Physico-Chemical Studies of Reactions of Alkalytion of Schiff's Bases

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الخلاصة:

تمت الكلة قواعد شيف (N-ارايليدين بنزايل امين 1-29) مع هاليدات الكيل متنوعة باستخدام نظام التحفيز بانتقال الطور (الصلب-السائل) (كربونات البوتاسيوم الصلبة، اسيتونايترايل، رباعي البيوتيل بروميد الامونيوم) وقد شخصت النتائج على انها قواعد شيف المقابلة وذلك بتحاليل بيانتها الطيفية (MS,NMR,IR,UV). وتم التحقق من الميكانيكية التي يمر عبرها التفاعل اعتمادا على المقاربة النظرية باستعمال موديل AM1(شبه الحرج) في برنامج من نوع ChemOffice الطراز الجزيئي.

Abstract

The Schiff's Bases (N-arylidene benzylamines) (1-29) have been alkylated with different alkyl halides by applying solid-liquid phase-transfer catalysis system (solid K_2CO_3, CH_3CN, TBAB). The products were identified as the corresponding alkylated Schiff's bases, by analyses of their spectral data (UV, IR, NMR, MS). The mechanism of the reaction was investigated on the basis of theoretical approach using semi-empirical AM1 module in the CS ChemOffice molecular modeling package.

Keywords: Schiffs bases,Alkylation, N-Arylidene benzylamine.

Introduction:

Phase-transfer catalysis (PTC) technique had been used in the beginning[1] of the sixties as a new method to overcome the difficulties met in some reactions within immiscible compounds (heterogeneous

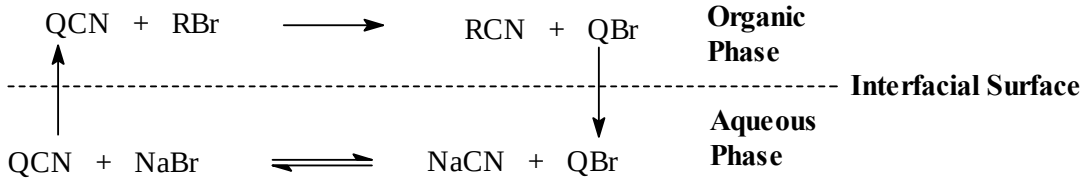
solution). As an example of these difficulties, consider[2] the following reaction:

$$n\text{-}C_8H_{17}Cl + NaCN \xrightarrow{H_2O} NaCl + n\text{-}C_8H_{17}CN$$

This reaction will not proceed even after a continuous stirring for several days. To solve this problem, some special solvents have been used which have polar and non-polar sites such as: DMSO, DMF. These solvents are able[3] to dissolve the polar (NaCN) and non-polar ($n\text{-}C_8H_{17}Cl$). They also have some disadvantages[4], like their high boiling points and being expensive and difficult to purify. It has been noticed that the reaction (below) is followed easily with good yield and rate when using a salt such as tetrabutyl ammonium cyanide[2] instead of insoluble sodium cyanide:

$$n\text{-}C_8H_{17}Br + (C_4H_9)_4\overset{\oplus\ \ominus}{N}CN \xrightarrow{H_2O} n\text{-}C_8H_{17}CN + (C_4H_9)_4\overset{\oplus\ \ominus}{N}Br$$

This is related to the lipophilic quaternary cation [$Q^+ = (C_4H_9)_4N^+$] which transfers the cyanide ion to the organic phase as (Q^+CN^-), and which in turn undergoes a reaction with ($n\text{-}C_8H_{17}Br$) to yield cyanootcane and (Q^+Br^-) which is quickly changed into (Q^+CN^-) either in the aqueous phase or in the interfacial surface as it is shown below:



For the control of infectious diseases, the discovery and development of antibiotics are aiming the most powerful and successful achievements to modern science an technology[5].
In the field of Schiff bases an extension investigations have been reported[6,7].

Chemical and Physical properties as well as their preparation have been described by various workers[8,9]. Many Workers denoted that Schiff bases formed from aromatic aldehydes or aromatic ketones and their substituents are quite stable. A wide range of these compounds have been synthesized due to the great diverse and flexibility in the structural aspects of Schiff bases, their complexation behavior had also been studied [10,11]. It was reported that nitro and halo derivatives of Schiff bases have antimicrobial and antitumor activites[12]. Antifugal and antimicrobial activates of various Schiff bases have also been reported[13,14,15]. Sahu et al [16]. reported fungi toxicity of some Schiff bases. Gawad et al[17].Synthesized some Schiff bases and observed high antimicrobial activites. Many Schiff bases are known to be medicinally important and are used to design medicinal compounds[18-20].

Experimental

Instrumentation

I. Boiling points were determined by inverted capillary in a Thiele tube using paraffin[21] colourless oil.

II. Ultra-violet spectra were obtained using Shimadzu UV-Vissible spectrophotometer UV-160.

III. Infra-red spectra were recorded on Perkin-Elmer 590 B spectrophotometer.

IV. a). Nuclear magnetic resonance (^{1}H-NMR) spectra were registered at 60 MHz. Hitachi Perkin-Elmer spectrometer, using tetramethyl silane (TMS) as an internal standard, and $CDCl_3$, d_6-DMSO as solvents.

b). Some compounds had been analysed in France* by Brucker AC 300, 400 MHz ^{1}H-NMR spectrometer, using $CDCl_3$ as a solvent.

The following abbreviations used to discuss the NMR data: s(singlet), d(doublet), 2d(two doublet signals), t(triplet), q(quartet), p(pentet), m(multiplet), br(broad).

V. Mass spectra (MS) were recorded in the laboratories of:

*UNIVERSITE` RENE` DESCARTES-PARIS V
DEPARTEMENT DE PHARMACOGNOSIE
FACULTE` DES SCIENCES PHARMACEU TIQUES ET BIOLOGIQUES

VI. Theoritical calculations based on the data obtained from the minimized geometery were computed using semi-empirical AM_1 module in the CS ChemOffice molecular modeling package.

VII. The preliminary biological study was carried out in Dept. of Biology, Coll. of Sci., Univ. of Mosul. The standard Kirby and Bauer method was used.

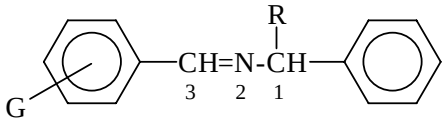
Alkylation of Schiff Bases Under (PTC) Conditions Using (Solid-Liquid) System

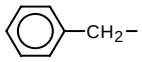
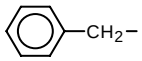
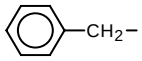
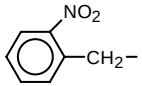
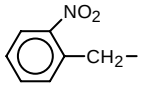
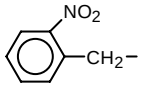
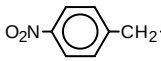
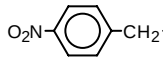
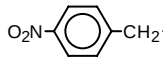
General Procedure [22]

In a 100 ml round-bottomed flask, a heterocyclic mixture of: Schiff base (10) mmole, catalyst (1) mmole, potassium carbonate (4 gm, 30 mmole), the corresponding electrophile (RX) (15) mmole and acetonitrile CH_3CN (30) ml was stirred at room temperature until no further change in colour. The resulting mixture was filtered, and the solvent was evaporated under vacuum. The liquid product was then distilled. The products were analyzed.

Table (1) illustrate the spectral data (U.V and I.R), elemental data and some physical properties of the alkylated Schiff bases (1-20), whereas table (2) illustrates the amounts of alkyl halides along with the names of products (1-29).

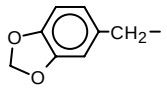
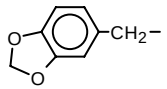
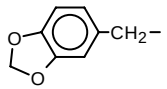
Table (1): Spectral and elemental data of alkylated Schiff bases (1-20).



Cpd. No.	R	G	b.p(°C) & colour*	Yield (%)	Reaction time (min.)	U.V ($CHCl_3$) λ_{max} (nm)	I.R (KBr) υ (cm^{-1})		Molecular formula	Elemental analysis (%) (Calc./Found)		
							C=N	Asym. N—O		C	H	N
1		H	101-102 Y-B	75	45	405	1660	---	$C_{21}H_{19}N$	88.77 87.96	6.70 6.60	4.90 4.74
2		p-NO_2	108-110 R-B	97	50	320	1675	1480	$C_{21}H_{18}N_2O_2$	76.32 75.98	5.49 5.39	8.48 8.32
3		m-NO_2	98-99 R-B	89	50	393	1640	1500	$C_{21}H_{18}N_2O_2$	76.32 75.99	5.49 5.34	8.48 8.29
4		H	168-170 Y-B	90	60	403	1655	---	$C_{21}H_{18}N_2O_2$	76.32 75.99	5.49 5.29	8.48 8.19
5		p-NO_2	97-99 Y-B	91	60	393	1675	1475	$C_{21}H_{17}N_3O_4$	67.17 66.88	4.56 4.41	11.20 11.09
6		m-NO_2	100-101 Y-B	98	70	343	1640	1500	$C_{21}H_{17}N_3O_4$	67.17 67.01	4.56 4.21	11.20 10.97
7		H	120-121 Y-B	95	70	344	1650	---	$C_{21}H_{18}N_2O_2$	76.32 76.29	5.49 5.39	8.48 8.46
8		p-NO_2	159-160 R	93	70	406	1670	1505	$C_{21}H_{17}N_3O_4$	67.17 67.21	4.56 4.39	11.20 11.12
9		m-NO_2	175-177 R	99	70	344	1640	1500	$C_{21}H_{17}N_3O_4$	67.17 67.12	4.56 4.40	11.20 11.18

*** Y: Yellow, R: Red, O: Orange, Y-B: Yellow-Brown, R-B: Reddish-Brown, P-B: Pale-Brown, D-B: Dark-Brown**

Table (1): Continued

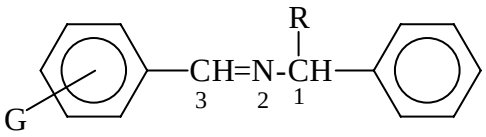
10	$CH_3CH=CHCH_2$-	H	123-124 P-B	97	30	343	1650	---	$C_{18}H_{17}NO$	87.39 86.98	6.93 7.06	5.66 5.49
11	$CH_3CH=CHCH_2$-	p-NO_2	136-139 D-B	91	30	344	1650	1500	$C_{18}H_{16}N_2O_3$	73.55 73.46	8.03 8.10	8.85 8.79
12	$CH_3CH=CHCH_2$-	m-NO_2	131.5-132 P-B	99	35	344	1640	1495	$C_{18}H_{16}N_2O_3$	73.55 73.50	8.03 8.00	8.85 8.32
13	$CH_2=CHCH_2$-	p-NO_2	128-130 R	96	25	404	1640	1500	$C_{17}H_{16}N_2O_2$	72.82 72.76	5.75 5.69	9.99 9.82
14	$CH_2=CHCH_2$-	m-NO_2	88-90 B	98	25	373	1650	1500	$C_{17}H_{16}N_2O_2$	72.82 72.70	5.75 5.66	9.99 9.82
15		H	99-99.5 B	96	20	344	1650	---	$C_{22}H_{17}NO_2$	89.44 89.32	5.80 5.69	4.74 4.62
16		p-NO_2	119-120 D-R	98	20	408	1675	1480	$C_{22}H_{16}N_2O_4$	70.94 70.69	4.33 4.24	7.52 7.41
17		m-NO_2	92-94 B	98	25	343	1680	1450	$C_{22}H_{16}N_2O_4$	70.94 70.72	4.33 4.28	7.52 7.44
18	Br-$(CH_2)_3$-CH_2-	H	101-102 Y	96	45	339	1650	---	$C_{18}H_{20}BrN$	62.21 62.60	5.80 5.73	4.03 4.10
19	Br-$(CH_2)_3$-CH_2-	p-NO_2	98-99 O	98	45	381	1650	1490	$C_{18}H_{19}BrN_2O_2$	57.59 57.34	5.10 5.21	7.46 7.13
20	Br-$(CH_2)_3$-CH_2-	m-NO_2	95-97 P-B	99	50	344	1675	1475	$C_{18}H_{19}BrN_2O_2$	57.59 57.22	5.10 4.98	7.46 7.22

*** Y: Yellow, R: Red, O: Orange, Y-B: Yellow-Brown, R-B: Reddish-Brown, P-B: Pale-Brown, D-B: Dark-Brown**

Table (2): Names of alkylated Schiff bases (1-29)

Cpd .No.	Alkyl halide (Name & amount)	Name of alkylated Schiff base	Cpd . No.	Alkyl halide (Name & amount)	Name of alkylated Schiff base
1	Benzyl chloride (1.72) ml	N-Benzylidene-α-benzyl benzyl amine	15	Methyl-3,4-dioxobenzyl chloride (2.4) gm	N-Benzylidene-α-(3,4-dioxymethyl benzyl) benzyl amine
2		N-(p-Nitrobenzylidene)-α-benzyl benzyl amine	16		N-(p-Nitrobenzylidene)-α-(3,4-dioxy methyl benzyl) benzyl amine
3		N-(m-Nitrobenzylidene)-α-benzyl benzyl amine	17		N-(m-Nitrobenzylidene)- α-(3,4-dioxy methyl benzyl) benzyl amine
4	o-Nitrobenzyl chloride (2.56) gm	N-Benzylidene-α-(o-nitrobenzyl) benzyl amine	18	1,4-Dibromo butane (1.79) ml	N-Benzylidene-1-phenyl-5-bromo pentyl amine
5		N-(p-Nitrobenzylidene)-α-(o-nitro- benzyl) benzyl amine	19		N-(p-Nitrobenzylidene)-1-phenyl-5-bromo pentyl amine
6		N-(m-Nitrobenzylidene)-α-(o-nitro-benzyl) benzyl amine	20		N-(m-Nitrobenzylidene)-1-phenyl-5-bromo pentyl amine
7	p-Nitrobenzyl chloride (2.56)	N-Benzylidene-α-(p-nitrobenzyl) benzyl amine	21	Methyl iodide (0.93) ml	N-Benzylidene-α-methyl benzyl amine
8		N-(p-Nitrobenzylidene)-α-(p-nitro- benzyl) benzyl amine	22		N-(p-Nitrobenzylidene)-α-methyl benzyl amine
9		N-(m-Nitrobenzylidene)-α-(p-nitro- benzyl) benzyl amine	23		N-(m-Nitrobenzylidene)-α-methyl benzyl amine
10	Crotyl chloride (1.47) ml	N-Benzylidene-1-phenyl-3-pentenyl amine	24	Butyl bromide (1.6) ml	N-Benzylidene-1-phenyl pentyl amine
11		N-(p-Nitrobenzylidene)- 1-phenyl-3-pentenyl amine	25		N-(p-Nitrobenzylidene)-1-phenyl pentyl amine
12		N-(m-Nitrobenzylidene)-1-phenyl-3-pentenyl amine	26		N-(m-Nitrobenzylidene)-1-phenyl pentyl amine
13	Allyl chloride (1.22) ml	N-(p-Nitrobenzylidene)-1-phenyl-3-butenyl amine	27	o-Bromobenzoyl chloride (2.19) ml	N-Benzylidene-α-(o-bromobenzoyl)-benzyl amine
14		N-(m-Nitrobenzylidene)-1-phenyl-3-butenyl amine	28		N-(p-Nitrobenzylidene)-α-(o-bromo benzoyl) benzyl amine
			29		N-(m-Nitrobenzylidene)-α-(o-bromo benzoyl) benzyl amine

Table (3): Spectral data, physical properties and elemental data of some alkylated Schiff bases(21-29).



Cpd. No.	b.p(°C) & colour*	G	R	UV ($CHCl_3$) λmax (nm)	IR(KBr) υ (cm^{-1})		^{1}H-NMR ($CDCl_3$) δ(ppm)	Yield (%)	Reaction time (min)	Molecular formula	Elemental analysis (%) (Calc./Found))		
					C=N	N—O asym					C	H	N
21	94-97 Y-B	H	CH_3-	304	1650	---	0.9(d,3H,CH_3), 3.0(q, 1H, H-1), 5.55(s, 1H, H-3), 6.9 (s, 10H, Ar-H)	88	15	$C_{15}H_{15}N$	86.07 86.17	7.22 7.01	6.69 6.42
22	84-85 Y-B	p-NO_2	CH_3-	302	1640	1500	1.1(d,3H,CH_3), 4.4(q, 1H, H-1), 4.9(m,1H, H-3), 6.3-6.9 (m, 5H, C_6H_5-), 6.8-7.1 (dd, 4H, p-$NO_2C_6H_4$-)	78	15	$C_{15}H_{14}N_2O_2$	70.83 70.68	5.55 5.48	11.02 10.42
23	87-88 Y-B	m-NO_2	CH_3-	302	1640	1500	1.0(m,3H,CH_3), 4.35(q, 1H, H-1), 5.5(s,1H, H-3), 6.8-7.5 (m, 9H, Ar-H)	87	15	$C_{15}H_{14}N_2O_2$	70.83 70.57	5.55 5.38	11.02 11.20
24	92-93 Y-B	H	$CH_3(CH_2)_2CH_2$-	302	1650	---	0.9(t,3H,CH_3), 1.4(m, 4H, -CH_2-CH_2), 1.7(m,2H, Ar-CH_2-), 3.0(m, 1H, H-1), 4.8 (m, 1H, H-3), 6.8-8.3 (m, 10H, Ar-H)	98	40	$C_{18}H_{21}N$	85.99 85.70	8.42 9.04	5.57 5.39

Table (3): Continued

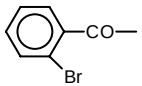
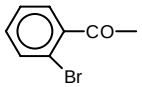
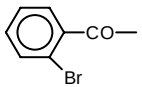
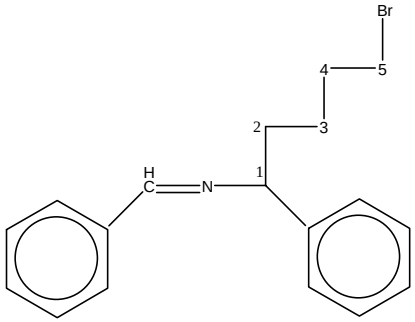
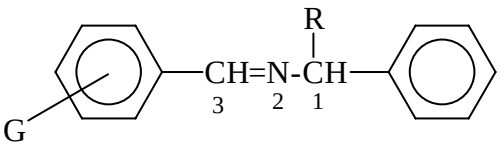
25	164-165 Y-B	p-NO_2	$CH_3(CH_2)_2CH_2$-	396	1640	1490	0.9(t,3H,CH_3), 1.4(m, 4H, -CH_2-CH_2),1.7(m,2H, Ar-CH_2),3.0(t, 1H, H-1), 4.9 (m, 1H, H-3), 6.5-8.0 (m, 5H, C_6H_5-),6.6-7.9(dd, 4H, p-NO_2 $_6H_4$)	92	40	$C_{18}H_{20}N_2O_2$	81.76 81.51	7.63 7.72	10.60 10.48
26	135-136 Y-B	m-NO_2	$CH_3(CH_2)_2CH_2$-	343	1640	1500	0.9(t,3H,CH_3), 1.5(m, 4H, -CH_2-CH_2-), 2.0(m,2H, Ar-CH_2-), 3.2(t, 1H, H-1), 5.0 (s, 1H, H-3), 6.5-8.6(m, 9H, Ar-H)	90	45	$C_{18}H_{20}N_2O_2$	81.76 81.62	7.63 7.45	10.60 10.62
27	89-90 B	H		300	1665	---	2.8(s, 1H, H-1), 4.65(s, 1H, H-3),6.0-6.7(m, 10H, Ar-H), 7.0-7.5(m,4H,o-Br($6H_4$))	97	80	$C_{21}H_{16}BrNO$	66.66 66.41	4.26 4.19	3.70 3.60
28	136-137 D-R	p-NO_2		399	1640	1465	3.2(s, 1H, H-1), 5.6(s, 1H, H-3), 6.6-7.5(m, 9H, Ar-H), 6.4-7.4(dd,4H,p-$NO_2C_6H_4$-)	98	80	$C_{21}H_{15}BrN_2O_3$	59.55 59.29	3.57 3.42	6.61 6.45
29	111-112 D-R	m-NO_2		344	1650	1505	3.3(m, 1H, H-1), 5.3(m, 1H, H-3), 6.2-8.0(m,13H, Ar-H)	98	90	$C_{21}H_{15}BrN_2O_3$	59.55 59.28	3.57 3.42	6.61 6.50

Table (4): The ^{1}H-NMR,Mass spectral and elemental data of compound (23)

Cdp. No.	NMR($CDCl_3$) Δ(ppm)		Molecular formula	Elemental Microanalysis % (Cal C. /Found)					Structure
				C	H	Hal	N	O	
23	1.4(P,4H,CH_2-3, CH_2-4) 1.7(q,2H, CH_2-2) 2.9 (t, CH_2-31H, CH-1) 3.55(5,2H, CH_2-5) 8.4(5,1H,CH=N) 7.2-7.9(m,10H,Ar-H)		$C_{18}H_{20}BrN$	65.43 65.46	6.10 6.16	24.20 24.19	4.24 4.24	-- --	
Cdp. No.	m/z	Relative intensity(%)	Reagent gas	Integral[27] collector reading (abundance)		Molecular ion[27] and base peak[28]			Parent molecule
									Elemental Composition / Exact mass / Molecular weight
23	196	100	NH_3	11.400		Base peak			$C_{18}H_{20}BrN$ / 329.10 / 330.26
	330	0.76		100		Molecular ion MH^+			

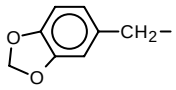
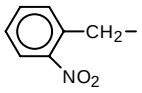
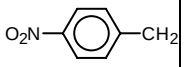
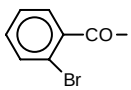
Resulst and Discussion

The alkylation of Schiff bases [N-benzylidene benzylamine (I), N-(p-nitrobenzylidene benzylamine) (II) and N-(m-nitrobenzylidene benzylamine (III)] under (PTC) conditions (solid-liquid system) with different alkyl halides afforded the corresponding alkylated Schiff bases (1-29):

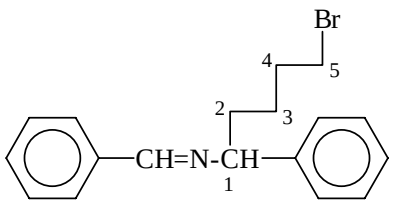


N-arylidene-α-substituted benzylamines (1-29)

The spectral and elemental data are used for the identification of the products (1-29) (tables: 1, 2, 3 and 4).

Cpd. No.	G	R	Cpd. No.	G	R
1	H	Ph-CH_2-	**15**	H	
2	p-NO_2	=	**16**	p-NO_2	=
3	m-NO_2	=	**17**	m-NO_2	=
4	H		**18**	H	$Br(CH_2)_3CH_2$-
5	p-NO_2	=	**19**	p-NO_2	=
6	m-NO_2	=	**20**	m-NO_2	=
7	H		**21**	H	CH_3-
8	p-NO_2	=	**22**	p-NO_2	=
9	m-NO_2	=	**23**	m-NO_2	=
10	H	$CH_3CH=CHCH_2$-	**24**	H	$CH_3(CH_2)_2CH_2$-
11	p-NO_2	=	**25**	p-NO_2	=
12	m-NO_2	=	**26**	m-NO_2	=
13	p-NO_2	$CH_2=CHCH_2$-	**27**	H	
14	m-NO_2	=	**28**	p-NO_2	=
			29	m-NO_2	=

As a representative model, the compound (18) is selected in the discussion of spectral data.



18

N-benzylidene-1-phenyl-5-bromo pentylamine (18)

The (^{1}H-NMR) spectrum[23,24] (table 4) shows a pentet signal resonates at δ(1.4) ppm (4H) related to the methylene protons at C-3 and C-4. A quartet signal at δ(1.7) ppm (2H) attributed to the methylene protons at C-2. A triplet signal resonates at δ(2.9) ppm (1H) corresponds to the proton at C-1. A singlet signal is appeared at δ(3.55) ppm (2H) due to the methylene protons at C-5. Another singlet signal resonates at δ(8.4) ppm (1H) referred to C<u>H</u>=N.

Finally, the multiplet signal at δ(7.2-7.9) ppm (10H) related to the aromatic protons.

The (IR) spectrum (tables 1) exhibits a strong absorption band at (1650) cm^{-1} attributed to υC=N.

The (UV) spectrum[25] (table 1) indicates a maximum absorption at wavelength λmax= (339) nm compared with λmax= (320) nm for the reacted Schiff base (I) which reflects a red shift.

The (MS) spectrum[26,27] (table 4) shows a base peak[28] (100%, abundance 11,400) for m/z= 196 and a molecular ion $(MH)^+$ (0.76%, abundance 100) for m/z= 330. The molecular ion $(MH)^+$ is in quite good agreement with the composition $C_{18}H_{20}BrN$.

The elemental analysis (table 4) shows a good agreement with the calculated (C, H, N, Br) values.

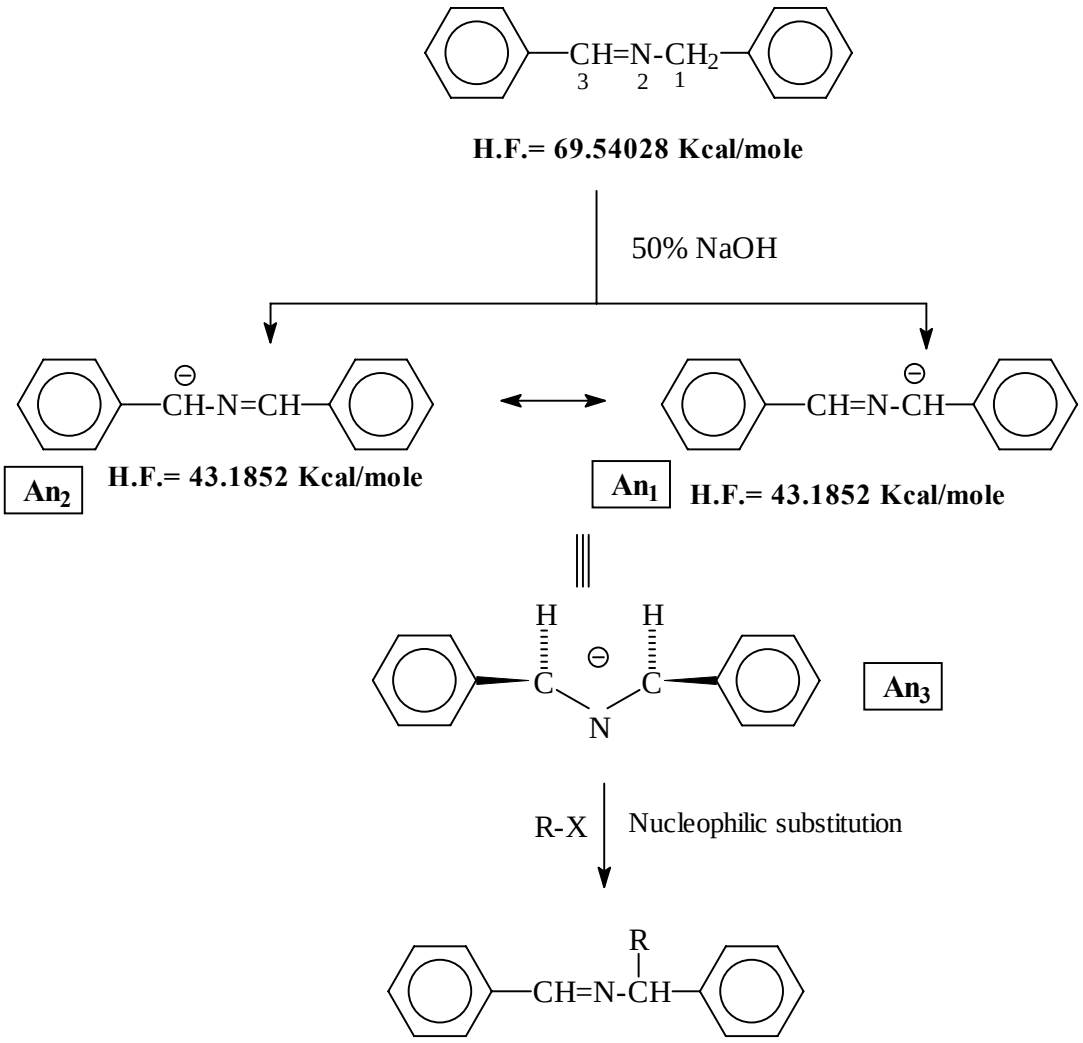
The alkylation of the Schiff base (N-benzylidene benzylamine I) using: benzyl chloride, crotyl chloride and methyl iodide are selected as a representative reactions for discussing the mechanism of the alkylation.

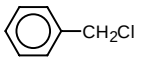
The suggested mechanism for such reaction (scheme 1) is initiated by the abstraction of the acidic proton from the Schiff base under the influence of the strong base (50% NaOH). The formed anion An_1 may attack the alkyl halide (RX) via nucleophilic substitution to afford the final products (1) (H.F= 93.98380, S.E= 0.206), (10) (H.F= 75.28176, S.E= 7.047) and (21) (H.F= 66.60970, S.E= 0.433).

An_1 may resonates to give the anion An_2 since An_1 and An_2 are the same, accordingly the same product is obtained whether the alkylation occurred at any one of the two carbons attached to the nitrogen, the mechanism may be suggested as the attack of the anion An_1 or An_2 on α-carbon of R-X or via the resonance hybride An_3.

Appendix (17) illustrates the minimized geometry data of the final product (21), whereas (Figure 1) illustrates the 3D-structure of (21). The 3D-structure of (21) reflects the planarity of the molecule where:

$C_2C_3C_4$ <u>C_5</u>=0.09484, $C_3C_2C_1$ <u>C_6</u>=0.05331, $C_3C_4C_5$ <u>C_7</u>= -179.75113, $C_4C_5C_7$<u>N_8</u>= -179.22244, $C_5C_7N_8$ <u>C_9</u>= 179.28763 and $C_9C_{10}C_{11}$<u>C_{12}</u>= -178.97775 (Appendix-1)



Cpd. No.	R-X	H.F.(Kcal/mole)	S.E.(Kcal/mole)
1		93.98380	0.206
10	$CH_3CH=CHCH_2Cl$	75.28176	4.047
21	CH_3I	66.60970	0.433

Scheme (1): Reaction of Schiff base (I) with benzyl chloride, crotyl chloride and methyl iodide

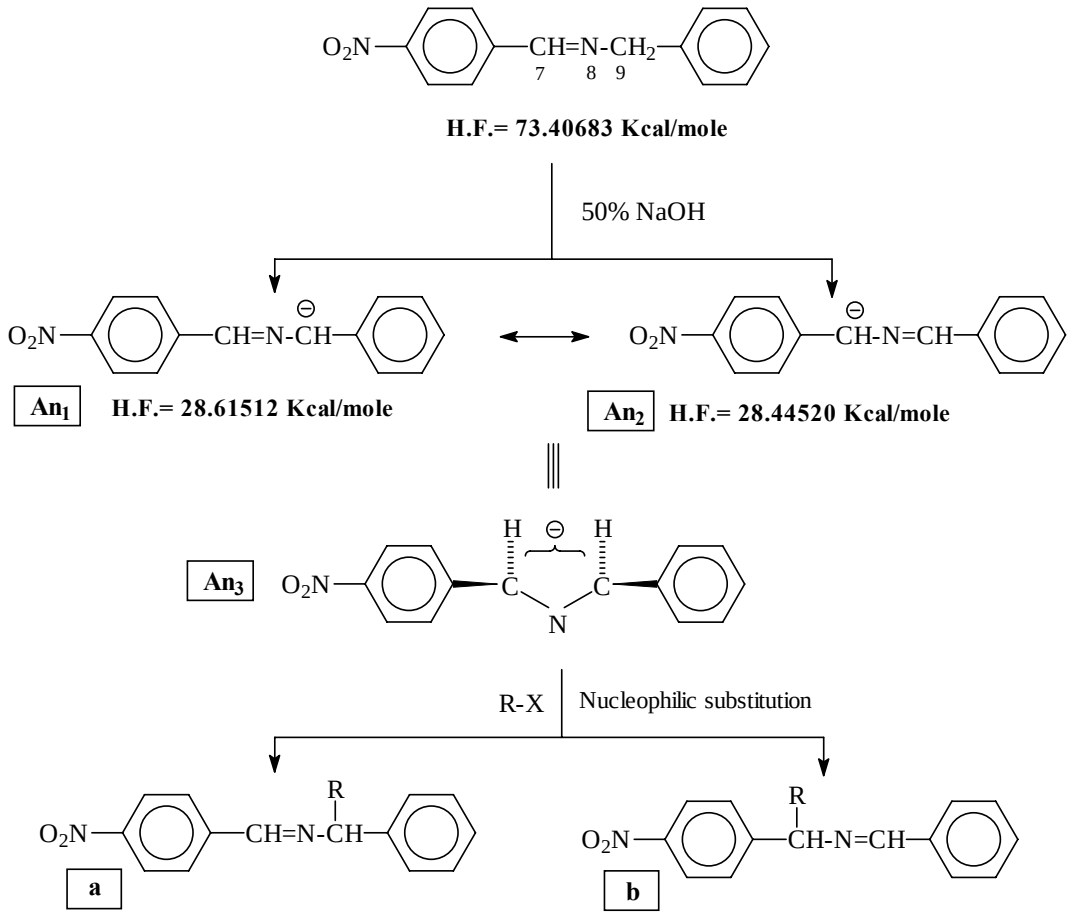
On the other hand, when asymmetric Schiff base is used, i.e.: with certain substituents on one of the two phenyls as Schiff base (N-p-nitrobenzylidene benzylamine), the attack may proceed via An_1 or An_2 (which may be represented by An_3) on the alkyl halide.

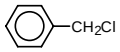
The alkylation of Schiff base with benzyl chloride, crotyl chloride and methyl iodide which afforded (2, 11 and 22) respectively are investigated in order to give some information on the mechanism of these reactions and show the effect of the alkyl groups on such reactions.

As such, the abstraction of the acidic proton from the Schiff base may leads to the liberation of the two anions An_1 and An_2 (scheme 2) which may be represented by the resonance hybrid An_3.

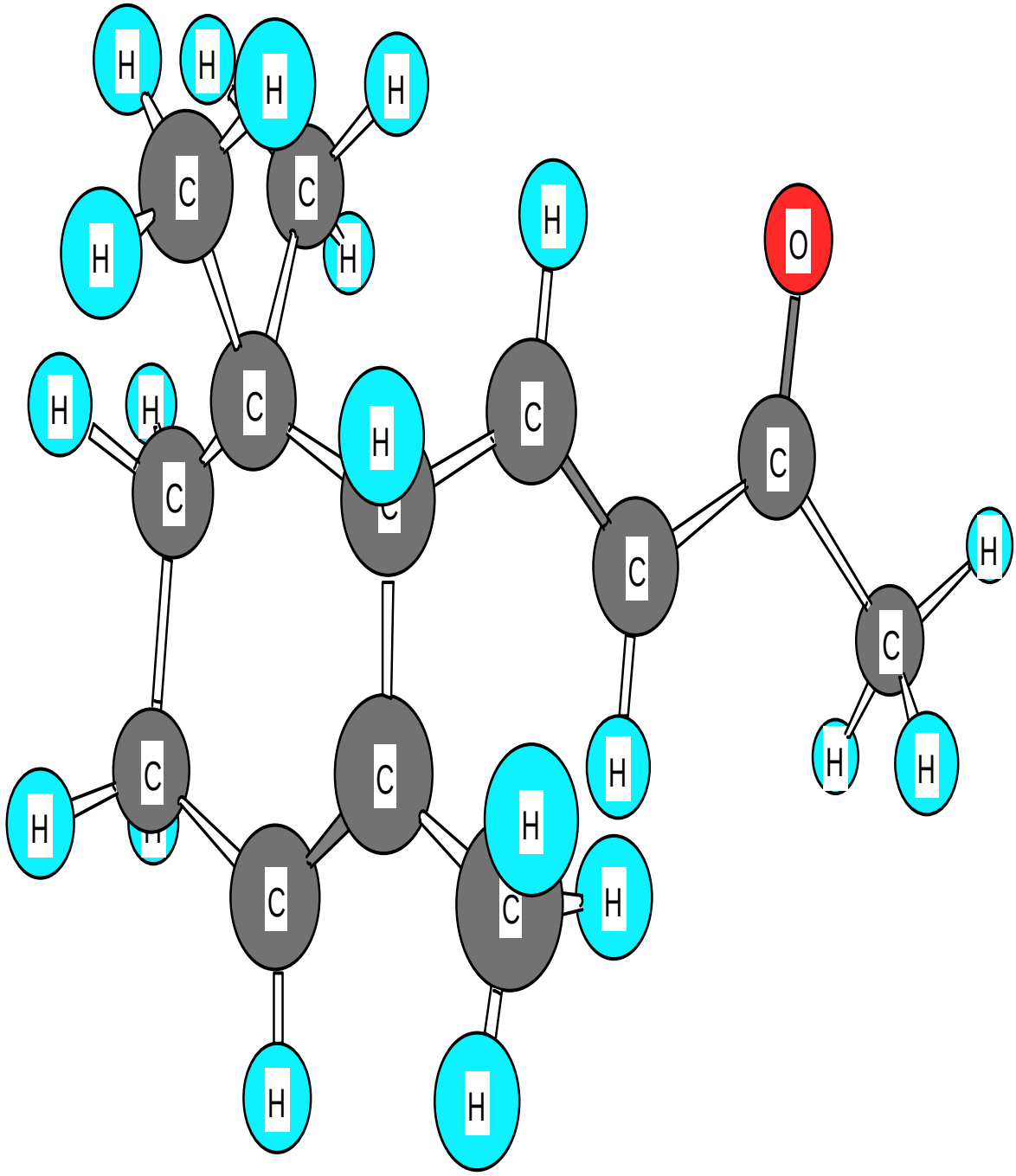
An_3 in turn may attack the carbon attached to the halogen in the alkyl halide molecule and upon substitution of the halide, the final products would be afforded either (2-a) (H.F= 97.86365, S.E= 44.642), (11-a) (H.F= 79.10883, S.E= 48.500) and (22-a) (H.F= 70.38823, S.E= 44.895) or (2-b) (H.F= 97.0400, S.E= 12.679), (11-b)(H.F= 78.25746, S.E= 15.223) and (22-b) (H.F= 70.16624, S.E= 13.938).

The analysis of the spectral data support the formation of the actual products (2-a), (11-a) and (22-a) rather than (2-b), (11-b) and (22-b) (the proposed products). Besides, it could be noticed that the (H.F.) increased as the size of the alkyl group (R-X) increase.



Cpd. No.	R-X	H.F.(Kcal/mole)	S.E.(Kcal/mole)
2a		97.86305	44.642
2b	=	97.04000	12.679
11a	$CH_3CH=CHCH_2Cl$	79.10883	48.500
11b	=	78.25746	15.223
22a	CH_3I	70.38823	44.895
22b	=	70.16624	13.938

Scheme (2): Reaction of Schiff base(II) with benzyl chloride, crotyl chloride and methyl iodide



Compound (2-a) Final product

Figure-1-

Preliminary Biological Study

In the present work, preliminary biological study is carried out. The biological inhibitory effect (s) of certain products such as: Schiff bases (1, 3, 4, 28, 29) against two types of bacterial groups such as: Gram-negative ***E. coli*** and Gram-positive ***Staphylococcus aureus*** were investigated (table 5).

The isolates were isolated and identified in Biology Dept. in the College of Science in Mosul Univ. The standard Kirby and Bauer[29] method was used.

A loopful of each bacterial species were cultured in nutrient broth and incubated at (37°C) for (14-16 hr.) and then evently distributed on the nutrient agar by using a sterile swab. The plates were incubated at (37°C) for (30) min.

The filter paper (Whatmann No.1) discs were distributed on the agar and a certain equal (1 mg/1 ml) or (1 ml/1 ml) of the compound per solvent (DMSO) was added. The controls here were the Chloramphenicol and / or Ampicillin for comparison. The plates were then incubated at (37°C) for (18-24) hr. (The interpretation of the results equal the diameter (mm) of the inhibition zone appeared around the discs[30].

The results were interpreted according to the report of the (W.H.O.).

The resistant (R) result represented the diameter of inhibition < (11) mm. However, the moderately sensitive (MS) result was regarded when the zone of inhibition was between (12-16) mm. The sensitive (S) result was over (16) mm.

Table (5): Inhibition effect of certain products on growth of staphylococcus aureus and Escherichia coli

Cpd. No.	Test Organism	
	Staph. Aureus	***E.Coli***
1	S	R
3	S	MS
4	S	S
28	S	S
29	S	S
Chloramphenicol	S	S
Ampicillin	S	S

Appendix (1)
Final Product, Compound (21)

Charges:

C_1= -0.141397	C_2= -0.115552	C_3= -0.139134	C_4= -0.112218
C_5= -0.067222	C_6= -0.083705	C_7= -0.026542	N_8= -0.175310
C_9= -0.010120	C_{10}= 0.069159	C_{11}= 0.121431	C_{12}= -0.127911
C_{13}= -0.128722	C_{14}= -0.129688	C_{15}= -0.117211	C_{16}= 0.235398
H_{17}= 0.134187	H_{18}= 0.132067	H_{19}= 0.132458	H_{20}= 0.130014
H_{21}= 0.154788	H_{22}= 0.098212	H_{23}= 0.114792	H_{24}= 0.129738
H_{25}= 0.131277	H_{26}= 0.131029	H_{27}= 0.131471	H_{28}= 0.133384
H_{29}= 0.081680	H_{30}= 0.088758	H_{31}= 0.076863	

Charges:
Bond Length (A°):

C_1C_2= 1.39389	C_2C_3= 1.39571	C_3C_4= 1.39244	C_4C_5= 1.40326
C_1C_6= 1.39497	C_5C_7= 1.47171	C_7N_8= 1.28639	N_8C_9= 1.44964
C_9C_{10}= 1.51135	$C_{10}C_{11}$= 1.39876	$C_{11}C_{12}$= 1.39367	$C_{12}C_{13}$= 1.39508
$C_{13}C_{14}$= 1.39443	$C_{10}C_{15}$= 1.39824	C_9C_{16}= 1.53121	C_1H_{17}= 1.10004
C_2H_{18}= 1.09983	C_3H_{19}= 1.09978	C_4H_{20}= 1.10049	C_6H_{21}= 1.10139
C_7H_{22}= 1.11529	C_9H_{23}= 1.13624	$C_{11}H_{24}$= 1.10060	$C_{12}H_{25}$= 1.09977
$C_{13}H_{26}$= 1.09958	$C_{14}H_{27}$= 1.09984	$C_{15}H_{28}$= 1.10029	$C_{16}H_{29}$= 1.11603
$C_{16}H_{30}$= 1.11616	$C_{16}H_{31}$= 1.11630		

Bond Angle (degree):

$C_1C_2C_3$=119. 85417	$C_2C_3C_4$= 120.11654	$C_3C_4C_5$= 120.24860	$C_2C_1C_6$= 120.31910
$C_4C_5C_7$= 118.26382	$C_5C_7N_8$= 123.19308	$C_7N_8C_9$= 121.72556	$N_8C_9C_{10}$= 112.21725
$C_9C_{10}C_{11}$= 120.67568	$C_{10}C_{11}C_{12}$= 120.20796	$C_{11}C_{12}C_{13}$=120.08087	$C_{12}C_{13}C_{14}$=119.86615
$C_9C_{10}C_{15}$=119.74720	$C_8C_9C_{16}$= 116.86926	$C_2C_1H_{17}$=119.99093	$C_1C_2H_{18}$=120.12964
$C_2C_3H_{19}$=120.00438	$C_3C_4H_{20}$=119.77640	$C_1C_6H_{21}$=119.75471	$C_5C_7H_{22}$=113.14297
$N_8C_9H_{23}$=103.23022	$C_{10}C_{11}H_{24}$=119.77215	$C_{11}C_{12}H_{25}$=119.89536	$C_{12}C_{13}H_{26}$=120.04793
$C_{13}C_{14}H_{27}$=120.02358	$C_{10}C_{15}H_{28}$=120.06444	$C_9C_{16}H_{29}$=110.68020	$C_9C_{16}H_{30}$=109.07180
$C_9C_{16}H_{31}$=111.14412			

Twist Angle (degree):

$C_1C_2C_3\underline{C_4}$= -0.10374	$C_2C_3C_4\underline{C_5}$= 0.09484	$C_3C_2C_1\underline{C_6}$= 0.05331
$C_3C_4C_5\underline{C_7}$= -179.75113	$C_4C_5C_7\underline{N_8}$= -179.22244	$C_5C_7N_8\underline{C_9}$= 179.28763
$C_7N_8C_9\underline{C_{10}}$= 97.57314	$N_8C_9C_{10}\underline{C_{11}}$= -62.36017	$C_9C_{10}C_{11}\underline{C_{12}}$= -178.97775
$C_{10}C_{11}C_{12}\underline{C_{13}}$= -0.06659	$C_{11}C_{12}C_{13}\underline{C_{14}}$= -0.19494	$N_8C_9C_{10}\underline{C_{15}}$= 118.19682
$C_7N_8C_9\underline{C_{16}}$= -28.91081	$C_3C_2C_1\underline{H_{17}}$= -179.96271	$C_6C_1C_2\underline{H_{18}}$= -179.95753
$C_1C_2C_3\underline{H_{19}}$= 179.91753	$C_2C_3C_4\underline{H_{20}}$= -179.97464	$C_2C_3C_4\underline{H_{21}}$= 179.96095
$C_4C_5C_7\underline{H_{22}}$= 7.28229	$C_7N_8C_9\underline{H_{23}}$= -146.20980	$C_9C_{10}C_{11}\underline{H_{24}}$= 1.31820
$C_{10}C_{11}C_{12}\underline{H_{25}}$= -179.89014	$C_{11}C_{12}C_{13}\underline{H_{26}}$= -179.98662	$C_{12}C_{13}C_{14}\underline{H_{27}}$=-179.71708
$C_9C_{10}C_{15}\underline{H_{28}}$= -1.38694	$N_8C_9C_{16}\underline{H_{29}}$= -49.7126	$N_8C_9C_{16}\underline{H_{30}}$= -169.244
$N_8C_9C_{16}\underline{H_{31}}$= 71.44688		

Final heat of formation = 66.60970 Kcal/mole = 278.69797 KJ

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