Reactions of Aldehydes with Hydrazine Hydrochlorides in the Presence of Dipolarophiles; Intra- and Intermolecular [3+ + 2] Cycloadditions

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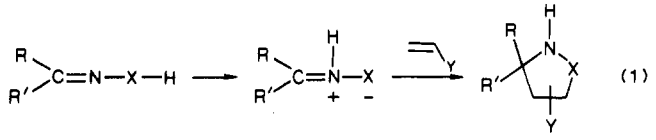
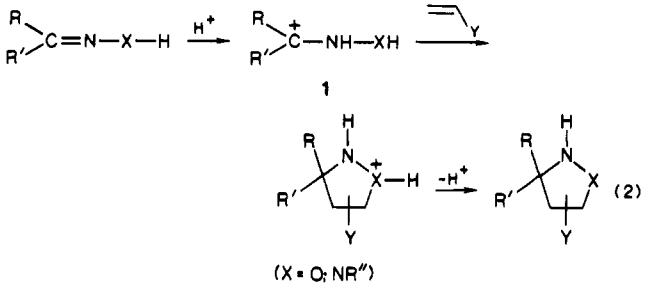
The reaction of 2 molar equiv of several 2-(alkenyloxy)-1-naphthaldehydes (**2**) with hydrazine dihydrochloride (**3**) and subsequent treatment of the mixture with triethylamine lead to intramolecular [3+ + 2] criss-cross cycloadducts **5**, 2:1 molar products of **2** and **3**, in high yields. On the other hand, naphtho[1′,2′:5,6]pyrano-[4,3-*c*]pyrazoles **11** and **12**, equimolar products of **2** and **3**, were obtained by a similar series of reactions using a large excess of **3**. Many pyrazolium chlorides (**25**), 2,2-dimethyl derivatives of **11**, were prepared in high yields from the equimolar reaction of **2** with 1,1-dimethylhydrazine hydrochloride (**24**). *N*-Phenyl, *N*-decyl, and *N*-dodecyl derivatives **29**, **31**, and **32**, respectively, of **25** were also prepared from the reaction using the corresponding *N*-phenyl, *N*-decyl, and *N*-dodecyl derivatives of **24**. Similarly, 1,2-dimethyl derivatives **41** of **11** were also prepared from an equimolar reaction of **2** with 1,2-dimethylhydrazine dihydrochloride. Intermolecular cycloadducts corresponding to these intramolecular ones were also obtained by the reactions of benzaldehyde with these hydrazine hydrochlorides in the presence of dipolarophiles. Formation of these cycloadducts can be explained as a result of intra- and intermolecular cycloadditions of cationic dipoles [RC+H–N(R′)NR″R‴ ↔ RCH=N+(R′)NR″R‴ (R′, R″, R‴ = H, alkyl, or phenyl)] with dipolarophiles.

Since the monumental work of Huisgen and co-workers in the early 1960s, which led to the general concept of 1,3-dipolar cycloaddition and the definition and classification of 1,3-dipoles,[1] a variety of 1,3-dipoles have been prepared.[2] According to the definition, compounds such as oximes and hydrazones should exhibit 1,3-dipolar character by the thermal isomerization to nitrones or azomethine imines, respectively (eq 1). Thus, the cyclo-



(X=O; NR″) (1)

addition of the compounds via thermal isomerization have been well studied.[3-5] An alternative procedure was found recently where the same cycloadducts were prepared conveniently under milder conditions by acid-catalyzed reaction of oximes or hydrazones with dipolarophiles and then deprotonation of the products, and this reaction has been explained in terms of the cycloaddition of cationic dipole **1** with the dipolarophiles and can be symbolized as [3+ + 2] cycloaddition[6-8] (eq 2). So far this type of reaction



(X = O; NR″) (2)

of hydrazones has been known only with N-monosubstituted hydrazones. We report here that some N-unsubstituted aldehyde hydrazones (RCH=NNH$_2$), N,N-disubstituted aldehyde hydrazones (RCH=NNR′R″), and aldehyde azines (RCH=NN=CHR) also underwent similar [3+ + 2] cycloadditions with dipolarophiles in the presence of acid. We also report that hydrazinocarbinol intermediates [RCH(OH)NR′NHR″] formed by the reaction of aldehydes with 1,2-disubstituted hydrazines underwent similar reaction via cationic dipoles [RCH=N+(R′)NHR″] in the presence of acid.

Results and Discussion

Cycloaddition Reactions Using Hydrazine. The reaction of 2-(allyloxy)-1-naphthaldehyde (**2a**) with hydrazine dihydrochloride (**3**) in 2:1 molar ratio was carried out in refluxing ethanol for 4 h, from which an intramolecular criss-cross cycloadduct, 8a,9b,17a,18b-tetrahydro-8*H*,9*H*,17*H*,18*H*-7,16-dioxa-9a,18a-diazapentaleno[2,1-*c*:5,4-*c*′]diphenanthrene hydrochloride (**4a**), was obtained, and subsequent treatment of **4a** with triethylamine afforded its free amine (**5a**) in 87% overall yield (Scheme I). The structure of **5a** was established by the comparison of the physical properties with those of authentic specimen.[9] Compound **5a** was also prepared in similar yields by reaction using a stoichiometric amount of hydrazine

(1) (a) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565, 633. (b) Huisgen, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; pp 1–176.

(2) (a) Reference 1b, pp 177. (b) Bianchi, G.; De Micheli, C.; Gandolfi, R. In "1,3-Dipolar Cycloadditions Involving X=Y Groups" *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1977; Supplement A, Part 1, Chapter 6, pp 369–532.

(3) (a) Grigg, R.; Jordan, M.; Tangthongkum, A.; Einstein, F. W. B.; Jones, T. *J. Chem. Soc., Perkin Trans. 1* **1984**, 47. (b) Oppolzer, W.; Keller, K. *Tetrahedron Lett.* **1970**, 1117. (c) Ochiai, M.; Obayashi, M.; Morita, K. *Tetrahedron* **1967**, *23*, 2641. (d) Lablache-Combier, A.; Villaume, M. L. *Tetrahedron* **1968**, *24*, 6951. (e) Winterfeldt, E.; Krohn, W. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 709.

(4) (a) Grigg, R.; Kemp, J.; Thompson, N. *Tetrahedron Lett.* **1978**, 2827. (b) Saxena, M. K.; Gudi, M. N.; George, M. V. *Tetrahedron* **1973**, *29*, 101. (c) Shimizu, T.; Hayashi, Y.; Kitora, Y.; Teramura, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2450.

(5) (a) Hamelin, J.; Le Fevre, G. *Tetrahedron Lett.* **1978**, 4503. (b) Le Fevre, G.; Hamelin, J. *Tetrahedron* **1980**, *36*, 887.

(6) (a) Le Fevre, G.; Hamelin, J. *Tetrahedron Lett.* **1979**, 1757. (b) Le Fevre, G.; Sinbandhit, S.; Hamelin, J. *Tetrahedron* **1979**, *35*, 1821. (c) Fouchet, B.; Joucla, M.; Hamelin, J. *Tetrahedron Lett.* **1981**, *22*, 1333.

(7) (a) Shimizu, T.; Hayashi, Y.; Nakano, M.; Teramura, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2456. (b) Shimizu, T.; Hayashi, Y.; Teramura, K. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 397.

(8) (a) Hesse, K.-D. *Justus Liebigs Ann. Chem.* **1971**, *743*, 50. (b) Wilson, R. M.; Rekers, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 4005.

(9) Mathur, S. S.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2479.

0022-3263/87/1952-2277$01.50/0

Scheme I

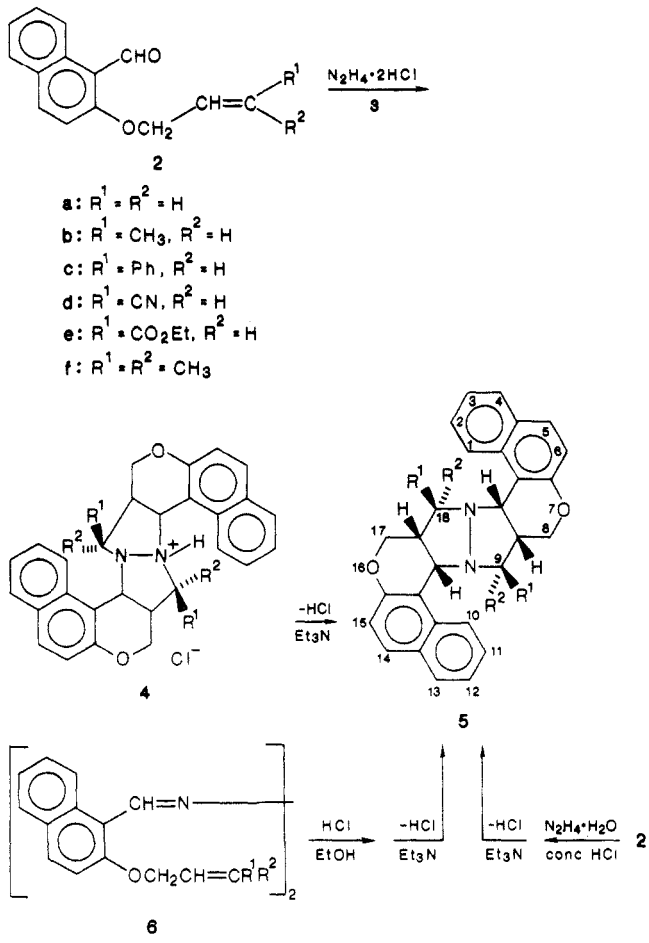
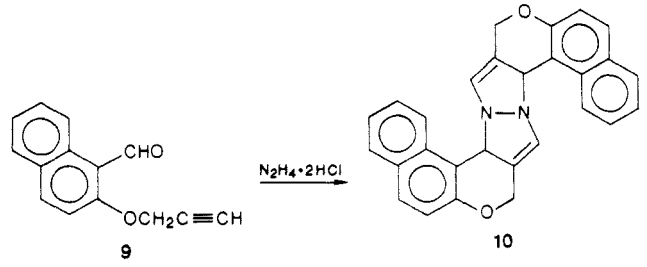


Table I. Yields and Melting Points of Criss-Cross Cycloadducts 5 and 10

compd	R^1	R^2	yield,[a] %	mp, °C
5a	H	H	87 (83)	273–275
5b	CH_3	H	71 (71)	242–245
5c	Ph	H	60 (54)	245–248
5d	CN	H	74 (68)	260 dec
5e	COOEt	H	87 (60)	240–243
5f	CH_3	CH_3	61 (37)	175 dec
10			42 (69)	276–278

[a] Yields from the reaction of **2** or **9** with **3** are shown, and those from the reaction with hydrazine hydrate and concentrated HCl are shown in parentheses.

hydrate and concentrated HCl instead of **3** or by treatment of the aldehyde azine **6a** with a stoichiometric amount of concentrated HCl (or gaseous dry HCl). Similar criss-cross adducts (**5b–f** and **10**) were obtained under the similar conditions from reactions using 2-[(3-substituted-2-propenyl)oxy]-1-naphthaldehydes **2b–f** or 2-(propargyloxy)-1-naphthaldehyde (**9**) in yields shown in Table I.



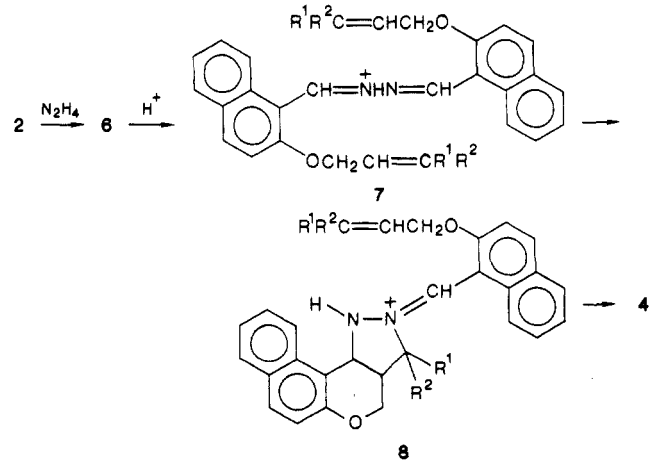
While some (**5a,b** and **10**) of these criss-cross adducts have already been prepared by the treatment of the corresponding azines in *N,N*-dimethylaniline at elevated temperature in the absence of acid,[9] the yields of the adducts were generally poor (for example, **5a** in 12% yield), and some troublesome procedures were required for isolation of the adduct from the reaction mixture owing to the formation of tarry byproducts. The method described here gave more satisfactory results. If the substituent (R^1) at 9- and 18-positions in compounds **5** is a methyl, phenyl, or ethoxycarbonyl group, i.e., in cases of **5b–f**, the chemical shifts of all of the protons on R^1 were found in upfield regions compared with those of normal ones, probably due to the steric compression between the substituent and naphthyl group or the shielding effect by naphthyl group.[9]

Table II. Products from the Reactions of 2 with an Excess Amount of 3

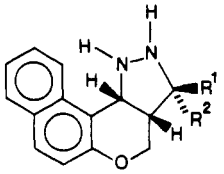
	20-fold amount of 3			4-fold amount of 3	
substrate	product	yield, %	mp (dec), °C	product	yield, %
2a	**12a**	63	115	**5a**	17
2a[a]	**11a**	40	oil		
	12a	50			
2b	**12b**	19	98	**5b**	23
				12b	25
2c	**11c**	70	140	**5c**	26
				11c	40
2d	**11d**	33	181	**11d**	31
2e	**11e**	30	111	**11e**	47
2f	**5f**	6		**5f**	38
	11f	33	80		
	12f	5	oil		

[a] This reaction was carried out under nitrogen.

Formation of **5** can be explained by the following consecutive reactions; (i) the formation of azines **6** from the acid-catalyzed reaction of aldehydes **2** and **9** with hydrazine, (ii) protonation of one of the nitrogen atoms of the azines, giving cationic dipole **7**, (iii) intramolecular [3⁺ + 2] cycloaddition of the dipole with one of the allyl double bonds, giving another cationic dipole **8**, and (iv) further intramolecular [3⁺ + 2] cycloaddition of the dipole with remaining allyl double bond, giving the criss-cross adduct **4**.



By refluxing an ethanol solution of the aldehydes **2** and a large excess of hydrazine dihydrochloride **3**, equimolar cycloadducts **11** and **12** were mainly obtained along with a small amount of the criss-cross adduct **5**. The results are summarized in Table II. The structures of **11** and **12** were established on the basis of elemental and mass, NMR, and IR spectral analyses and comparison with an authentic specimen, 3,3a,4,9b-tetrahydro[1]benzopyrano[4,3-*c*]-pyrazole (**13**).[10] The structure of the pyrazolidine **11c** was



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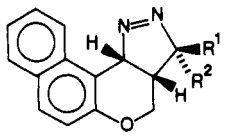

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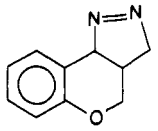
further supported by analysis of diacetyl derivative **14** prepared in 95% yield from the reaction of **11c** and acetyl chloride.



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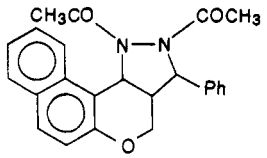

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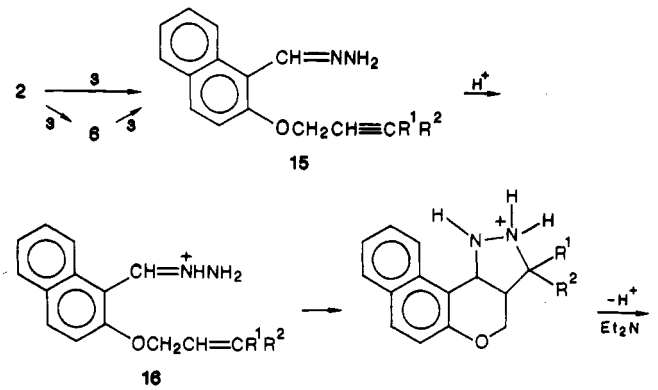
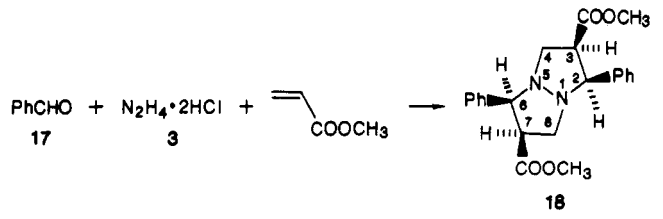
The formation of pyrazolidines **11** can be ascribed to the result of intramolecular [3⁺ + 2] cycloaddition of cationic dipole **16** generated by protonation of N-unsubstituted hydrazones **15**, following deprotonation by Et_3N. Hydrazones **15** may be produced by either an equimolar reaction of **2** with **3** or an exchange reaction between azines **6** and **3**. The dehyrogenation of pyrazolidines **11** to pyrazolines



11 $\xrightarrow{-H_2}$ **12**

12 under the reaction conditions is well-known.[6] In fact, pyrazolidine **11a** was obtained in 40% yield along with **12a** (50%) by reaction under nitrogen, while **11a** was not obtained by similar reaction under atomosphere.

We successfully applied these reactions to the intermolecular ones as described below. A mixture of hydrazine dihydrochloride **3** and 2 equiv of benzaldehyde (**17**) was refluxed in methanol for 4 h in the presence of a large excess (ca. 10-fold excess) of methyl acrylate. A desired intermolecular criss-cross cycloadduct, dimethyl 2,6-diphenyl-1,5-diazabicyclo[3.3.0]octane-3,7-dicarboxylate (**18**), was obtained in 20% yield after the treatment of the mixture with triethylamine. The other possible structures as the regioisomers (**19** and **20**) were ruled out by the analysis of the ^1H NMR spectra of the product: the chemical shift of multiplet observed at δ 2.7–3.3 is not consistent with that (δ 2.0–2.7) expected for the methylene protons at the 3- and 7-positions of the structure **19** but is consistent with that of the 4- and 8-positions of the structure **18**. The chemical shift of the two methyl groups was observed in the same position at δ 3.1 and was in upfield regions (ca. 0.5 ppm) compared with normal methyl ester group (ca. δ 3.7). This phenomenon is well-known



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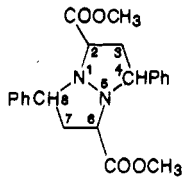

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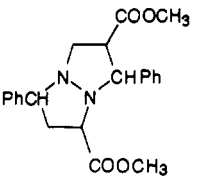
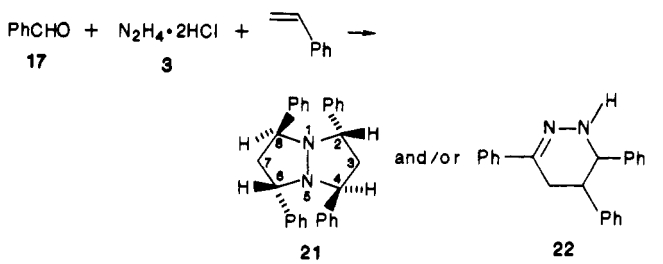


20

in analogous five-membered heterocyclic compounds and has been explained by vicinal cis relationship of the ester and aryl groups.[11]

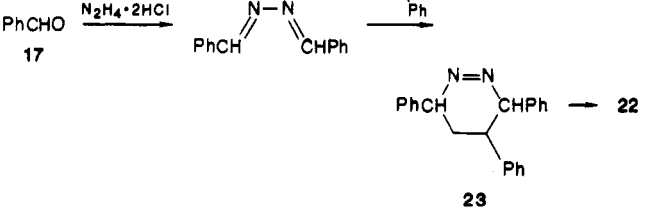
While we failed to detect **19** and **20** in the reaction mixture, regioisomer **21**, similar to **19**, was the only isolable criss-cross adduct from the reaction mixture using styrene as the dipolarophile; i.e., 2,4,6,8-tetraphenyl-1,5-diazabicyclo[3.3.0]octane (**21**) was obtained in 17% yield along with a trace amount (3%) of 3,5,6-triphenyl-1,4,5,6-tetrahydropyridazine (**22**) by the reaction of 2:1:6 molar mixture of **17**, **3**, and styrene, respectively, in refluxing ethanol for 4 h. On the other hand, pyridazine **22** was the only



21 and/or **22**

isolable compound from the reaction mixture of 2:1:2 molar ratio of these substrates. The structure of **21** and **22** was established by elemental and mass, NMR, and IR spectral analyses; compound **22** showed only a singlet and two triplets owing to the symmetrical structure, i.e., a triplet at δ 2.63 for four methylene protons at the 3- and 7-positions, a triplet at δ 4.2 for four methine protons at the 2-, 4-, 6-, and 8-positions, and a singlet at δ 7.2 for 20 protons of four phenyl groups at the 2-, 4-, 6-, and 8-positions.

The formation of **22** may be explained on the basis of initial Diels–Alder addition of benzaldehyde azine with styrene and following tautomerization of the product **23** to hydrazo compound.



23

Many intermolecular criss-cross cycloadditions of azines with olefins have been reported.[12,13] Reaction of benz-

(10) (a) Shimizu, T.; Hayashi, Y.; Yamada, K.; Nishio, T.; Teramura, K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 217. (b) Kirmse, W.; Dietrich, H. *Chem. Ber.* **1967**, *100*, 2710.

(11) (a) Joucla, M.; Gree, D.; Hamelin, J. *Tetrahedron* **1973**, *29*, 2315. (b) Joucla, M.; Hamelin, J. *Tetrahedron Lett.* **1978**, 2885. (c) Sinbandhit, S.; Hamelin, J. *J. Chem. Soc., Chem. Commun.* **1977**, 768.

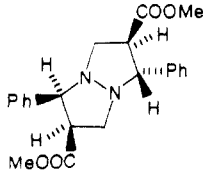
(12) (a) Haring, M.; Wagner-Jauregg, T. *Helv. Chim. Acta* **1957**, *40*, 852. (b) For reviews, see ref 1b, pp 153–155, 757–763, and: Wagner-Jauregg, T. *Synthesis* **1976**, 349.

Table III. Yields and Melting Points of Cycloadducts 25, 26, and 28–32

aldehyde	hydrazine	product	yield,[a] %	mp,[b] °C
2a	1,1-dimethylhydrazine	**25a**	100 (100)	249
2b		**25b**	79	265
2c		**25c**	70	251
2d		**25d**	90	212
2e		**25e**	100	188
2f		**25f**	51	264
9		**26**	100	200
27		**28**	15	251
2a	1-methyl-1-phenylhydrazine	**29a**	72 (30)	*b*
2b		**29b**	69	*b*
2c		**29c**	11	*b*
9		**30**	40	*b*
2a	1-decyl-1-methylhydrazine	**31**	(82)	181, 191
2a	1-dodecyl-1-methylhydrazine	**32**	(80)	187, 197

[a] Yields from the reaction using 1,1-disubstituted hydrazine hydrochlorides are shown and those from the reaction using 1,1-disubstituted hydrazines and concentrated HCl are shown in parentheses. [b] Decomposition points are shown and those of **29** and **30** were unambiguous owing to the mixture of two stereoisomers.

aldehyde azine with methyl acrylate in an autoclave at 130 °C has been reported by Wagner-Jauregg et al.[12a] to give a criss-cross adduct (mp 137 °C) in 22% yield. They proposed the structure **18** (or the diastereomers; the stereochemistry was not mentioned) for the criss-cross adduct. The disagreement of the melting points between our specimen (mp 186 °C) and their specimen led us to reexamination of their experiment. The products prepared under the conditions according to the literature were found to be a mixture of cis-cis and cis-trans stereoisomers **18** and **18′** by analysis of the ^{1}H NMR spectrum, which were managed to isolate in pure form (about 5% and 20% yields, respectively): the stereochemistry of **18′** was established from the evidence that two methyl groups were observed at δ 3.1 and 3.67, respectively. The difference

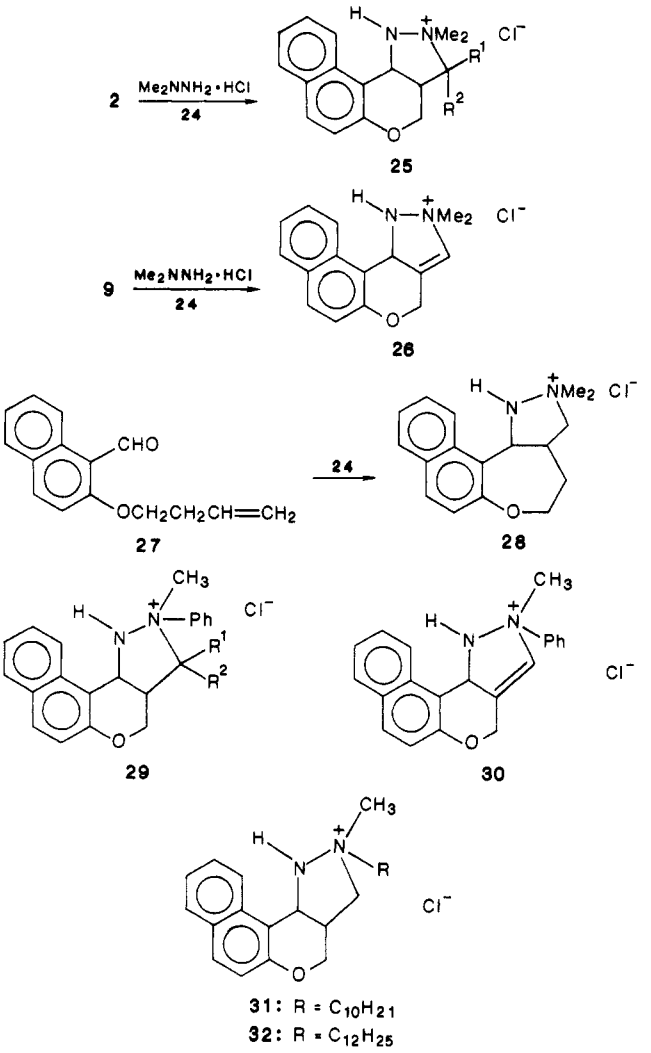


18′

between the result obtained by the method described here and that by Wagner-Jauregg et al. can be ascribed to the result of isomerization of **18** to the thermodynamically more stable diastereomer **18′** because **18** was found to be isomerized to **18′** by heating under Wagner-Jauregg's conditions. In general, predominant formation of diastereomers such as **18** bearing cis relationship between phenyl and ester groups is well-known in the kinetically controlled 1,3-dipolar cycloaddition reactions and has been explained as the result of secondary orbital interaction.[11]

Cycloaddition Reactions Using 1,1-Disubstituted Hydrazines. The reaction of an equimolar mixture of **2** and 1,1-dimethylhydrazine hydrochloride (**24**) was carried out in ethanol at the refluxing temperature for 3 h, from which 2,2-dimethyl-1,2,3,3a,4,11c-hexahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazolium chlorides **25** were isolated in yields shown in Table III (Scheme II). Similarly, 1,2,4,11c-tetrahydro derivative **26** and 2,2-dimethyl-1,2,3,3a,4,5,12c-hexahydronaphtho[1′,2′:6,7]oxepino[5,4-c]pyrazolium chloride (*28*) were also prepared from **9** or 2-(3-butenoxy)-1-naphthaldehyde (**27**), respectively, instead of **2**. Similar results were also obtained from the reactions using a combination of stoichiometric amount of 1,1-dimethylhydrazine and concentrated HCl instead of **24**. *N*-Phenyl derivatives **29** and **30** and long *N*-alkyl derivatives **31** and **32** were also prepared similarly by the reaction using asymmetrically 1,1-substituted hydrazines shown in Table III. Different from the cases of 1,1-dimethylhydrazine, these adducts bear two different substituents at the same nitrogen atom and, therefore, the structure of two stereoisomers may be expected. In fact, the formation of both stereoisomers was observed in many cases and the sum yield of these isomers is shown in Table III.

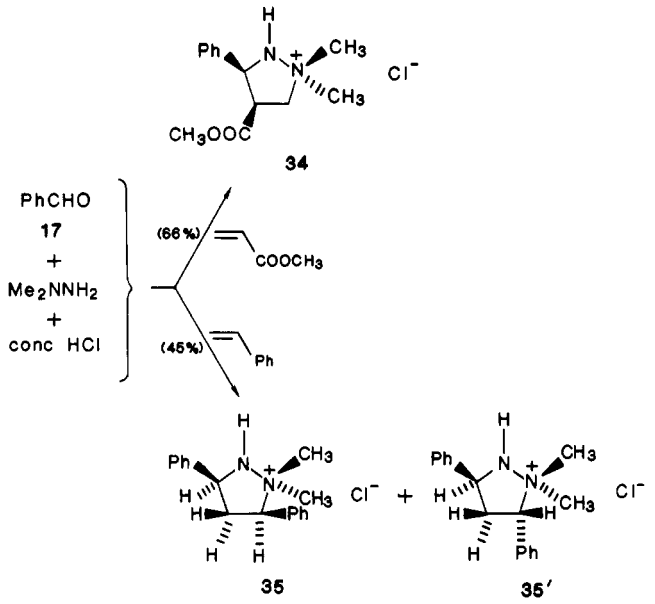
Scheme II



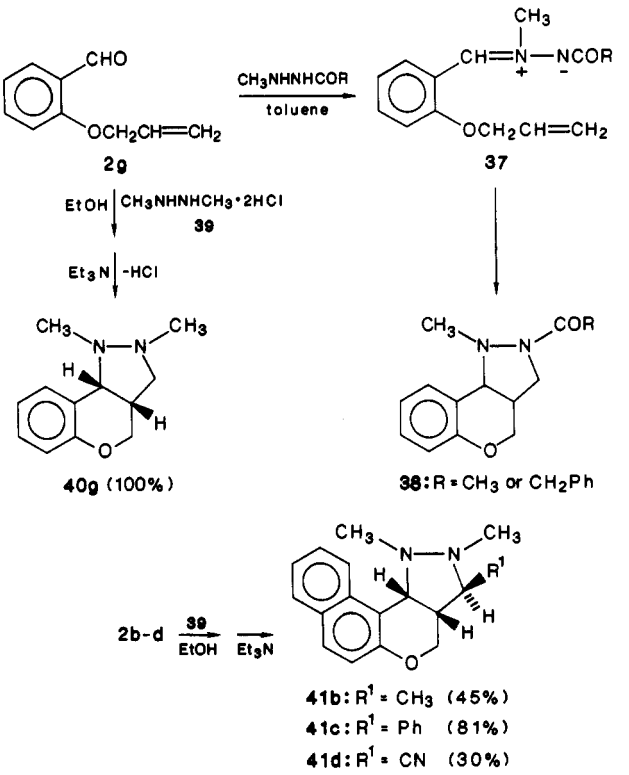
The structure of cycloadducts **25**, **26**, and **28–32** was established by elemental and mass, NMR, and IR spectral analyses. Mass spectra by electron ionization (EI) method of these compounds did not show the molecular ion peak (M^+) but the peak corresponding to $M^+ - HCl$ and $M^+ - CH_3Cl$. This phenomena is well-known in the mass spectra of quaternary ammonium salts.[14] Secondary ion mass

(13) (a) Wagner-Jauregg, T. *Chem. Ber.* **1930**, *63*, 3213. (b) Wagner-Jauregg, T.; Zirngibl, L.; Demolis, A.; Gunther, H.; Tam, S. W. *Helv. Chim. Acta* **1969**, *52*, 1672. (c) Burger, K.; Thenn, W.; Rauh, R.; Schickaneder, H.; Gieren, W. *Chem. Ber.* **1975**, *108*, 1460. (d) Burger, K.; Schickaneder, H.; Thenn, W.; Ebner, G.; Zettl, C. *Justus Liebigs Ann. Chem.* **1976**, 2156. (e) Burger, K.; Hein, F.; Zettl, C.; Schickanader, H. *Chem. Ber.* **1979**, *112*, 2609. (f) Burger, K.; Hein, F. *Justus Liebigs Ann. Chem.* **1979**, 133. (g) Forshaw, T. P.; Tipping, A. E. *J. Chem. Soc. C* **1971**, 2404. (h) Armstrong, S. E.; Tipping, A. E. *J. Chem. Soc., Perkin Trans. 1* **1975**, 538. (i) Armstrong, S. E.; Tipping, A. E. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1411.

Scheme III

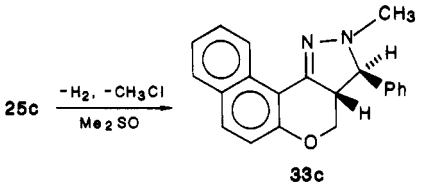


Scheme IV



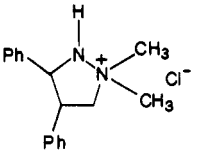
spectrometry (SIMS) has recently been shown to be a sensitive method for the characterization of these salts[15] because the method consists of a desorption ionization (DI)[16] which is well-suited to the sampling of preformed ions directly from the condense phase. With this technique, the formation of a cation (M^+ – Cl) and a cluster ion ($2M^+$ – Cl) has been known.[17] We employed this method and could observe the formation of these ions in all cases.

Though the pyrazolium chlorides **25** prepared here were stable under the dealkylation conditions,[18] the pyrazolium chloride **25c** was converted to 2-methyl-3-phenyl-2,3,3a,4-tetrahydronaphtho[1′,2′:5,6]pyrano[4,3-*c*]pyrazole (**33**) by refluxing it in dimethyl sulfoxide. The physical properties of **33c** agreed in all respects with those of an authentic specimen.[7a]



Application of these reactions to intermolecular one was successfully effected for preparation of pyrazolidinium salts. A *Z* cycloadduct, 1,1-dimethyl-4-(methoxycarbonyl)-3-phenylpyrazolidinium chloride (**34a**), was obtained in 66% yield from the reaction mixture of benzaldehyde (**17**), 1,1-dimethylhydrazine, and methyl acrylate in the presence of concentrated HCl (Scheme III). On the other hand, the two diastereomers (**35** and **35′**) of 1,1-dimethyl-3,5-diphenylpyrazolidinium chloride were obtained in 45% yield from the reaction with styrene.

A distinction between the possible isomers was made on the basis of the observed upfield shift (0.5 ppm) of the methyl protons of the ester group of compound **34** and the presence of two methine protons at the 3- and 5-positions of the rings of the compounds **35** and **35′** at δ 4.7–6.0; if the structure is 4-phenyl regioisomer **36**, the methine proton at the 4-position of the ring would appear at about δ 3.0–4.0 in the NMR spectra.



Cycloaddition Reactions Using 1,2-Disubstituted Hydrazines. Reaction of 2-(allyloxy)benzaldehyde (**2g**) with 1-acyl-2-methylhydrazine in refluxing toluene leads to 2-acyl-1-methyl-1,2,3,3a,4,9b-hexahydro[1]benzopyrano[4,3-*c*]pyrazoles (**38**) via the stabilized azomethine imine intermediate **37**[19a] (Scheme IV). The corresponding 1,2-dimethyl derivative **40g** has now been prepared by the acid-catalyzed reaction of **2g** with dimethylhydrazine dihydrochloride (**39**). Analogous cycloadducts **41b–d** were also prepared by the reaction using **2b–d** in the place of **2g**.

Similarly, several 1,2-dimethylpyrazolidines (**42–44**) were also prepared by an intermolecular application of this reaction. A mixture of two regioisomers, 1,2-dimethyl-4-(methoxycarbonyl)-3-phenylpyrazolidine (**42**) and 1,2-dimethyl-5-(methoxycarbonyl)-3-phenylpyrazolidines (**43** and **43′**), was obtained in 40% yield from the reaction of benzaldehyde (**17**) with **39** in the presence of a large excess of methyl acrylate. On the other hand, a predominant formation of one regioisomer which is a mixture of 1,2-dimethyl-*trans*-3,5-diphenylpyrazolidine (**44**) and trace

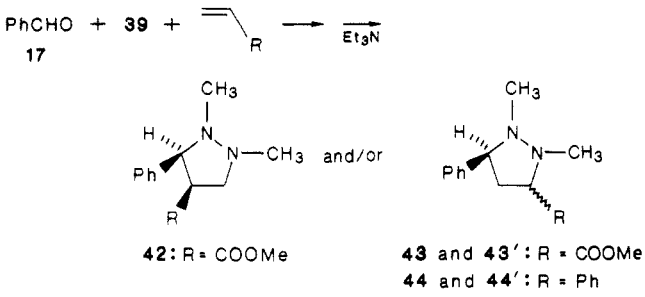
(14) (a) Duffield, A. M.; Djerassi, C.; Balaban, A. T. *Org. Mass. Spectrom.* **1971**, *5*, 87. (b) Hvistendahl, G.; Undheim, K.; Gyorosi, P. *Org. Mass. Spectrom.* **1974**, *7*, 903. (c) Gardner, R. J. *Org. Mass. Spectrom.* **1971**, *5*, 83. (d) Salsmans, R.; VanBinst, G. *Org. Mass. Spectrom.* **1974**, *8*, 357.

(15) Ryan, T. M.; Day, R. J.; Cooks, R. G. *Anal. Chem.* **1980**, *52*, 2054 and references cited therein.

(16) Bush, K. L.; Cooks, R. G. *Science (Washington, D. C.)* **1982**, *218*, 247.

(17) (a) Schueler, B.; Krueger, F. R. *Org. Mass. Spectrom.* **1979**, *14*, 439. (b) Larsen, E.; Egsgaard, H.; Holmen, H. *Org. Mass. Spectrom.* **1978**, *13*, 417. (c) Heller, D. N.; Yergey, J.; Cotter, R. J. *Anal. Chem.* **1983**, *55*, 1310. (d) Gierlich, H. H.; Rollgen, F. W.; Borchers, F.; Levsen, K. *Org. Mass. Spectrom.* **1977**, *12*, 387.

(18) (a) Huning, S.; Baron, W. *Chem. Ber.* **1957**, *90*, 395. (b) Ho, T.-L. *Synthesis* **1972**, 702.



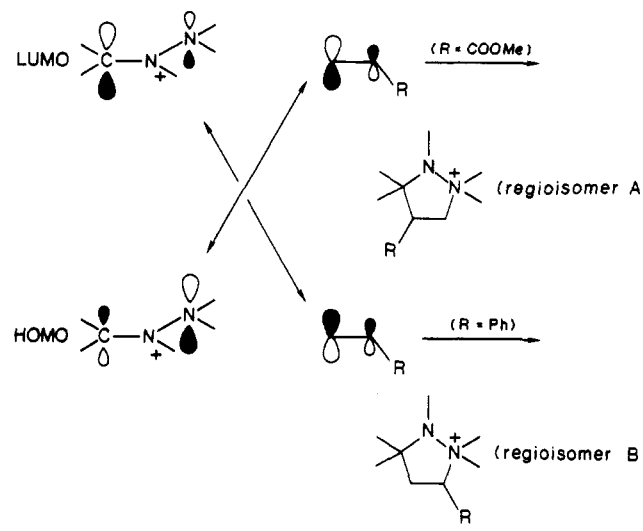
amount of the cis isomer **44′** was observed in the reaction with styrene. Cycloadduct **5c** was obtained in 79% yield by the reaction of **2c** with the N,N′-unsubstituted pyrazolidine **11c** in the presence of a stoichiometric amount of concentrated HCl.

The structure of these pyrazolidines (**40**–**44′**) was established on the basis of elemental and mass, IR and ^{1}H NMR spectral analyses. The stereochemistry of the compounds **40g** and **41b–d** was decided by the ^{1}H NMR spectra; the coupling constant (J = ca. 8 Hz) of the proton at 9b-(or 11c-) position are in accord with cis coupling constant of analogous compounds **38**.[19] The regio- and stereochemistry of compound **42** were established on the basis of the observed upfield shift (ca. 0.5 ppm) of protons of the methyl ester group at the 4-position which was similar to that described in compound **18**. Those of the trans compound **44** were established by the evidence that the coupling pattern (A_2X_2), and the coupling constants of ring protons of the compound were fully consistent with those of **21**. In cis compound **44′**, an ABX_2 coupling pattern was observed for the ring protons because the methylene protons at the 4-position of the ring were in different circumstances with each other. We failed to establish the stereochemistry of the diastereomers **43** and **43′**.

Stereo- and Regioselectivities of the Reactions. Cycloadducts bearing the cis-fused 5,6-ring system were obtained from the intramolecular cycloaddition reactions described above. The cis-fused compounds appear to be formed exclusively by the reactions because any trace of the corresponding trans-fused cycloadducts were not detected in the NMR spectra of the reaction mixture. This result may be ascribed to the result that the transition state giving the trans-fused 5,6-ring system is more highly strained than that giving cis-fused one. Retention of the configuration of the dipolarophile during the reaction was also observed in substrates **2b–e**, and this results is in accord with the character of concerted 1,3-dipolar cycloaddition reaction.

The difference of the regioselectivity observed between the intermolecular reaction with methyl acrylate and those with styrene may be explained in terms of FMO theory as follows. Cationic dipoles, whose structure is similar to those of the dipoles described here, have been known to have a large coefficient at the carbon atom than the terminal nitrogen atom in LUMO and vice versa in HOMO.[6b] A remarkable difference between the molecular orbitals of methyl acrylate and styrene is that the latter compound has higher HOMO energy level than the former one. Consequently, a dipole–HOMO/dipolarophile–LUMO interaction would be predominant in the reactions with methyl acrylate, whereas a dipole–LUMO/dipolarophile–HOMO interaction giving regioisomer B such as 5-phenylpyrazolidines may be predominant in the reaction with styrene.

(19) (a) Oppolzer, W. *Tetrahedron Lett.* **1970**, 3091. (b) Oppolzer, W. *Tetrahedron Lett.* **1970**, 2199.



Conclusions

A variety of cationic dipoles written by general formula $RC^+HN(R')NR''R''' \rightleftharpoons RCH{=}N^+(R')NR''R'''$ (R′, R″, R‴ = H, alkyl, or aryl) were found to be prepared by the reaction of aldehydes with a variety of hydrazines (mono-, 1,1-di-, 1,2-disubstituted hydrazines and unsubstituted hydrazine) in the presence of acid.

With the intra- and intermolecular [3$^+$ + 2] cycloadditions described here, various 1,5-diazabicyclo[3.3.0]-octanes, naphtho[1′,2′:5,6]pyrano[4,3-*c*]pyrazoles, and the quaternary ammonium chlorides were prepared. The corresponding benzopyrano derivatives can also be prepared similarly by reactions using 2-(alkenyloxy)benzaldehydes instead of **2a–f**. Some benzopyranopyrazoles have been known to exhibit a broad range of pharmacological activities, such as antiarrhythmic activity,[20a] central nervous system depressant,[20b] antiinflammatory activity,[20c] and anticonvulsive activity,[20c] and industrially useful chemical properties, such as pressure- or heat-sensitive imaging properties[21] and bleaching properties.[22] Pyrazolium chlorides prepared here have pharmaceutically important functional groups, a pyrazole ring and an ammonium group. Furthermore, introduction of a long alkyl group into these ammonium salts gives surfactants (**31** and **32**) with surface activity. Further details of these properties of the cycloadducts are under investigation and will be reported in the near future.

Experimental Section

All melting points, decomposition points, and boiling points are uncorrected. The IR spectra were determined on a Hitachi 215 infrared spectrophotometer. The ^{1}H NMR spectra were measured on a Varian T-60A instrument with Me_4Si as an internal standard: chemical shifts are given in δ units and coupling constants (J) are in herz: d = doublet; t = triplet; q = quartet; m = multiplet; br = broad singlet. High-resolution mass spectra were measured on a Hitachi M-80 mass spectrometer.

Materials. 2-(Alkenyloxy)-1-naphthaldehydes **2a–f** and 2-propargyl-1-naphthaldehyde (**9**) were prepared according to the methods in the literature.[4c,9] 2-(3-Butenyloxy)-1-naphthaldehyde (**27**) was prepared by an equimolar reaction of 2-hydroxy-1-naphthaldehyde with 4-bromo-1-butene in acetone in the presence of an equimolar amount of anhydrous potassium fluoride at the

(20) (a) Eiden, F.; Breugst, I. Ger. Offen. 2917575, 1980; *Chem. Abstr.* **1981**, *94*, 139801. (b) Brown, R. E.; Shavel, J., Jr. U.S. Pat. 3624102, 1971; *Chem. Abstr.* **1972**, *76*, 59618. (c) Oppolzer, W. U. Ger. Offen. 1926023, 1969; *Chem. Abstr.* **1970**, *72*, 43671.

(21) Kamio, T.; Kato, H. Jpn. Kokai Tokkyo Koho 79126114, 1979; *Chem. Abstr.* **1980**, *92*, 119745.

(22) Imperial Chemical Industries Ltd. Neth. Appl. 6511492, 1966; *Chem. Abstr.* **1966**, *65*, 2271.

refluxing temperature for 30 h; after filtration of inorganic salts and evaporation of the solvent, the oily residue was chromatographed (silica gel) with chloroform to give pure oily **27** in 38% yield: ^{1}H NMR ($CDCl_3$) δ 2.55 (q, 2 H, J = 7 Hz), 4.15 (t, 2 H, J = 7 Hz), 4.9–5.35 (m, 2 H), 5.5–6.3 (m, 1 H), 6.9–8.3 (m, 5 H), 9.27 (d, 1 H, J = 9 Hz), 10.85 (s, 1 H); IR (neat) 1660 cm^{-1} (CHO). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.47; H, 6.20. 1-Dodecyl-1-methylhydrazine was prepared according to the method described in the literature:[23] 82% yield; bp 120–122 °C (1 mmHg) [lit. bp 150–153 °C (11 mmHg)]. 1-Decyl-1-methylhydrazine was prepared similarly in 64% yield: bp 135–139 °C (21 mmHg); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3 H, J = 7 Hz), 1.03–1.80 (m, 16 H), 2.45 (s, 3 H), 2.83 (br, 2 H); IR (neat) 3350 cm^{-1} (NH_2). The other chemicals were of commercial origin and were used without further purification.

Reaction of Hydrazine Dihydrochloride (3) with 2 Equivalents of 2 or 9. A mixture of **3** (260 mg, 2.5 mmol) and aldehyde **2** or **9** (5 mmol) was refluxed in ethanol (80 mL) for 4 h with stirring. After the mixture was cooled to room temperature, 0.5 g (5 mmol) of triethylamine was added to the reaction mixture, and the mixture was further stirred for 1 h at the temperature. Crystals precipitated directly from the mixture were filtered and recrystallized from appropriate solvent to give pure criss-cross adducts **5** or **10** in the yields shown in Table I.

Compound **5a**: mp 273–275 °C (lit.[9] mp 273–275 °C).

Compound **5b**: mp 242–245 °C (lit.[9] mp 243–245 °C).

Compound **5c**: mp 245–248 °C; ^{1}H NMR ($CDCl_3$) δ 2.5–3.0 (m, 2 H), 3.8 (dd, 2 H, J = 5 Hz, 12 Hz), 4.1 (dd, 2 H, J = 4 Hz, 12 Hz), 4.26 (d, 2 H, J = 8 Hz), 5.63 (d, 2 H, J = 10 Hz), 6.4–6.9 (m, 10 H), 6.9–7.6 (m, 10 H), 8.1 (d, 2 H, J = 8 Hz); MS, m/e calcd for $C_{40}H_{32}N_2O_2$ (M^+) 572.2456, found 572.2459. Anal. Calcd for $C_{40}H_{32}N_2O_2$: C, 83.89; H, 5.63; N, 4.89. Found: C, 83.77; H, 5.58; N, 5.02.

Compound **5d**: mp 260 °C dec; MS, m/e calcd for $C_{30}H_{22}N_4O_2$ (M^+) 470.1738, found 470.1739. Anal. Calcd for $C_{30}H_{22}N_4O_2$: C, 76.58; H, 4.71; N, 11.91. Found: C, 76.59; H, 4.54; N, 11.77.

Compound **5e**: mp 240–243 °C; ^{1}H NMR ($CDCl_3$) δ 0.7 (t, 6 H, J = 7 Hz), 2.5–3.3 (m, 6 H), 3.8 (d, 2 H, J = 8 Hz), 4.05 (d, 4 H, J = 6 Hz), 5.55 (d, 2 H, J = 9 Hz), 7.0–7.9 (m, 10 H), 8.33 (d, 2 H, J = 8 Hz); IR (Nujol) 1710 cm^{-1} (COO); MS, m/e calcd for $C_{34}H_{32}N_2O_6$ (M^+) 564.2252, found 564.2250. Anal. Calcd for $C_{34}H_{32}N_2O_6$: C, 72.32; H, 5.71; N, 4.96. Found: C, 72.06; H, 5.65; N, 5.21.

Compound **5f**: mp 175 °C dec; ^{1}H NMR δ 0.7 (s, 6 H), 1.73 (s, 6 H), 2.0–2.47 (m, 2 H), 4.15 (dd, 2 H, J = 5, 11 Hz), 4.5 (d, 2 H, J = 11 Hz), 5.07 (d, 2 H, J = 5 Hz), 7.0–7.9 (m, 10 H), 8.27 (d, 1 H, J = 8 Hz); MS, m/e calcd for $C_{32}H_{32}N_2O_2$ (M^+) 476.2456, found 476.2452. Anal. Calcd for $C_{32}H_{32}N_2O_2$: C, 80.64; H, 6.77; N, 5.88. Found: C, 80.38; H, 6.61; N, 5.99.

Compound **10a**: mp 282–284 °C (lit.[9] mp 285–287 °C).

Reaction of Hydrazine Monohydrate with 2 Equivalents of 2 in the Presence of Concentrated HCl. General Procedure. To an ethanol solution (80 mL) of hydrazine monohydrate (130 mg, 2.6 mmol) and aldehydes **2** (5 mmol) was added 0.26 g of concentrated HCl (35%). The mixture was refluxed for 4 h with stirring. After the mixture was cooled to room temperature, 0.25 g (2.5 mmol) of triethylamine was added to the solution and further stirred for 1 h at room temperature. Then, the reaction mixture was treated similarly as described above to give criss-cross adducts **5** in the yields shown in Table I.

Reaction of 2-(Allyloxy)-1-naphthaldazine with Concentrated HCl. An ethanol solution (80 mL) of 2-(allyloxy)-1-naphthaldazine (2.1 g, 5 mmol) and concentrated HCl (0.26 g) was refluxed for 4 h with stirring. After similar workup as described above, criss-cross adduct **5a** was obtained in 80% yield.

Reaction of 2 with a Large Amount of 3. General Procedure. **3** (5.25 g, 50 mmol) was added to 95% ethanol (100 mL), and the mixture was refluxed with stirring. After a large part of **3** was dissolved, aldehyde **2** (5 mmol) was added, and the mixture was refluxed for 4 h. Evaporation of the solvent gave a crystalline mass, which was well mixed with chloroform and washed with water several times. The chloroform layer was dried over anhydrous sodium sulfate, from which the solvent was evaporated to give crude products. Crystalline crude products were recrystallized from appropriate solvents several times, and the oily crude product was chromatographed (silica gel) with chloroform to give a pure oily material. The structure of the products was found to be 1,2,3,3a,4,11c-hexahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazoles **11** and/or 3,3a,4,11c-tetrahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazoles **12** by following their spectral data.

Compound **11c**: mp 140 °C dec; ^{1}H NMR ($CDCl_3$) δ 3.4 (br, 2 H, NH), 3.83 (dd, 1 H, J = 9, 11 Hz), 4.0 (d, 1 H, J = 5 Hz), 4.3 (dd, 1 H, J = 5, 11 Hz), 4.73 (d, 1 H, J = 8 Hz), 7.0–7.9 (m, 10 H), 8.33 (d, 1 H, J = 8 Hz); IR (Nujol) 3200 cm^{-1} (NH); MS, m/e calcd for $C_{20}H_{18}N_2O$ (M^+) 302.1415, found 302.1415. Anal. Calcd for $C_{20}H_{18}N_2O$: C, 74.99; H, 6.00; N, 9.27. Found: C, 74.98; H, 6.03; N, 9.18.

Compound **11d**: mp 179–181 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.6–3.4 (m, 1 H), 3.7–5.3 (m, 6 H), 7.0–7.9 (m, 5 H), 8.25 (d, 1 H, J = 8 Hz); IR (Nujol) 3300 cm^{-1} (NH); MS, m/e calcd for $C_{15}H_{13}N_3O$ (M^+) 251.1056, found 251.1054. Anal. Calcd for $C_{15}H_{13}N_3O$: C, 71.69; H, 5.21; N, 16.72. Found: C, 71.67; H, 5.30; N, 16.44.

Compound **11e**: mp 111 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.3 (t, 3 H, J = 7 Hz), 2.6–3.1 (m, 1 H), 3.5–4.6 (m, 8 H), 7.0–7.9 (m, 5 H), 8.27 (d, 1 H, J = 8 Hz); IR (Nujol) 3220 (NH), 1720 cm^{-1} (COO); MS, m/e calcd for $C_{17}H_{18}N_2O_3$ (M^+) 298.1313, found 298.1318. Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.21; H, 6.20; N, 9.30.

Compound **11f**: mp 80 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 3 H), 1.37 (s, 3 H), 2.0–2.6 (m, 1 H), 3.2 (br, 2 H, NH), 3.87 (dd, 1 H, J = 9, 12 Hz), 4.3 (dd, 1 H, J = 5, 12 Hz), 4.7 (d, 1 H, J = 8 Hz), 6.95–7.9 (m, 5 H), 8.15 (d, 1 H, J = 8 Hz); IR (Nujol) 3200 cm^{-1} (NH); MS, m/e calcd for $C_{16}H_{18}N_2O$ (M^+) 254.1415, found 254.1417. Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.02. Found: C, 75.79; H, 7.10; N, 10.75.

Compound **12a**: mp 115 °C dec; ^{1}H NMR ($CDCl_3$) δ 2.4–3.0 (m, 1 H), 3.17 (t, 1 H, J = 11 Hz), 4.12 (dd, 1 H, J = 5, 11 Hz), 4.45–4.7 (m, 2 H), 5.3–5.6 (m, 1 H), 7.0–7.95 (m, 5 H), 8.65 (d, 1 H, J = 8 Hz); MS, m/e calcd for $C_{14}H_{12}N_2O$ (M^+) 224.0947, found 224.0944. Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.99; H, 5.38; N, 12.49. Found: C, 75.25; H, 5.34; N, 12.40.

Compound **12b**: mp 98 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.43 (d, 3 H, J = 7 Hz), 2.0–2.45 (m, 1 H), 3.3 (t, 1 H, J = 11 Hz), 4.13 (dd, 1 H, J = 5, 11 Hz), 4.5–5.0 (m, 1 H), 5.73 (d, 1 H, J = 7 Hz), 6.95–7.9 (m, 5 H), 8.67 (d, 1 H, J = 8 Hz); MS, calcd for $C_{15}H_{14}N_2O$ (M^+) 238.1103, found 238.1103. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76. Found: C, 75.30; H, 5.92; N, 12.00.

Compound **12f**: oil; ^{1}H NMR ($CDCl_3$) δ 1.3 (s, 3 H), 1.6 (s, 3 H), 2.0–2.5 (m, 1 H), 3.2 (t, 1 H, J = 11 Hz), 4.1 (dd, 1 H, J = 5, 11 Hz), 5.55 (d, 1 H, J = 7 Hz), 7.0–7.9 (m, 5 H), 8.57 (d, 1 H, J = 8 Hz).

Reaction of 2a with a 10-Fold Amount of 3 under Nitrogen. The reaction of **2a** (1.02 g, 5 mmol) and a 10-fold amount (5.0 g, 50 mmol) of **3** described above was carried out under nitrogen for 4 h. After the usual workup, an oily material (950 mg) was obtained. It was found from ^{1}H NMR spectra that the oily material was a 4:5 molar ratio mixture of **11a** and **12a**, and the yields of these compounds were 40% and 50%, respectively. The ^{1}H NMR spectral data of compound **11a** is as follows: ($CDCl_3$) δ 2.5–3.0 (m, 3 H), 3.4 (br, 2 H, NH), 3.4–4.3 (m, 3 H), 7.0–7.9 (m, 5 H), 8.2 (d, 1 H, J = 8 Hz).

Reaction of 11c with Acetyl Chloride. To a chloroform solution (50 mL) of **11c** (300 mg, 1 mmol) and acetyl chloride (0.78 g, 10 mmol) was added triethylamine (1.0 g, 10 mmol), and the mixture was refluxed for 2 h with stirring. After cooling to room temperature, the mixture was washed with water several times and dried over anhydrous sodium sulfate. The subsequent evaporation of the solvent gave crystals, which were recrystallized from ethanol to give pure 1,2-diacetyl-1,2,3,3a,4,11c-hexahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazole (**14c**) in 95% yield: mp 203–205 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 2.0 (s, 3 H), 3.15–3.6 (m, 1 H), 4.0–4.6 (m, 2 H), 5.77 (d, 1 H, J = 7 Hz), 6.57 (d, 1 H, J = 8 Hz), 6.9–7.9 (m, 10 H), 8.25 (d, 1 H, J = 8 Hz); IR (Nujol) 1650 cm^{-1} (CON); MS, m/e calcd for $C_{24}H_{22}N_2O_3$ (M^+) 386.1625, found 386.1627. Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.38; H, 5.66; N, 7.32.

Reaction of Benzaldehyde (17) with 3 in the Presence of Methyl Acrylate. A mixture of benzaldehyde (**17**) (20 mmol),

(23) Westphal, O. *Chem. Ber.* **1941**, *74*, 759.

3 (1.0 g, 10 mmol), and methyl acrylate (ca. 20 g, 0.23 mol) was refluxed in methanol (50 mL) for 4 h in the presence of small amount of hydroquinone. Evaporation of the solvent and an excess amount of acrylate from the reaction mixture by rotary evaporation gave a viscous oil, which was redissolved with methanol. Triethylamine (2.0 g, 20 mmol) was then added at room temperature, and the mixture was cooled to 0 °C. White crystals of 3,7-bis(methoxycarbonyl)-2,6-diphenyl-1,5-diazabicyclo-[3.3.0]octane (18) precipitated and were filtered and washed with a small amount of methanol: mp 185–186 °C; ^{1}H NMR ($CDCl_3$) δ 2.7–3.3 (m, 4 H), 3.07 (s, 6 H), 3.6–4.15 (m, 4 H), 7.1–7.5 (m, 10 H); MS, m/e calcd for $C_{22}H_{24}N_2O_4$ (M^+) 202.1130, found 202.1128. Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.39; H, 6.20; N, 7.26.

Reaction of Benzaldehyde Azine with Methyl Acrylate in an Autoclave at 130 °C. This reaction was carried out according to the literature.[12a] Diastereomer 18′ was obtained in 20% yield via the picrate, and the other diastereomer 18 was obtained in 5% yield by column chromatography on silica gel. 18′: mp 134–136 °C (lit.[12a] mp 137 °C); ^{1}H NMR ($CDCl_3$) δ 3.10 (s, 3 H), 2.8–4.1 (m, 6 H), 3.67 (s, 3 H), 4.3 (d, 1 H, J = 8 Hz), 4.73 (d, 1 H, J = 9 Hz), 7.1–7.7 (m, 10 H).

Reaction of Benzaldehyde (17) with 3 in the Presence of Styrene. A mixture of benzaldehyde (17) (2.2 g, 20 mmol), 3 (1.0 g, 10 mmol), and styrene (6.2 g, 60 mmol) was refluxed for 4 h in ethanol (50 mL) with stirring in the presence of a small amount of hydroquinone. After the mixture was cooled to room temperature, triethylamine (2.0 g, 20 mmol) was added to the reaction mixture, and then the mixture was cooled to 0 °C. The white crystals that precipitated were filtered off and washed with ethanol. Fractional recrystallization of the crystals from ethanol gave pure 2,4,6,8-tetraphenyl-1,5-diazabicyclo[3.3.0]octane (21) and 3,5,6-triphenyl-1,4,5,6-tetrahydropyridazine (22) in 17% and 3% yields, respectively.

Compound 21: mp 152–156 °C; ^{1}H NMR ($CDCl_3$) δ 2.63 (t, 4 H, J = 7.5 Hz), 4.2 (t, 4 H, J = 7.5 Hz), 7.2 (s, 20 H); MS, m/e calcd for $C_{30}H_{28}N_2$ (M^+) 416.2246, found 416.2244. Anal. Calcd for $C_{30}H_{28}N_2$: C, 86.50; H, 6.78; N, 6.73. Found: C, 86.61; H, 6.90; N, 6.71.

Compound 22: mp 212–215 °C; ^{1}H NMR ($CDCl_3$) δ 2.8–3.2 (m, 2 H), 3.4–3.55 (m, 1 H), 4.4–4.6 (m, 1 H), 5.9–6.1 (br, 1 H, NH), 6.8–7.9 (m, 15 H); IR (Nujol) 3400 cm^{-1} (NH); MS, m/e calcd for $C_{22}H_{20}N_2$ (M^+) 312.1622, found 3.12.1623. Anal. Calcd for $C_{22}H_{20}N_2$: C, 84.58; H, 6.45; N, 8.97. Found: C, 84.47; H, 6.40; N, 8.95.

Reaction of 2 or 9 or 27 with 1,1-Dimethylhydrazine Hydrochloride (24). General Procedure. A mixture of 2, 9, or 27 (5 mmol) and 24 (0.5 g, 5 mmol) was refluxed in ethanol (80 mL) for 3 h. After the mixture was cooled to room temperature, triethylamine (0.5 g, 5 mmol) was added to the reaction mixture, and the mixture was further stirred for 0.5 h. White crystals of cycloadducts were precipitated out from the reaction mixture by cooling to 0 °C and were filtered and washed with a small amount of ethanol to give pure 25, 26, or 28 in the yields shown in Table III.

Compound 25a: mp 249 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.0–4.0 (m, 1 H), 3.6 (s, 3 H), 3.77 (s, 3 H), 4.2–4.8 (m, 4 H), 5.32 (dd, 1 H, J = 6.5, 11 Hz), 7.2–8.4 (m, 7 H); MS, m/e 254 (M^+ – HCl), 240 (M^+ – CH_3Cl); SIMS, 545 (2M – Cl), 255 (M – Cl). Anal. Calcd for $C_{16}H_{19}N_2OCl$: C, 66.09; H, 6.59; N, 9.63. Found: C, 65.82; H, 6.70; N, 9.52.

Compound 25b: mp 265 dec; ^{1}H NMR (Me_2SO-d_6) δ 1.7 (d, 3 H, J = 7 Hz), 3.0–4.1 (m, 3 H), 3.43 (s, 3 H), 3.50 (s, 3 H), 4.4 (d, 1 H, J = 4 Hz), 5.4 (t, 1 H, J = 9 Hz), 7.2–8.3 (m, 7 H); MS, m/e 268 (M^+ – HCl), 254 (M^+ – CH_3Cl); SIMS, 573 (2M – Cl), 269 (M – Cl). Anal. Calcd for $C_{17}H_{21}N_2OCl$: C, 66.99; H, 6.94; N, 9.19; Cl, 11.63. Found: C, 66.70; H, 7.10; N, 8.94; Cl, 11.38.

Compound 25c: mp 251 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.3 (s, 3 H), 3.35 (s, 3 H), 4.3 (br, 3 H), 5.17 (d, 1 H, J = 10 Hz), 5.73 (t, 1 H, J = 8 Hz), 7.2–8.5 (m, 12 H); MS, m/e 330 (M^+ – HCl), 316 (M^+ – CH_3Cl); SIMS, m/e 697 (2M – Cl), 331 (M – Cl). Anal. Calcd for $C_{22}H_{23}N_2OCl$: C, 72.02; H, 6.32; N, 7.64. Found: C, 71.96; H, 6.21; N, 7.91.

Compound 25d: mp 212 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.4–4.2 (m, 1 H), 3.67 (s, 3 H), 3.87 (s, 3 H), 4.4 (d, 2 H, J = 6 Hz), 5.2–5.7 (m, 2 H), 7.1–8.5 (m, 7 H); MS, m/e 279 (M^+ – HCl); SIMS, m/e 595 (2M – Cl), 280 (M – Cl). Anal. Calcd for $C_{17}H_{18}N_3OCl$: C, 64.66; H, 5.75; N, 15.45. Found: C, 64.92; H, 5.74; N, 15.38.

Compound 25e: mp 188 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 1.45 (t, 3 H, J = 7 Hz), 3.4–4.1 (m, 1 H), 3.6 (s, 3 H), 3.65 (s, 3 H), 4.2–4.7 (m, 4 H), 4.93 (d, 1 H, J = 9 Hz), 5.5 (t, 1 H, J = 9 Hz), 7.2–8.5 (m, 7 H); MS, m/e 326 (M^+ – HCl), 312 (M^+ – CH_3Cl); SIMS, m/e 689 (2M – Cl), 327 (M – Cl). Anal. Calcd for $C_{19}H_{23}N_2O_3Cl$: C, 62.89; H, 6.39; N, 7.72. Found: C, 62.66; H, 6.55; N, 7.55.

Compound 25f: mp 264 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 1.6 (s, 3 H), 1.75 (s, 3 H), 3.0–3.9 (m, 1 H), 3.3 (s, 3 H), 3.65 (s, 3 H), 4.2 (dd, 1 H, J = 4.5, 13 Hz), 4.7 (d, 1 H, J = 13 Hz), 5.5 (t, 1 H, J = 10 Hz), 7.1–8.3 (m, 7 H); MS, m/e 282 (M^+ – HCl), 268 (M^+ – CH_3Cl); SIMS, m/e 601 (2M – Cl), 283 (M – Cl). Anal. Calcd for $C_{18}H_{23}N_2OCl$: C, 67.81; H, 7.27; N, 8.79. Found: C, 67.64; H, 7.24; N, 8.85.

Compound 26: mp 200 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.55 (s, 3 H), 3.7 (s, 3 H), 4.8 (d, 1 H, J = 13 Hz), 5.25 (d, 1 H, J = 13 Hz), 6.2 (dd, 1 H, J = 3, 10 Hz), 7.05–8.3 (m, 7 H), 8.4 (s, 1 H); MS, m/e 253 (M^+ – HCl), 238 (M^+ – CH_3Cl); SIMS, m/e 541 (2M – Cl), 253 (M – Cl). Anal. Calcd for $C_{16}H_{17}N_2OCl$: C, 66.55; H, 5.93; N, 9.70. Found: C, 66.27; H, 5.85; N, 9.52.

Compound 28: mp 251 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 1.63 (d, 2 H, J = 7 Hz), 2.9–4.1 (m, 3 H), 3.3 (s, 3 H), 3.4 (s, 3 H), 4.1–4.6 (m, 2 H), 5.33 (t, 1 H, J = 9 Hz), 7.0–8.3 (m, 7 H); SIMS, m/e 573 (2M – Cl), 269 (M – Cl). Anal. Calcd for $C_{17}H_{21}N_2OCl$: C, 66.99; H, 6.94; N, 9.19. Found: C, 66.80; H, 7.04; N, 8.92.

Reaction of 2 or 9 with 1-Methyl-1-phenylhydrazine Hydrochloride. The reaction was carried out by the general procedure described just above. Yields of the cycloadducts 1,2,3,3a,4,11c-hexahydro- or 1,2,4,11c-tetrahydronaphtho-[1′,2′:5,6]pyrano[4,3-c]pyrazoles (29 or 30) are shown in Table III. These cycloadducts are so hygroscopic that the accurate melting points of them could not be recorded. The cycloadducts except 29c were found to be a mixture of two stereoisomers by the ^{1}H NMR spectra, and the characteristic peaks of both isomers are shown below.

Compound 29a: ^{1}H NMR ($CDCl_3$) N-CH_3 [δ 3.90 (s) and 3.95 (s); ca. 1:1 ratio]; SIMS, m/e 669 (2M – Cl), 317 (M – Cl).

Compound 29b: ^{1}H NMR ($CDCl_3$) 3-CH_3 [δ 1.43 (d, J = 6 Hz) and 1.83 (d, J = 6 Hz); ca 2:1 ratio], N-CH_3 [δ 3.73 (s) and 3.83 (s); 2:1 ratio]; SIMS, m/e 697 (2M – Cl), 331 (M – Cl).

Compound 29c: ^{1}H NMR ($CDCl_3$) δ 2.9–3.5 (m, 1 H), 3.8 (s, 3 H), 4.0–4.8 (m, 2 H), 5.3 (d, 1 H, J = 12 Hz), 6.0 (t, 1 H, J = 8 Hz), 6.9–8.0 (m, 16 H), 8.3 (d, 1 H, NH, J = 8 Hz); SIMS, m/e 393 (M – Cl).

Compound 30: ^{1}H NMR ($CDCl_3$) N-CH_3 [δ 4.1 (s) and 4.3 (s); 2:3 ratio]; SIMS, m/e 665 (2M – Cl), 315 (M – Cl).

Reaction of 2a with 1-Decyl-(or 1-Dodecyl-)1-methylhydrazine in the Presence of Concentrated HCl. A mixture of 2a (5 mmol) and 1-decyl-(or 1-dodecyl-)1-methylhydrazine was refluxed in ethanol for 3 h in the presence of concentratedc HCl (0.26 g). After the mixture was cooled to room temperature, triethylamine (0.5 g, 5 mmol) was added to the reaction mixture, and the mixture was further stirred for 0.5 h at the temperature. Evaporation of the solvent from the reaction mixture gave an oily material, which was crystallized by adding acetone (20 mL). The crystals precipitated were filtered to give pure 31 (or 32) in the yields shown in Table III.

Compound 31: mp 181 and 191 °C dec; ^{1}H NMR ($CDCl_3$) N-CH_3 [δ 3.2 (s) and 3.5 (s); ca. 4:5 ratio]; SIMS, m/e 797 (2M – Cl), 381 (M – Cl). Anal. Calcd for $C_{25}H_{37}N_2OCl$: C, 72.00; H, 8.94; N, 6.72. Found: C, 71.88; H, 8.96; N, 6.72.

Compound 32: mp 187 and 197 °C dec; ^{1}H NMR ($CDCl_3$) N-CH_3 [δ 3.17 (s) and 3.57 (s); ca. 5:4 ratio]; SIMS, m/e 853 (2M – Cl), 409 (M – Cl). Anal. Calcd for $C_{27}H_{41}N_2OCl$: C, 72.86; H, 9.29; N, 6.29. Found: C, 72.83; H, 9.27; N, 6.45.

Conversion of 25c into 2-Methyl-2,3,3a,4-tetrahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazole 33c. 25c (1.1 g, 3 mmol) was dissolved in Me_2SO (10 mL), and the solution was heated to reflux for 4 h. Distillation of the solvent from the reaction mixture gave a crystalline mass, which was recrystallized from ethanol to give pure 33c in 46% yield (0.43 g): mp 175–177 °C (lit.[7a] mp 177–178 °C).

Reaction of Benzaldehyde (17) with 1,1-Dimethylhydrazine Hydrochloride (24) in the Presence of a Dipola-

rophile. A mixture of **17** (20 mmol), **24** (1.93 g, 20 mmol), and a dipolarophile [methyl acrylate (15 mL, 167 mmol) or styrene (10 mL, 87 mmol)] was refluxed in metahnol (80 mL) for 4 h with stirring in the presence of a small amount of hydroquinone. Evaporation of the solvent and an excess amount of the dipolarophile from the reaction mixture by rotary evaporation gave a generally crystalline mass, which was filtered with acetone (30 mL) to give analytically pure pyrazolidinium chlorides **34**, **35**, and **35′** in the yields shown in the text.

Compound **34**: mp 195 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.1 (s, 3 H), 3.7 (s, 3 H), 3.8 (s, 3 H), 3.7–4.6 (m, 3 H), 5.1–5.4 (m, 1 H), 7.3 (s, 5 H), 8.4 (br, 1 H, NH); IR (Nujol) 3100, 3300 (NH), 1725 (COO) cm^{-1}; SIMS, m/e 505 (2M – Cl), 235 (M – Cl), 149 (M – Cl – dipolarophile). Anal. Calcd for $C_{13}H_{19}N_2O_2Cl$: C, 57.67; H, 7.07; N, 10.34. Found: C, 57.44; H, 7.07; N, 10.26.

Compounds **35** and **35′** (mixture of two stereoisomers): mp 223 °C dec; ^{1}H NMR ($CDCl_3$) (one isomer) N-CH_3 [δ 2.75 (s) and 3.73 (s)], (the other isomer) N-CH_3 [δ 3.33 (s) and 3.50 (s)] (in 1:4 ratio); SIMS, m/e 541 (2M – Cl), 253 (M – Cl), 149 (M – Cl – dipolarophile). Anal. Calcd for $C_{17}H_{21}N_2Cl$: C, 70.70; H, 7.33; N, 9.70. Found: C, 70.45; H, 7.40; N, 9.81.

Reaction of 2 with 1,2-Dimethylhydrazine Dihydrochloride (39). General Procedure. A mixture of **2** (5 mmol) and **39** (5 mmol) was refluxed in ethanol (80 mL) for 3 h with stirring. After the mixture was cooled to room temperature, triethylamine (1.0 g, 10 mmol) was added to the reaction mixture, and the mixture was further stirred for 1 h at the temperature. Evaporation of the solvent from the reaction mixture gave a crystalline residue, which was dissolved with chloroform and washed with water several times. The chloroform layer was dried over anhydrous sodium sulfate, from which the solvent was evaporated to give crude product. Crystalline crude products obtained from the reaction using aldehydes **2b–d** were recrystallized from ethanol to give pure 3-substituted 1,2-dimethyl-1,2,3,3a,4,11c-hexahydronaphtho[1′,2′:5,6]pyrano[4,3-c]pyrazoles **41b–d** in the yields shown in the text. The oily product **40g** obtained from the reaction of **2g** with **39** was purified by distillation.

Compound **41b**: mp 48–51 °C; ^{1}H NMR ($CDCl_3$) δ 1.32 (d, 3 H, J = 6 Hz), 2.33 (s, 3 H), 2.63 (s, 3 H), 2.3–3.0 (m, 2 H), 4.0 (dd, 1 H, J = 3.5, 11.5 Hz), 4.25 (dd, 1 H, J = 4, 11.5 Hz), 4.4 (d, 1 H, J = 8 Hz), 6.95–7.9 (m, 5 H), 8.1 (d, 1 H, J = 8 Hz); MS, m/e calcd for $C_{17}H_{20}N_2O$ (M^+) 268.1571, found 268.1566. Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51; N, 10.44. Found: C, 76.02; H, 7.47; N, 10.18.

Compound **41c**: mp 120–122 °C; ^{1}H NMR ($CDCl_3$) δ 2.2 (s, 3 H), 2.8 (s, 3 H), 2.5–3.1 (m, 1 H), 3.82 (d, 1 H, J = 9 Hz), 3.9 (dd, 1 H, J = 3, 11.5 Hz), 4.2 (dd, 1 H, J = 3, 11.5 Hz), 4.5 (d, 1 H, J = 8 Hz), 6.95–7.85 (m, 10 H), 8.1 (d, 1 H, J = 8 Hz); MS, m/e calcd for $C_{22}H_{22}N_2O$ (M^+) 330.1731, found 330.1733. Anal. Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71; N, 8.48. Found: C, 79.84; H, 6.69; N, 8.23.

Compound **41d**: mp 117–120 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.17 (s, 3 H), 2.77 (s, 3 H), 3.4–3.9 (m, 1 H), 3.93 (d, 1 H, J = 8 Hz), 4.15 (dd, 1 H, J = 2.5, 12 Hz), 4.45 (dd, 1 H, J = 3, 12 Hz), 4.7 (d, 1 H, J = 7.5 Hz), 6.9–8.1 (m, 6 H); MS, m/e calcd for $C_{17}H_{17}N_3O$ (M^+) 279.1368, found 279.1366. Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.09; H, 6.13; N, 15.04. Found: C, 72.95; H, 6.10; N, 14.88.

Compound **40g**: bp 138 °C (1.8 mmHg); ^{1}H NMR ($CDCl_3$) δ 2.2–3.0 (m, 2 H), 2.47 (s, 3 H), 2.6 (s, 3 H), 3.3–3.7 (m, 1 H), 3.5 (d, 1 H, J = 7 Hz), 4.05 (d, 2 H, J = 6 Hz), 6.75–7.3 (m, 4 H); MS, m/e calcd for $C_{12}H_{16}N_2O$ (M^+) 204.1259, found 204.1263. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.72. Found: C, 70.33; H, 7.71; N, 13.55.

Reaction of 17 with 39 in the Presence of a Dipolarophile. General Procedure. A mixture of **17** (20 mmol), **39** (2.66 g, 20 mmol), and a dipolarophile [methyl acrylate (15 mL, 0.17 mol) or styrene (10 mL, 0.09 mol)] was refluxed in methanol (or ethanol) (80 mL) for 3 h with stirring in the presence of a small amount of hydroquinone. Evaporation of the solvent and an excess amount of the dipolarophile from the reaction mixture by rotary evaporation gave an oily residue, which was dissolved with chloroform (80 mL) and to which triethylamine (4.0 g, 40 mmol) was added at room temperature, and then the mixture was washed with water several times. The chloroform layer was dried over anhydrous sodium sulfate, and the solvent was evaporated to give an oily residue. The oily residue was distilled in vacuo to give pure 1,2-dimethylpyrazolidines **42–44′**. Products obtained by the distillation are the mixture of two or three stereo- and regioisomers. Boiling points, mass spectral data, and elemental analyses of the mixture are as follows.

Compounds **42**, **43**, and **43′**: bp 110–120 °C (0.9 mmHg); MS, m/e calcd for $C_{13}H_{18}N_2O_2$ (M^+) 234.1346, found 234.1374. Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.56; H, 7.71; N, 11.84.

Compounds **44** and **44′**: bp 138–146 °C (0.5 mmHg); MS, m/e calcd for $C_{17}H_{20}N_2$ (M^+) 252.1622, found 252.1627. Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.90; H, 7.99; N, 11.05. Separation of the mixture into their components was effected by chromatography (silica gel; chloroform). **44**: 60% yield; ^{1}H NMR ($CDCl_3$) δ 2.3 (t, 2 H, J = 8.5 Hz), 2.4 (s, 6 H), 3.6 (t, 2 H, J = 8.5 Hz), 7.15–7.6 (m, 10 H). **44′**: 3% yield; ^{1}H NMR ($CDCl_3$) δ 2.1–3.1 (m, 2 H), 2.37 (s, 6 H), 4.1 (dd, 2 H, J = 7 and 9.5 Hz), 7.15–7.6 (m, 10 H).

Reaction of 2c with 11c in the Presence of Concentrated HCl. To an ethanol solution (50 mL) of **2c** (0.48 g, 1.66 mmol) and **11c** (0.5 g, 1.66 mmol) was added concentrated HCl (0.17 g, calcd for HCl: 1.66 mmol), and the mixture was refluxed for 3 h with stirring. After the mixture was cooled to room temperature triethylamine (0.2 g) was added to the reaction mixture, and then, crystals that precipitated directly from the mixture were filtered and recrystallized from ethanol to give pure **5c** in 79% yield.

Cycloaddition Routes to Azaanthraquinone Derivatives. 2. Use of Aza Dienes[1]

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Azanaphthoquinones and 1-(dimethylamino)-3-methyl-1-azabuta-1,3-diene (methacrolein N,N-dimethylhydrazone) underwent extremely facile cycloaddition to aza- and polyazaanthraquinones after elimination of dimethylamine from the initial 1:1 cycloadduct and its subsequent oxidation. Introduction of a basic side chain into the 8-position of the azaanthraquinone occurred readily with primary amines and the 8-(tosyloxy) derivative, but more complex substitution patterns resulted with 5,8-bis(tosyloxy) derivatives and primary amines.

In an earlier publication[2] the cycloaddition of 1- and 2-azanaphthoquinones and also 1,3- and 1,4-diazanaphthoquinones with a variety of alicyclic and cyclic dienes led to azaanthraquinones with nitrogen atoms in

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