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Electrosynthesis of New Xanthene-1,8(2*H*)-Dione Derivatives-A Green Chemistry Approach

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The xanthene-1,8(2*H*)-dione group is a constituent of the structures of a series of natural products with interesting biological and pharmacological activities such as anticoagulant, anticancer, spasmolytic, antianaphylactic, *etc*. The importance of these compounds has led many workers to synthesize these compounds using different methods. Each of the reported methods has its own merits and demerits, such as limitations of poor yields, difficult work-up and toxic. An efficient and convenient synthesis of tetrahydrobenzo[b]pyrans is described, using an electro generated base of the anion of dimedone in a one-pot, condensation of an aromatic aldehyde, and two molecules of dimedone compound. The reaction is carried out at room temperature in water/acetonitrile solution with the use of an anode in a single- compartment cell.

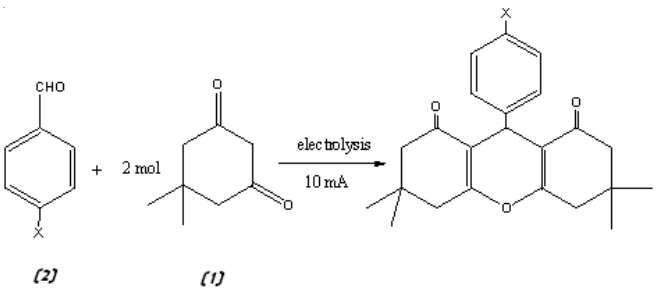
Key Words: Electrosynthesis, Xanthene-1,8(2*H*)-dione derivatives, Green chemistry, Electro generated base.

INTRODUCTION

The xanthene-1,8(2*H*)-dione group is a constituent of the structures of a series of natural products with interesting biological and pharmacological activities such as anticoagulant, anticancer, spasmolytic, antianaphylactic, *etc*.[1-4] Furthermore, these compounds can be employed as pigments, photoactive materials and utilized as potential biodegradable agrochemicals. The importance of these compounds has led many workers to synthesize them using methods including microwave[5] and ultrasonic irradiation[6] or by using tetrabutylammonium bromide[7], (S)-proline,[8] rare earth perfluorooctanoates[9] and hexadecyltrimethylammonium bromide[10] as basic catalysts in one-pot reactions. Each of the above methods has its own merits, while some are plagued by limitations of poor yields, difficult work-up and toxic effluents.

For about 20 years there has been a growing realization that the deliberate cathodic generation of anionic bases, in aprotic solvents, might be extremely convenient and offer possibilities for control of such factors as base strength and base concentration. The term probase has come into regular use to describe a compound which on reduction is converted into an intermediate that acts predominantly as a base and which is described as an electrogenerated base (EGB).

Recently, it was found that chemical bases could be replaced with an electrogenerated base to promote reactions in higher yields[11]. Electroorganic reactions proceed generally smoothly with easy work-up and do not require the use of harsh conditions such as high temperatures and expensive reagents. Up to now, no reports have been published on the electrosynthesis of xanthene-1,8(2*H*)-dione and we devoted the electrosynthesis of heterocycles as a part of our program.[11] We decided to investigate the electrochemical synthesis of xanthene-1,8(2*H*)-dione. Herein we reported the synthesis of various xanthene-1,8(2*H*)-dione derivatives *via* electroreduction of dimedone at a platinum electrode (**Scheme-I**).



X = H, Cl, NO_2, OH, F, Br, $-CH_3$

Scheme-I General reaction

EXPERIMENTAL

The reactions were performed in an Autolab 302 (potentiostate/ galvanostate). Melting points was measured on the Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Bomem FT-IR-MB 100 spectrometer. ^{1}H and ^{13}C NMR spectra were measured by a Bruker

DRX-300 Avance spectrometer at 300 MHz and 75 MHz respectively, using TMS as internal standard. Chemical shifts are reported (δ) relative to TMS and coupling constant (*J*) is reported in hertz (Hz). Mass spectra were recorded on a MS model 5973 Network apparatus at ionization potential of 70 eV. All other reagents were purchased from commercial sources and were freshly used after being purified by standard procedures.

Typical procedure for the preparation of (4a-4g): Electroorganic synthesis of xanthene-1,8(2*H*)-dione: In a typical procedure, the mixture of sodium acetate solution (0.2 M, 50 mL)/acetonitrile (30 mL), dimedone (2 mmol) and benzaldehyde derivatives (1 mmol) were added in the 100 mL beaker. Sodium acetate solution was used as a supporting electrolyte in an undivided cell fitted with a consumable graphite anode and a Pt sheet as cathode was subjected to electrolysis at room temperature and at a constant current (10 mA). The progress of the reaction was monitored by thin layer chromatography. The reaction time was in all the cases about 5 h. The resulting precipitate was filtered and recrystallized from an ethanol/water (3:1) mixture. All the products were characterized by spectroscopy and physical data.

Compound 4a: 3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2956, 1736, 1712, 1455, 1229, 1203; ^{1}H NMR (DMSO-d_6) : 7.23-7.33 (m, 5H, Ar), 4.77 (s, 1H, CH), 2.71 (d, 2H, 14 Hz), 2.58 (d, 2H, 14 Hz), 2.11 (d, 2H, 14 Hz), 2.07 (d, 2H, 14 Hz), 1.09 (s, 6H, CH_3), 1.06 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 201.1, 157.3, 137.6, 129.6, 129.2, 128.9, 113.8, 64.0, 53.5, 50.1, 30.2, 28.9, 26.8; Ms (EI): m/z (relative intensity): 350 [M^{+o}] (12), 282 (31), 254 (100), 128 (26), 83 (55), 55 (29).

Compound 4b: 3,3,6,6-tetramethyl-9-*p*-tolyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2949, 1731, 1710, 1435, 1225, 1201, ^{1}H NMR (DMSO-d_6): 7.39 (d, 2H, 8.4 Hz), 7.28 (d, 2H, 8.4 Hz), 4.82 (s, 1H, CH), 2.70 (d, 2H, 15 Hz), 2.58 (d, 2H, 15Hz), 2.35 (s, CH_3), 2.16 (d, 2H, 15 Hz), 2.10 (d, 2H, 15 Hz), 1.08 (s, 6H, CH_3), 1.03 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 200.9, 152.5, 136.6, 133.1, 131.5, 129.3, 113.7, 63.2, 53.9, 50.1, 30.1, 28.8, 26.7.

Compound 4c: 3,3,6,6-tetramethyl-9-(4-nitrophenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2960, 1741, 1710, 1431, 1199, ^{1}H NMR (DMSO-d_6): 8.19 (d, 2H, 8.1 Hz), 7.55 (d, 2H, 8.1 Hz), 5.00 (s, 1H, CH), 2.50-2.77 (m, 4H), 2.10-2.22 (m, 4H), 1.14 (s, 6H, CH_3), 1.02 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 202. 8, 168.5, 148.0, 145.1, 142.6, 131.0, 113.7, 74.5, 53.9, 51.3, 31.2, 28.9, 26.7; Ms (EI): m/z (relative intensity): 395 [M^{+o}] (5), 327 (25), 299 (50), 83 (100).

Compound 4d: 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2520 broad peak, 1735, 1712, 1424, 1201, ^{1}H NMR (DMSO-d_6): 7.33 (d, 2H, 8.4 Hz), 7.12 (d, 2H, 8.4 Hz), 4.54 (s, 1H, CH), 2.45-2.74 (m, 4H), 2.08-2.16 (m, 4H), 1.09 (s, 6H, CH_3), 1.01 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 201. 4, 152.5, 134.0, 132.1, 131.6, 128.0, 113.7, 59.8, 52.8, 50.2, 31.1, 27.6, 25.4; Ms (EI): m/z (relative intensity): 366 [M^{+o}] (4), 271 (30), 243 (29), 215 (89), 94 (95), 43 (100).

Compound 4e: 9-(4-fluorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2968, 1742, 1711, 1469, 1162, ^{1}H NMR (DMSO-d_6): 7.29 (d, 2H, 8.1 Hz), 7.15 (d, 2H, 8.1 Hz), 4.81 (s, 1H, CH), 2.54-2.73 (m, 4H), 2.03-2.10 (m, 4H), 1.08 (s, 6H, CH_3), 1.04 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 201. 6, 152.4, 133.8, 131.7, 131.6, 126.2, 115.9, 58.4, 52.4, 50.3, 31.0, 28.4, 25.7.

Compound 4f: 9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR (KBr, ν_{max}, cm^{-1}): 2970, 1735, 1708, 1459, 1174, ^{1}H NMR (DMSO-d_6): 7.25 (d, 2H, 8.4 Hz), 7.12 (d, 2H, 8.4 Hz), 4.71 (s, 1H, CH), 2.44-2.63 (m, 4H), 2.01-2.08 (m, 4H), 1.06 (s, 6H, CH_3), 1.02 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 200. 3, 151.2, 131.6, 130.4, 130.2, 124.6, 114.3, 57.3, 51.9, 50.7, 30.9, 27.9, 25.4.

Compound 4g: 9-(4-bromophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione: IR(KBr, ν_{max}, cm^{-1}): 2973, 1738, 1710, 1455, 1169, ^{1}H NMR (DMSO-d_6): 7.21 (d, 2H, 8.1 Hz), 7.10 (d, 2H, 8.1 Hz), 4.70 (s, 1H, CH), 2.42-2.60 (m, 4H), 2.02-2.10 (m, 4H), 1.07 (s, 6H, CH_3), 1.02 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): 201. 5, 151.1, 132.8, 130.7, 129.6, 126.0, 114.9, 57.3, 51.8, 50.2, 30.9, 28.1, 24.9.

RESULTS AND DISCUSSION

Electro synthesis at constant current of aryl aldehydes (**2**) and dimedone (**1**) proceeded in an undivided cell containing a Pt electrode as cathode and a graphite electrode as anode to avoid electrochemical side reactions. The reactions were completed after 5 h and afforded high yields of the desired products under mild conditions. The results have been summarized in Table-1.

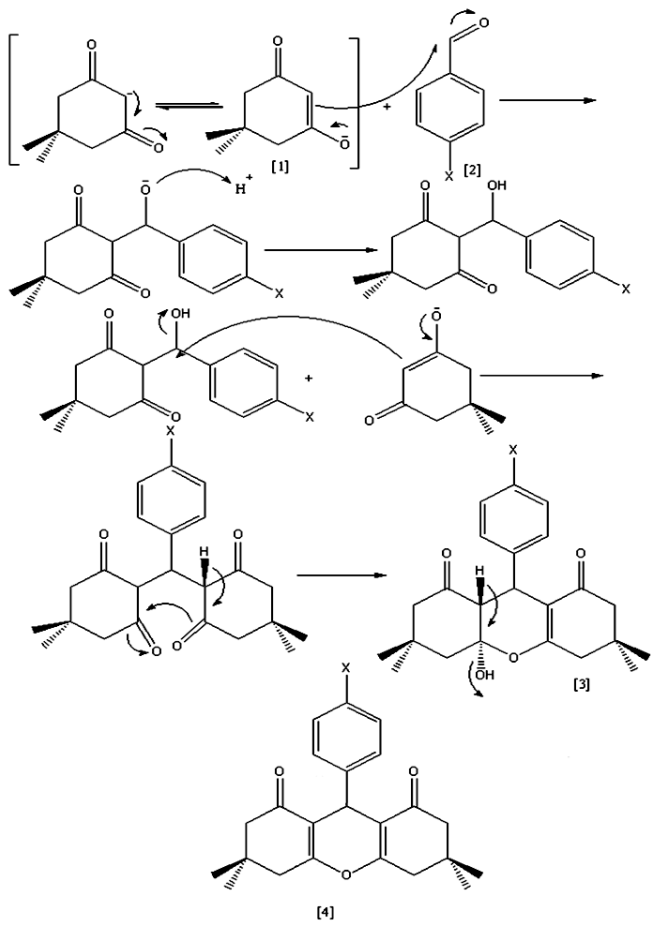
TABLE-1
ISOLATED YIELD OF DIFFERENT XANTHENE-1,8(2*H*)-DIONE DERIVATIVES SYNTHESIZED BY ELECTROGENERATED BASE

Entry	R	Yield (%)	m.p. (ºC)[a]
4a	H	85	268-269
4b	CH_3	80	255-256
4c	NO_2	95	237-239
4d	OH	75	199-201
4e	F	89	245-247
4f	Cl	87	241-243
4g	Br	85	247-249

a: all compounds decomposed at these temperatures

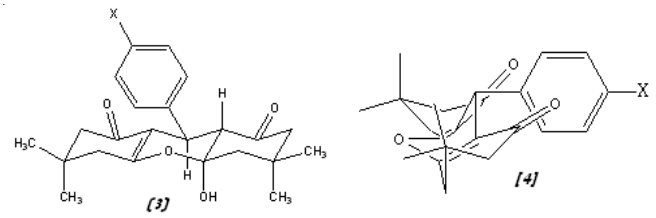
After the characterization of product by ^{1}H NMR, ^{13}C NMR, FT-IR, MS spectroscopy and also monitoring of that by TLC, it has been conclusively proved that progress of this reaction is highly depended on the time of current influence and if the current is switched off after 1 h, the main product of this reaction is compound (**3**), that can be counted as an intermediate for final product, whereas if it is continued up to 5 h, the final product can be obtained. According to the isolated intermediate (**3**), the proposed mechanism for this reaction has been shown in **Scheme-II**.

According to the spectra of this compound that have obtained only after 1 h of current influence, it can be deduced that the elimination of water hasn't occurred. This phenomena can be proved by the *ax-ax* coupling constant of hydrogen (δ = 3.64 ppm) with its *vicinal* hydrogen that is equal with 15 Hz. (**Scheme-III**). These coupling constant has been omitted in compound (**4**) by *virtue* of elimination of water (**Scheme-III**).



X=H, OH, NO_2, F, Cl, Br

Schem-II Proposed mechanism



Scheme-III Eliminating of water by continuing of current influence

Conclusion

The use of an electrogenerated base[11] in comparison with conventional chemistry[12-15] has advantages such as:

(i) *in situ* generation of base.

(ii) a one-pot reaction in excellent yields under milder conditions.

(iii) avoidance of polluting or hazardous chemicals or the addition of base or probase.

(iv) involves an easy work-up procedure.

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REFERENCES

1. S. Hatakeyama, N. Ochi, H. Numata, S. Takano, *J. Chem. Soc. Chem. Commun*., **17**, 1202 (1988).
2. R. Gonzalez, N. Martin, C. Seoane, J.L. Marco, A. Albert and F.H. Cano, *Tetrahedron Lett*., **33,** 3809 (1992).
3. G.R. Green, J.M. Evans and A.K. Vong, in eds: A.R. Katritzky, C.W. Rees and E.F. Scriven, Comprehensive Heterocyclic Chemistry II, Pergamon Press Oxford, 5, 469 (1995).
4. L. Bonsignore, G. Loy, D. Secci and A. Calignano, *Eur. J. Med. Chem.*, **28**, 517 (1993).
5. J.F. Zhou, S.J. Tu, Y. Gao and M. Ji, *Chin. J. Org. Chem*., **21**, 742 (2001).
6. S.J. Tu, H. Jiang, Q.Y. Zhuang, C.B. Miao, D.Q. Shi, X.S. Wang and Y. Gao, *Chin. J. Org. Chem.*, **23**, 488 (2003).
7. T.S. Jin, J.C. Xiao, S.J. Wang, T.S. Li and X.R. Song, *Synlett*, 2001 (2003).
8. S. Balalaie, M. Bararjanian, A.M. Amani and B. Movassagh, *Synlett*, 263 (2006).
9. L.M. Wang, J.H. Shao, H. Tian, Y.H. Wang and B.J. Liu, *Fluorine Chem.*, **127**, 97 (2006).
10. T.S. Jin, A.Q. Wang, X. Wang, J.S. Zhang and T.S. Li, *Synlett*, 871 (2004).
11. B. Mirza, D. Nematollahi, J. Azizan, M. Sargordan-Arani, M. Hesari, S. Jameh-Bozorghi, A. Alizadeh and L. Fotouhi, *Chem. Pharm. Bull.*, **56**, 1562 (2008).
12. X.S. Wang, D.Q. Shi, S.J. Tu, C.S. Yao, *Synth. Commun.*, **33**, 119 (2003).
13. S.J. Tu, Y. Gao, C. Guo, D.Q. Shi and Z.S. Lu, *Synth. Commun.*, **32**, 2137 (2002).
14. S.E. Treimer and D.K.J. Evans, *Electroanal. Chem.*, **455**, 19 (1998).
15. K. Singh, J. Singh and H. Singh, *Tetrahedron*, **52**, 14273 (1996).