Synthesis of Diimines and Dihydropyrimidines

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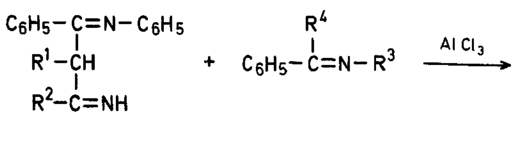
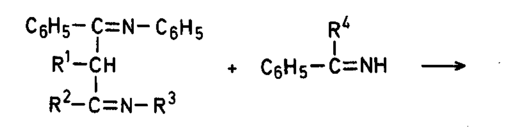
It has been shown recently[1] that diimines **1**, obtained by addition of Schiff bases to nitriles, are able to react with nitriles under mild conditions in a cycloaddition to give substituted pyrimidines[2].

In view of their high reactivity towards nitriles and their ready accessibility, these diimines may be suitable starting materials for cycloaddition reactions[3]. The aim of this work is to examine the reactions of these compounds with aldimines and ketimines[4].

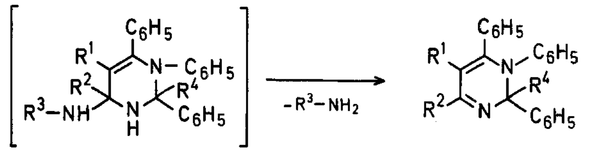
1,2-Dihydropyrimidines **4** are obtained from the reactions of the 1,3-diimino compounds **1** with benzylideneaniline at room temperature in the presence of aluminium chloride as catalyst. When *N*-benzylidenecyclohexylamine ($R^3=c$-C_6H_{11}, $R^4=H$) is used under the same conditions, the 1,2-dihydropyrimidines obtained are identical to those obtained when benzylideneaniline is employed. These results can be explained by the following reaction sequence.



1 (tautomer) **2**



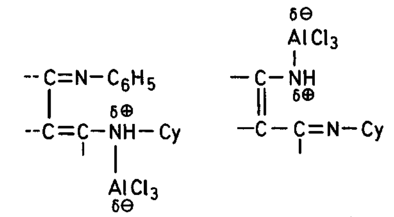
3 (tautomer)



4

The reaction of **1** with **2** when $R^3=C_6H_5$, c-C_6H_{11} and $R^4=H$ gives the product **4** via the diimine **3**. The same results were observed when ketimines of aliphatic amines are used ($R^3=c$-C_6H_{11} and $R^4=CH_3$, C_2H_5); in these cases the reaction proceeds under more severe conditions (temperatures of 90°), probably because of steric effects. The dihydropyrimidines **4** obtained in this way are summarised in Table 1.

The higher reactivity of the diimine in the presence of aluminium chloride can be explained by the formation of a complex of aluminium chloride and the diimine utilising one of the free electron pairs of the nitrogen atoms[2].



a **b**

According to the results shown in Table 1, the diimine reacts, not surprisingly, as indicated in complex **a**. This assumes that complex formation occurs with the more basic nitrogen atom of the diimine.

When ketimines of aromatic amines ($R^3=C_6H_5$, $R^4=CH_3$, C_2H_5, i-C_3H_7) are used in the reaction of **1** with **2** at 90°, only products **3**, resulting from exchange reactions, are obtained instead of the corresponding 1,2-dihydropyrimidines. Even under more vigorous conditions, no cycloaddition products are obtained, probably because of electronic and steric effects.

Table 1. 1,2-Dihydropyrimidines **4** Prepared by Reaction of Schiff Bases **2** with Diimines **3**

Product	R^1	R^2	R^4	M.p.	Yield (%) $R^3=C_6H_5$	Yield (%) $R^3=c$-C_6H_{11}
4a	CH_3	C_6H_5	H	142–144°	88	85
4b	CH_3	4-H_3C–C_6H_4	H	158°	80	80
4c	CH_3	4-Cl–C_6H_4	H	143–145°	76	80
4d	H	C_6H_5	H	193–194°	85	82
4e	CH_3	C_6H_5	CH_3	154°	—	75
4f	CH_3	C_6H_5	C_2H_5	163–165°	—	73

Table 2. Diimines **3** Prepared by Reaction of Diimines **1** with Ketimines **2**

Product	R^1	R^2	R^3	M.p.	Yield (%) (R^4)
3a	CH_3	C_6H_5	C_6H_5	136–138°	80 ($R^4=CH_3$) 80 ($R^4=C_2H_5$) 70 ($R^4=i$-C_3H_7)
3b	H	C_6H_5	C_6H_5	183–185°	85 ($R^4=CH_3$) 85 ($R^4=C_2H_5$)
3c	CH_3	4-H_3C–C_6H_4	C_6H_5	105–107°	75 ($R^4=CH_3$)

Table 3. ^{1}H-N.M.R. and Elemental Analyses for Products **3** and **4**

Product	^{1}H-N.M.R. ($CDCl_3$) δ (ppm)	Elemental Analyses				
3a	1.7 (s, CH_3), 6.7—7.3 (m, 20H_{arom}).	$C_{28}H_{24}N_2$ (388.5)	calc. found	C 86.59 86.24	H 6.18 6.03	N 7.21 7.10
3b	5.4 (s, CH), 6.7—7.4 (m, 20H_{arom}).	$C_{27}H_{22}N_2$ (347.5)	calc. found	C 86.63 86.32	H 5.82 5.79	N 7.48 7.32
3c	1.5 (s, CH_3), 2.3 (s, CH_3), 6.7—7.7 (m, 19H_{arom}).	$C_{29}H_{26}N_2$ (402.5)	calc. found	C 86.56 85.92	H 6.46 6.37	N 6.96 6.53
4a	1.8 (s, CH_3), 6.8 (s, CH), 7.0—7.7 (m, 20H_{arom}).	$C_{29}H_{24}N_2$ (400.5)	calc. found	C 87.00 86.72	H 6.00 5.92	N 7.00 6.75
4b	1.8 (s, CH_3), 2.4 (s, CH_3), 6.7 (s, CH), 7.0—7.6 (m, 19H_{arom}).	$C_{30}H_{26}N_2$ (414.6)	calc. found	C 86.95 86.75	H 6.28 6.12	N 6.76 6.52
4c	1.8 (s, CH_3), 6.7 (s, CH), 7.0—7.8 (m, 19H_{arom}).	$C_{29}H_{23}ClN_2$ (434.9)	calc. found	C 79.90 79.54	H 5.48 5.37	N 6.44 N 6.25
4d	6.6 (s, CH), 6.8 (s, CH), 7.0—8.0 (m, 20H_{arom}).	$C_{28}H_{22}N_2$ (386.5)	calc. found	C 87.05 86.92	H 5.69 5.36	N 7.25 6.92
4e	1.4 (s, CH_3), 1.6 (s, CH_3), 7.0—8.0 (m, 20H_{arom})	$C_{30}H_{26}N_2$ (414.6)	calc. found	C 86.95 86.72	H 6.28 6.05	N 6.76 6.28
4f	0.8—1.0 (t, CH_3), 1.7 (s, CH_3), 1.8—2.2 (q, CH_2), 7.1—8.0 (m, 20H_{arom})	$C_{31}H_{28}N_2$ (428.6)	calc. found	C 86.59 86.24	H 6.18 6.03	N 7.21 7.10

All starting diimines prepared for the first time were obtained as indicated in Ref. 1.

5-Methyl-1,2,4,6-tetraphenyl-1,2-dihydropyrimidine (4a):

To a stirred solution of 3-imino-1-phenylimino-2-methyl-1,3-diphenylpropane[1] (6.24 g, 20 mmol) and benzylideneaniline (9.1 g, 50 mmol) in dioxan (100 ml) was added aluminium chloride (2.7 g, 20 mmol). The mixture was stirred at room temperature for 48 h. The reaction mixture was then cooled, acidified with 2 *N* sulfuric acid (100 ml), and treated with 3 *N* potassium hydroxide until basic. The mixture was then extracted with ether and the solvents removed from the extract under reduced pressure to give the crude product; yield: 7 g; m.p. 142—144° (from hexane).

I.R. (nujol): ν = 1610, 760, and 690 cm^{-1}.

Mass spectrum: m/e = 400 (M^+), 385, 323, 180, 104, 77.

1,3-Diphenylimino-2-methyl-1,3-diphenylpropane (3a):

To a stirred solution of 3-imino-1-phenylimino-2-methyl-1,3-diphenylpropane[1] (6.24 g, 20 mmol) and 1-phenyl-1-phenylimino-propane (10.5 g, 50 mmol) in dioxan (100 ml) was added aluminium chloride (2.7 g, 20 mmol). The mixture was heated and stirred at 90° for 14 h, allowed to cool, acidified with 2 *N* sulfuric acid (100 ml), and then treated with 3 *N* potassium hydroxide solution until basic. The mixture was extracted with ether, all solvent was removed from the ether extract under reduced pressure, and the crude solid recrystallised from hexane; yield (crude): 6.2 g; m.p. 136—138°.

I.R. (nujol): ν = 1640, 770, and 700 cm^{-1}.

Mass spectrum: m/e = 388 (M^+), 373, 311, 180, 104, 77.

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[1] H. Hoberg, J. Barluenga, *Synthesis* **1970**, 142.

[2] H. Hoberg, J. Barluenga, *Synthesis*, **1970**, 363.

[3] Diimines derived from 1-aza-1,3-butadiene have not been studied with respect to 1,4-cycloaddition reactions. J. Hamer, "*1,4-Cycloaddition Reactions*" J. Hamer, Ed., 1967, Academic Press, New York, London.

[4] Schiff bases have been the subject of only little research with respect to reaction with diimines; M. Lora Tamayo, R. Madroñero, "*1,4-Cycloaddition Reactions*" J. Mamer, Ed., 1967, Academic Press, New York, London.