134 © *1984 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn., 57, 134—141 (1984)* [Vol. 57, No. 1

Intra- and Intermolecular [3^++2] Cycloadditions of Aldehyde or Ketohydrazones[1)]

Tomio Shimizu,* Yoshiyuki Hayashi, Mineo Nakano, and Kazuhiro Teramura
Department of Color Chemistry and Technology, Faculty of Industrial Arts,
Kyoto Technical University, Matsugasaki, Sakyo-ku, Kyoto 606

(Received August 1, 1983)

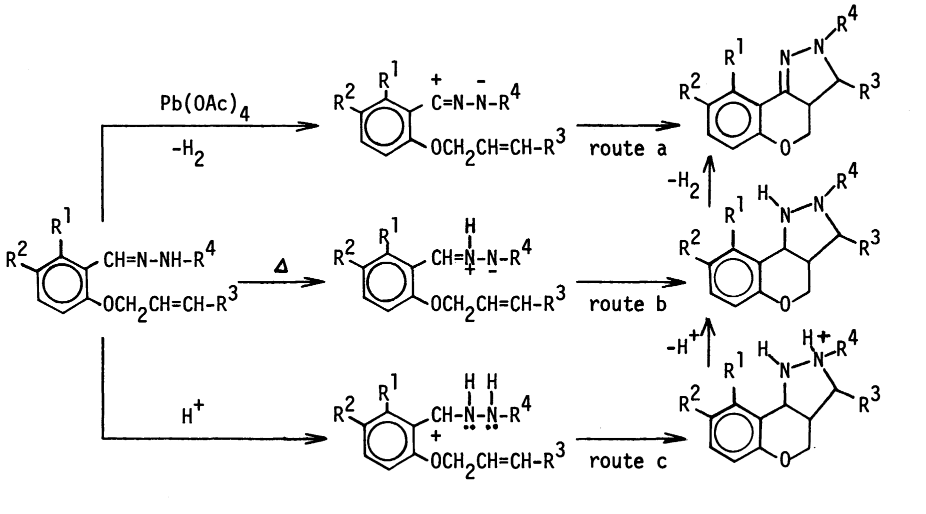
The reaction of several 2-(alkenyloxy)benzaldehydes (or 1-naphthaldehydes) (**1**) with arylhydrazine hydrochlorides leads to intramolecular [3^++2] cycloadducts, 3-substituted 2-aryl-1,2,3,3a,4,9b(or 1,2,3,3a,4,11c)hexahydro[1]benzopyrano (or naphtho[1′,2′:5,6]pyrano)[4,3-*c*]pyrazole hydrochlorides (**4**), in good yields. Free bases (**5**) were obtained in high yields after the treatment of **4** with triethylamine. The thermal treatment of **5** at 150 °C gave 3-substituted 2-aryl-2,3,3a,4-tetrahydro[1]benzopyrano (or naphtho[1′,2′:5,6]pyrano)[4,3-*c*]pyrazoles. The reaction of **1** with methylhydrazine sulfate gave the corresponding 2-methyl derivatives. Analogous intramolecular [3^++2] cycloadducts were obtained from the reaction of 2′-(alkenyloxy)acetophenones with arylhydrazine hydrochlorides. Intermolecular [3^++2] cycloadducts were also obtained from a reaction mixture of 1-naphthaldehyde, arylhydrazine hydrochlorides, and styrene.

Many heterocyclic compounds containing nitrogen atoms show a broad range of phermacological activities and industrially useful chemical properties. Several studies aimed at the synthesis of biologically important [1]benzopyrano[4,3-*c*]pyrazoles have been done by a number of investigators.[2-4)] In a series of investigations of the intramolecular 1,3-dipolar cycloaddition reactions of 2-(alkenyloxy)benzaldehyde arylhydrazones,[5)] we ourselves have prepared several [1]benzopyranopyrazoles in relatively good yields, but some desirable cycloadducts could not be brought about because of the weak reactivity of some substrates. (see Routes a and b in Scheme 1)

The acid-catalyzed [3^++2] 1,3-dipolar cycloaddition of hydrazones with olefins reported recently byHamelin *et al.*[6)] is a fruitful alternative for the prepatation of the cycloadducts *via* an interesting type of dipole bearing a cationic center. However, their method, using an excess amount of sulfuric acid as a catalyst, is unsuitable for substrates bearing substituents which are labile in a strong acid. In the course of the application of their method to the synthesis of benzopyranopyrazoles, we have found that hydrochloride or sulfate of aryl(or alkyl)hydrazines itself acts as an acid-catalyst and that cycloadducts were obtained very easily from the reaction in good yields. (Route c in Scheme 1)

Results and Discussion

The reaction of 2-(alkenyloxy)benzaldehydes(or 1-naphthaldehydes) (**1**) with an equimolar amount of arylhydrazine hydrochlorides was carried out in ethanol for several hours at room temperature. 3-Substituted 2-aryl-1,2,3,3a,4,9b (or 1,2,3,3a,4,11c)hexahydro[1]benzopyrano(or naphtho[1′,2′:5,6]pyrano)[4,3-*c*]pyrazole hydrochlorides (**4**) were obtained from the reaction mixture in the yields shown in Table 1. The structure of **4** was established on the basis of elemental analyses and spectral data; the IR spectra show an NH-streching vibration of quarternary ammonium salts around 2500 cm^{-1} and no carbonyl-streching vibration of the formyl group observed at **1**. The NMR spectra show saturated methine and methylene protons at δ 3.0—5.0 and no alkenyl protons. The assignment of the structure was further supported by the transformation to known compounds, 3-substituted 2-aryl-2,3,3a,4-tetrahydro[1]benzopyrano(or 1-naphtho[1′,2′:5,6]-pyrano)[4,3-*c*]pyrazoles (**6**).[5c,d)] The treatment of **4** with triethylamine in chloroform at room temperature afforded the free bases (**5**) and/or further dehydrogenated compounds (**6**). Refluxing a xylene solution of pyrazolidines (**5**) at 150 °C for several hours resulted in pyrazolines (**6**) and/or further dehy-



Scheme 1.

TABLE 1. YIELDS, MELTING POINTS, AND SPECTRAL DATA OF **4**

	R^1	R^2	R^3	R^4	Yield %	Mp θ_m/°C	IR($\tilde{\nu}$/cm^{-1})	NMR (δ) in DMSO-d_6
4a	-$(CH)_4$-		CO_2Et	CH_3	82	168—188	2450 (N^+H) 1750 (COO)	1.2(t, 3H, J=7 Hz), 2.2(s, 3H), 3.12—3.7 (m, 1H), 4.0—4.73(m, 5H), 5.33(d, 1H, J=7 Hz), 6.6—8.1(m, 9H), 8.53(d, 1H, J=8 Hz)
4c	-$(CH)_4$-		CO_2Et	Cl	55	103—109	2450 (N^+H) 1730 (COO)	1.2(t, 3H, J=7 Hz), 3.2—3.57(m, 1H), 4.0—4.53(m, 5H), 5.12(d, 1H, J=7 Hz), 6.6—7.9(m, 9H), 8.43(d, 1H, J=8 Hz)
4e	-$(CH)_4$-		CN	H	95	120—125	2700 (N^+H) 2230 (CN)	3.0—3.8(m, 1H), 4.0—4.6(m, 2H), 4.85—5.3(m, 2H), 6.8—8.4(m, 10H), 9.2(d, 1H, J=8 Hz)
4f	-$(CH)_4$-		CN	Cl	96	a)	2430 (N^+H) 2230 (CN)	3.0—3.6(m, 1H), 4.15—4.53(m, 2H), 4.9—5.3(m, 2H), 6.85—8.75(m, 9H), 9.27(d, 1H, J=8 Hz)
4g	-$(CH)_4$-		Ph	CH_3	80	a)	2430 (N^+H)	2.2(s, 3H), 2.85—3.3(m, 1H), 4.0—4.5 (m, 2H), 4.8(d, 1H, J=6 Hz), 5.65(d, 1H, J=8 Hz), 6.9—8.0(m, 14H), 8.3(d, 1H, J=8 Hz)
4h	-$(CH)_4$-		Ph	H	81	112—116	2480 (N^+H)	2.7—3.4(m, 1H), 4.0—5.0(m, 3H), 5.6 (d, 1H, J=7 Hz), 6.8—8.1(m, 15H), 8.75 (d, 1H, J=8 Hz)
4i	-$(CH)_4$-		Ph	Cl	64	148—150	2460 (N^+H)	2.7—3.35(m, 1H), 4.0—4.6(m, 2H), 4.8 (d, 1H, J=6 Hz), 5.4(d, 1H, J=8 Hz), 6.7—8.0(m, 14H), 8.23(d, 1H, J=8 Hz)
4j	-$(CH)_4$-		H	CH_3	74	147—150	2550 (N^+H)	2.3(s, 3H), 3.7—5.0(m, 5H), 5.46(d, 1H, J=6 Hz), 7.0—8.0(m, 9H), 8.25(d, 1H, J=8 Hz)
4k	-$(CH)_4$-		H	H	82	133—137	2500 (N^+H)	3.0—3.5(m, 1H), 4.15—4.53(m, 2H), 4.9—5.3(m, 2H), 6.85—8.75(m, 10H), 9.27(d, 1H, J=8 Hz)
4l	-$(CH)_4$-		H	Cl	74	150—155	2550 (N^+H)	2.9—3.5(m, 1H), 3.6—4.6(m, 4H), 5.1 (d, 1H, J=6 Hz), 6.9—8.0(m, 9H), 8.2(d, 1H, J=8 Hz)
4m	-$(CH)_4$-		CH_3	CH_3	85	155—167	2470 (N^+H)	1.55(d, 3H, J=6 Hz), 2.2(s, 3H), 3.46—5.0(m, 5H), 7.0—8.03(m, 9H), 9.2(d, 1H, J=8 Hz)
4n	-$(CH)_4$-		CH_3	H	80	135—139	2460 (N^+H)	1.41(d, 3H, J=6 Hz), 2.7—3.2(m, 1H), 3.46—4.8(m, 3H), 5.56(d, 1H, J=7 Hz), 7.0—8.0(m, 9H), 9.2(d, 1H, J=8 Hz)
4o	-$(CH)_4$-		CH_3	Cl	83	135—140	2460 (N^+H)	1.43(d, 3H, J=6 Hz), 2.7—3.3(m, 1H), 3.85—4.7(m, 3H), 5.53(d, 1H, J=7 Hz), 6.85—8.1(m, 9H), 8.7(d, 1H, J=8 Hz)
4p	H	H	CO_2Et	CH_3	77	a)	2460 (N^+H) 1750 (COO)	1.3(t, 3H, J=7 Hz), 2.17(s, 3H), 2.6—3.0(m, 1H), 3.95—4.75(m, 6H), 6.7—7.55(m, 8H)
4q	H	H	CO_2Et	H	64	a)	2660 (N^+H) 1720 (COO)	
4s	H	H	Ph	CH_3	69	193—195	2550 (N^+H)	2.2(s, 3H), 4.2—5.9(m, 5H), 6.77—7.8 (m, 13H)
4t	H	H	Ph	H	56	133—135	2540 (N^+H)	4.1—6.4(m, 5H), 6.7—7.8(m, 14H)
4u	H	H	Ph	Cl	91	161—163	2490 (N^+H)	4.1—6.2(m, 5H), 6.7—7.6(m, 13H)
4v	H	H	H	CH_3	39	127—130	2550 (N^+H)	2.23(s, 3H), 3.1—5.2(m, 6H), 6.9—8.1 (m, 8H)
4x	H	H	H	Cl	37	117—124	2530 (N^+H)	2.9—5.7(m, 5H), 6.7—8.4(m, 8H)

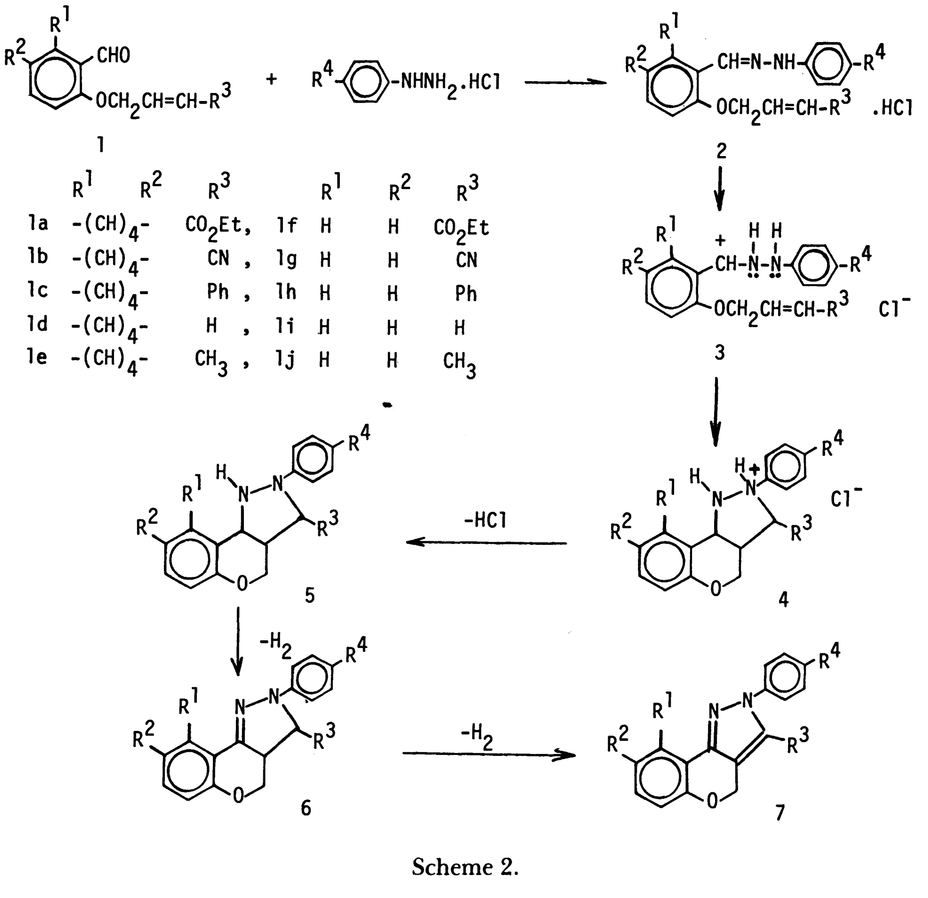
a) The melting-point range was very broad because of the contamination of a small amount of **5** and/or **6**.

drogenated pyrazoles (**7**). (Table 3) The structure of **5** was established on the basis of elemental analyses and spectral data. (Table 2) Some of the **4** and **5** are so hygroscopic or easily oxidized to **5** or **6** that they are difficult to isolate in a pure state; thus, the range of the melting points of those compounds is relatively broad. **4** could also be obtained after the treatment of hydrazones (**2**) with ethanolic hydrogen chloride. The formation of **4** can not be accounted for in terms of the [3+2] 1,3-dipolar cycloaddition reaction after the thermal isomerization of hydrazones (**2**) to azomethine imine tautomers, for such isomerization can not be observed under the thermal conditions up to 100 °C.5c) In fact, **2** are infinitely stable in refluxing ethanol. From these results, it is most plausible to explain the formation of **4** in terms of a [3^++2] 1,3-dipolar

TABLE 2. YIELD, MELTING POINTS, AND SPECTRAL DATA OF 5[a)]

	R^1 R^2	R^3	R^4	Yield[b)] %	Mp[c)] θ_m/°C	IR($\tilde{\nu}$/cm^{-1})	NMR (δ)[d)]
5a	-$(CH)_4$-	CO_2Et	CH_3	80	104—105	3130 (NH)	1.33(t, 3H, J=7 Hz), 2.17(s, 3H), 2.88—3.33(m, 1H), 3.67—4.56(m, 5H),4.66—5.2(m, 1H), 6.54—7.9(m, 9H), 8.43(d, 1H, J=8 Hz)
5d	-$(CH)_4$-	CN	CH_3	72	222—225	3270 (NH) 2250 (CN)	2.48(s, 3H), 2.8—3.5(m, 1H), 3.9—4.95 (m, 4H), 7.15—8.1(m, 9H), 8.38(d, 1H, J=8 Hz)
5e	-$(CH)_4$-	CN	H	31	208—210	3270 (NH) 2250 (CN)	2.9—3.56(m, 1H), 4.1—4.6(m, 2H), 5.12 (d, 1H, J=7 Hz), 5.8(d, 1H, J=13 Hz), 6.7—8.0(m, 10H), 8.33(d, 1H, J=8 Hz)
5f	-$(CH)_4$-	CN	Cl	85	203—205	3270 (NH) 2230 (CN)	3.0—3.2(m, 1H), 3.8—6.0(m, 4H), 6.95—7.95(m, 9H), 8.25(d, 1H, J=8 Hz)
5i	-$(CH)_4$-	Ph	Cl	84	180—182	3170 (NH)	2.5—3.0(m, 1H), 3.6—4.5(m, 3H), 4.85 (dd, 1H, J=6 and 10 Hz), 6.45—7.8(m, 9H), 8.49(d, 1H, J=8 Hz)
5p	H H	CO_2Et	CH_3	62	130—131	3230 (NH) 1740 (COO)	1.46(t, 3H, J=7 Hz), 2.23(s, 3H), 2.68 (hex, 1H, J=5 Hz), 3.7—4.5(m, 6H), 4.65(dd, 1H, J=5 and 10 Hz), 6.7—7.5 (m, 8H)
5s	H H	Ph	CH_3	71	188—190	3280 (NH)	2.2(s, 3H), 2.77—4.66(m, 5H), 6.67—7.42(m, 13H)
5t	H H	Ph	H	70	184—194	3250 (NH)	2.7—3.2(m, 1H), 3.6—5.0(m, 4H), 6.6—7.8(m, 13H), 8.2(d, 1H, J=8 Hz)
5u	H H	Ph	Cl	60	101—103	3270 (NH)	3.6—4.8(m, 5H), 6.4—8.2(m, 13H)
5v	H H	H	CH_3	40	116—123	3260 (NH)	2.2(s, 3H), 2.4—4.8(m, 6H), 6.8—7.6 (m, 8H)

a) Satisfactory anlytical data were obtained for these compounds. b) **5d** was obtained in the yield from **1b** without isolation of **4d**; the yields of the other substances were based on **4**. c) Recrystallized from ethanol. d) **5e** was dissolved in DMSO-d_6; the other substances were dissolved in $CDCl_3$.



	R^1	R^2	R^3		R^1	R^2	R^3
1a	-$(CH)_4$-		CO_2Et,	1f	H	H	CO_2Et
1b	-$(CH)_4$-		CN ,	1g	H	H	CN
1c	-$(CH)_4$-		Ph ,	1h	H	H	Ph
1d	-$(CH)_4$-		H ,	1i	H	H	H
1e	-$(CH)_4$-		CH_3 ,	1j	H	H	CH_3

Scheme 2.

Table 3. Yield, melting points, and spectral data of **6** and **7**[a]

	R^1	R^2	R^3	R^4	Yield[b] %	Mp θ_m/°C[c] (lit)	NMR (δ) in $CDCl_3$
6a	-$(CH)_4$-		CO_2Et	CH_3	81	145—147 (148—151)[d]	
6b	-$(CH)_4$-		CO_2Et	H	28	133—136 (134—136)[d]	
6c	-$(CH)_4$-		CO_2Et	Cl	58	166—168 (162—165)[d]	
6g	-$(CH)_4$-		Ph	CH_3	67	206—208 (208—210)[d]	
6h	-$(CH)_4$-		Ph	H	51	199—201 (194—195)[d]	
6i	-$(CH)_4$-		Ph	Cl	74	206—208 (206—208)[d]	
6j	-$(CH)_4$-		H	CH_3	71	103—105	2.43(s, 3H), 3.0—3.3(m, 1H), 3.4—4.9(m, 4H), 6.95—7.9(m, 9H), 9.2(d, 1H, J=8 Hz)
6k	-$(CH)_4$-		H	H	57	72—76	2.84—4.82(m, 5H), 6.66—7.9(m, 10H), 9.35 (d, 1H, J=8 Hz)
6l	-$(CH)_4$-		H	Cl	75	117—119	3.1—4.85(m, 5H), 6.8—7.8(m, 9H), 9.2(d, 1H J=8 Hz)
6m	-$(CH)_4$-		CH_3	CH_3	73	128—129	1.6(d, 3H, J=7 Hz), 2.3(s, 3H), 3.1—4.8(m, 4H), 6.9—7.8(m, 9H), 9.33(d, 1H, J=8 Hz)
6n	-$(CH)_4$-		CH_3	H	50	102—103	1.63(d, 3H, J=7 Hz), 3.2—4.9(m, 4H), 6.8—7.9 (m, 10H), 9.25(d, 1H, J=8 Hz)
6o	-$(CH)_4$-		CH_3	Cl	83	129—131	1.63(d, 3H, J=7 Hz), 3.15—4.8(m, 4H), 6.63—7.9(m, 9H), 9.1(d, 1H, J=8 Hz)
6r	H	H	CO_2Et	Cl	8	128—129 (121—122)[e]	
6s	H	H	Ph	CH_3	50	143—145 (148—150)[d]	
6t	H	H	Ph	H	70	143—146 (146—147)[d]	
6u	H	H	Ph	Cl	34	180—183 (180—183)[d]	
6v	H	H	H	CH_3	71	127—128	2.25(s, 3H), 2.9—4.4(m, 3H), 4.76(q, 1H, J=7 Hz), 6.73—7.95(m, 8H)
6x	H	H	H	Cl	44	105—107	2.93—4.84(m, 5H), 6.74—7.93(m, 8H)
7q	H	H	CO_2Et	H	5	129—131 (129—130)[e]	

a) Satisfactory analytical data were obtained for the new compounds. b) **6b**, **r**, and **7q** were obtained in these yields from **1** without the isolation of any precursors; **6c**, **j**, **k**, **l**, **m**, **n**, **o**, **t**, and **6x** were obtained in these yields from **4**; the yields of the other substances were based on **5**. c) Recrystallized from ethanol. d) Lit, 5c. e) Lit, 5d.

cycloaddition reaction of the cationic intermediate (**3**) (see Scheme 2). No remarkable substituent effects in these cycloaddition were observed except for the few examples described below. In the cases of $R^1=R^2=H$ and $R^3=CN$, hydrazones (**2**) were the only isolable products, and no cycloadducts were detected. However, the cycloadducts (**4**) could be obtained in good yields after the treatment of the hydrazones (**2**) in ethanol containing 8% hydrogen chloride. While the quantitative formation of hydrazones was also observed in the case of $R^4=NO_2$, these hydrazones were stable even in refluxing ethanol containing 8% hydrogen chloride. This result may be explained in terms of the electronic effect of the nitro group; the same effect was observed in the relatively poor 1,3-dipolar reactivity of *N*-(*p*-nitrophenyl)nitrilimines.[7]

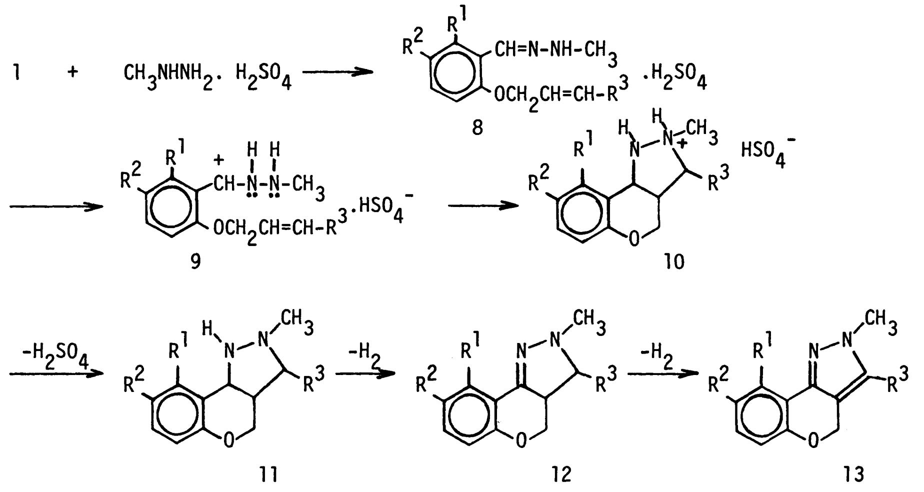
A 1,3-dipolar cycloaddition reaction can generally be explained in terms of the frontier molecular orbital (FMO) theory,[8] but so far the FMO of the cationic dipole **3** has not been calculated accurately. The observed good reactivity toward both the electron-rich and electron-poor alkenes is consistent with the interactions of a relatively low LUMO and a high HOMO in the 1,3-dipole and alkenes, and Sustmann, Type-II behavior.[9] An alternative explanation for the reactivity of **3** may be proposed on the basis of the entropically favoured intramolecular reaction, while previous studies of an intramolecular 1,3-dipolar cycloaddition[5c,d] with analogous compounds showed a substantial rate dependence on substituents.

The method described here can readily be effected with olefins and hydrazones bearing many types of functional groups, thus greatly extending the usefulness of the cycloaddition. Much better yields of **6** were obtained after consecutive treatment with the base and the thermal treatment of the reaction mixture without the isolation of **4** and **5**.

It is now shown that the [3^++2] cycloaddition is not restricted to some aldohydrazones but also to a variety of hydrazones, derived from ketones and alkylhydrazines. Some of the results are shown below.

The reaction of a suspension of methylhydrazine sulfate in ethanol with **1** proceed to completion within a few hours at room temperature. A subsequent work-up of the reaction mixtures gave the expected salts (**10**) and/or free bases (**11**) (Scheme 3). The same procedure in the case of **4** also gave **11**,**12**, and/or **13** (Table 4).

The reaction of 2′-(alkenyloxy)acetophenones(**14**) with arylhydrazine hydrochlorides in ethanol proceeded sluggishly at room temperature, but occurred smoothly at 80 °C to give cycloadducts (**17**) in the yields shown in Table 5. The structure of **17** was

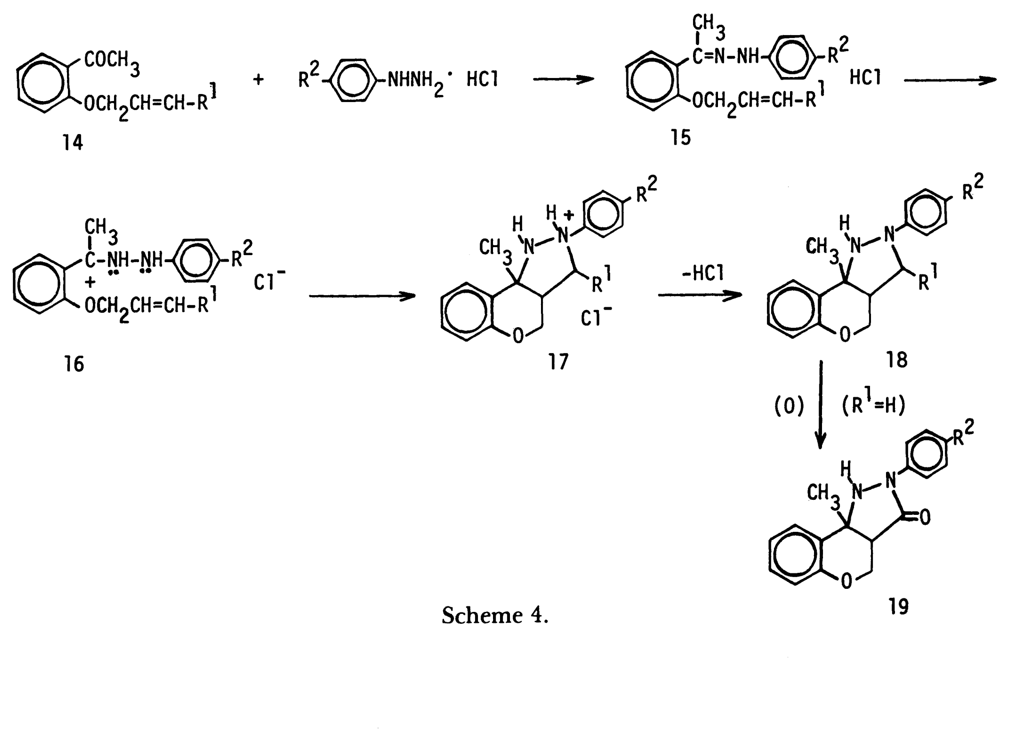


Scheme 3.

TABLE 4. YIELDS, MELTING POINTS, AND SPECTRAL DATA OF **10**—**13**[a)]

	R^1 R^2	R^3	Yield[b)] %	Mp[c)] θ_m/°C	NMR (δ)[d)]
10c	-(CH)₄-	Ph	66	275—277	2.67(s, 3H), 3.0—5.2(m, 5H), 6.2—8.3(m, 11H)
11g	H H	CN	48	*ca.* 160	2.9(s, 3H), 3.0—5.0(m, 4H), 6.8—8.0(m, 4H)
11b	-(CH)₄-	CN	35	167—169	2.8(s, 3H), 3.0—3.2(m, 1H), 3.8—4.8(m, 5H), 7.0—7.8 (m, 5H), 8.3(d, 1H, *J*=8 Hz)
12c	-(CH)₄-	Ph	70	177—178	2.9(s, 3H), 3.65—4.75(m, 4H), 6.85—7.8(m, 10H), 9.4 (d, 1H, *J*=8 Hz)
12g	H H	CN	22	127—128	3.0(s, 3H), 3.36—4.15(m, 3H), 4.66—4.85(m, 1H), 6.7—8.0(m, 4H)
13a	-(CH)₄-	CO_2Et	24	179—180	1.33(t, 3H, *J*=7 Hz), 4.2(q, 2H, *J*=7 Hz), 5.26(s, 2H), 7.0—7.8(m, 5H), 10.27(d, 1H, *J*=8 Hz)

a) Satisfactory analytical data were obtained for these compounds. b) **12c** was obtained in this yield from **10c**; **12g** was obtained in this yield from **11g**; the yields of the other substances were based on **1**. c) Rectystallized from ethanol. d) **10c** was dissolved in DMSO-d_6; the other substances were dissolved in $CDCl_3$.

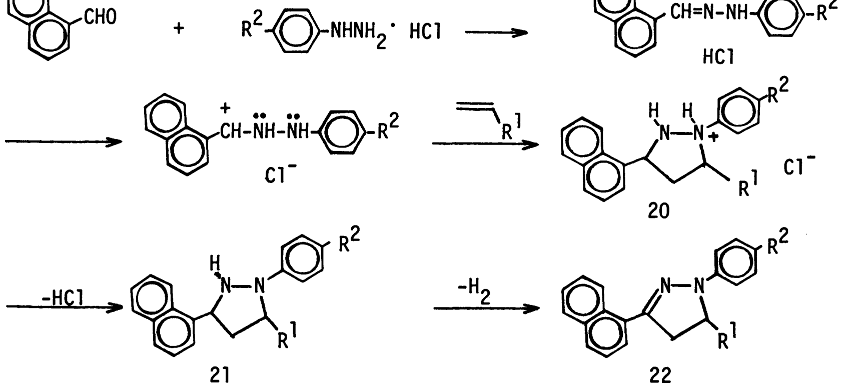


Scheme 4.

Table 5. Yields, melting points, and spectral data of **17**, **18**, and **19**[a)]

	R^1	R^2	Yield %	Mp[b)] θ_m/°C	IR($\tilde{\nu}$/cm^{-1})	NMR (δ)[c)]
17a	H	CH_3	61	120—130 (decomp)	2400 (N^+H)	1.87(s, 3H), 2.17(s, 3H), 2.7—4.3(m, 5H), 7.1—7.6 (m, 7H), 8.13(dd, 1H, *J*=2 and 8 Hz)
17b	H	H	62	130—150 (decomp)	2450 (N^+H)	1.9(s, 3H), 2.8—3.8(m, 2H), 3.85—4.5(m, 3H), 6.85—7.6(m, 8H), 8.23(dd, 1H, *J*=2 and 8 Hz)
17c	H	Cl	42	107—108 (decomp)	2450 (N^+H)	1.83(s, 3H), 2.7—3.5(m, 1H), 3.7—4.4(m, 2H), 4.56 (d, 1H, *J*=5 Hz), 6.8—7.7(m, 7H), 8.06(dd, 1H, *J*=2 and 7 Hz)
17d	CH_3	CH_3	31	167—169 (decomp)	2430 (N^+H)	1.43(d, 3H, *J*=6 Hz), 1.85(s, 3H), 2.17(s, 3H), 3.45—3.93(m, 1H), 4.05—4.63(m, 3H), 6.8—7.6(m, 7H), 8.1 (dd, 1H, *J*=2 and 7 Hz)
18b	H	H	77	131—132	3170 (NH)	1.33(s, 3H), 2.52(heptet, 1H, *J*=4 Hz), 3.22(dd, *J*=4 and 10 Hz), 3.45—4.05(m, 2H), 4.15(dd, 1H, *J*=12 and 5 Hz), 6.63—7.63(m, 8H), 7.5(dd, 1H, *J*=7 and 2 Hz)
19a	H	CH_3	25	239—240	3230 (NH) 1680 (CON)	1.66(s, 3H), 2.23(s, 3H), 2.94(t, 1H, *J*=4 Hz), 4.33—4.85(m, 2H), 6.65—7.85(m, 8H)
19c	H	Cl	37	202—203	3230 (NH) 1690 (CON)	1.66(s, 3H), 2.9(t, 1H, *J*=3 Hz), 4.23(dd, 1H, *J*=4 and 12 Hz), 4.53(dd, 1H, *J*=4 and 12 Hz), 6.7—7.8(m, 8H)

a) Satisfactory analytical data were obtained for these compounds. b) **17a**—**d** were recystallized from benzene; the other substances were recrystallized from ethanol. c) **17a**—**d** were dissolved in DMSO-d_6; the other substances were dissolved in $CDCl_3$.



Scheme 5.

Table 6. Yields, melting points, and spectral data of **20** and **22**[a)]

	R^1	R^2	Yield %	Mp[b)] θ_m/°C	NMR (δ)[c)]
20a	Ph	CH_3	53	177—178	2.23(s, 3H), 2.4—2.9(m, 1H), 3.0—3.7(m, 1H), 4.9—5.4(m, 1H), 5.7—6.2(m, 1H), 6.9—8.2(m, 15H), 8.3—8.6(m, 1H)
20c	Ph	Cl	64	134—138	2.8—3.4(m, 2H), 3.7—4.3(m, 1H), 4.8—5.6(m, 2H), 6.4—8.4 (m, 15H), 8.1—8.4(m, 1H)
20d	CO_2Et	Cl	64	d)	1.15(t, 3H, *J*=7 Hz), 3.2—4.3(m, 7H), 5.75(d, 1H, *J*=6 Hz), 7.3—8.2(m, 10H), 9.5—9.8(m, 1H)
22a	Ph	CH_3	87	172—173	2.36(s, 3H), 2.7—4.2(m, 2H), 4.75(dd, 1H, *J*=7 and 10 Hz), 6.9—7.9(m, 15H), 8.3—8.6(m, 1H)
22b	Ph	H	80	167—168	2.9—4.2(m, 2H), 5.05(dd, 1H, *J*=7 and 12 Hz), 6.7—8.0(m, 16H), 9.4—9.7(m, 1H)
22c	Ph	Cl	100	155—157	2.1—4.3(m, 2H), 4.56(dd, 1H, *J*=7 and 10 Hz), 6.8—7.9(m, 15H), 8.2—8.3(m, 1H)
22d	CO_2Et	Cl	50	d)	1.2(t, 3H, *J*=7 Hz), 3.5—5.8(m, 5H), 6.9—8.0(m, 10H), 8.9—9.3 (m, 1H)

a) Satisfactory analytical data were obtained for **20a**, **c**, **22a**, **b**, and **22c**. b) The compounds **20** were recystallized from benzene; the compounds **22** were recrystallized from ethanol. c) **20a**, **c**, and **20d** were dissolved in DMSO-d_6; the other compounds were dissolved in $CDCl_3$. d) The melting points of **20d** and **22d** were very broad because a contamination of alcohol, which could not be removed completely by recystallization from other solvents or by drying under reduced pressure at 80 °C.

assigned on the basis of the results of elemental analyses and the spectral data. Although some of the **17** gave crystalline free bases (**18**) upon treatment of triethylamine, some of the oily free bases (**18**) gave air-oxidation products (**19**) after the reaction mixture had been allowed to stand at room temperature for several days. The structure of **19** was assigned on the basis of the results of elemental analyses and the spectral data (see Table 5). The methylene at the 3-position of **18** is labile to air-oxidation. Thus, **18a—c** gave the 3-oxo products, while **18d** (with methyl substituted for one hydrogen) was stable for the oxidation under the same conditions.

While an intermolecular $[3^{+}+2]$ cycloaddition proceeds well in the presence of an excess of sulfuric acid,[6] our procedure under much milder conditions also gave the intermolecular cycloadducts (**20**) in higher yields (see Scheme 5 and Table 6). 1-Aryl-3-(1-naphthyl)-5-phenyl-2-pyrazolines (**22**) were obtained after the treatment of **20** with triethylamine. The intermediate, 1-aryl-3-(1-naphthyl)-5-phenylpyrazolidines (**21**), would be unstable and oxidized to **22** under the reaction conditions. The assignment of the structure was supported by a comparison of the physical properties of **22** with those of authentic specimens prepared according to the previously published procedures.[10] The cycloaddition with such dipolarophiles as acrylonitrile, methyl methacrylate, dimethyl maleate, dimethyl fumarate, *N*-phenylmaleimide, norbornene, dimethyl acethylenedicarboxylate, and phenylacetylene afforded cycloadducts in poor yields. The cycloadducts (**20**) were also obtained in good yields after the treatment of 1-naphthaldehyde arylhydrazones with olefins in ethanol containing 8% hydrogen chloride at room temperature.

Experimental

All the melting points are uncorrected. The IR spectra were recorded on a Hitachi 215 Infrared Spectrophotometer. The NMR spectra were measured on a Varian T-60A instrument, using suitable solvents and TMS as an internal standard.

Materials. The 2-(alkenyloxy)benzaldehydes(or 1-naphthaldehydes) (**1**) and their arylhydrazones were prepared according to the method previously reported.[5] The arylhydrazine hydrochlorides and methylhydrazine sulfate were commercially available (Nakarai Chem. Co.) and were used without further purification. The 2′-(alkenyloxy)-acetophenones (**14**) were prepared by the reaction of 2′-hydroxyacetophenone and ω-bromoalkenes in acetone in the presence of an equimolar amount of anhydrous potassium carbonate at 60°C for 20h. The 2′-allyloxyacetophenone (**14a**) was obtained in an 83% yield; bp 125—126°C (7mmHg), IR (neat): 1670cm^{-1} (C=O) and NMR ($CDCl_3$): δ 2.6 (s, 3H), 4.6 (d, 2H, J=5Hz), 5.1—5.6 (m, 2H), 5.75—6.4 (m, 1H), and 6.75—7.85 (m, 4H). The 2′-(2-butenyloxy)acetophenone(**14b**) was obtained in an 81% yield; bp 136—138°C (7mmHg), IR (neat): 1670cm^{-1} and NMR ($CDCl_3$) δ 1.7 (d, 3H, J=5Hz), 2.6 (s, 3H), 4.5 (d, 2H, J=4 Hz), 5.6—5.95 (m, 2H), and 6.75—7.85 (m, 4H).

Reaction of 1 with Arylhydrazine Hydrochlorides. General Procedure: An equimolar mixture (5 mmol) of **1** and arylhydrazine hydrochlorides was stirred in ethanol (50ml) for several hours at room temperature. The crystals of arylhydrazine hydrochlorides are only slightly soluble in the solvent at this temperature, but the mixture became homogenous after 1 h, and then a crystalline precipitate of 3-substituted 2-aryl-1,2,3,3a,4,9b(or 1,2,3,3a,4,11c)hexahydro[1]-benzopyrano(or naphtho[1′,2′:5,6]pyrano)[4,3-*c*]pyrazole hydrochlorides (**4**) appeared within additional few hours. The evaporation of the solvent gave another corp of **4** or an oily residue. Scratching a benzene solution of the oily residue gave **4**. The yields, melting points, and spectral data are shown in Table 1. Almost all the **4** which could be recrystallized from ethanol gave correct elemental analyses. A solution of **1** and arylhydrazine hydrochlorides in warm ethanol (50—60°C) gave results similar to those described above.

The Treatment of 2-(Alkenyloxy)benzaldehyde(or 1-naphthaldehyde) Arylhydrazones in Ethanol Containing 8% HCl. 2-(Alkenyloxy)benzaldehyde (or 1-naphthaldehyde) arylhydrazones (**2**)[5c,d] was added to an ethanol containing 8% HCl at room temperature and the mixture was stirred for an additional hour after the complete dissolution of **2**. The subsequent evaporation of the solvent and the hydrogen chloride at 70°C in a rotary evaporator gave an oily residue. The residue was recrystallized from benzene to afford **4** in 90—100% yields.

The Treatment of 4 with Triethylamine. Into a suspension of **4** in chloroform we added an excess mol of triethylamine, after which the mixture was stirred for 30min. The reaction mixture was then washed with water several times, and the organic layer was dried over anhydrous sodium sulfate. The subsequent evaporation of the solvent yielded 3-substituted 2-aryl-1,2,3,3a,4,9b(or 1,2,3,3a,4,11c) hexahydro[1]benzopyrano(or naphtho[1′,2′,:5,6]pyrano)[4,3-*c*]pyrazoles (**5**) in the yields shown in Table 2.

Preparation of 3-Substituted 2-Aryl-2,3,3a,4-tetrahydro(or -2,4-dihydro)[1]benzopyrano(or naphtho[1′,2′:5,6]pyrano)[4,3-c] pyrazoles (6 and/or 7). A xylene solution (50ml) of **5** (1mmol) was refluxed for 4h. After the evaporation of the solvent, the residue was mixed with a small amount of ehtanol (10ml) and allowed to stand for several hours, and the precipitate (**6**) that thus formed was filtered off. The filtrate was chromatographed (silica gel) with chloroform to give another crop of **6** and/or **7**.

The Reaction of 1 with Methylhydrazine Sulfate. Into a suspension of methylhydrazine sulfate (10mmol) in ethanol (50ml) we added **1** (10mmol), after which the mixture was stirred at room temperature. After the complete dissolution of the methylhydrazine sulfate, the mixture was stirred for an additional 4 h. The subsequent work-up of the reaction mixture gave 3-substituted 2-methyl-1,2,3,3a,4,9b (or 1,2,3,3a,4,11c)hexahydro[1]benzopyrano(or naphtho[1′2′:5,6]-pyrano)[4,3-*c*]pyrazole sulfates (**10**) in a rather impure crystalline or oily state because of the contamination of a small amount of **11** and/or **12**. Free bases (**11**) and dehydrogenated products (**12** and **13**) were prepared following procedures similar to those described in the cases of **4**→**7**.

The Reaction of 14 with Arylhydrazine Hydrochlorides. A mixture of **14** (10mmol) and arylhydrazine hydrochloride (10mmol) in ethanol (70ml) was refluxed for 20h. After the evaporation of the solvent, benzene was added (30ml) to the residue; crystalline **17** was then precipitated immediately from the benzene solution. Recrystallization from benzene gave pure **17**. 2′-(3-Phenyl-2-propenyloxy)acetophenone arylhydrazones were the only isolable products from the reaction of 2′-(3-phenyl-2-propenyloxy)acetophenone (**14c**) with arylhydrazine hydrochlorides; no cycloadducts were detected.

The Treatment of 17 with Triethylamine. To a solution of **17b** (1.8g) in chloroform (70ml) we added triethylamine (1ml), after which the mixture was stirred for 30 min at room temperature. The reaction mixture was then washed with water several times, and the organic layer was dried over anhydrous sodium sulfate. The subsequent evaporation of the solvent yielded crystals of 9b-methyl-2-phenyl-1,2,3,3a,4,9b-hexahydro[1]benzopyrano[4,3-*c*]pyrazole (**18b**) in a 77% yield (1.22 g). Recrystallization from ethanol gave pure **18b**. On the other hand, an oily mass was obtained after the similar treatment of **17a** (or **17c**) with triethylamine. The exposure of the ethanol solution of the oily mass to the atmosphere for several days yielded white crystals of 2-aryl-9b-methyl-1,2,3,3a,4,9b-hexahydro[1]benzopyrano[4,3-*c*]pyrazol-3-ones (**19a** or **19c**) in the yields shown in Table 5.

The Reaction of 1-Naphthaldehyde with Arylhydrazine Hydrochlorides in the Presence of Dipolarophiles. An ethanol solution (80 ml) of an equimolar (10 mmol) mixture of 1-naphthaldehyde and arylhydrazine hydrochlorides was stirred for 20 h at room temperature in the presence of dipolarophile (4 ml of dipolarophiles which exhibit boiling points less than 150 °C, and an equimolar amount (10 mmol) of other high-boiling dipolarophiles). After the evaporation of the solvent, the residue was mixed with hot benzene (20 ml) and the mixture was cooled to room temperature. The 5-substituted 1-aryl-3-(1-naphtyl)pyrazolidine hydrochlorides (**20**) thus precipitated filtered and were recrystallized from benzene. The yields and melting points are shown in Table 6.

The Reaction of 1-Naphthaldehyde p-*Chlorophenylhydrazone and Styrene in Ethanol Containing 8% HCl.* The reaction of 0.3 g (2 mmol) of 1-naphthaldehyde *p*-chlorophenylhydrazone and 1.0 g (10 mmol) of styrene was carried out in ethanol (30 ml) containing 8% HCl at toom temperature for 20 h. After the evaporation of the solvent and the excess amount of HCl and styrene, the residue was mixed with benzene (10 ml) to give white crystals (0.34 g, 82% yield) which shows the same physical properties as those of **20c**.

References

1) Presented in part at the 46th National Meeting of the Chemical Society of Japan, Niigata, October 1982, Abstr. 725.

2) a) W. Oppolzer, Ger. Offen., 1926023 (1969); *Chem. Abstr.*, **72**, 43671 (1970); b) R. E. Brown and J. Shavel, Jr., U. S. Patent 3624102 (1971); *Chem. Abstr.*, **76**, 59618 (1972); c) M. T. Di Parsia, C. Suarez, M. J. Vitolo, V. E. Marguez, C. Urbina, and I. Hurtado, *J. Med. Chem.*, **24** 117 (1981); d) F. Eiden and I. Breugst, Ger. Offen., 2917575 (1980); *Chem. Abstr.*, **94**, 139801 (1981); e) N. K. Sangwan and S. N. Rastogi, *Indian J. Chem., Sec.* B, **20**, 135 (1981).

3) a) Imperial Industries, Ltd., Neth. Appl., 6511492 (1966); *Chem. Abstr.*, **65**, 2271 (1966); b) T. Kamino and H. Kato, Jpn. Kokai Tokkyo Koho, 79126114 (1979); *Chem. Abstr.*, **92**, 119745 (1980).

4) a) H. Meier, W. Heinzelman, and H. Heimgartner, *Chimica*, **34**, 506 (1980); b) A. Padwa, S. Nahn, and E. Kato, *J. Org. Chem.*, **43**, 1664 (1978); c) G. Schmitt and B. Laude, *Tetrahedron Lett.*, **1978**, 3727; d) F. M. Dean, K. B. Hindley, S. Murray, and W. Taylor, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2444; e) H. Meier and H. Heimgartner, *Helv. Chim. Acta*, **60**, 3035 (1977); f) W. Oppolzer, *Tetrahedron Lett.*, **1971**, 3091; g) W. Kirmse and H. Dietrich, *Chem. Ber.*, **100**, 2710 (1967).

5) a) T. Shimizu, Y. Hayashi, Y. Nagano, and K. Teramura, *Bull. Chem. Soc. Jpn.*, **53**, 429 (1980); b) T. Shimizu, Y. Hayashi, K. Yamada, T. Nishio, and K. Teramura, *ibid.*, **54**, 217 (1981); c) T. Shimizu, Y. Hayashi, Y. Kitora, and K. Teramura, *ibid.*, **55**, 2450 (1982); d) T. Shimizu, Y. Hayashi, S. Ishikawa, and K. Teramura, *ibid.*, **55**, 2456 (1982).

6) a) G. Le Fevre, S. Sinbandhit, and J. Hamelin, *Tetrahedron*, **35**, 1821 (1979); b) G. Le Fevre and J. Hamelin, *Tetrahedron Lett.*, **1979**, 1757.

7) R. S. Tewari and P. Parihar, *Tetrahedron*, **39**, 129 (1983).

8) a) I. Fleming, "Frontier Orbitals and Organic Chemical Reactons," John Wiley and Sons, New York (1976); b) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Stronzier, and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973); c) K. N. Houk in "Pericyclic Reactions, II," ed by R. E. Lehr and A. P. Marchand, Academic Press, New York (1977).

9) R. Sustmann, *Tetrahedron Lett.*, **1971**, 2717.

10) R. Huisgen, M. Siedel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, **17**, 3(1962).