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Decarboxylation Reactions. V.[1] Reaction of N-Benzylideneanilines with Propiolic Acid

Osamu Iwamoto, Kunio Suzuki, Yoshiyasu Terao, and Minoru Sekiya

Shizuoka College of Pharmacy[2]

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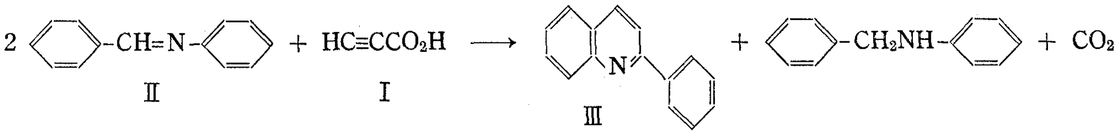
It has been found that a decarboxylation reaction of propiolic acid proceeds with N-benzylideneaniline to give 2-phenylquinoline. Extention of this reaction furnishes generality for a convenient synthesis of 2-phenylquinoline derivatives. A plausible reaction path involving 3-anilino-3-phenyl-1-propyne intermediate is proposed.

We now wish to disclose our recent finding on a new decarboxylation reaction between N-benzylideneanilines and propiolic acid (I) producing 2-phenylquinolines. The reaction was first realized on refluxing a benzene solution of N-benzylideneaniline (II) and I in 2:1 molar proportion, where process of the reaction was indicated by observation of carbon dioxide evolution. Treatment of the reaction mixture gave 2-phenylquinoline (III) in 35% yield with an equimolar amount of N-benzylaniline.



The side formation of N-benzylaniline indicates that a part of the starting II acts as a hydrogen acceptor. Realization of this reaction by the use of other hydrogen acceptor was successful in carrying out the reaction with dibenzoyldiimide in place of a half equivalent of II, whereupon 1,2-dibenzoylhydrazine was obtained in addition to III.

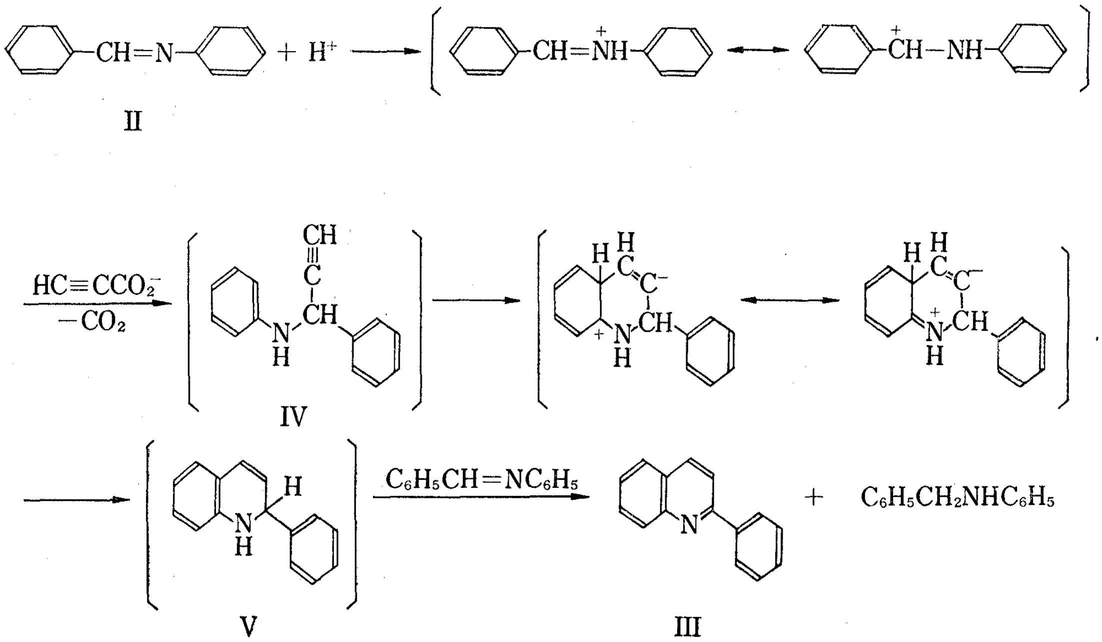


Chart 1

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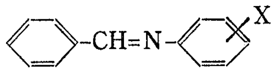
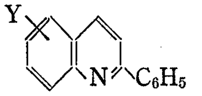
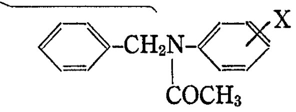
[1] Part IV: M. Sekiya and T. Morimoto, *Chem. Pharm. Bull.* (Tokyo), 23, 2353 (1975).

[2] Location: *2-2-1 Oshika, Shizuoka-Shi, 422, Japan*·

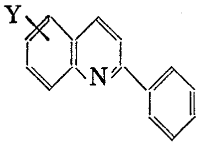
As indicated in Chart 1, the reaction path probably involves 3-anilino-3-phenyl-1-propyne (IV) as an intermediate. Understanding of the formation of IV by action of I may be given on the analogy of the previously known decarboxylation reactions of N-benzylideneanilines

Table I. Reaction[a] of N-Benzylideneanilines with Propiolic Acid

Substrate	Products and Yields[b] (%)			
				
X	Y	%	X	%
H	H	35	H	35
m-Cl	7-Cl	35	*m*-Cl	35
m-CH_3	7-CH_3	51	*m*-CH_3	46
p-Cl	6-Cl	20	*p*-Cl	20
p-CH_3	6-CH_3	42	*p*-CH_3	42
p-OCH_3	6-OCH_3	28	*p*-OCH_3	28

[a] conditions: see Experimental
[b] based on the products actually isolated

Table II. Physical, Spectral and Analytical Data of 2-Phenylquinolines



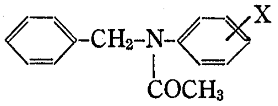
Y	Appearance (recryst. solvt.)	mp (°C) (lit. mp)	IR ν_{max}^{KBr} cm^{-1}	UV λ_{max}^{EtOH} nm (ε)	NMR τ (in $CDCl_3$)[a]	Analysis (%) Calcd. (Found) C	H	N
H	needles (petr. ether)	77—78 (83[b])	1600 829 774	258 (42000) 323 (7300)	1.6—2.7 (11H, m, ar-H)	87.77 (87.94)	5.40 (5.30)	6.82 (7.15)
7-Cl	needles (ether)	105—106	1600 885 843	259 (50800) 327 (9600)	1.6—2.8 (10H, m, ar-H)	75.16 (75.19)	4.20 (4.20)	5.84 (5.68)
7-CH_3	needles (ether)	92—93 (100.5[c])	1600 895 840	257 (45600) 325 (8900)	7.47 (3H, s, CH_3) 1.6—2.8 (10H, m, ar-H)	87.63 (87.67)	5.97 (5.95)	6.38 (6.40)
6-Cl	leaflets (ether)	103—104	1598 885 875 833	261 (37200) 327 (8000)	1.6—2.7 (10H, m, ar-H)	75.16 (75.37)	4.20 (4.20)	5.84 (5.69)
6-CH_3	needles (ether)	61—62 (69[d])	1600 893 834	258 (42800) 326 (8200)	7.48 (3H, s, CH_3) 1.6—2.7 (10H, m, ar-H)	87.63 (87.55)	5.97 (5.75)	6.38 (6.36)
6-CH_3O	plates (EtOH)	125—126 (133[e])	1598 861	263 (31800) 334 (7000)	6.14 (3H, s, OCH_3) 1.6—2.9 (10H, m, ar-H)	81.68 (81.59)	5.57 (5.55)	5.95 (6.27)

[a] Following abbreviations were used: s: singlet, m: multiplet, ar-H: aromatic protons
[b] O. Doebner and W. v. Miller, *Ber.*, **16**, 1665 (1883)
[c] T. Kaku, *Yakugaku Zasshi*, **47**, 577 (1927)
[d] J. v. Braun and L. Brauns, *Ber.*, **60B**, 1253 (1927)
[e] O. Doebner, *Ann. Chem.*, **249**, 106 (1888)

with formic acid[3] and trihaloacetic acids.[4] A 1,2-dihydroquinoline-ring closure of N-propargylaniline analog, such as shown by the succeeding transfer of IV in Chart 1, has rarely appeared in the literature. A U.S. Patent[5] describing the formation of 2,2-dimethyl-1,2-dihydroquinoline from 3-anilino-3-methyl-1-butyne under the $CuCl_2$- and Cu-catalyzed reaction conditions is only an example in the ring closure. The literature, however, contains several reports describing 2H-pyran-[6] and 2H-thiopyran-ring[7] closure of O- and S-propargyl-substituted aromatic compounds. These facts seem to offer an analogy to the transfer of IV into 2-phenyl-1,2-dihydroquinoline (V) shown in Chart 1. The resulting V may successively undergo dehydrogenation induced by action of II as a hydrogen acceptor, being led to III.

In the hope of obtaining 2-phenylquinolines possessing substituents, the reaction was extensively examined with a number of N-benzylideneanilines. The reactions were processed

TABLE III. Physical, Spectral and Analytical Data of N-Benzylacetanilides



X	Appearance (recryst. solvt.)	mp (°C) (lit. mp)	bp(°C/mmHg) (lit. bp)	IR ν_{max}^{KBr} cm^{-1} (>NCO)	NMR τ (in $CDCl_3$)[a]	Analysis (%) Calcd. (Found)		
						C	H	N
H	plates (ether)	57—58 (57—58[b])	147—149/0.3	1651	8.11(3H, s, $COCH_3$) 5.12(2H, s, $-CH_2-$) 2.6—3.1(5H, m, ar-H) 2.80(5H, s, ar-H)	79.97 (79.91)	6.71 (6.58)	6.22 (6.41)
m-Cl	liquid		151—154/0.07	1648	8.11(3H, s, $COCH_3$) 5.15(2H, s, $-CH_2-$) 2.6—3.3(4H, m, ar-H) 2.80(5H, s, ar-H)	69.37 (69.20)	5.43 (5.31)	5.39 (5.24)
m-CH_3	liquid		144—146/0.07	1655	8.10(3H, s, $COCH_3$) 7.70(3H, s, $-CH_3$) 5.10(2H, s, $-CH_2-$) 2.6—3.3(4H, m, ar-H) 2.81(5H, s, ar-H)	80.30 (80.33)	7.16 (7.13)	5.85 (5.81)
p-Cl	plates (ether)	87—88 (91—91.5[c])	140—143/0.05	1655	8.12(3H, s, $COCH_3$) 5.16(2H, s, $-CH_2-$) 2.81(5H, s, ar-H) 2.93(4H, q, ar-H J=9 and 23 Hz)	69.37 (69.34)	5.43 (5.39)	5.39 (5.46)
p-CH_3	liquid		135—137/0.03	1650	8.17(3H, s, $COCH_3$) 7.74(3H, s, $-CH_3$) 5.18(2H, s, $-CH_2-$) 3.40(4H, q, ar-H J=9 and 16 Hz) 2.80(5H, s, ar-H)	80.30 (79.94)	7.16 (7.04)	5.85 (6.08)
p-OCH_3	liquid		140—143/0.09 (174—176/0.7[b])	1658	8.17(3H, s, $COCH_3$) 6.32(3H, s, $-OCH_3$) 5.18(2H, s, $-CH_2-$) 3.17(4H, s, ar-H) 2.81(5H, s, ar-H)	75.27 (75.69)	6.71 (6.89)	5.49 (5.43)

a) Following abbreviations were used: s: singlet, q: quartet, m: multiplet, ar-H: aromatic protons
b) J. H. Billman and J. W. McDowell, *J. Org. Chem.*, **27**, 2640 (1962)
c) J.H. Billman and J.W. McDowell, *J. Org. Chem.*, **26**, 1437 (1961)

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3) M. Sekiya, *J. Syn. Org. Chem. Japan*, **34**, 67 (1976).
4) A. Lukasiewicz, *Tetrahedron*, **20**, 1, (1964); A. Lukasiewicz and J. Lesiuska, *ibid.*, **21**, 3247 (1965); A. Lukasiewicz, *ibid.*, **21**, 193 (1965); *idem*, *ibid.*, **23**, 1713 (1967).
5) N.R. Easton and G.F. Hennion, U.S. Patent, 3331846 (1967) [*C.A.*, **67**, P 99627 *c* (1967)].
6) I. Iwai and J. Ide, *Chem. Pharm. Bull.* (Tokyo), **10**, 926 (1962); *idem*, *ibid.*, **11**, 1042 (1963); J. Zsindely and H. Schmid, *Helv. Chim. Acta*, **51**, 1510 (1968).
7) H. Kwart and T.J. Geoge, *Chem. Commun.*, **1970**, 433.

under the conditions similar to those described for II in the above. Basic liquids obtained by the isolation procedures were composed of 2-phenylquinolines and N-benzylanilines, which were separately isolated by acetylation with acetic anhydride, converting the latter into N-acetyl derivatives. Results are summarized in Table I. Physical and spectral data of the obtained 2-phenylquinolines and N-benzylacetanilides are listed in Tables II and III.

In the reactions with N-benzylidene-*m*-chloroaniline and N-benzylidene-*m*-toluidine, it was needed to determine whether the quinoline-ring closure favors 7-substituted or 5-substituted 2-phenylquinoline formation. 7- and 5-chloro-substituted 2-phenylquinolines have not been described in the literature. Since complexities of their infrared (IR) and nuclear magnetic resonance (NMR) spectra made it difficult to distinguish between the 7- and 5-chloro-substituted or 7- and 5-methyl-substituted 2-phenylquinolines, identities of the products were made by comparison of their physical data with those of authentic specimens prepared by other routes. Started from 7-chloro- and 7-methyl-substituted quinolines, N-oxidation followed by the reaction with phenylmagnesium bromide suited the preparation of the authentic specimens. The starting 7-chloro-[8] and 7-methyl-substituted[8,9] quinolines were obtained by separation as their bichromates from the mixtures of the 7- and 5-substituted isomers obtained by the Skraup reactions of *m*-chloroaniline and *m*-toluidine. The products exhibited IR, NMR and ultraviolet (UV) spectra, which were well identical with those of the authentic 7-chloro- and 7-methyl-substituted materials prepared, and no depression of their melting points on admixture.

Experimental[10]

Reactions of N-Benzylideneanilines with Propiolic Acid General Procedures——The following six N-benzylideneanilines were subjected to the reaction with propiolic acid. N-Benzylideneaniline, mp 48°; N-benzylidene-*m*-chloroaniline, bp 142—144° (3 mmHg); N-benzylidene-*p*-chloroaniline, mp 61—63°; N-benzylidene-*m*-toluidine, bp 153—156° (4 mmHg); N-benzylidene-*p*-toluidine, mp 34—36°; N-benzylidene-*p*-anisidine, mp 71—72°.

To a solution of each 0.08 mole of N-benzylideneaniline in 80 ml of benzene propiolic acid (2.8 g, 0.04 mole) was added. On refluxing, the heterogeneous reaction mixture became homogeneous with evolution of CO_2. Refluxing was continued until evolution of CO_2 almost ceased. On cool, the reaction solution was washed with 20% aq. KOH to remove unreacted propiolic acid and dried over anhyd. K_2CO_3. Benzene was evaporated under reduced pressure and the resulting residue was extracted with several portions of 10% aq. HCl to remove an insoluble residue. The aqueous extracts combined were concentrated under reduced pressure and 20% aq. KOH was added to the resulting residue. A liberated oily material was extracted with benzene and the benzene solution was dried over anhyd. K_2CO_3. After evaporation of benzene, the resulting residue was subjected to distillation under reduced pressure, whereupon, after removal of low boiling aniline, a mixture of 2-phenylquinoline and N-benzylaniline was obtained as a higher boiling fraction. Then, this mixture was refluxed together with 20 g of acetic anhydride for 2 hr. After evaporation under reduced pressure the resulting residue was dissolved in benzene and dry HCl was introduced into the benzene solution, whereupon 2-phenylquinoline was deposited as the hydrochloride. Usual treatment with aq. KOH gave the free amine crystals, which were purified by recrystallization from appropriate solvent and weighed.

The foregoing benzene filtrate was washed with aq. $NaHCO_3$ and dried over anhyd. K_2CO_3. N-Benzylacetanilide was obtained by evaporation followed by distillation of the resulting residue under reduced pressure.

The two products, 2-phenylquinoline and N-benzylacetanilide, obtained in each run were identified by their spectral and analytical data shown in Tables II and III, and their yields are listed in Table I.

Acknowledgement We thank Mr. K. Narita and other members of the Analysis Center of this college for microanalyses and NMR measurements.

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[8] L. Bradford, T.J. Elliott, and F.M. Rowe, *J. Chem. Soc.*, **1947**, 437.

[9] M.H. Palmer, *J. Chem. Soc.*, **1962**, 3645.

[10] All melting and boiling points are uncorrected. Spectra reported herein were determined with a Hitachi EPI-G2 IR spectrophotometer, a Hitachi EPS-3T UV spectrophotometer and a JEOL JNM-60H spectrometer using tetramethylsilane as an internal standard.