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Synthesis of Some New Heterocyclic Compounds Using Phase Transfer Catalysis Technique (PTC)

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ABSTRACT

A series of substituted chalcones (1-6) were synthesized and used to prepare some new five membered heterocyclic compounds (pyrazolines) (7-12) by their condensation with phenylhydrazine, and six membered heterocyclic compounds (pyrimidinones) (13-18) by their condensation with urea.

All reactions were carried out under phase transfer catalysis (PTC) technique, employing tributylbenzylammonium bromide (TBBAB) as a catalyst in 50% aqueous sodium hydroxide in benzene (liquid-liquid system) .The structures of products were identified by physical and spectroscopic methods.

تحضير بعض المركبات الحلقية غير المتجانسة الجديدة باستعمال تقنية التحفيز بانتقال الطور

الملخص

يتضمن البحث تحضير سلسلة من الجالكونات المعوضة (1-6) واستخدامها لتحـضير مركبـات حلقية غير متجانسة (البايرازوليات) (7-12) بتكاثفها مع الفنيل هيدرازين وكذلك تحضير مركبات حلقية سداسية غير متجانسة (البايريميدينونات) (13-18) بتكاثفها مع اليوريا.

اجريت كل التفاعلات باستعمال تقنية التحفيز بانتقال الطور.وظفت لذلك أملاح الامونيوم الرباعية كحفازات مثل ثلاثي بيوتيل بنزيل امونيوم بروميد (TBBAB) وهيدروكسيد الصوديوم المـائي (50%) كقاعدة في البنزين كمذيب في نظام يدعى نظام (سائل-سائل)، وتم دعـم الـصيغ التركيبيـة المحـضرة والمتوقعة باستخدام الطرق الفيزياوية والطيفية.

INTRODUCTION

Michael addition (1,4) is one of the most important reactions in the organic synthesis especially when causes ring closure of the reactant (Bergmann,1959; Fieser and Fieser,1967). Most of heterocyclic compounds obtained from such reactions have important values in industry and for their biological activity (Katrizky and Rees,1984). However, satisfactory yield of Michael products from α, β-unsaturated carbonyl compounds especially the chalcones (Shandala et al., 1990; Salih et al., 1995) are

obtained in rare cases. Now, it is well known that many reactions proceeded via carbanions, can be carried out efficiently using phase transfer catalysts technique (PTC)(Ghazal, 1999; AL-Hamdany, 2000; AL-Rubay, 2001; AL-Bazi, 2001; Arslan, 2002; Soliman, 2002; AL-Hamdany, 2002; AL-Nakshabandy, 2005) and as a logical extension of this work we report here a very simple and smooth reaction to synthesize a series of pyrazolines and pyrimidinones through the reaction of phenylhydrazine and urea with chalcones (1-(9`-anthryl)-3-phenyl-2-propene-1-one) under phase transfer catalysis (PTC). The versatility of (PTC) is well established (Dehmlow,1983).

The pyrazoline, pyrimidinone and their derivatives represent one of the most biologically active classes of compounds, and its nucleus is associated with diverse pharmacological activities such as potent GnRH receptor antagonists (Zhu et al.,2003), for medicinal and pharmaceutical applications (Cebasek et al.,2004), as anti-inflammatory, antiarthritic agents (Nugent et al.,1993) and other biological activities (Chimenti et al., 2004).

EXPERIMENTAL

Melting points were measured on Electrothermal 9300 melting point apparatus and are uncorrected,IR spectra were recorded in KBr disc using a Bruker FT-IR, spectrophotometer tensor 27.UV spectra were performed on Shimadzu UV-Visible spectrophotometer UV-1650PC using chloroform as a solvent.

Table 1: Physical and spectral data for compounds (1-6).

Comp No.	X	m.p (°C)	Yield (%)	UV $CHCl_3$ λ_{max} (nm)	IR (KBr) $\upsilon(cm^{-1})$	
					C=O	C=C
1	4-Cl	132-133	90	280	1640	1601
2	*m*-NO_2	138-139	85	292	1650	1609
3	4-CH_3	95-96	70	276	1660	1606
4	3,4-diOCH_3	144-145	70	280	1665	1641
5	4-OH	142-143	73	276	1670	1644
6	4-$N(CH_3)_2$	157-158	80	276	1660	1638

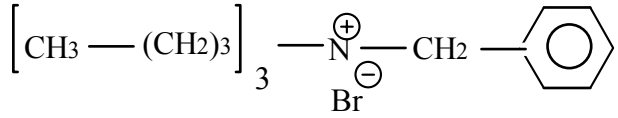
Preparation of chalcones (1-6)(vogel, 1981)

9-Acetyl anthracene (0.005 mol) was added to a stirred ice-cooled solution of sodium hydroxide (2.2 g) in water (20ml) and ethanol (15 ml), then substituted benzaldehydes (0.005 mol) were added. The stirring was continued for 2-4 hrs until the mixture is so thick that stirring became no longer effective. The reaction mixture was kept in refrigerator overnight (for chalcone 5, the mixture was acidified with dilute hydrochloric acid). The precipitate was filtered off, washed with cold water until the filtrate became neutral, then with (5 ml) of cold ethanol, dried and recrystallized from ethanol.The physical and spectral data of chalcones (1-6) are listed in Table 1. (Vogel,1981).

Preparation of the phase transfer catalyst (tributylbenzylammonium bromide) (TBBAB)

General Procedure: (AL-Nakshabandy,2005)

A mixture of 10 gm (0.053 mole) of tri-butylamine, 9.22 gm (0.053 mole) benzylbromide and (50 ml) of dry benzene was placed in a (250 ml) dry round-bottomed flask fitted with a condenser. The mixture was refluxed for (30) minutes, resulting in a thick solution. After cooling the precipitate was filtered and the resulting white powder was washed with benzene and recrystallized from a mixture of ethyl acetate and ethanol ,giving white crystals of tributylbenzylammonium bromide, m.p(174-175 ºC) agrees with the reported m.p (176 ºC) (Aldrich,1989).



Condensation reaction of chalcones (1-6) with phenylhydrazine or urea using phase transfer catalysis technique using (liquid-liquid) system.

General Procedure:

A solution of chalcone (1-6) (0.01 mol), phenylhydrazine or urea (0.01 mol), TBBAB (0.02 moles),and 50% aqueous sodium hydroxide solution (3 ml) in benzene (25 ml) was stirred for (3-6) hours at 50ºC. (for chalcone 5, the reaction mixture was neutralized with dilute hydrochloric acid solution). The aqueous layer was separated and the organic layer was washed repeatedly with cold water,(to get rid of the base and the catalyst), dried with anhydrous magnesium sulfate then the solvent was evaporated under reduced pressure. The residue was dissolved in a smaller amount of boiling ethanol and upon cooling a solid product was precipitated. The product was filtered off, then recrystallized from ethanol. The physical and spectral data of the products (7-12) and (13-18) are listed in Tables 2 and 3 respectively.

Table 2: Physical and spectral data for compounds (7-12)

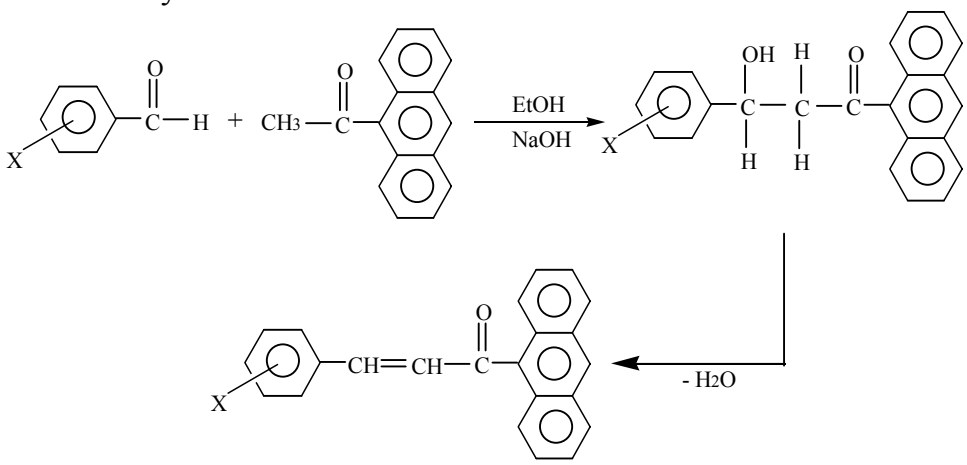
Comp. No.	X	m.p (ºC)	Yield (%)	UV $CHCl_3$ λ_{max} (nm)	IR (KBr) υ(cm^{-1})	
					C=C	N–H
7	4-Cl	189-190	77	250	1602	3411
8	*m*-NO_2	180-181	65	250	1610	3399
9	4-CH_3	134-135	70	254	1604	3421
10	3,4-diOCH_3	174-175	65	254	1600	3433
11	4-OH	195-196	55	250	1605	3400
12	4-$N(CH_3)_2$	191-192	70	258	1611	3402

Table 3: Physical and spectral data for compounds (13-18)

Comp No.	X	m.p (°C)	Yield (%)	UV $CHCl_3$ λ_{max} (nm)	IR (KBr) υ(cm^{-1})		
					C=O	C=C	N-H
13	4-Cl	195-196	65	256	1670	1600	3423
14	*m*-NO_2	214-215	53	256	1684	1617	3442
15	4-CH_3	220-221	62	254	1670	1601	3444
16	3,4-diOCH_3	210-211	54	248	1674	1615	3424
17	4-OH	200-201	52	256	1675	1610	3442
18	4-$N(CH_3)_2$	215-216	60	260	1670	1602	3422

RESULTS AND DISCUSSION

The chalcones (1-6) were synthesized by condensation of 9-acetylanthracene with substituted benzaldehydes as shown in Scheme 1:



(1-6)

X= 4-Cl, *m*-NO_2, 4-CH_3
3,4-diOCH_3, 4-OH, 4-$N(CH_3)_2$

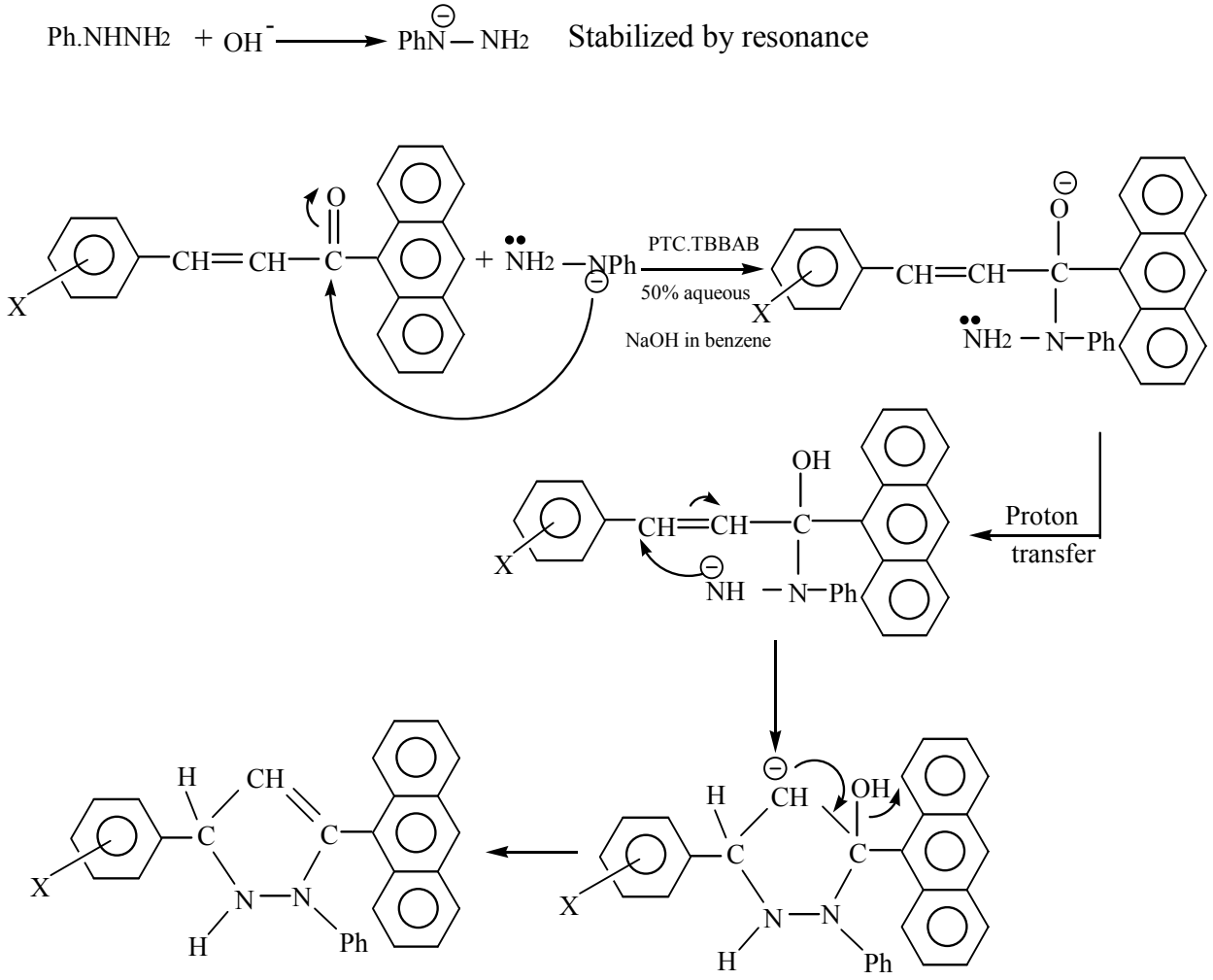
Scheme (1)

The structure of these compounds was substantiated spectroscopically. IR spectra [Table (1)] showed significant absorption peaks at (1670 – 1640 cm^{-1}) and (1644 -1601 cm^{-1}) related to υ(C=O) and υ(C=C) bond stretching, respectively (Parikh, 1974). The depression in the absorption frequencies of the (C=O) was attributed to the resonance of the conjugated system. The infrared spectrum of compound (2) exhibited an additional absorption peaks at (1511 and 1269 cm^{-1}) for asymmetrical and symmetrical NO_2 bond stretching, while the IR spectrum of compound 5 showed absorption peak at (3300 cm^{-1}) which is attributed to the O-H bond stretching. The electronic spectra of compounds (1-6) showed λ_{max} at (276-292 nm) which indicate the presence of conjugaed system.

The introduction of aromatic moiety into the terminal positions of the conjugated system (C=C-C=O), as in chalcones appears to increase its polar character and therefore its tendency to undergo condensation reaction with nucleophiles (Mohamed et al., 1980).

Thus, chalcones (1-6) condensed with phenylhydrazine under phase transfer catalysis conditions yield the corresponding pyrazolines (7-12) either through Claisen addition (route 1) or Michael addition (route 2) as shown in Schemes 2a, 2b:

Rout 1: claisen addition

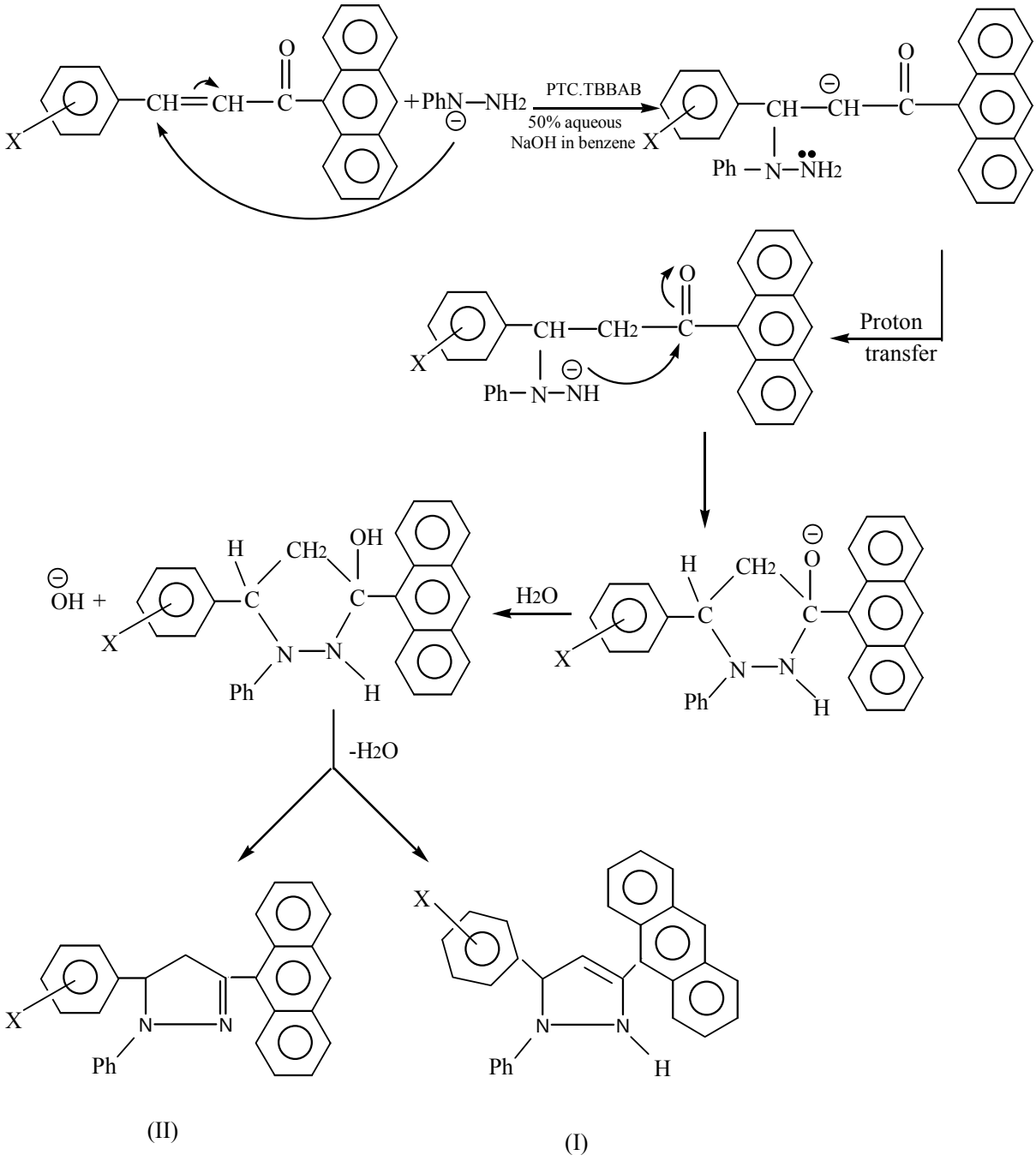


Scheme (2a)

The previous literature (AL-Hamdany,2005) illustrated through the theoretical study for the heat of formation and steric hindrance energy for similar compounds that this reaction proceeds exclusively via Michael addition to form the most stable product (II).

The structure of the pyrazolidines (7-12) was supported by IR spectroscopy, which showed a characteristic absorption peaks at (1600 -1611 cm^{-1}), (3399-3411 cm^{-1}) attributed to the C=C and N – H bonds stretching, respectively of the pyrazoline ring. The absence of absorption peak for the C=O bond stretching supported the formation of structure I. The UV spectra showed a blue shift for the pyrazolines relative to that of chalcones. This indicates that the conjugation is reduced in the pyrazoline compounds.

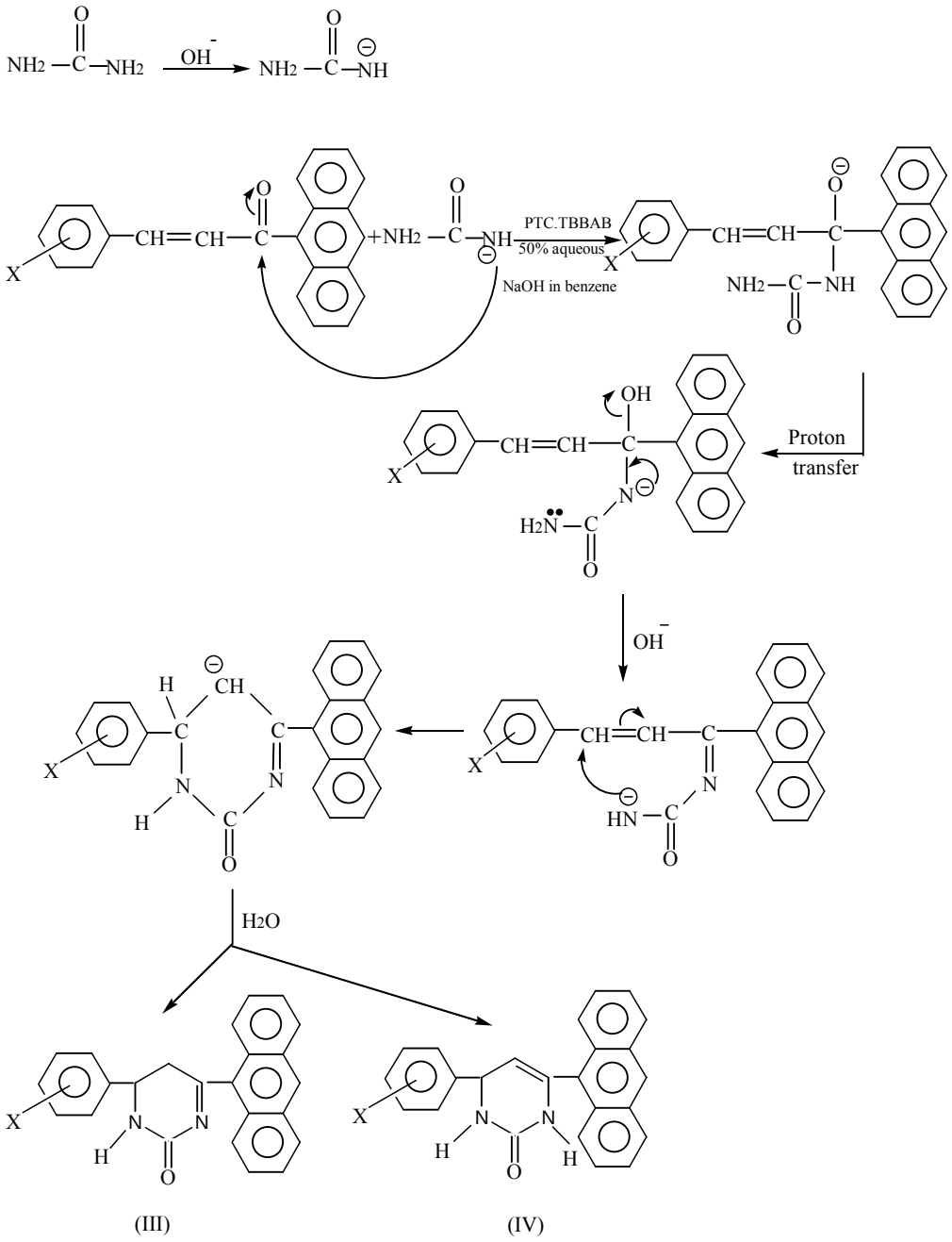
Rout 2: Michael addition



Scheme (2b)

The action of urea on the chalcones was also studied. The condensation of chalcones (1-6) with urea under phase transfer catalysis condition leads to the corresponding substituted pyrimidinones (13-18). The formation of these compounds may proceed through one of two routes: Claisen or Michael routes (Al-Nakshabandy, 2005). (Schemes 3a, 3b):

Rout 1: claisen addition



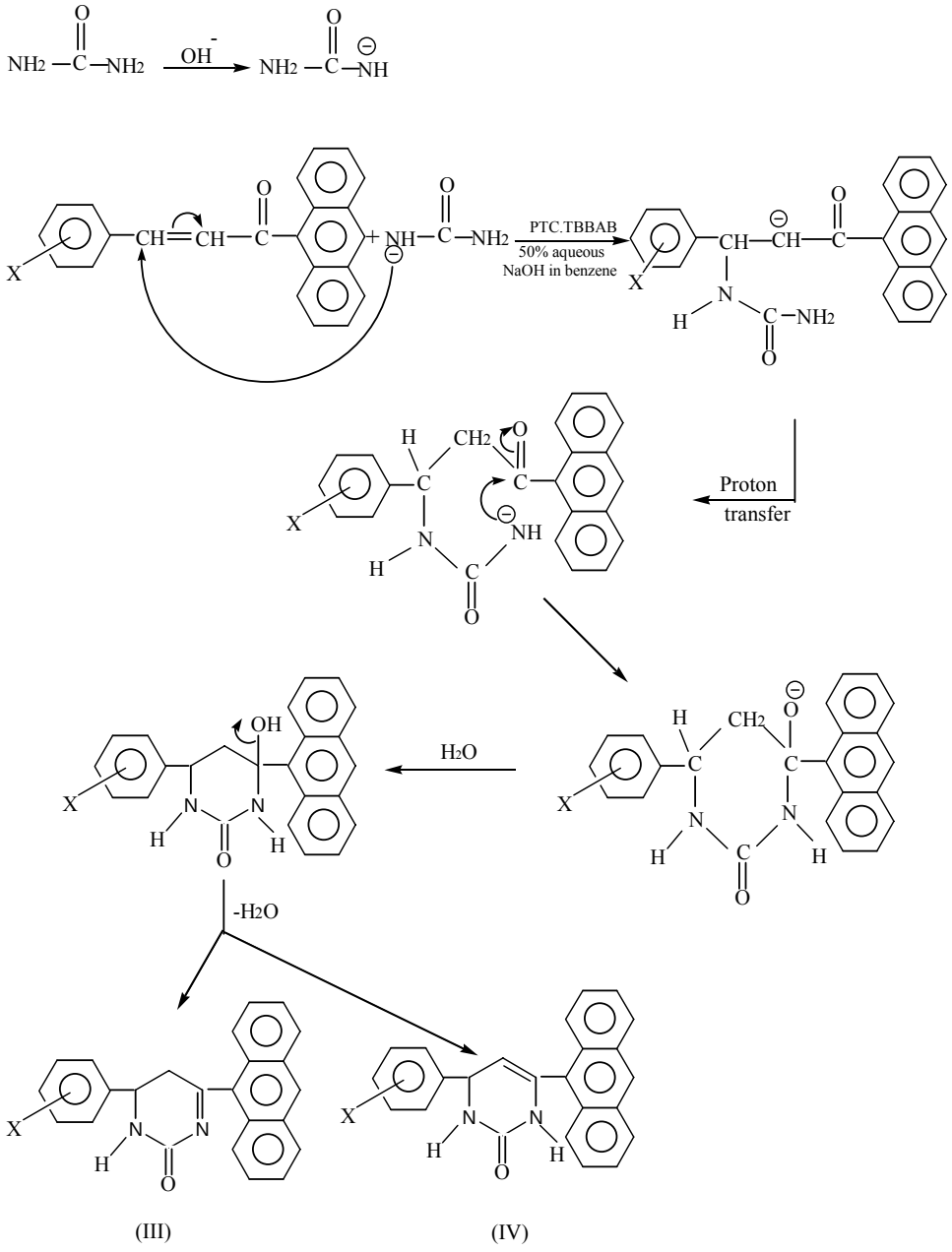
Scheme (3a)

The theoretical studies for the heat of formation and steric energy of the products illustrate that this reaction proceeds via Michael addition to form the most stable product IV.

The structures of pyrimidinones (13-18) were supported by IR spectroscopy. The IR spectra, Table (3) of compound (13-18) showed absorption peaks at (3422-3444 cm^{-1}), (1600-1617 cm^{-1}) and (1670-1684cm^{-1}) assigned to N–H ,C=C and C=O bonds stretching respectively. The UV spectra of compounds (13-18) showed absorption peak at λ_{max} (248-260 nm), i.e. there is a blue shift relative to that of chalcones which indicates that the conjugation was reduced in the pyrimidinone compounds due to the absence of the C=C

and the configuration of these compounds i.e. the pyrimidine ring is not in the same plane with the aryl rings (AL-Nakshabandy, 2005).

Route 2: Micheal addition



(III) (IV)

Scheme (3b)

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