Jour. Chem. Soc. of Pak. Vol. 12, No. 3, 1990

Cycloaddition Reaction on Naphthopyran-2-one Derivatives

S.EL-NAGDY, A.Y. SOLIMAN, H.M. BAKEER* AND A.M. YOUSSEF
Faculty of Science, Ain Shams University, Cairo, Egypt
**Faculty of Education at El-Fayoum, El-Fayoum, Egypt.*

(Received 27th July, 1989, revised 29th March, 1990)

Summary:4-Methyl-2H-naphtho[1,2-b]pyran-2-one (I), 2-oxo-2H- naphtho[1,2-b]pyran-4-acetic acid (II), 1-methyl-3H-naphtho[2,1- b]pyran-3-one (III) and 3-oxo-3H-naphtho [2,1-b]pyran-1-acetic acid (IV), have been synthesized. Compound (I) and (II) condensed with aromatic aldehydes to give 2-naphthalene acrylic acid (Va- d), and 4-styryl pyranones (VIa-e) derivatives. Va and/or Vd reacted with maleic anhydride under Diels-Alder condition to give 2- naphthalenyl cyclohex-4-ene 1,2,3-tricarboxylic acid derivatives (VIIIa & b), decarboxylation of VIIa gave 2-naphthalenyl cyclohex-2-ene-1-carboxylic acid derivative (VIII). The 4-styryl pyranones derivatives (VId & e) reacted with maleic anhydride to give benzo[d]naphtho[1,2-b]pyranone deriatives (Xa & b). Compound (Xa) condensed with hydrazines, amines and thiourea to give naphthalenyl-N-substituted cyclohexene carboxamide derivatives (XIa-d), while (Xa) reacted with Grignard reagents to give naphthalenyl cyclohexenyl aryl ketone derivatives (XIIa-c), also (Xa) reacted with benzene under Friedel-Crafts condition to give (XIIa).

A number of publications have appeared on the synthesis of anti- bacterial and biological activities of different types of α-pyrones [1-4]. Thus it appeared of interest to synthesis a series of 4-arylvinylnaphtho-pyran-2-ones as intermediate compounds to synthesize a different heterocyclic compounds. In continuation of our previous works [5-8], 4-methyl- 2*H*-naphtho[1,2-*b*]pyran-2-one (I) and 2-oxo-2*H*-naphtho [1,2-*b*]pyran-4-acetic acid (II) were obtained from the condensation of α-naphthol with citric acid in the presence of conc. H_2SO_4 [7]. Similarly 1-methyl-3*H*-naphtho [2,1-*b*] pyran-3-one (III) and 3-oxo-3*H*-naphtho [2,1-*b*] pyran-1-acetic acid (IV) were obtained by the condensation of β-naphthol with citric acid in conc. H_2SO_4. Also, compound (I or III) was obtained by the reaction of α or β-naphthol with ethyl acetoacetate in conc. H_2SO_4 [5].

Condensation of compounds I and II with aromatic aldehydes in the presence of sodium ethoxide gave the corresponding 1-hydroxy- β-styryl-2-naphthalene acrylic acid (Va-d) and 4-styryl-2*H*-naphtho[1,2-*b*] pyran-2-ones VIa-e. The structures of compounds V and VI were confirmed by analytical data and hyderivatization (Va) reacts with maleic anhydride in boiling xylene for 40 hrs under Diels-Alders condition to give 2-(1- hydroxy-2-naphthyl)-4-phenylcyclohex-2-ene-1-carboxylic acid (VIII).

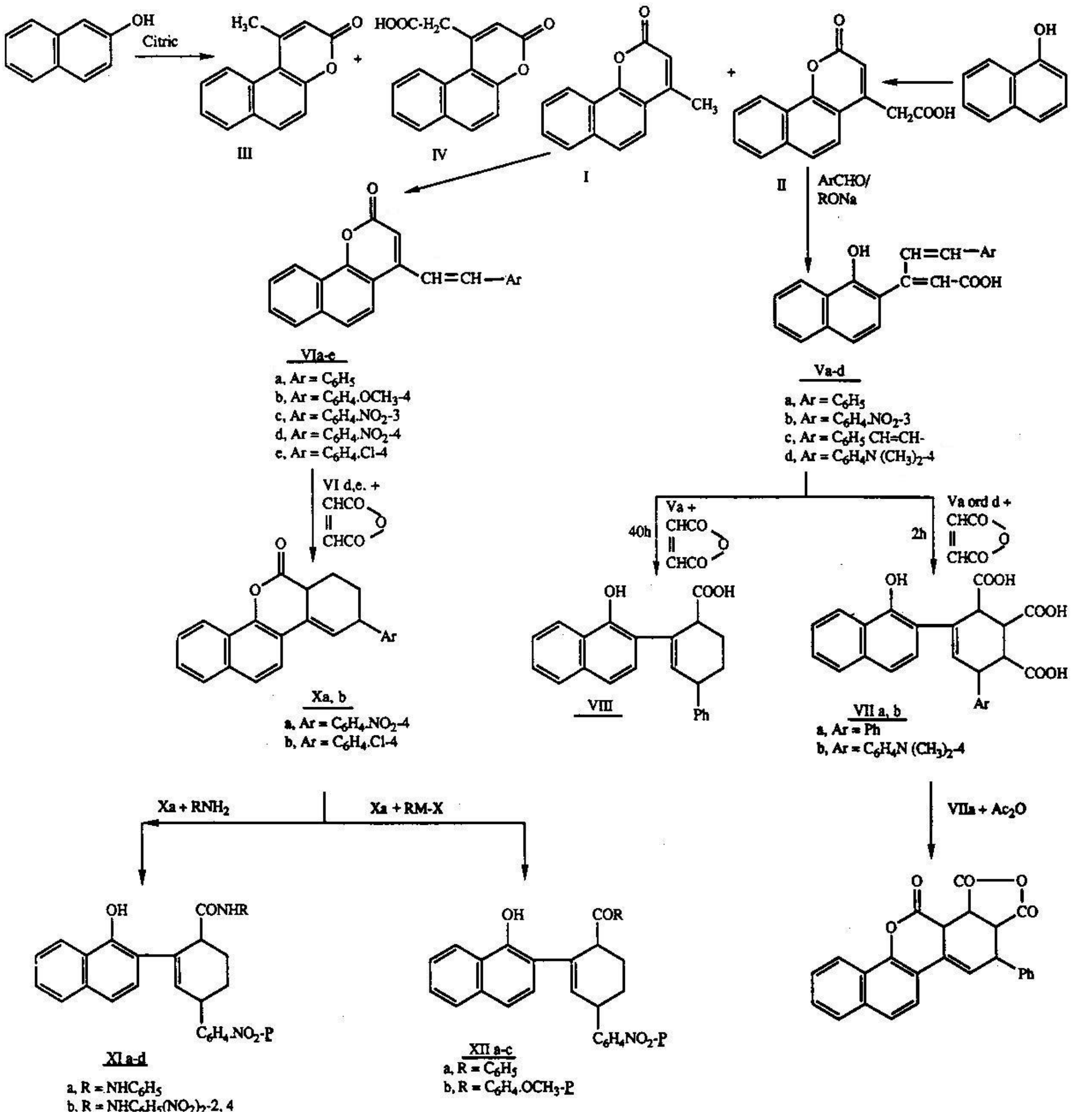
The cyclocondensation of (Va or Vd) with maleic anhydride in boiling xylene for 20 hrs under Diels-Alder's condition gave 4-(1-hydroxy-2-naphthyl)-6-aryl cyclohex-4-ene 1,2,3- tricarboxylic acids (VIIa & b), while fusion of compound VIIa at its m.p. for 2 hrs gave VIII. The structures of VII and VIII were supported by IR and NMR spectra.

More evidence for the structures VIIa, on refluxing it with acetic anhydride for 2 hrs, gave 6a, 7, 8,9-tetrahydro-6-oxo-9-phenyl-6*H*-benzo [*d*] naphtho [1,2-*b*] pyran-7, 8-dicarboxylic anhydride (IX)

Compound (VId & e) reacted with maleic anhydride under Diels- Alders condition to give 6a, 7, 8,9-tetrahydro-9-aryl-6*H*-benzo[*d*]naphtho[1,2-*b*] pyran-6-one (Xa & b).

The condensation of Xa with nitrogen nucleophiles such as phenylhydrazine, 2,4-dinitro- phenylhydrazine, α-naphthylamine and/or thiourea in boiling alcohol gave 2-(1- hydroxy-2-naphthyl) -N-substituted-4(*p*-nitrophenyl)-cyclohex-2-ene-carboxamide (XIa-d). The structure of (XIa-d) were confir -med by their solubility in aqueous KOH and IR spectra exhibit bands at 1660-1670 (νCO, amide) and 3390- 3410 cm^{-1} (νOH and νNH).

Also compound Xa reacted with Grignard reagents as a carbon nucleophiles and gave 2-(1-hydroxy-2-naphthyl)-4-(*p*- nitrophenyl)cyclohex-2-enyl-1-aryl ketones (XIIa-c). On the other hand Xa reacted with benzene under Friedel-Crafts condition to give XIIa.


OH
Citric
H_3C
O
O
+
$HOOC\text{-}H_2C$
O
O
III
IV
O
O
CH_3
I
+
O
O
CH_2COOH
OH
II
ArCHO/
RONa
O
O
CH=CH—Ar
VIa-e
a, Ar = C_6H_5
b, Ar = $C_6H_4.OCH_3$-4
c, Ar = $C_6H_4.NO_2$-3
d, Ar = $C_6H_4.NO_2$-4
e, Ar = $C_6H_4.Cl$-4
OH
CH=CH—Ar
C=CH-COOH
Va-d
a, Ar = C_6H_5
b, Ar = $C_6H_4.NO_2$-3
c, Ar = C_6H_5 CH=CH-
d, Ar = $C_6H_4N(CH_3)_2$-4
VI d,e. +
CHCO
CHCO
O
Va +
CHCO
CHCO
O
40h
Va ord d +
CHCO
CHCO
O
2h
O
O
Ar
Xa, b
a, Ar = $C_6H_4.NO_2$-4
b, Ar = $C_6H_4.Cl$-4
OH
COOH
VIII
Ph
OH
COOH
COOH
COOH
Ar
VII a, b
a, Ar = Ph
b, Ar = $C_6H_4N(CH_3)_2$-4
Xa + RNH_2
Xa + RM-X
VIIa + Ac_2O
OH
CONHR
$C_6H_4.NO_2$-P
XI a-d
a, R = NHC_6H_5
b, R = $NHC_6H_5(NO_2)_2$-2, 4
OH
COR
$C_6H_4NO_2$-P
XII a-c
a, R = C_6H_5
b, R = $C_6H_4.OCH_3$-P
O
CO
O
CO
O
Ph

Experimental

All the melting points are uncorrected and the IR spectra were determined by a Unicam SP 1200 spectrophotometer and. the NMR spectra were determined by BM 360 A Varian (60 MHz).

Formation of 4-methyl-2*H*-naphtho[1,2-*b*] pyran-2-one(I),1-methyl-3-2*H*-naphtho[1,2,-*b*] pyran-3-one (III), 2-oxo-2*H*-naphtho [1,2-*b*]pyran-4-acetic acid (II) and/or 3-oxo-3*H*-naphtho [2,1-*b*] pyran-1-acetic acid (IV)

A mixture of 210 g (1 mole) of citric acid monohydrate and 280 ml of conc. H_2SO_4 was stirred at room temperature for one hour, then slowly heated at 70°C. After 1/2 hr at this temperature with stirring through the evolution of carbon monoxide had slackened and the clear solution was rapidly cooled to 0°C. To this stirred solution was added 144 g (1 mol) of α- or β-naphthol and 112 ml of conc. H_2SO_4, each in three equal portions, while the temperature did not exceed 10°C. The resulting mixture was stored at 0°C for 16 hrs, poured into two litre of ice and the resulting crystalline precipitate was filtered off and washed with water. The precipitate was stirred with 1000 ml of 1N Na_2CO_3 solution at 65°C for 15 minutes, filtered the insoluble material, washed with water and crystallised to give I or III, respectively.

Acidification of the filtrate, washed with water, then the obtained solid was crystallised to give II or IV.

On the other hand, I or III was prepared by Beckmann reaction; a mixture of α- and β-naphthol (1 mol) and acetylacetoacetate (1 mol) in 200 ml conc. H_2SO_4 was refluxed for 7 hrs on a water bath, cooled, poured into ice (100g), the solid that separated was filtered off and crystallised from a suitable solvent to give I or III respectively.

The NMR of II ($CDCl_3$) showed signals at δ 5.45 (*s2H*,CH_2COOH), 6.8-8.3 (*m*,*7H*, aromatic and olefinic protons).

Condensation of (I) and/or (II) with aromatic aldehydes. Formation of (Va-d) and (VIa-e)

A mixture of compound I and/or II (0.01 mol) and aromatic aldehydes, namely, benzaldehyde, anisaldehyde, *m*-nitrobenzaldehyde, *p*-nitrobenzaldehyde, cinnamaldehyde, N,N-dimethyl-*p*-amino benzaldehyde or *p*-chlorobenzaldehyde (0.016 mol) and sodium ethoxide (0.015 mol) was heated at 130°C in an oil bath for 3 hrs. Poured the reaction mixture into ice/HCl, the solid that separated was filtered off and crystallised from the proper solvent to give 1-hydroxy-β-styryl-2-naphthalene acrylic acid (Va-d), 4-styryl-2*H*-naphtho [1,2- *b*]pyran-2-ones (VIa-d), respectively. The IR spectra of compounds Va-d showed bands at the region 1660-1680 (νCO, carboxylic group), 1590-1610 (νC=C, olefinic), 3410-3500 cm^{-1} (νOH) and compounds (VIa-e) exhibit bands at 1700- 1720 cm^{-1})νCO, , α,β- unsaturated δ lactone).

Cyclocondensation of Va,d and VId,e with maleic anhydride; Formation of VIIa,b, VIII and Xa,b respectively.

A mixture of Va, d (0.01 mol) and maleic anhydride (1 g) in dry xylene (50 ml) was refluxed for 2 hrs or a mixture of Va or VId, e (0.01 mol) and maleic anhydride (1 g) in dry xylene (50 ml) was refluxed for 40 hrs. The solid that separated after concentration and cooling was crystallised from the proper solvent to give 4 (1-hydroxy-2-naphthyl)-6-phenylcyclohex-4-ene-1,2,3-tricarboxylic acids (VIIa,b), 2-(1-hydroxy-2-naphthyl)-4-phenylcyclohex-2-ene-1-carboxylic acid (VIII) or 6a,7,8,9-tetra hydro-9-aryl-6-benzo[*d*]naphtho[1,2-b]pyran-6-ones (Xa,) respectively. The IR spectra of VII and VIII showed bands at 1650-1710 cm^{-1} (broad, νCO, carboxylic groups) and 3300 cm^{-1} (broad, νOH), while the NMR spectrum of VIII (DMSO) showed signals at δ 2.5-3.3 (*m-6H*, cyclohexene), 6.5 (*s*, *1H*, olefinic proton) and 7.7- 8.4 (*m*, *11H*, Ar-H). The IR spectra of Xa,b showed absorption bands at 1705-1710 (νCO, δ-lactone) and 1620-1635 cm^{-1} (ν C=C).

Decarboxylation of VIIa; Formation of VIII

Fusion of VIIa (2 g) at its melting point (200 °C) for 1/2 hr then cooled and crystallised the solid product separated from acetic acid to give 2-(1-hy droxy-2-napthyl)-4-phenylcyclohex-2-ene-1-carboxylic acid (VIII) identified by melting point and mixed melting point determination.

Dehydration of VIIa; Formation of IX

A solution of VIIa (2 g) in acetic anhydride (50 ml) was refluxed for 2 hrs, cooled and con-

Table-1: Physical Data of Prepared Compounds

Compd.	M.p.°C (colour)	Solvent* yield %	Formula M.Wt.	Analysis % Calc./Found C	H	N
I	145	B(40)	$C_{14}H_{10}O_2$	80.0	4.76	
	(pale yellow)		(210)	80.3	5.00	
II	150	A(45)	$C_{15}H_{10}O_4$	70.86	3.93	
	(orange)		(254)	70.9	4.2	
III	172	B(55)	$C_{14}H_{10}O_2$	80.0	4.76	
	(yellow)		(210)	80.1	5.08	
IV	125	A(45)	$C_{15}H_{10}O_4$	70.86	3.93	
	(yellow)		(254)	70.7	4.1	
Va	136	B(40)	$C_{21}H_{16}O_3$	79.74	5.06	
	(pale yellow)		(361)	79.3	5.20	
b	130	A(40)	$C_{21}H_{15}O_5N$	69.80	4.15	
	(yellow)		(316)	69.90	4.3	
c	210	A(50)	$C_{23}H_{18}O_3$	86.7	5.26	
	(brown)		(342)	86.9	5.30	
d	155	A(60)	$C_{23}H_{21}O_3N$	76.88	5.84	
	(brown)		(359)	76.81	6.12	
VIa	165	A(50)	$C_{21}H_{14}O_2$	84.56	4.69	
	(colourless)		(298)	84.35	4.80	
b	135	B(50)	$C_{22}H_{16}O_3$	80.48	4.87	
	(brown)		(328)	80.55	4.60	
c	166	A(35)	$C_{21}H_{13}O_4N$	73.46	3.79	
	(yellow)		(343)	73.50	3.50	
d	115	L.P(50)	$C_{21}H_{13}O_4N$	73.46	3.79	
	(orange)		(343)	73.70	3.60	
e	220	A(55)	$C_{21}H_{13}O_2Cl$	75.58	3.90	
	(brown)		(332.5)	75.65	4.12	
VIIa	200	T(70)	$C_{25}H_{20}O_7$	69.44	4.62	
	(brown)		(432)	69.60	4.8	
b	145	B(75)	$C_{27}H_{25}O_7N$	68.21	5.26	2.94
	(brown		(475)	68.10	5.10	3.20
VIII	156	A(60)	$C_{23}H_{20}O_3$	80.23	5.81	
	(brown)		(344)	80.50	5.58	
IX	110	A(60)	$C_{25}H_{16}O_5$	75.75	4.04	
	(brown)		(396)	75.80	4.20	
Xa	175	B(70)	$C_{23}H_{17}O_4N$	74.39	4.58	3.77
	(brown)		(371)	74.5	4.41	3.95
b	156	A(50)	$C_{23}H_{17}O_2Cl$	76.66	4.72	9.72
	(brown)		(360)	76.80	4.55	9.60
XIa	335	B(60)	$C_{29}H_{25}O_4N_3$	72.65	5.21	8.79
	(brown)		(479)	72.8	5.40	8.6
b	120	B(65)	$C_{29}H_{23}O_6N_5$	64.8	4.28	13.03
	(red)		(537)	64.5	4.4	13.2
c	340	B(55)	$C_{33}H_{26}O_4N_2$	77.04	5.05	5.44
	(brown)		(514)	77.2	5.3	5.28
d	140	B(60)	$C_{24}H_{21}O_4N_3S$	64.42	4.69	9.39
	(brown)			64.5	4.5	9.2
XIIa	110	B(60)	$C_{29}H_{23}O_4N$	77.50	5.12	3.11
	(pale brown)		(449)	77.6	5.2	3.2
b	150	B(65)	$C_{30}H_{25}O_4N$	77.75	5.39	3.02
	(brown)		(463)	77.8	5.4	3.1
c	250	B(75)	$C_{30}H_{25}O_5N$	75.15	5.21	2.92
	(brown)		(479)	75.3	5.3	3.1

B = Benzene, A = Acetic acid, L.P = Ligh petroleum (60-80) T = Toluene

centrated to give 6a,7,8,9-tetrahydro-9- phenyl-6-oxo-6*H*-benzo[*d*]naphtho [1,2-b]pyran-7,8- dicarboxylic anhydride (IX). The IR spectrum of IX showed bands at 1700-1720 and 1730-1740 cm^{-1} (νCO of δ-lactone and anhydride) and 1620 cm^{-1} (ν C = C olefinic). The NMR spectrum of IX ($CDCl_3$) showed signals at δ 2.9-4.8 (broad, *m*, 4*H*, saturated carbon skeletons), 6.7-8.4 (*m*, 12*H*, aromatic and olefinic protons).

Condensation of Xa with nitrogen nucleophiles; Formation of 2-(1-hydroxy-2-naphthyl)-N-substituted-4-(p- nitrophenyl)cyclohex-2-ene-1-carboxamide (XIa-d)

A mixture of Xa (0.01 mol) and nitrogen nucleophiles, namely, phenyl hydrazine, 2,4-dinitrophenylhydrazine, α- naphthylamine or thiourea (0.015 mol) in ethanol (50 ml) was refluxed for 6 hrs, the solid that separated after concentrawtion and cooling was crystallised from the proper solvent to give (XIa-d) respectively.

Reaction of Xa with Grignard reagents; Formation of 2-[1- hydroxy-2-naphthyl)-4-(p-nitrophenyl)cyclohex-2-enyl alkyl or aryl ketones (XIIa-c)

The Grignard reagent prepared from (0.04 mol) magnesium, and bromobenzene, *p*-bromoanisol or *o*-bromotoluene (0.04 mol) in 100 ml dry ether was added to a suspension of Xa (0.01 mol) in 50 ml dry ether. The reaction mixture was distilled under pressure, the solid obtained was crystallised from the proper solven to give (XIIa-c).

The IR spectra of XIIa-c exhibit bands at 1680-1705 (νCO, ketonic group) and 3370-3410 cm^{-1} (νOH).

References

1. R. Kugler, Czech Pat. cs 222,535 (cl. Co 7D 311/48), 15 Mar. 1986, Appl. 821667, 01 Feb. 1983, 3 pp., *C.A.*, **105**, 190936 (1986).
2. D.P. Chakraborty, A. Dasgupta, P.K. Bose, *Ann.Biochem.Exp.Med.*, **17**, 59 (1957). *C.A.*, **52**, 1352 (1958).
3. Troponwerke Dinklog, Co. Belgium Pat. 843-810 (Nov. 3, 1976), Cussela Farb Maink AG. USSR Pat. 489-319 (March 10, 1976).
4. D.R. Shridar, C.V.Reddy, N.K. Vaida, G.S. Reddi, G.S. Thapar, and S.K. Gupta, *Indian J.Chem.*, **16B**, 704 (1978).
5. A.I. Essawy, M. El-Kady and A.Y. Soliman, *Indian J.Chem.*,**19**, 567 (1980).
6. M. El-Garby Younes, M. El-Kady, A.I. Essawy and A.Y. Soliman, *Indian J.Chem.* **20**, 747 (1981).
7. A.F. El-Farargy, A.Y. Soliman, M. El-Mobayed and S. El- Esser, *Revue Roumaine de Chimie* **32**, 435 (1987).

8. M. El-Mobayed, A.Y. Soliman, A.F. El-Farargy (accepted for publication, *Oriental J. Chem.* **4**, (1988).

9. S.C. Laskawski, R.D. Clinton, *J.Am.Chem.Soc.,* **72**, 3989 (1950).