b), mp. 90–92°C; IR: 3065, 2988, 2938, 1736, 1609, 1469, 1356, 1286, 1216, 1195, 1089, 759 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.40 (3H, t, $J = 11.5$, CH_3), 3.81 (2H, q, $J = 11.5$, CH_2), 7.10–7.54 (2H, m, ArH), 7.70–8.00 (2H, m, ArH); Mass Spec. m/z(EI): 195 (M-C = O, 100), 167 (54), 139 (17), 115 (6), 90 (9), 77 (16).

Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89

Found: C, 65.25; H, 4.63; N, 6.80

N-Ethyl-3,3-dihydroxyquinoline-2,3,4-trione (3b), mp. 126–128°C; IR: 3330, 3100, 3060, 2900, 2800, 1708, 1618, 1595, 1460, 1395, 1270, 1180, 1000, 922, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.22 (3H, t, $J = 9.5$, CH_3), 4.02 (2H, q, $J = 9.5$, CH_2), 3.16 (2H, br, 2OH), 7.050–7.86 (4H, m, ArH); Mass Spec. m/z(EI): 189 (M- H_2O, 6), 161 (14), 133 (31), 104 (100), 90 (26), 77 (39).

Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73, H: 5.01; N, 6.33

Found: C, 60.02, H: 5.26; N, 6.08

N-Phenylquinoline-2,3,4-trione (2c), mp. 136–138°C; IR: 3030, 2800, 1715, 1603, 1460, 1355, 1295, 1175, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.00–7.81 (9H, m, ArH); Mass Spec. m/z(EI): 206 (M-C = O, 6), 175 (19), 145 (23), 132 (57), 119 (100), 90 (69), 77 (73).

Anal. Calcd for $C_{15}H_9NO_3$: C, 71.71; H, 3.61; N, 5.58

Found: C, 71.85; H, 3.45; N, 5.46

N-Phenylquinoline-2,3,4-trione trihydrates (2c), mp. 255–257°C; IR: 3432, 3050, 1722, 1693, 1597, 1490, 1460, 1336, 1297, 1246, 1069, 846, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.53 (9H, d, $J = 8.4$), 7.28–7.25 (13H, m, ArH+hydrates), 8.16 (1H, d, $J = 7.2$); Mass Spec. m/z(EI): 305 (10), 270 (100, M-H_2O-OH), 242 (15), 195 (21), 167 (8).

Anal. Calcd for $C_{15}H_{15}NO_6$: C, 59.01; H, 4.95; N, 4.59

Found: C, 58.85; H, 5.15; N, 5.60

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