CATALYTIC CLAISEN AMINO REARRANGEMENT OF N-(CYCLO)ALKENYLARYLAMINES AND INTRAMOLECULAR CYCLIZATION OF ortho-ALKENYLARYLAMINES

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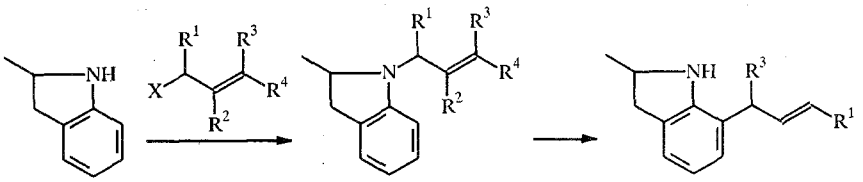
Aromatic Claisen amino rearrangements of N-alkenyl-2-methylindoline under the action of Lewis acids leads to 7-alkenyl-2-methylindolines in high yield. Cyclization of ortho-alkenyl compounds was effected in polyphosphoric acid (PPA) and by UV irradiation. Heating 7-(1-methyl-2-butenyl)-2-methylindoline in PPA is accompanied by 1,3-methyl shift in the alkenyl substituent with subsequent cyclization at the aromatic nucleus.

Only a few examples of Claisen rearrangements in heterocyclic compounds have been studied [1-3]. At the same time, ortho-alkenyl compounds of arylamines offer extensive possibilities for the synthesis of interesting heterocyclic compounds [4-5].

Continuing the study of relationships in this reaction, we have examined rearrangements in the 2-methylindoline series. The initial N-alkenylindolines were prepared by the reaction of the corresponding alkenyl halides with 2-methylindoline (I). Rearrangement of the N-alkenyl compounds IIa-d so prepared was effected under the action of Lewis acids. Reaction conditions and product yields are set out in Table 1.



I IIa-g IIIa-d

II—III a $R^1 = R^2 = R^3 = R^4 = H$; b $R^1 = R^3 = CH_3$, $R^2 = R^4 = H$; c $R^2 = R^4 = H$, $R^1 + R^3 = (CH_2)_2$; d $R^2 = R^4 = H$, $R^1 + R^3 = (CH_2)_3$; e $R^1 = R^3 = R^4 = H$, $R^2 = Cl$; f $R^1 = R^2 = H$, $R^3 = Cl$, $R^4 = CH_3$; g $R^1 = R^3 = R^4 = H$, $R^2 = Me$; X = Cl, Br

It has been established that rearrangement proceeds smoothly in the case of compounds IIa-d ($R^2 = R^4 = H$), compounds IIe,f rapidly form tars, and compound IIg remains unchanged under the conditions employed (Table 1). Probably, the methyl group in the β-position of the allyl substituent hinders the formation of the transition complex [6].

It has been shown previously that N-alkenyltetrahydroquinolines very readily undergo rearrangement in the presence of various catalysts [3]. 2,2,4-Trimethylhydroquinoline even forms the 8-alkenyl derivative VI under N-alkenylation conditions.

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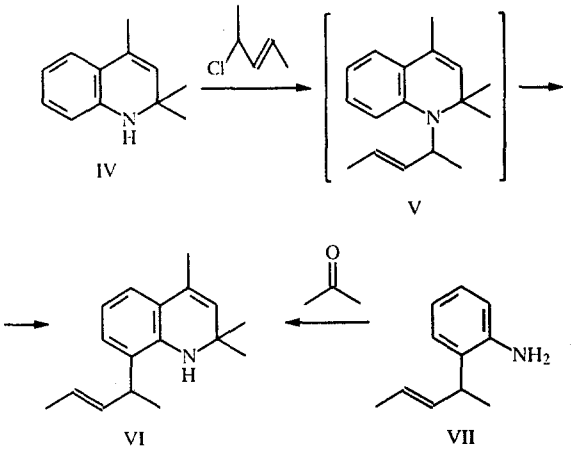
TABLE 1. Reaction Conditions and Product Yields in the Rearrangement of N-(Cyclo)alkenylarylamines IIa-d

Compound	Catalyst, solvent	Reaction conditions		Reaction product	Yield, %
		T, °C	Time, h		
IIa	$ZnCl_2$, xylene	140	6	IIIa	52
	$AlCl_3$, xylene	140	8	IIIa	43
	$BF_3(Et_2O)_2$*	170	6	IIIa	75
IIb	$ZnCl_2$, xylene	140	2	IIIb	78
	$AlCl_3$, xylene	140	5	IIIb	75
	$BF_3(Et_2O)_2$*	170	3	IIIb	70
IIc	$ZnCl_2$, xylene	140	1	IIIc	81
	$AlCl_3$, xylene	140	4	IIIc	77
	$BF_3(Et_2O)_2$*	170	5	IIIc	66
IId	$ZnCl_2$, xylene	140	1	IIId	79
	$AlCl_3$, xylene	140	4	IIId	75
	$BF_3(Et_2O)_2$*	170	5	IIId	61

*Without solvent.

It seems that the N-alkenyl compound V which is formed is unstable on account of steric reactions of the α-methyl group of the alkenyl substituent with the geminal methyl groups at the quaternary carbon and is readily rearranged into VI. Gas–liquid chromatographic analysis shows it to be identical with the compound obtained by a different route from compound VII on reaction with acetone [8].



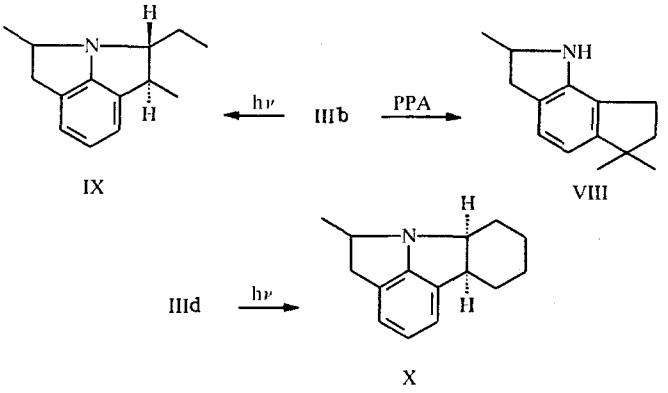
The ortho-alkenylarylamines thus prepared are convenient synthons for the preparation of tri- and tetracyclic compounds. Thus, heating compound III in PPA proceeds with a 1,3-methyl shift in the alkenyl substituent with subsequent cyclization at the aromatic nucleus. A proposed mechanism for the cyclization was given in [7]. Photochemical cyclization of compounds IIIb,d leads to high yields of the heterocycles IX and X. In the PMR spectra of compound I, the coupling constant $J_{7,8}$ = 9.9 Hz shows a trans arrangement of the 7- and 8-hydrogen atoms. A coupling constant of 8.2 Hz for these hydrogens in compound X points to their cis arrangement.

EXPERIMENTAL

Infrared spectra were run on a UR-20, PMR spectra on a Tesla BS-567A in $CDCl_3$ and CCl_4 with TMS internal standard. Mass spectra were recorded on an MKh-13-06 with ionization energy 70 eV and ionization chamber temperature

TABLE 2. Boiling Points and Spectroscopic Characteristics of Compounds IIa-g, IIIa-d, VI, VIII-X

Compound	bp °C (mm)	IR spectrum, ν cm^{-1}	PMR spectrum, δ ppm; J Hz; in $CDCl_3$
IIa	92...95 (3)	740, 910, 1610, 2990, 3050	1,24 (3H, d, CH_3, J = 7), 2,2...3,31 (3H, m, CH_2, CH), 3,62 (2H, d, CH_2, J = 7), 4,88...5,36 (3H, m, $CH=CH_2$), 6,20...7,15 (4H, m, ArH)
IIb	102...106 (3)	760, 990, 1490, 1610, 2980, 3030	1,25 (3H, d, CH_3, J = 7), 1,35 (3H, d, CH_3, J = 7), 1,46 (3H, d, CH_3, J = 4), 2,03...3,33 (3H, m, CH_2, CH), 4,16 (1H, m, CH), 5,5...5,66 (2H, m, CH=CH), 6,3....7,66 (2H, m, CH=CH), 6,3...7,6 (4H, m, ArH)
IIc	110....112 (3)	760, 1490, 1610, 3060	1,20 (3H, d, CH_3, J = 7), 1,98...3,3 (6H, m, $3CH_2$), 3,41...3,83 (1H, m, CH), 4,33...4,75 (1H, m, CH), 5,75...5,81 (2H, m, CH=CH), 6,33...7,05 (4H, m, ArH)
IId	115....118 (3)	760, 1480, 1610, 2940, 3030	1,15 (3H, d, CH_3, J = 7), 1,41...2,08 (6H, m, $3CH_2$), 2,10...3,2 (4H, m, 2CH, CH_2), 5,5...5,8 (2H, m, CH=CH), 6,16...7,0 (4H, m, ArH)
IIe	101...102 (3)	740, 890, 1600, 2960, 3030	1,25 (3H, d, CH_3, J = 7), 2,33...3,33 (3H, m, CH_2, CH), 3,73 (2H, s, CH_2), 5,18...5,48 (2H, d.d, CH_2=C), 6,01...7,01 (4H, m, ArH)
IIf	126...129 (3)	765, 1490, 1580, 1610, 2980	1,33 (3H, d, CH_3, J = 7), 2,01 (3H, s, CH_3), 2,41...3,75 (4H, m, $2CH_2$), 3,81...4,0 (1H, m, CH), 5,41...5,71 (2H, m, CH=CH), 6,40...7,33 (4H, m, ArH)
IIg	99...101 (3)	760, 910, 1490, 1600, 2980, 3030	1,16 (3H, d, CH_3, J = 7), 1,66 (3H, s, CH_3), 2,20...3,03 (3H, m, CH_2, CH), 3,43 (2H, s, CH_2), 4,60...4,95 (2H, m, CH_2=C), 6,08...6,9 (4H, m, ArH)
IIIa	103...105 (3)	760, 910, 1450, 1600, 2850, 3360	1,22 (3H, d, CH_3, J = 7), 2,5...3,62 (3H, m, CH_2, CH), 3,7 (2H, d, CH_2), 4,03 (1H, s, NH), 5,01...5,46 (3H, m, $CH=CH_2$), 6,33...7,30 (3H, m, ArH)
IIIb	110...113 (3)	760, 1460, 1660, 2970, 3030, 3375	1,15 (3H, d, CH_3, J = 7), 1,28 (3H, d, CH_3, J = 7), 1,61 (3H, d, CH_3, J = 4), 2,25...3,41 (3H, m CH_2, CH), 3,66...4,66 (2H, m, CH, NH), 5,40...5,60 (2H, m, CH=CH), 6,50...7,01 (3H, m, ArH)
IIIc	115...117 (3)	760, 1460, 3055, 3380	1,25 (3H, d, CH_3, J = 7), 1,66...3,33 (7H, m, $3CH_2$, CH), 3,61...4,01 (2H, m, CH, NH), 5,66...6,33 (2H, m, CH=CH), 6,45...7,16 (3H, m, ArH)
IIId	123...126 (3)	760, 1620, 2935, 3370	1,20 (3H, m, CH_3, J = 7), 1,40...1,92 (6H, m, $3CH_2$), 2,20...2,70 (3H, m, CH, CH_2), 3,20 (1H, m, CH), 3,70 (H, s, NH), 6,0 (2H, m, CH=CH), 6,60...7,0 (3H, m, ArH)
VI	142...145 (1)	760, 980, 1610, 3025, 3400	1,15 (3H, s, CH_3), 1,35 (3H, d, CH_3, J = 7), 1,67 (3H, d, CH_3, J = 4), 1,86 (3H, s, CH_3), 3,25...3,40 (H, m, CH), 3,5...5,0 (H, s, NH), 5,36...5,63 (3H, m, CH=C, CH=CH), 6,53...7,26 (3H, m, ArH)
VIII	150...153 (2)	800, 1585, 1615, 3020, 3370	1,20 (6H, s, $2CH_3$), 1,30 (3H, d, CH_3, J = 7), 2,33...3,46 (7H, m, $3CH_2$, CH), 3,20 (H, s, NH), 6,46 (1H, d, ArH), 3,86 (1H, d, ArH)
IX	145...147 (2)	790, 1575, 2940, 2980	0,96 (3H, t, CH_3, J = 7,5), 1,26 (3H, d, CH_3, J = 6,5), 1,28 (3H, d, CH_3, J = 6), 2,40...2,86 (4H, m, $2CH_2$), 2,98 (1H, m, CH, J = 9,9), 3,10 (1H, m, CH), 3,32 (1H, d.t, CH, J_1 = 9,9, J_2 = 4,2), 6,30...7,0 (3H, m, ArH)
X	165...168 (2)	750, 1600, 3025, 3055	1,16...2,26 (11H, m, $4CH_2$, CH_3), 1,82 (2H, d, CH_2, J = 7), 3,65 (1H, m, CH, J = 8,2), 3,83...4,03 (2H, m, 2CH, J_1 = 8,2, J_2 = 7), 6,63...7,48 (3H, m, ArH)



200°C. The GLC analysis was carried out on a Crom-5 with a column of SE-30 on Chromaton N–AW–DMCS with a flame-ionization detector.

The 2,2,4-trimethyldehydroquinoline starting material was prepared by the method of [8].

General Method of N-Alkenylation. Synthesis of N-(Cyclo)alkenyl-2-methylindolines (IIa-g). To a solution of 5 g (35 mmole) arylamine in 20 ml triethylamine was added an equimolar quantity of alkenyl halide and the mixture heated 1 h at 80-90°C. An equal volume of water was added to the reaction mixture, the organic layer separated, washed with water (3 × 20 ml) and dried over KOH. The product was isolated by distillation in vacuum.

Catalytic Rearrangement of N-Alkenylarylamines. Synthesis of 7-(Cyclo)alkenyl-2-methylindolines (IIa-d). A. To a solution of 35 mmole N-alkenyl-2-methylindoline in 20 ml xylene was added 7 mmole catalyst (Table 1). The reaction mixture was washed with aqueous KOH and the organic layer separated, dried over KOH, and distilled in vacuum.

B. To 1.7 g (8 mmole) N-alkenyl-2-methylindoline IIa-d was added 2.6 ml $BF_3(Et_2O)_2$ and the mixture heated at 170°C for the times shown in Table 1. The mixture was treated with Na_2CO_3 solution and extracted with ether. The products IIIa-d were purified by column chromatography on Al_2O_3 with 1:3 benzene–hexane eluent.

Cyclization of 7-(1-Methyl-2-butenyl)-2-methylindoline (IIIb). To a PPA prepared from 20 g H_3PO_4 (85%) and 5 g P_2O_5 was added 2.5 g (12.5 mmole) compound IIIb and the mixture heated 5 h at 140-145°C. Water was added to the cooled mixture which was then carefully neutralized with conc. aqueous KOH. The organic layer was separated and the aqueous portion extracted with 3 × 50 ml ether, the combined extracts dried over KOH, the solvent evaporated, and the residue distilled in vacuum. The yield of compound VIII was 61%.

Photochemical Cyclization of Compounds IIIb,d. A solution of 1 g (5 mmole) compound IIIb or IIId in 800 ml hexane was irradiated by a DRT-375 lamp in a quartz reactor for 1 h in an atmosphere of argon. The solvent was removed and the residue chromatographed on a column of Al_2O_3 using 1:4 benzene–hexane eluent. The yield of compound IX was 64%, of X, 45%.

Spectroscopic data and constants for the compounds prepared are given in Table 2.

REFERENCES

1. H. Katayama, Y. Higuchi, and K. Kaneko, Chem. Pharm. Bull., **32**, 2218 (1984).
2. H. Katayama, M. Ohkoshi, and K. Kaneko, Chem. Pharm. Bull, **32**, 1770 (1984).
3. I. B. Abdrakhmanov, A. G. Mustafin, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1852 (1988).
4. I. B. Abdrakhmanov, A. G. Mustafin, V. M. Sharafutdinov, A. S. Taichinova, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 839 (1985).
5. I. B. Abdrakhmanov, A. G. Mustafin, G. A. Tolstikov, and U. M. Dzhemilev, Khim. Geterotsikl. Soedin., No. 4, 505 (1987).
6. I. B. Abdrakhmanov, A. G. Mustafin, G. A. Tolstikov, L. V. Spirikhin, and L. M. Khalilov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 613 (1987).
7. I. B. Abdrakhmanov, A. G. Mustafin, L. V. Spirikhin, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 1214 (1985).
8. D. Craig, J. Am. Chem. Soc., **60**, 1458 (1938).