

DIPOLAR ADDITION REACTIONS ON ALDAZINES AND ANILS

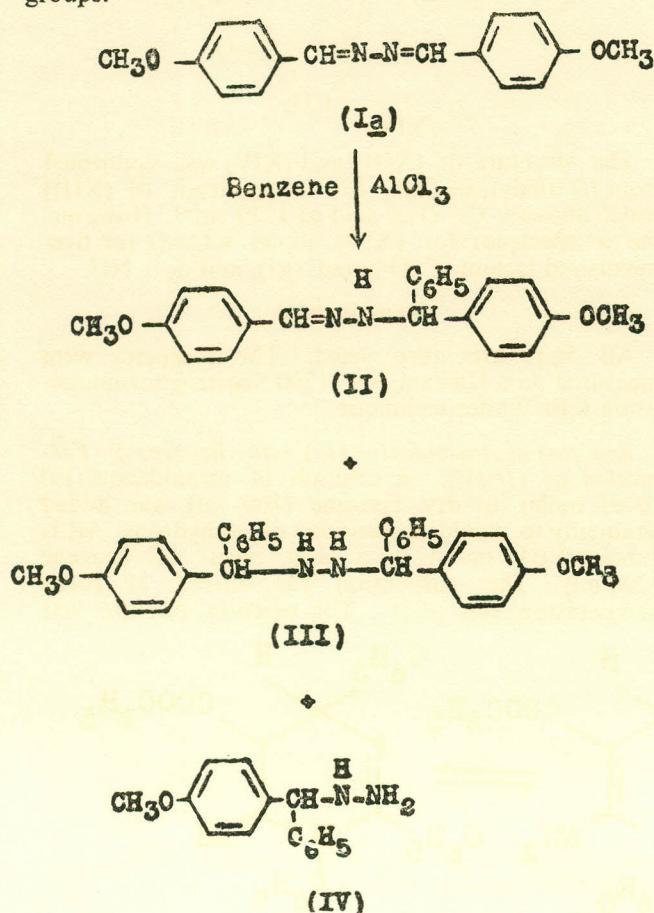
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Abstract. Aldazines (Ia, b) add aromatic hydrocarbons in the presence of anhydrous $AlCl_3$ to give (II), (III) and (IV). The cyclo dipolar addition of ethyl cyanoacetate, ethyl bromoacetate, and thioglycolic acid on anils was used as a useful method for synthesis of some large and small ring heterocycles (VI), (VII), (X) and (XIV).

In the present investigation the hitherto unknown 1,2-dipolar addition of aromatic hydrocarbon substrates to aldazines under the condition of the Friedel-Crafts reaction was discovered. Anisaldazine (I) reacts with benzene in the presence of anhydrous $AlCl_3$ to give three products, namely, (i) anisaldehyde-(*p*-anisyl, phenyl)-methyl hydrazone (II) via addition of one mole of benzene; (ii) symmetrical di-*p*-anisyl, phenyl-dimethylhydrazine (III) via addition of two moles of benzene; (iii) asymm. *p*-anisyl-phenyl methylhydrazine (IV) via addition of one mole of benzene and dearylation of one of the arylidene groups.



Structure (II) was confirmed from analytical data and ir spectrum which shows ν_{NH} at $3300-3250\text{ cm}^{-1}$.

Structure (III) was confirmed from (i) analytical data, (ii) ir spectrum which shows ν_{NH} at $(3500-3450\text{ cm}^{-1})$ (br.) and (iii) authentically via the reaction of anisole with benzalazine (Ib) in the presence of anhydrous $AlCl_3$.

It was found also that ethylcyanoacetate undergoes base catalyzed 1,4-cyclodipolar addition with benzylidene acetophenone anil (V) via two competitive routes to give 1,4,6-triphenyl-3-cyano-2(1H)-pyridene (VI) in major yield, and ethyl-2-amino-1,4,6-triphenyl-dihydropyridine (VII).

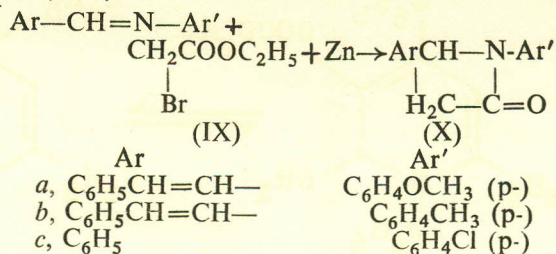
A more reasonable explanation of the preference of route (a) is that $C\equiv N$ is less reactive than $COOEt$ and the reaction with $C\equiv N$ is reversible.

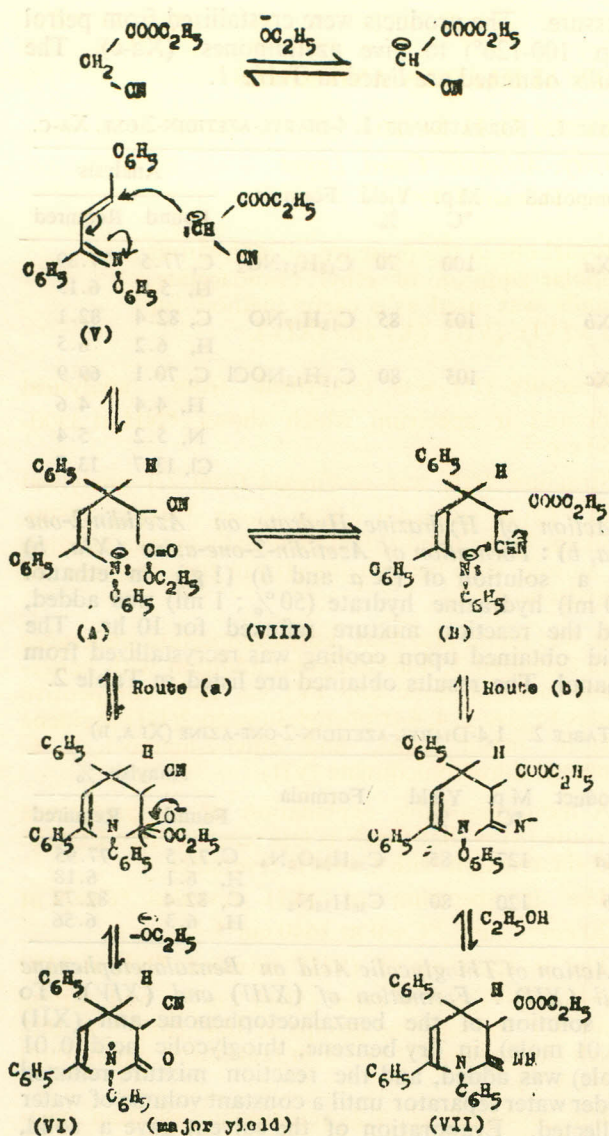
The ir spectrum of (VI) revealed $\nu_{C\equiv N}$ at 2220 cm^{-1} , and $\nu_{C=O}$ at 1640 cm^{-1} .

The ir spectrum of (VII) revealed ν_{NH} at 3450 cm^{-1} , and $\nu_{C=O}$ of ester (1690 cm^{-1}), and strong band for the kitimine groups at 1640 cm^{-1} , a fact which shows that VII exists in tautomeric equilibrium (VII. A-C).

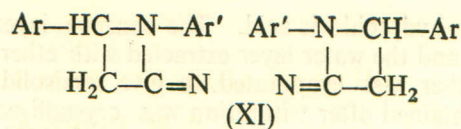
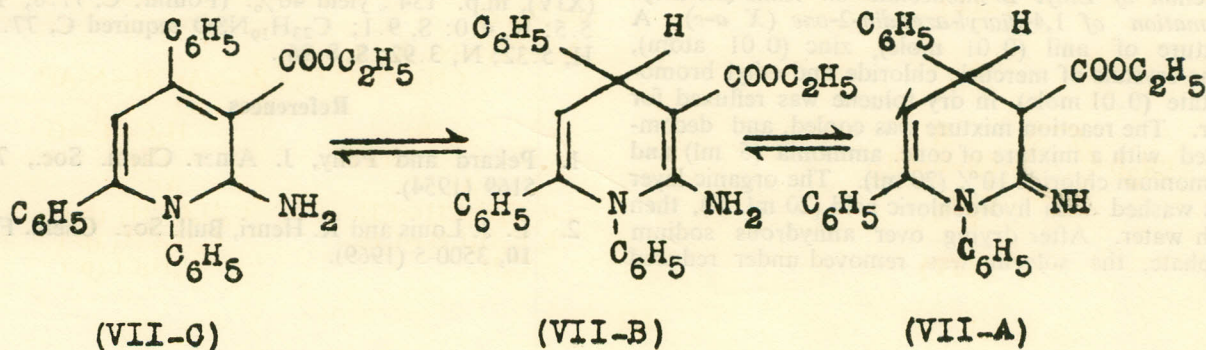
The problem² of 1,2-cyclodipolar addition reaction of ethyl bromoacetate under the condition of the Reformatsky reaction was reinvestigated by using differently substituted anils to see the effect of substitution on the mode of addition.

Cinnamal-*p*-anisidine (IXa), cinnamal-*p*-toluidine (IXb), and benzal-*p*-chloro-aniline (IXc) undergo acyclodipolar addition reaction with ethyl bromoacetate to give the corresponding 1,4-diaryl-azetidino-2-one (Xa-c)





The structure of (X) was confirmed from: (i) analytical data, (ii) ir spectra for (X) which show a band in the region ($1760-1730\text{ cm}^{-1}$) which is characteristic for four membered ring of ν -lactams, (iii) chemically via the reaction of hydrazine hydrate on (Xa, b) to give the corresponding, 1,4-diaryl-azetidin-2-one-azine (XIa, b).

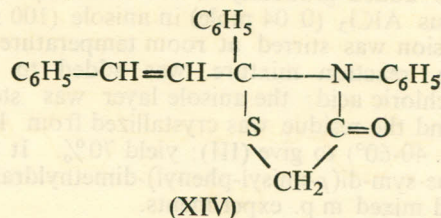
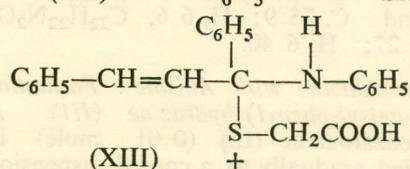
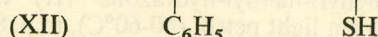
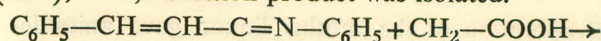


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a, $\text{C}_6\text{H}_5\text{CH}=\text{CH}-$ $\text{C}_6\text{H}_4\text{OCH}_3$ (*p*-)

b, $\text{C}_6\text{H}_5-\text{CH}=\text{CH}-$ $\text{C}_6\text{H}_4\text{CH}_3$ (*p*-)

It was found that thioglycolic acid undergoes 1,2-cyclodipolar addition to benzalacetophenone anil (XII), to give a mixture of open chain product (XIII), and cyclic 2-phenyl-3-styryl-4-thiazolidene (XIV); no 1,4-addition product was isolated.



The structure of (XIII) and (XIV) was confirmed from (i) analytical data, (ii) ir spectrum of (XIII) which shows $\nu\text{ C}=\text{O}$ of acid at 1720 cm^{-1} . However, the ir spectrum for (XIV) shows $\nu\text{ C}=\text{O}$ for five-membered lactam of (1740 cm^{-1})⁽¹⁾, and no $\nu\text{ NH}$.

Experimental

All m.p. are uncorrected. The ir spectra were measured on a Unicam S.p., 1200 Spectrophotometer, using KBr Waffer technique.

Reaction of Anisaldehyde (Ia) with Benzene: Formation of (II-IV). A solution of anisaldehyde (Ia) (0.01 mole) in dry benzene (100 ml) was added gradually to a cold suspension of anhydrous AlCl_3 (about 0.04 mole) in a large excess of benzene (200 ml). The suspension was stirred at room temperature for 10 hr. The reaction mixture was

then added to hydrochloric acid. The benzene layer was distilled and the water layer extracted with ether, and then ether was evaporated, to give semisolid. The solid obtained after trituration was crystallized from light petrol (40-60°) to give (III), m.p. 140°; yield 40%. Found C, 79.21; H, 6.65; $C_{28}H_{28}N_2O_2$ required C, 79.21; H, 6.65.

Leaving the oil for a long period resulted in a semisolid which was crystallized from light petrol (80-100°) to give (IV), m.p. 110° (decomposition) yield 20%. Found: C, 73.3; H, 6.6; $C_{14}H_{16}N_2O$ required C, 73.76; H, 7.06.

Evaporation of the mother liquor gave anisaldehyde-(*p*-anisyl-phenyl)-methyl-hydrazone (II) which was crystallized from light petrol (40-60°C), m.p. 85°C, yield 15%. Found: C, 75.9; H, 6.6, $C_{22}H_{22}N_2O_2$ required: C, 76.27; H, 6.40.

Reaction of Benzalazine with Anisole: Formation of Sym. di-(p-anisyl-phenyl)-hydrazine (III). A solution of benzaldazine (Ib) (0.01 mole) in anisole was added gradually to a cooled suspension of anhydrous $AlCl_3$ (0.04 mole) in anisole (100 ml). The suspension was stirred at room temperature for 10 hr. The reaction mixture was added to ice-cold hydrochloric acid; the anisole layer was steam distilled; and the residue was crystallized from light petrol (b. p. 40-60°) to give (III); yield 70%. It was proved to be sym-di(*p*-anisyl-phenyl)-dimethylhydrazine by m.p. and mixed m.p. experiments.

Action of Ethyl Cyanoacetate on Benzylidene Acetophenone anil V: Formation of (VI and VII). A mixture of benzylidene acetophenone anil (V) (0.01 mole), sodium ethoxide (.02 mole) and ethyl cyanoacetate (0.01 mole) was heated for (7 hr) at 185°. After cooling, the reaction mixture, the product obtained was washed with cold ethanol and the residue was crystallized from butyl alcohol to give (VI), m.p. over 300° (Found: C, 82.0; H, 5.6; N, 7.5; $C_{24}H_{18}N_2O$ required: C, 83.26; H, 5.8; N, 8.0).

The ethyl alcohol washing solution was evaporated and the semisolid left was trituated and crystallized from light petrol (80-110°), to give (XII), m.p. 14° (Found: C, 78.4; H, 6.0; N, 7.4; $C_{26}H_{24}N_2O_2$ required: C, 78.76; H, 6.1; N, 7.07).

Action of Ethyl Bromoacetate on Anils (IX a-c): Formation of 1,4-diaryl-azetidin-2-one (X a-c). A mixture of anil (0.01 mole), zinc (0.01 atom), some crystals of mercuric chloride and ethyl bromoacetate (0.01 mole) in dry toluene was refluxed for 2 hr. The reaction mixture was cooled, and decomposed with a mixture of conc. ammonia (5 ml) and ammonium chloride 10% (20 ml). The organic layer was washed with hydrochloric acid (20 ml. N), then with water. After drying over anhydrous sodium sulphate, the solvent was removed under reduced

pressure. The products were crystallized from petrol (b.p. 100-120°) to give azetidinones (Xa-c). The results obtained are listed in Table 1.

TABLE 1. FORMATION OF 1,4-DIARYL-AZETIDIN-2-ONE, XA-C.

Compound	M.p. °C	Yield %	Formula	Analysis	
				Found	Required
Xa	100	70	$C_{18}H_{17}NO_2$	C, 77.5 H, 5.9	77.39 6.13
Xb	103	85	$C_{18}H_{17}NO$	C, 82.4 H, 6.2	82.1 6.5
Xc	105	80	$C_{15}H_{12}NOCl$	C, 70.1 H, 4.4 N, 5.2 Cl, 13.7	69.9 4.6 5.4 13.7

Action of Hydrazine Hydrate on Azetidin-2-one (Xa, b): Formation of Azetidin-2-one-azine (XIa, b) To a solution of (Xa and b) (1 g.) in ethanol (20 ml) hydrazine hydrate (50%; 1 ml) was added, and the reaction mixture refluxed for 10 hr. The solid obtained upon cooling was recrystallized from ethanol. The results obtained are listed in Table 2.

TABLE 2. 1,4-DIARYL-AZETIDIN-2-ONE-AZINE (XI A, B)

Product	M.p. °C	Yield %	Formula	Analysis %	
				Found	Required
XIa	127	85	$C_{36}H_{34}O_2N_4$	C, 77.5 H, 6.1	77.95 6.18
Xb	120	80	$C_{36}H_{34}N_4$	C, 82.4 H, 6.3	82.72 6.56

Action of Thioglycolic Acid on Benzalacetophenone anil (XII): Formation of (XIII) and (XIV). To a solution of the benzalacetophenone anil (XII) (0.01 mole) in dry benzene, thioglycolic acid (0.01 mole) was added, and the reaction mixture refluxed under water separator until a constant volume of water collected. Evaporation of the solvent gave a solid, which was recrystallized from ethanol to give (XIII), m.p. 129° (Found C, 73.2; H, 5.6; N, 3.5; S, 8.9 $C_{23}H_{21}NSO_2$ required: C, 73.58; H, 5.64; N, 3.73; S, 6.5).

The yellow crystals that remained after evaporation of alcohol, were recrystallized from light petrol (b.p. 100-120°) to give 2-phenyl-3-styryl-4-thiazolidone (XIV), m.p. 134°, yield 40%. (Found: C, 77.6; H, 5.5; N, 4.0; S, 9.1; $C_{23}H_{19}NSO$ required C, 77.3; H, 5.32; N, 3.92; S, 8.96).

References

1. Pekard and Polly, J. Amer. Chem. Soc., **76**, 5169 (1954).
2. L. J. Louis and K. Henri, Bull. Soc. Chem. Fr., **10**, 3500-5 (1969).

(A-IV)

(B-IV)

(C-IV)