

Enamine Chemistry. Synthesis of Substituted Benzenes and Dihydro- α -pyrones

P.W. Hickmott, B.J. Hopkins, and C.T. Yoxall

University of Salford, Salford, M5 4WT

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Although numerous syntheses of carbocyclic and heterocyclic systems by the enamine method are now available,¹ syntheses of aromatic compounds by this method are relatively few. Aromatic compounds have been obtained by cycloaddition of alkyl pentadienates to enamines,² by cycloaddition of α -chloroacrylonitrile to dienamines³, by dehydrogenation of cyclic enamines with tetraphenylcyclopentadienone,⁴ and by distillation of the enamine (not isolated) from 2-acylfurans⁵. We now wish to report two new one-step syntheses of the benzene ring system.

The first method involves reaction of enamines of acyclic ketones with halogeno- α,β -unsaturated acid chlorides, in boiling benzene, and gives substituted *m*-aminophenols (IV, V, or VI). We have previously shown⁶ that acryloyl chloride (II, X=Y=H) gives the cyclohexenone (III, X=Y=H). When β -chloro - (or α,β - dibromo) acryloyl chloride is used the cyclohexenone is not isolated but undergoes dehydrohalogenation (or elimination of bromine) to give the aromatised product (IV, V, or VI; Table I) as illustrated in Scheme I.

TABLE I.

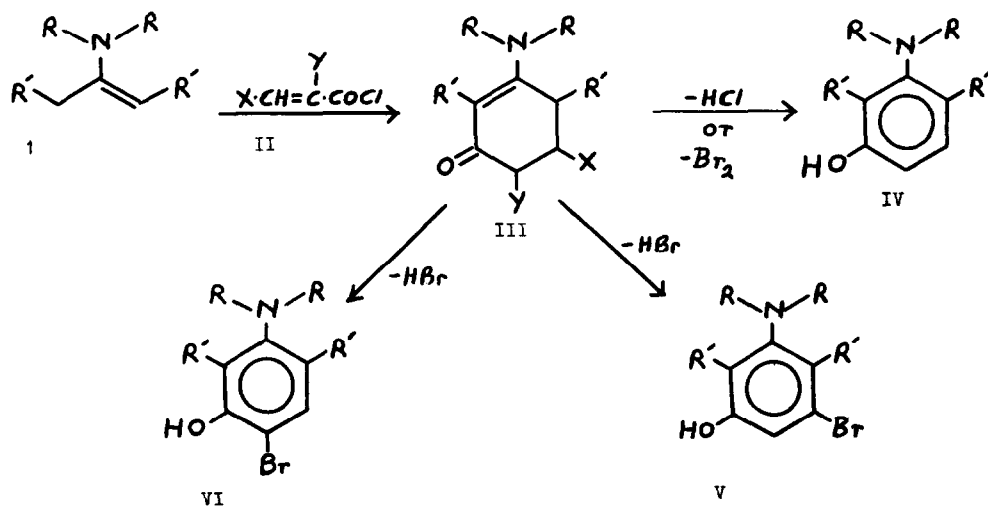
Enamine (I)		Acid chloride (II)		% Yield of <i>m</i> -aminophenol (m.p.°)	
R ₂ N	R'	X	Y	IV	V + VI
Morpholino	CH ₃	Br	Br	5 (227-230)	7(165)
Morpholino	C ₆ H ₅	Cl	H	48 (230-231)	-
N-Phenyl- piperazino	C ₆ H ₅	Cl	H	32 (86.5-87.5)	-

The second method involves reaction of aliphatic or aromatic acid chlorides with acyclic cross-conjugated dienamines (VII).⁷ This gives pentasubstituted benzenes (X) or dihydro- γ -pyrones (XII) in variable yields depending upon the acid chloride and the experimental conditions used (Table II). Possible mechanisms for the formation of these two products are given in Scheme II. As shown in Table II, low temperatures seem to favour the formation of the γ -pyrone. We suggest that at high temperatures proton loss from the intermediate iminium salt (VIII) occurs to give a mixture of C-acylated cross conjugated and linear dienamines (IXa and IXb), the latter cyclising to the benzene derivative (X) under the reaction conditions (path C). The dihydro- γ -pyrone must be formed during the aqueous work-up, either by hydrolysis of the pyran (XIII), formed by collapse of the iminium salt (VIII) (path A), or cyclisation of the β -diketone (enolic form XI) liberated by hydrolysis of the uncyclised C-acylated dienamines (IXa and IXb) (path B). Further investigation is necessary to distinguish between these two possibilities.

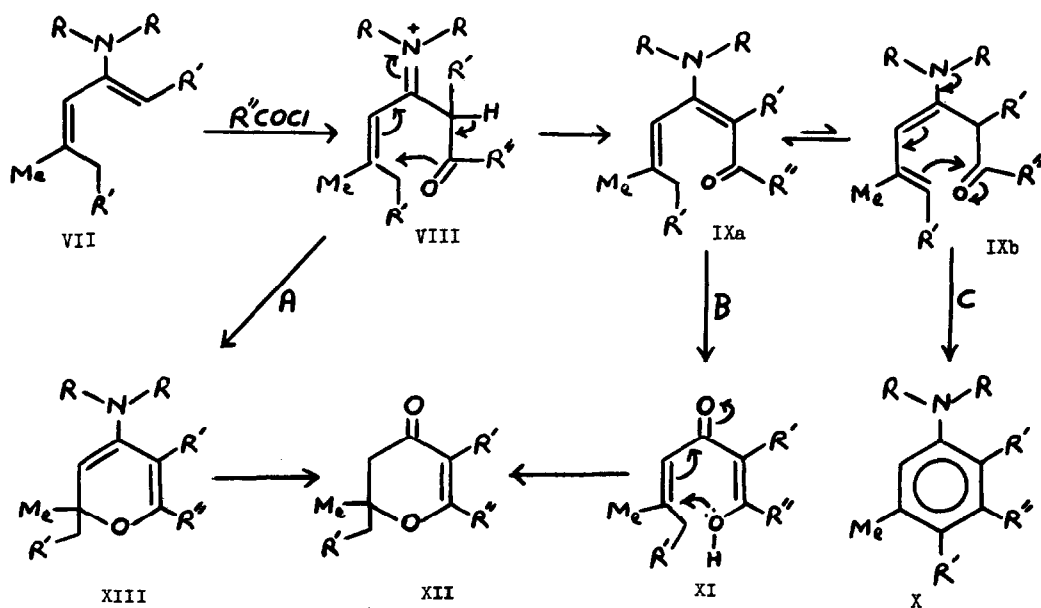
TABLE II

Dienamine (VII)	Acid Chloride		Reaction temperature	Dihydro- γ -pyrone (XII)	Benzene (X)	
R ₂ N	R'	R''	°C	% Yield	% Yield	m.p. °C
Morpholino	CH ₃	C ₆ H ₅	20	24	-	-
Morpholino	CH ₃	C ₆ H ₅	80	-	67	82.5-83.5
Morpholino	CH ₃	p-NO ₂ C ₆ H ₄	20	24	-	-
Morpholino	CH ₃	p-NO ₂ C ₆ H ₄	80	-	35	222-223
Morpholino	CH ₃	p-CH ₃ OC ₆ H ₄	80	-	41	139-140
Morpholino	CH ₃	C ₆ H ₅ ·CH=CH	80	-	20	93
Morpholino	C ₂ H ₅	C ₆ H ₅	80	17	17	111-112
Morpholino	C ₂ H ₅	p-NO ₂ C ₆ H ₄	80	20	32	222-223
Morpholino	C ₂ H ₅	p-CH ₃ OC ₆ H ₄	80	-	31	165-166
Pyrrolidino	CH ₃	CH ₃	20	60	-	-
Pyrrolidino	CH ₃	C ₆ H ₅	20	34	-	-

Scheme I



Scheme II



The structures of all products are supported by full analytical and spectroscopic data. Further exemplification of these new synthetic methods is in progress.

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