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Synthesis of Dibenzo[*b,f*]cycloprop[*d*]azepine Derivatives. II.[1] Introduction of a Cyclopropane Ring by the Dichloromethylene Transfer Reaction[2]

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An improved method for the synthesis of 1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**3**) was described. Thus, 5*H*-dibenz[*b,f*]azepine (**1**) was formylated and dichlorocyclopropanated with dichloromethylene generated from chloroform and aqueous sodium hydroxide in the presence of a phase-transfer catalyst to yield 1,1-dichloro-1a,10b-dihydrodibenzo[*b,f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (**2**). The latter compound and its deformylated product, 1,1-dichloro-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**5**), were reduced to **3** with sodium in liquid ammonia.

5-Acetyl-, 5-carbamoyl, 5-methyl- and 5-(3-chloropropyl)-5*H*-dibenz[*b,f*]azepines (**6**, **8**, **11** and **14**), when treated with the dichloromethylene, gave the corresponding dichlorocyclopropanation products and some other products, in which the substituents had reacted simultaneously with dichloromethylene in several fashions.

The reduction of **5** under drastic conditions yielded 5,6,7,12-tetrahydrodibenz[*b,g*]azocine (**20**) and 10*H*-indolo[1,2-*a*]indole (**21**). *cis*- and *trans*-1-Chloro-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepines (**23**, R=H and **24**, R=H), on the other hand, were the main products of catalytic hydrogenation of **5**. Conformational aspects of the N-methyl derivatives **23** ($R=CH_3$) and **24** ($R=CH_3$) were discussed.

Keywords——dibenzocyclopropazepine; dibenzazepine; dichlorocyclopropane; dichloromethylene; phase-transfer catalyst; dechlorination; dibenzazocine; indoloindole; conformation

1,1a,6,10b-Tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**3**) is a useful intermediate for the synthesis of psychotropic drugs recently described by the present authors.[1] The previous method for the synthesis of **3** comprises cyclopropanation of the N-methyl derivative of 5*H*-dibenz[*b,f*]azepine[4] (**1**) followed by the demethylation. The present paper describes an improved method of synthesis utilizing the dichloromethylene transfer reaction.[5]

Chart 1 illustrates the present method for the synthesis of **3** which comprises essentially two steps, *i.e.*, dichlorocyclopropanation of 5*H*-dibenz[*b,f*]azepine (**1**) and the dechlorination. Thus, **3** was obtained in a superior yield to and in shorter steps than the previous method. The individual step of the reaction will be described in detail together with some findings obtained in the course of the investigation.

Dichlorocyclopropanation of 5*H*-Dibenz[*b,f*]azepine (1) and 5*H*-Dibenz[*b,f*]azepine-5-carbaldehyde (4)

It has been well documented[5] that dichloromethylene ($:CCl_2$) adds to carbon-carbon double bonds to afford dichlorocyclopropanes; dichloromethylene can be generated by several methods, for example, dehydrochlorination of chloroform, dechlorination of carbon tetrachlo-

1) Part I: K. Kawashima and Y. Kawano, *Chem. Pharm. Bull.* (Tokyo), **24**, 2751 (1976).
2) A part of this study was presented at the 23rd Meeting of Kinki Branch, Pharmaceutical Society of Japan, Nov. 1973, Kyoto and described in the following patent application. K. Kawashima, T. Saraie, Y. Kawano, and T. Ishiguro, Japan. Patent Application 48-13987 (1973). For foreign patents see, for example: *Idem*, U.S. Patent Application 435965 (1974).
3) Location: *17–85, Jusohonmachi 2-chome, Yodogawa-ku, Osaka 532, Japan.*
4) W. Schindler and H. Blattner, *Helv. Chim. Acta*, **44**, 753 (1961).
5) W. Kirmse, "Carbene Chemistry," 2nd ed., Academic Press, Inc., New York, 1971.

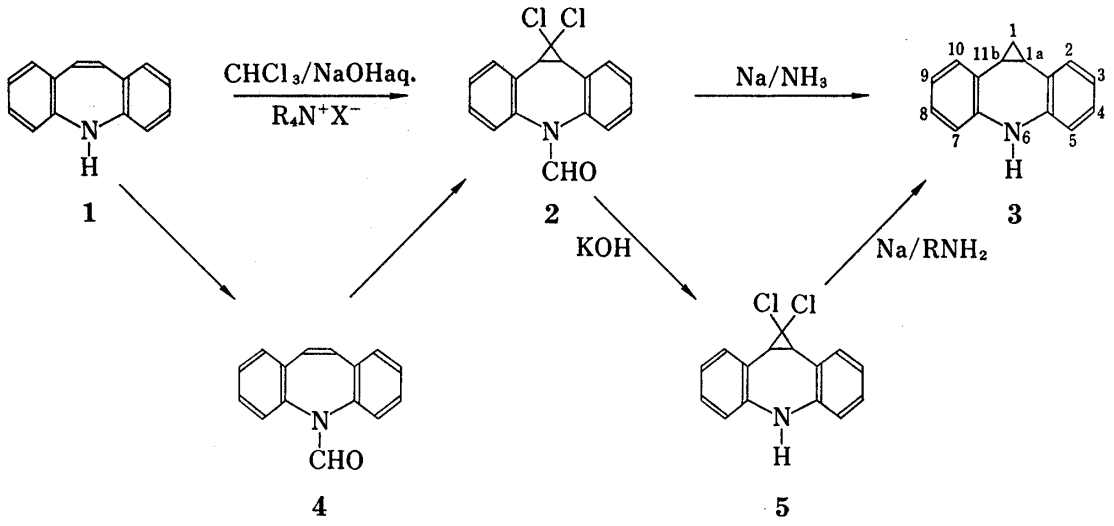


Chart 1

ride, and thermal decomposition of trichloroacetic acid and phenyl(trichloromethyl)mercury. Of several methods for the generation of dichloromethylene by dehydrochlorination of chloroform, the method described by Makosza[6] which utilizes a phase-transfer catalyst[7] was applied to the dichlorocyclopropanation of 5*H*-dibenz[*b*,*f*]azepine (**1**) and derivatives because of the greater simplicity of the procedure than the other methods.

Since a preliminary investigation revealed that 5*H*-dibenz[*b*,*f*]azepine (**1**) was first formylated[8] to yield 5*H*-dibenz[*b*,*f*]azepine-5-carbaldehyde[9] (**4**) under the reaction conditions described by Makosza for the dichlorocyclopropanation of styrene,[6] this latter compound **4** was further treated with the same reagent under similar conditions to yield the desired compound **2** in poor yields. Therefore, the extensive investigation of the reaction conditions was started to optimize the yield of the dichlorocyclopropanation of **4**.[10] Relative amounts of chloroform, sodium hydroxide and the catalyst as well as reaction temperature turned out to be very critical for the success of the reaction. Finally, 1,1-dichloro-1a,10b-dihydrodibenzo[*b*,*f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (**2**) was obtained in 67% yield when **4** was treated with 60 mol equivalents of chloroform and 80 mol equivalents of 50% aqueous sodium hydroxide solution at 40° for three hours in the presence of 0.03 mol equivalent of benzyltriethylammonium chloride as a catalyst. Of several quarternary ammonium halides tested for the catalytic activity benzyltrimethyl-, benzyldimethylphenyl-, and tetraethylammonium chlorides led us to almost comparative yields. The presence of benzene or carbon tetrachloride as a co-solvent did not affect the yield.

When **1** was subjected to the reaction under similar conditions, the yield of **2** was rather poor, because the formation of a tar competed with the N-formylation in the strongly alkaline medium. After a number of unrewarded trials, however, a single-flask synthesis was successfully achieved by the following manner: the N-formylation reaction was carried out first in somewhat milder alkaline solution using 33% aqueous sodium hydroxide, and then the dichlorocyclopropanation was set forth by addition of solid sodium hydroxide into the reaction

6) M. Makosza and M. Wawrzyniewicz, *Tetrahedron Lett.*, **1969**, 4659.
7) C.M. Starks, *J. Am. Chem. Soc.*, **93**, 195 (1971); C.M. Starks and R.M. Owens, *ibid.*, **95**, 3613 (1973).
8) Dichloromethylene generated by other methods has been known to react with secondary amines to give N,N-dialkylformamides (ref. 5, p. 410).
9) E. Gibstein, E.M. Barrall II, and K.E. Bredfeldt, "Anal. Calorimetry, Proc. Symp.," 2nd ed., ed. by R.S. Porter, Plenum, New York, 1970, p. 127 [*C.A.*, **74**, 125016*u* (1971)].
10) The requirement of a wide range of reaction conditions according to the nature of substrates in dibromocyclopropanation catalyzed by a phase-transfer catalyst has been noted (L. Skatteboel, G.A. Abskharoun, and T. Greibrokk, *Tetrahedron Lett.*, **1973**, 1367).

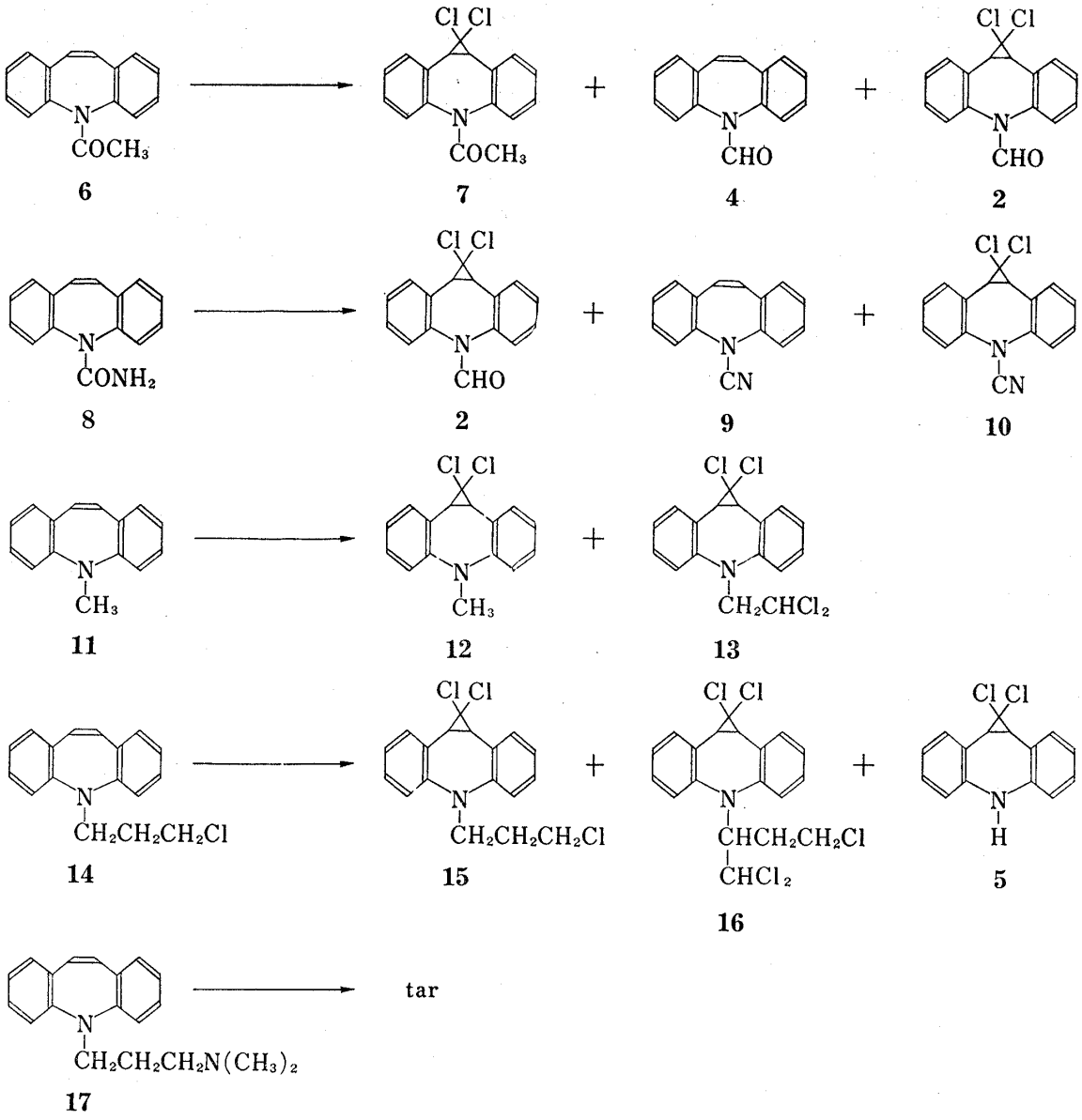


Chart 2

mixture thereby adjusting the concentration of the alkali to the optimum point. The overall yield of **2** was 77.5% and a small amount of the hydrolyzed product **5** was also obtained. If the reaction was quenched at the first stage, **4** was obtained in 95% yield.

Dichlorocyclopropanation of Some 5-Substituted 5*H*-Dibenz[*b*,*f*]azepines

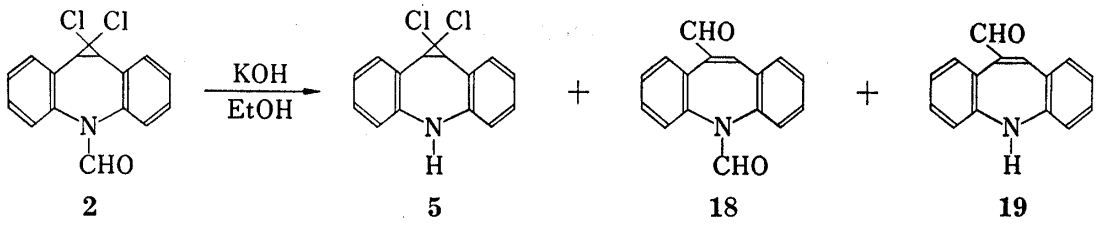
Results obtained in dichlorocyclopropanation of some other 5-substituted 5*H*-dibenz[*b*,*f*]azepines under similar reaction conditions are summarized in Chart 2. Because of the modest yields and side reactions, these routes are not suited for the synthesis of **3** and its pharmacologically active congeners, which include the carbamoyl and 3-(dimethylamino)-propyl derivatives.[1] The side reactions encountered are acyl interchange (**6**→**4** and **8**→**2**), dehydration of the carbamoyl into the cyano group (**8**→**9**), insertion of dichloromethylene into a carbon-hydrogen single bond[11] (**11**→**13** and **14**→**16**) and N-dealkylation (**14**→**5**). The dehydration of the carbamoyl group attracted our attention and the reaction was further

11) I. Tabushi, Z. Yoshida, and N. Takahashi, *J. Am. Chem. Soc.*, **92**, 6670 (1970).

investigated and shown to be generally applicable to the synthesis of nitriles from amides, thioamides and aldoximes, and cyanamides from ureas under the alkaline conditions.[12]

Hydrolysis of 1,1-Dichloro-1a,10b-dihydrodibenzo[*b*,*f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (2)

2 was easily hydrolyzed with potassium hydroxide in ethanol to give **5** in 73% yield. 5*H*-Dibenz[*b*,*f*]azepine-5,10-dicarbaldehyde (**18**) and 5*H*-dibenz[*b*,*f*]azepine-10-carbaldehyde (**19**) were obtained as minor by-products (Chart 3).

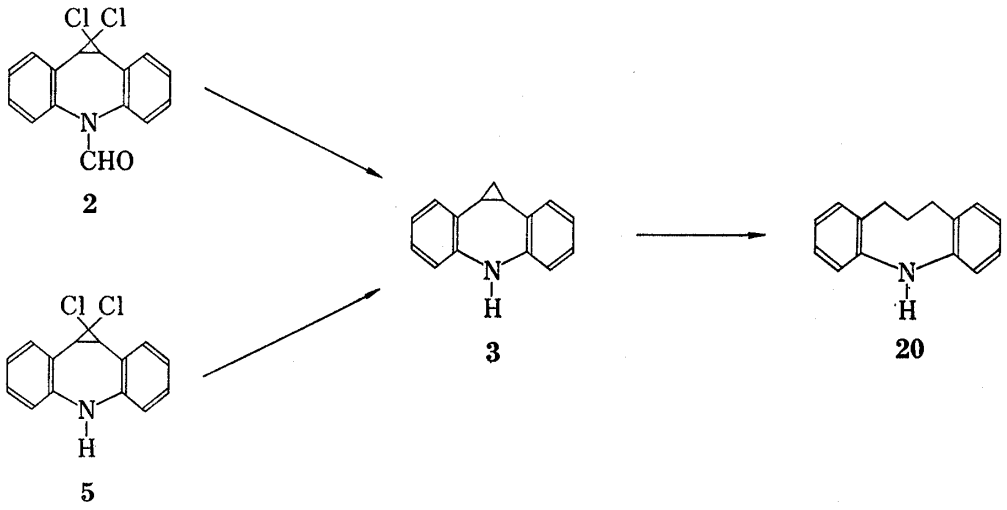


2 **5** **18** **19**

Chart 3

Dechlorination of 1,1-Dichloro-1a,10b-dihydrodibenzo[*b*,*f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (2) and 1,1-Dichloro-1,1a,6,10b-tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepine (5)

Of several methods[13] for the dechlorination of dichlorocyclopropanes, sodium in liquid ammonia[14] or amines gave the most successful result in conversion of **2** and **5** into **3**. When **5** was treated with five equivalents of sodium in liquid ammonia at the temperature, −50° to −40°, for 1 hr, **3** was obtained in 80.5% yield (Chart 4). A large excess of sodium led to cleavage of the C–C bond of the cyclopropane to yield 5,6,7,12-tetrahydrodibenz[*b*,*f*]azocine[15] (**20**) as the main product. Since **3** is transformed into **20** under the same conditions, a plausible reaction mechanism would be the one as depicted in Chart 4. When **2** was treated under similar conditions, the same product **3** was obtained in 53% yield with concomitant reductive deacylation.[16]

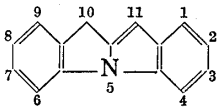


2 **5** **3** **20**

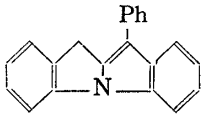
Chart 4

12) T. Saraie, T. Ishiguro, K. Kawashima, and K. Morita, *Tetrahedron Lett.*, 1973, 2121.
13) D. Wendisch, "Methoden der Organischen Chemie," Vol. IV/3, ed. by E. Müller, Georg Thieme Verlag, Stuttgart, 1971, p. 202; T. Ando and H. Yamanaka, *Yuki Gosei Kagaku Kyokai Shi*, **29**, 480 (1971).
14) G.L. Closs and L.E. Closs, *J. Am. Chem. Soc.*, **82**, 5723 (1960); M. Schlosser and G. Heinz, *Angew. Chem. Inter. Ed. Engl.*, **6**, 629 (1967); D. Klamann and C. Finger, *Chem. Ber.*, **101**, 1291 (1968).
15) R.M.Jacob and J.C.L. Fouche, Ger. Patent 1180751 (1964) [*C.A.*, **62**, 13132*c* (1965)].
16) G.W. Watt, *Chem. Rev.*, **46**, 318 (1950); A.J. Birch and H. Smith, *Quart. Rev.*, **12**, 17 (1958).

The dechlorination was also effected by the use of sodium in aliphatic amines at room temperature. Thus, **5** was reduced to **3** in 71.1% yield by treatment with ten equivalents of sodium in di-*iso*-propylamine for 70 hr. An attempt to shorten the reaction time by the use of sodium dispersion resulted in formation of another product **21** in 25.6% yield. The 10*H*-indolo[1,2-*a*]indole structure was assigned to **21** on the spectral evidence: the methylene and olefinic protons are clearly visualized as singlets at δ 3.74 and 6.30, respectively, with a 2: 1 integral ratio in the nuclear magnetic resonance (NMR) spectrum. The ultraviolet (UV) spectrum of **21** (λ_{max}^{EtOH} nm (ε): 215 (27100), 259 (35000), 309 (18000)) is quite similar to the publised data for the 11-phenyl derivative **22** (λ_{max}^{EtOH} nm (ε): 222 (28600), 257 (36800), 315 (18300).[17] **2** was unaffected by sodium in aliphatic amines.



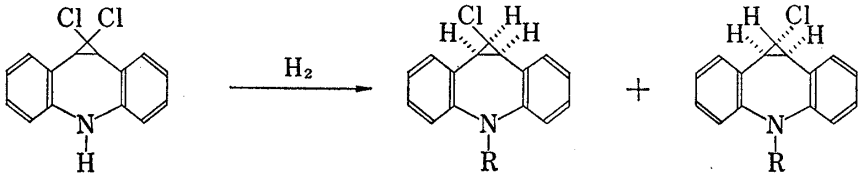
21



22

1-Chloro-1,1a,6,10b-tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepines

When 1,1-dichloro-1,1a,6,10b-tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepine (**5**) was subjected to catalytic hydrogenation, the monodechlorinated substances (**23**, R=H) and (**24**, R=H) were the main products (Chart 5) and the didechlorinated product **3** was obtained only in a trace amount even under the vigorous conditions. This is in accord with the fact that dichlorocyclopropanes generally give monochlorocyclopropanes on catalytic hydrogenation.[18] The kind of catalysts largely affected the *cis*: *trans* ratio of the products; thus, W7 Raney nickel, W7 Raney cobalt and Urushibara nickel B[19] gave the ratio of 2: 1 for *cis* and *trans*, and the catalytic activities for the reaction decreased in this order, while *ca.* 1: 1 mixture of the isomers was obtained by the use of platinum oxide as a catalyst. On the other hand, palladium on charcoal catalyzed the cleavage of the C–C bond, as well as didechlorination, giving rise to **20** as the sole product.



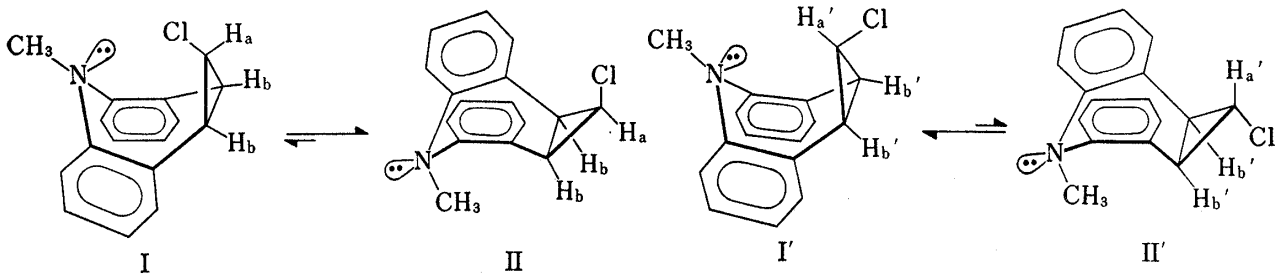
5 **23** : R=H **24** : R=H

Chart 5

cis- and *trans*-1-Chloro-1,1a,6,10b-tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepines (**23**, R=H and **24**, R=H) were methylated with methyl iodide to yield **23** (R=CH_3) and **24** (R=CH_3), respectively. **23** (R=CH_3) was also obtained by the lithium aluminum hydride reduction of **2** as the sole product. The configurational assignment is based on the NMR spectroscopic evidence;[20] the coupling constants for the carbinyl protons attached to the carbon bearing

17) L.J. Dolby and P.D. Lord, *J. Org. Chem.*, **34**, 2988 (1969).
18) W. von E. Doering and A.K. Hoffmann, *J. Am. Chem. Soc.*, **76**, 6162 (1954); K. Hofmann, S.F. Orochena, S.M. Sax, and G.A. Jeffrey, *ibid.*, **81**, 992 (1959); A.J. Birch, G.M. Iskander, B.I. Magboul, and F. Stansfield, *J. Chem. Soc.* (*C*), **1967**, 358; K. Isogai and T. Kazama, *Nippon Kagaku Zasshi*, **88**, 106 (1967); K. Isogai and S. Kondo, *ibid.*, **89**, 97 (1968); K. Isogai, S. Kondo, K. Katsura, S. Sato, N. Yoshihara, Y. Kawamura, and T. Kazama, *ibid.*, **90**, 561 (1970).
19) Y. Urushibara and S. Nishimura, *Bull. Chem. Soc. Japan*, **27**, 480 (1954).
20) J.W. Emsley, J. Feeney, and L.H. Sutchiffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press Ltd., New York, 1966, p. 690.

chlorine atom are 8 Hz for the *cis*-isomer **23** (R=CH_3) and 4 Hz for the *trans*-isomer **24** (R=CH_3), respectively. It should be noted that these carbinyl protons resonate at quite different frequencies, *i.e.*, δ 3.77 for the *cis*-isomer and δ 5.86 for the *trans*-isomer. The large difference of the chemical shift values for *cis*- and *trans*-isomers is accounted for by conformational considerations (Chart 6). In the preferred conformation I′ for the *trans*-isomer,[21] the proton Ha′ is subjected to an extremely large deshielding effect by the proximate nitrogen lone-pair electrons. On the other hand, the *cis*-isomer is not expected to involve such an effect in the both conformers I and II. The conformation II would be the preffered one for the *cis*-isomer, because the molecular model demonstrates a large steric hindrance between the chlorine atom and the nitrogen lone-pair electrons in the conformation I.



23 : R=CH_3 (*cis*) **24** : R=CH_3 (*trans*)

Chart 6

Experimental

Melting points are uncorrected. The UV and infrared (IR) spectra were taken with Perkin-Elmer 450 and Hitachi EPI-S2 models, respectively. NMR spectra were recorded with Varian T-60 (60 MHz) and HR-100 (100 MHz) models, the chemical shifts being expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Mass spectra were measured with a Hitachi RMU-6D double focussing mass spectrometer.

5*H*-Dibenz[*b*,*f*]azepine-5-carbaldehyde[9] (**4**)——A mixture of 38.6 g (0.2 mol) of 5*H*-dibenz[*b*,*f*]azepine[4] (**1**), 716 g (6.0 mol) of $CHCl_3$, 1.36 g (6.0 mmol) of benzyltriethylammonium chloride and 640 g (4.0 mol) of 25% NaOH aq. was stirred vigorously at 40° for 21 hr. The reaction mixture was extracted with $CHCl_3$, the $CHCl_3$ solution was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure to yield a white residue. The residue was recrystallized from benzene–cyclohexane (1: 1) to yield 41.8 g of **4** (95% yield).

1,1-Dichloro-1a,10b-dihydrodibenzo[*b*,*f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (**2**)——a) By Dichlorocyclopropanation of **4** under Various Reaction Conditions: Table I summarizes the effect of various reaction conditions on the yield of **2**. Entry 3 represents the experimental procedure: A mixture of 4.42 g (20 mmol) of **4**, 143.2 g (1.2 mol) of $CHCl_3$, 0.136 g (0.6 mmol) of benzyltriethylammonium chloride and 128 g of 50% NaOH aq. (1.6 mol of NaOH) was stirred vigorously at 40° for 3 hr. The reaction mixture was extracted with $CHCl_3$, the $CHCl_3$ solution was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure to yield a white residue. The residue was recrystallized from benzene to yield white crystals of **2**, mp 213° (dec.). IR ν_{max}^{Nujol} cm^{-1}: 1692 (C=O). NMR (60 MHz) δ^{CDCl_3}: 3.35 (s, benzylic), 7.2—7.7 (m, aromatic), 8.53 (s, CHO). *Anal.* Calcd. for $C_{16}H_{11}Cl_2NO$: C, 63.18; H, 3.65; N, 4.61. Found: C, 63.28; H, 3.64; N, 4.58.

b) By a One-flask Synthesis from **1**: A mixture of 14.48 g (0.075 mol) of **1**, 538 g (4.5 mol) of $CHCl_3$, 0.57 g (0.0023 mol) of benzyldimethylphenylammonium chloride and 360 g of 33% NaOH aq. was stirred vigorously at 40° for 6 hr, after which time 216 g (5.4 mol) of solid NaOH and 60 g of H_2O were added. The mixture was stirred at 40° for 16 hr and the resulting solution was extracted with chloroform. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated under reduced pressure to yield a residue, which was recrystallized from benzene to give 17.67 g of **2** (77.5% yield).

Dichlorocyclopropanation of 5-Substituted 5*H*-Dibenz[*b*,*f*]azepines——A mixture of 10 mmol of a substrate, 71.6 g (0.6 mol) of $CHCl_3$, 68 mg (0.3 mmol) of benzyltriethylammonium chloride and 32 g (0.4 mol) of 50% NaOH aq. was stirred vigorously at 40° for 21 hr. A crude product obtained by extraction with $CHCl_3$ was separated and purified by column chromatography on silica gel.

21) It has been discussed in detail that the conformers like I′ are preferred to the conformers like II′ in these ring systems, although the former appears, at a glance, to involve a large steric hindrance (K. Kawashima and E. Mizuta, *Chem. Pharm. Bull.* (Tokyo), **24** 2761 (1976)).

Table I. 1,1-Dichloro-1a,10b-dihydrodibenzo[*b,f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (**2**) by Dichlorocyclopropanation of 5*H*-Dibenz[*b,f*]-azepine-5-carbaldehyde (**4**) under Various Reaction Conditions

Entry	Catalyst	50% NaOH aq. (mol)[a]	Time (hr)	Yield of **2**
1	$C_6H_5CH_2N(C_2H_5)_3Cl$	0.8	21	47
2	$C_6H_5CH_2N(C_2H_5)_3Cl$	1.2	21	57
3	$C_6H_5CH_2N(C_2H_5)_3Cl$	1.6	3	67
4	$C_6H_5CH_2N(C_2H_5)_3Cl$	2.0	3	64
5	$C_6H_5CH_2N(C_2H_5)_3Cl$	1.6	3	67
6	$C_6H_5CH_2N(CH_3)_3Cl$	1.6	3	64
7	$C_6H_5CH_2N(C_6H_5)(CH_3)_2Cl$	1.6	3	70
8	$(C_2H_5)_4NCl$	1.6	3	61
9	$(CH_3)_4NCl$	1.6	3	38
10	n-$C_{16}H_{33}N(CH_3)_3Br$	1.6	3	52

a) 20 mmol of the substrate **4** was used.

a) From 5-acetyl-5*H*-dibenz[*b,f*]azepine[4] (**6**) were obtained 6-acetyl-1,1-dichloro-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**7**), **4** and **2** in yields of 10, 1.5 and 3%, respectively, 5% of **6** being recovered. **7** is a white crystalline substance, mp 162—163°. IR ν_{max}^{Nujol} cm^{-1}: 1665 (C=O). NMR (60 MHz) δ^{CDCl_3}: 2.05 (s, CH_3), 3.32 (s, benzylic), 7.2—7.6 (m, aromatic). *Anal.* Calcd. for $C_{17}H_{13}Cl_2NO$: C, 64.16; H, 4.12; N, 4.40. Found: C, 64.68; H, 3.95; N, 4.42.

b) From 5*H*-dibenz[*b,f*]azepine-5-carboxamide[22] (**8**) were obtained **2**, 5*H*-dibenz[*b,f*]azepine-5-carbonitrile[12] (**9**) and 1,1-dichloro-1a,10b-dihydrodibenzo[*b,f*]cycloprop[*d*]azepine-6(1*H*)-carbonitrile[12] (**10**) in yields of 12, 21 and 41%, respectively. **9** is a white crystalline substance, mp 109—110°. IR ν_{max}^{Nujol} cm^{-1}: 2225 (C≡N). NMR (60 MHz) δ^{CDCl_3}: 6.75 (s, olefinic), 7.1—7.6 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{10}N_2$ (**9**): C, 82.55; H, 4.62; N, 12.83. Found: C, 82.30; H, 4.73; N, 12.80. **10** is a white crystalline substance, mp 205—206°. IR ν_{max}^{Nujol} cm^{-1}: 2225 (C≡N). NMR (60 MHz) δ^{CDCl_3}: 3.38 (s, benzylic), 7.2—7.7 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{10}Cl_2N_2$ (**10**): C, 63.80; H, 3.35; N, 9.30. Found: C, 63.73; H, 3.35; N, 9.16.

c) From 5-methyl-5*H*-dibenz[*b,f*]azepine[1,23] (**11**) were obtained 1,1-dichloro-1,1a,6,10b-tetrahydro-6-methyldibenzo[*b,f*]cycloprop[*d*]azepine (**12**) and 1,1-dichloro-6-(2,2-dichloroethyl)-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**13**) in yields of 33 and 37%, respectively. **12** is a white crystalline substance, mp 197—200° (dec.). IR ν_{max}^{Nujol} cm^{-1}: 1585 (aromatic). NMR (60 MHz) δ^{CCl_4}: 3.20 (s, benzylic), 3.27 (s, CH_3), 6.8—7.5 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{13}Cl_2N$ (**12**): C, 66.22; H, 4.52; N, 4.83. Found: C, 65.87; H, 4.41; N, 4.60. **13** is a white crystalline substance, mp 105—107°. IR ν_{max}^{Nujol} cm^{-1}: 1580, 1490 (aromatic). NMR (60 MHz) δ^{CDCl_3}: 3.32 (s, benzylic), 4.32 (d, J=6.8 Hz, CH_2), 5.60 (t, J=6.8 Hz, $CHCl_2$), 6.8—7.6 (m, aromatic). *Anal.* Calcd. for $C_{17}H_{13}Cl_4N$ (**13**): C, 54.73; H, 3.51; N, 3.75. Found: C, 54.81; H, 3.37; N, 3.75.

d) From 5-(3-chloropropyl)-5*H*-dibenz[*b,f*]azepine[24] (**14**) were obtained 1,1-dichloro-6-(3-chloropropyl)-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**15**), 1,1-dichloro-6-[(3-chloro-1-dichloromethyl)propyl]-1,1a,6,10b-tetrahydrodibenzo[*b,f*]cycloprop[*d*]azepine (**16**) and 1,1-dichloro-1,1a,6,10b-tetrahydrodibenzo-[*b,f*]cycloprop[*d*]azepine (**5**) in yields of 15, 50 and 4%, respectively. **15** is a pale yellow oily substance. NMR (60 MHz) δ^{CDCl_3}: 1.7—2.2 (m, C–CH_2–C), 3.23 (s, benzylic), 3.46 (t, J=6.5 Hz, NCH_2 or CH_2Cl), 3.75 (t, J=6.5 Hz, NCH_2 or CH_2Cl), 6.8—7.5 (m, aromatic). **16** is a pale yellow oily substance. NMR (60 MHz) δ^{CDCl_3}: 2.1—2.6 (m, C–CH_2–C), 3.39 (s, benzylic), 3.5—3.9 (m, CH_2Cl), 4.15—4.45 (br, N–CH), 5.96 (d, J= 2 Hz, $CHCl_2$), 7.1—7.6 (m, aromatic). **5** is a white crystalline substance, mp 162—163°. IR ν_{max}^{Nujol} cm^{-1}: 3370 (NH), 1585 (aromatic). NMR (60 MHz) δ^{CDCl_3}: 3.26 (s, benzylic), 5.60 (br, NH), 6.7—7.5 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{11}Cl_2N$ (**5**): C, 65.23; H, 4.02; N, 5.07. Found: C, 65.52; H, 3.77; N, 4.82.

Hydrolysis of 1,1-Dichloro-1a,10b-dihydrodibenzo[*b,f*]cycloprop[*d*]azepine-6(1*H*)-carbaldehyde (**2**)——A suspension of 3.65 g (12 mmol) of **2** and 3.36 g (60 mmol) of KOH in 63.8 g of EtOH was stirred at 50° for 4 hr. The reaction mixture was neutralized with HCl aq., concentrated and extracted with AcOEt. The extract was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. The resulting residue was recrystallized from benzene–hexane to yield 2.40 g of **5** (73% yield). Column chromatography of the mother liquor on silica gel afforded a small amount of 5*H*-dibenz[*b,f*]azepine-5,10-dicarbaldehyde (**18**) and 5*H*-dibenz[*b,f*]azepine-10-carbaldehyde (**19**). **18** is a white crystalline substance, mp 147—148°. NMR

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24) P.N. Craig, B.M. Lester, A.J. Saggiomo, C. Kaiser, and C.L. Zirkle, *J. Org. Chem.*, **26**, 135 (1961).

(60 MHz) δ^{CDCl_3}: 7.3—8.0 (m, aromatic and olefinic), 8.34 (s, N–CHO), 9.90 (d, J=1 Hz, C–CHO). *Anal.* Calcd. for $C_{16}H_{11}NO_2$ (**18**): C, 77.09; H, 4.45; N, 5.62. Found: C, 77.55; H, 4.45; N, 5.33. **19** is a red oily substance. NMR (60 MHz) δ^{CDCl_3}: 6.50 (br, NH), 6.6—7.6 (aromatic and olefinic), 9.77 (s, CHO).

1,1a,6,10b-Tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepine[1] (**3**)——a) By Reduction of **5** with Sodium in Liquid Ammonia: In 20 ml of liquid NH_3 were suspended 1.10 g (4 mmol) of **5** and 0.46 g (20 mmol) of Na was added in small pieces with stirring at −40° to −50°. The mixture was stirred at the same temperature for 1 hr, after which time 1.0 g of NH_4Cl was added. The liquid NH_3 was distilled off and 20 ml of H_2O were added. The mixture was then extracted three times with 20 ml portions of benzene and the extracts were washed with H_2O and dried. The benzene was distilled off and the residue was purified by column chromatography on silica gel using benzene–cyclohexane (6: 4) as a solvent; 0.667 g of **3** was obtained (80.5% yield). This substance was identical in all respects with **3** obtained previously by present authors.[1]

b) By Reduction of **2** with Sodium in Liquid Ammonia: Treatment of 1.82 g (6 mmol) of **2** with 0.69 g (30 mmol) of Na in 20 ml of liquid NH_3 in the same manner as in a) afford 0.66 g of **3** (53% yield).

c) By Reduction of **5** with Sodium in Di-*iso*-propylamine: In 20 ml of di-*iso*-propylamine was suspended 0.552 g (2 mmol) of **5** and 0.46 g of Na in small pieces was added. The mixture was stirred for 70 hr at room temperature, after which time the excess Na was decomposed with 10 ml of MeOH. The mixture was poured into 20 ml of H_2O and extracted three times with 20 ml portions of benzene. After washing with H_2O and drying, the solvent was evaporated under reduced pressure and the residue was purified by chromatography as described in a); 0.297 g of **3** was obtained (71.7% yield).

d) By Reduction of **5** with Sodium in *n*-Butylamine: Treatment of 1.1 g (4 mmol) of **5** with 0.46 g (20 mmol) of Na in 10 ml of *n*-butylamine in the same manner as in c) afforded 0.53 g of **3** (64% yield), 0.03 g of **5** (3%) being recovered unchanged.

5,6,7,12-Tetrahydrodibenz[*b*,*g*]azocine[15] (**20**)——a) From **5**: In 20 ml of liquid NH_3 was suspended 0.552 g (2 mmol) of **5** and 0.46 g (20 mmol) of Na was added in small pieces with stirring at −60°. The mixture was stirred at −33° for 1 1/2 hr, after which time 1.0 g of NH_4Cl was added. The liquid NH_3 was distilled off and H_2O was added. The mixture was then extracted with $CHCl_3$ and the extract was washed with H_2O and dried. The $CHCl_3$ was distilled off and the residue was purified by column chromatography on silica gel using benzene–hexane (6: 4) as a solvent; 0.211 g of **20** was obtained (50.5% yield), mp 61—62° (lit.[15] 55—57°). IR ν_{max}^{Nujol} cm^{-1}: 3360 (NH), 1585, 1485 (aromatic). NMR (60 MHz) δ^{CDCl_3}: 1.4—1.9 (m, CH_2–$C\underline{H}_2$–CH_2), 2.70 (t, J=7.0 Hz benzylic), 5.70 (br s, NH), 6.6—7.4 (m, aromatic).

b) From **3**: Treatment of 0.414 g (2 mmol) of **3** with 0.138 g (6 mmol) of Na in 20 ml of liquid NH_3 in the same manner as in a) afforded 0.411 g of a mixture comprizing **20** and **3**. The mol ratio **20**: **3** was measured to be 55: 45 by the use of the NMR signal integration.

10*H*-Indolo[1,2-*a*]indole (**21**)—A suspension of 1.1 g (4 mmol) of **5** and 0.46 g (20 mmol) of Na dispersion in 20 ml of di-*iso*-propylamine was stirred for 20 hr at room temperature. An usual working-up followed by column chromatography on silica gel using benzene–hexane (3: 7) as a solvent afforded 0.21 g of **21** (25.6% yield), mp 86—87°. IR ν_{max}^{Nujol} cm^{-1}: 3020, 1600, 1570 (aromatic). NMR (60 MHz) δ^{CDCl_3}: 3.74 (s, CH_2), 6.30 (s, olefinic), 6.7—7.7 (m, aromatic). MS *m/e*: 205 (M^+, base peak). *Anal.* Calcd. for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.90; H, 5.20; N, 6.77.

Catalytic Hydrogenation of 5——a) Preparation of *cis*- and *trans*-1-Chloro-1,1a,6,10b-tetrahydrodibenzo[*b*,*f*]cycloprop[*d*]azepines (**23**, R=H and **24**, R=H): In 200 ml of EtOH was suspended 5.52 g (20 mmol) of **5**, and 3.96 g of KOH (>85% pure, 60 mmol) and 2.0 g of PtO_2 were added. The mixture was stirred for 60 hr in an atmosphere of H_2. After removing the catalyst by filtration, the filtrate was neutralized with conc. HCl aq. and concentrated. H_2O was added to the residue and extracted with $CHCl_3$. The extract was washed, dried and evaporated under reduced pressure. The resulting residue was recrystallized from EtOH to give 1.48 g of **23** (R=H). The mother liquor was separated by column chromatography on silica gel. Benzene–hexane (1: 1) eluted 2.07 g of **24** (R=H) (42.8% yield). From the fractions eluted with benzene–hexane (2: 1) was obtained an additional amount of **23** (R=H) (1.17 g, 54.8% total yield). **23** (R=H) melted at 160—161°. IR ν_{max}^{Nujol} cm^{-1}: 3280 (NH), 1590 (aromatic). NMR (100 MHz) δ^{CDCl_3}: 2.72 (d, J=8.0 Hz benzylic), 3.82 (t, J=8.0 Hz, CHCl), 5.48 (s, NH), 6.6—7.4 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{12}ClN$ (**23**, R=H): C, 74.53; H, 5.00; N, 5.80. Found: C, 74.76; H, 4.76; N, 5.46. **24** (R=H) melted at 96—97°. IR ν_{max}^{Nujol} cm^{-1}: 3320 (NH), 1590 (aromatic). NMR (100 MHz) δ^{CDCl_3}: 2.52 (d, J=4.0 Hz benzylic), 4.50 (t, J=4.0 Hz, CHCl), 4.97 (s, NH), 6.5—7.4 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{12}ClN$ (**24**, R=H): C, 74.53; H, 5.00; N, 5.80. Found: C, 74.87; H, 4.81; N, 5.80.

b) Effect of Various Catalysts on Product Ratio: **5** was hydrogenated in the presence of various catalysts and KOH in EtOH solution. The results are summarized in Table II.

***cis*-1-Chloro-1,1a,6,10b-tetrahydro-6-methyldibenzo[*b*,*f*]cycloprop[*d*]azepine** (**23**, **R=CH_3**)——a) From **23** (R=H): 0.144 g of NaH containing 50% mineral oil (3 mmol) was washed three times with 2 ml each of hexane and 3 ml of dry DMSO and 0.242 g (1 mmol) of **23** (R=H) were added successively. The mixture was stirred for 1 hr in an atmosphere of N_2 and 0.426 g (3 mmol) of CH_3I was added. After 5 hr stirring H_2O was added to the mixture and extracted with benzene. The extract was washed with H_2O, dried and evaporated under reduced pressure. Column chromatography of the resulting residue on silica gel yielded 0.20 g of **23** (R=CH_3) (78% yield), mp 182° (dec.) (from benzene). IR ν_{max}^{Nujol} cm^{-1}: 1575, 1485 (aromatic).

Table II. Effect of Various Catalysts on Product Ratio in the Catalytic Hydrogenation of 1,1-Dichloro-1,1a,6,10b-tetrahydrodibenzo[b,*f*]cycloprop[*d*]azepine (**5**)

Catalyst	Temperature	Pressure (atm)	Time (hr)	Product ratio[a] **23**: **24** (R=H)
W7 Raney nickel	Room temp.	1	36	2:1[b]
W7 Raney nickel	74°	108	6.5	2:1[b]
Platinum oxide	Room temp.	1	24	1:1
Platinum oxide	93°	130	7	1:1
Urushibara nickel B	Room temp.	1	45	2:1[b,c]
Urushibara nickel B	93°	132	6.5	2:1[b,c]
W7 Raney cobalt	Room temp.	1	45	2:1
10% Palladium on charcoal	Room temp.	1	42	[c,d]

a) Estimated from the NMR integral ratio for the benzylic protons at δ 2.72 and 2.52.
b) A trace amount of **3** was formed.
c) Some amounts of the starting material were recovered unchanged.
d) **20** was the sole product.

NMR (100 MHz) δ^{CDCl_3}: 2.75 (d, J=8.0 Hz, benzylic), 3.32 (s, CH_3), 3.77 (t, J=8.0 Hz, CHCl), 6.8—7.4 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{14}ClN$: C, 75.14; H, 5.52; N, 5.48. Found: C, 75.26; H, 5.50; N, 5.52.

b) From **2**: To a solution of 0.304 g (1 mmol) of **2** in 6 ml of hot THF was added 0.190 g (5.0 mmol) of $LiAlH_4$ and refluxed for 20 min in an atmosphere of N_2. The mixture was chilled with ice and excess $LiAlH_4$ was decomposed by addition of 3 drops of H_2O. The precipitate formed was filtered and washed three times with 5 ml each of THF. The combined filtrate and washings were evaporated to give 0.248 g of **23** (R=CH_3) (97% yield).

***trans*-1-Chloro-1,1a,6,10b-tetrahydro-6-methyldibenzo[*b*,*f*]cycloprop[*d*]azepine (24, R=CH_3)**——0.242 g of **24** (R=H) was reacted with CH_3I in the same manner as in the case of *cis*-isomer to yield 0.172 g of **24** (R=CH_3) (67% yield), mp 149—150°. IR ν_{max}^{Nujol} cm^{-1}: 1575, 1485 (aromatic). NMR (100 MHz) δ^{CDCl_3}: 2.45 (d, J=4.0 Hz, benzylic), 3.08 (s, CH_3), 5.86 (t, J=4.0 Hz, CHCl), 6.8—7.3 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{14}ClN$: C, 75.14; H, 5.52; N, 5.48. Found: C, 75.53; H, 5.42; N, 5.51.

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