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Substituent Effects in the Diels-Alder Reaction of Substituted Benzynes with Hexamethylcyclohexa-2,4-dienone

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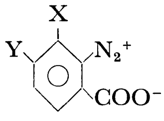
The Diels-Alder reaction of unsymmetrically substituted benzynes that had been generated from 3-Me-, 4-Me-, 5-Me-, 6-Me-, 3,4-Me_2-, 3-NO_2-, 4-NO_2-, 5-NO_2-, and 3-Cl-benzenediazonium-2-carboxylates, with hexamethylcyclohexa-2,4-dienone gave a mixture of 5- or 6-substituted-1,2,3,4,10,10-hexamethyl-1,4-dihydro-1,4-ethanonaphthalene-9-one (Type **7**) and its 8- or 7-substituted isomer (Type **8**). The **7**/**8** isomer ratios varied from 1.0 to 2.0 depending substantially on the size and the position of substituents of the benzynes and also on the temperature and the solvent. The ratios were the same when two positionally isomeric acids, *i.e.*, 3- and 6-, or 4- and 5-substituted acids, were used as the precursors. Thus, the identity of the benzynes generated from these paired isomeric precursors was proved, ruling out the possibility of an inherent memory effect of the precursors. The factor that controls the isomer ratios is discussed in terms of the steric repulsive interaction between the substituents of benzynes and the *gem*-dimethyl groups of the dienone.

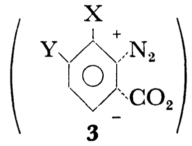
In view of the chemical interest in benzyne chemistry, the structure of benzyne does not seem to have been fully elucidated, particularly with regard to that in the transition state of chemical reactions. Triple-bond (**1a**), biradical (**1b**), and ion-pair (**1c**) structures have most often been proposed and discussed in numerous reactions.[1] Among them, the Diels-Alder-type reactions of benzyne with conjugated dienes, for example, have been considered to proceed mainly by means of the **1a** structure with symmetrical bonding, though there is some possibility of **1b** and **1c**.[2]

In our previous study of the synthesis of polymethylnaphthalenes, the reaction of hexamethylcyclohexa-2,4-dienone with unsymmetrically substituted benzynes that were generated from the corresponding benzenediazonium-2-carboxylates has been shown to give two isomeric adducts (Type **7** and Type **8**) in an unequal ratio.[3] Therefore, in the present study, our first interest was focussed on the characterization of the factors controlling the stereoselectivity in the formation of these adducts. We presumed, first of all, that when two different benzenediazonium-2-carboxylates, **2** and **4**, are used as the precursors of an identical benzyne, then the structure of the benzyne adducts may inherit the memory of the ionic structure of the diazonium carboxylates in certain reactions in which a substantial polar reactant interaction exists either prior to the benzyne generation or in the transition state, regardless of the substituent effect of the benzynes. Hexamethylcyclohexa-2,4-dienone (**6**),[4] for instance, seems to be a suitable dipolar diene for examining this memory effect. On the other hand, if this memory effect does not operate, then the reaction will be controlled by the benzyne structure, **1a** (or **1b**) or **1c**, only when there is a polar effect of the benzyne substituents. In this case, the isomer ratio, **7**/**8**, obtained from the reaction of **2** with **6** (Eq. 1) should be the same as that of **4** with **6** (Eq. 2), and the substituent effect that determines the **7**/**8** isomer ratio, will be either a steric effect, an inductive effect, or a dipole-dipole interaction between reactants.

In the present study, the reactions of hexamethylcyclohexa-2,4-dienone (**6**) with several unsymmetrically substituted benzynes that are generated from the corresponding arenediazonium-2-carboxylates (**2** and **4**, where X and Y are H, CH_3, Cl, or/and NO_2) are carried out under controlled conditions, and a qualitative diagnosis of the substituent effects in the transition state is deduced from the isomer ratios of the adducts.



2a—**2f**



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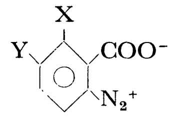
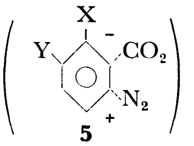


4a—**4f**



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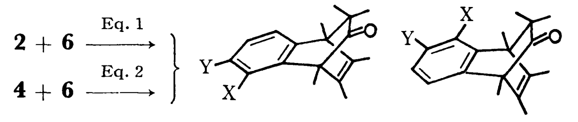
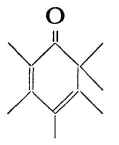


7a—**7f** **8a**—**8f**



6

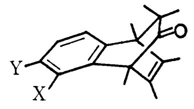
	X	Y
a:	X=Me	Y=H
b:	X=H	Y=Me
c:	X=NO_2	Y=H
d:	X=H	Y=NO_2
e:	X=Cl	Y=H
f:	X=Me	Y=Me

Results and Discussion

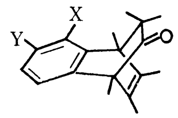
Substituted benzenediazonium-2-carboxylates, as the aryne precursors, were prepared in the form of hydrochlorides from the corresponding anthranilic acids. They can be handled safely in the dried-powder state, except for the nitro derivatives, which are detonated by heat or impact. Most anthranilic acids were synthesized, after testing several procedures, *via* the corresponding isatines,[5] except in the case of nitroanthranilic acids, which were synthesized from the corresponding nitrophthalamic acids.

The reactions of unsymmetrically substituted benzenediazonium-2-carboxylate hydrochlorides (**2** and **4**) with hexamethylcyclohexa-2,4-dienone (**6**) were carried out under controlled conditions—constant rate of rising

Table 1. Structures and NMR chemical shifts of the benzyne-adducts



7a—7f



8a—8f

Compd	Substituents		Chemical shifts of Me-groups (δ)					
			7			**8**		
	X	Y	*syn*-Me	*anti*-Me	Ar-Me	*syn*-Me	*anti*-Me	Ar-Me
a	Me	H	0.54	1.02	2.47	0.61	0.99	2.52
b	H	Me	0.48	1.03	2.29	0.48	1.03	2.31
c	NO_2	H	0.68	1.04		0.57	1.08	
d	H	NO_2	0.52	1.10		0.53	1.10	
e	Cl	H	0.67	1.03		0.57	1.06	
f	Me	Me	0.56	1.00	2.21 2.37	0.62	0.97	2.23 2.41

temperatures and a constant concentration of reagents. The product analysis of these reactions, mainly by means of NMR, proved that the products were mixtures of two structurally isomeric adducts, **7** and **8**. Their NMR assignments were performed as follows (see Table 1).

The Assignment of Adduct Structures and the Determination of Isomer Ratios. The NMR spectrum of the adduct obtained from the reaction of **2a** with **6** was identical with that obtained from the reaction of **4a** with **6**, and it has been clarified that the adduct consisted of two structural isomers, **7a** and **8a**.[6,7] These isomers could not be separated, but their spectral assignment was achieved by a means analogous to that employed in the assignment of **7f** and **8f**, which was carried out with the aid of a lanthanoid shift reagent, $Eu(fod)_3$.[3] The **7a**/**8a** isomer ratio was determined mainly by the comparison of the NMR integration of the geminate methyl groups that are at the 9-position of the 1,4-dihydro-1,4-ethanonaphthalene ring and oriented *syn* to the benzene ring, since the difference in chemical shifts between the *syn*-methyls of **7a** and **8a** ($\Delta\delta$=0.07 ppm) is large enough to discriminate the two isomers. The ratios obtained from **2a** and **4a** are 1.73 and 1.75 respectively.

The same mixtures of isomeric adducts, **7b** and **8b**, were obtained from both benzyne precursors, **2b** and **4b**. The VPC separation of these two isomers was unsuccessful, and the NMR chemical shifts of the *syn*-*gem*-methyl groups were almost identical and undiscriminative. Fortunately, however, the chemical shifts of aryl methyl groups were slightly different between **7b** and **8b** ($\Delta\delta$= 0.02 ppm), and this difference could be enlarged clearly enough to distinguish the two isomers by the aid of the lanthanoid shift reagent, $Eu(fod)_3$ (0.30 mol equivalent). The isomer ratios obtained from **2b** and **4b** are 1.01 and 1.00 respectively. The assignment of NMR spectra to these isomers is based on the assumption that the aryl methyl group situated farther from the carbonyl group shows a lower field absorption than the one situated closer to the carbonyl group, which is analogous to the finding in the cases of **7a** and **8a**.

The reaction of 3-nitrobenzenediazonium-2-carboxylate hydrochloride (**4c**) with **6** gave a mixture of **7c** and **8c**. The NMR spectra of this mixture showed a clear difference in the chemical shift of the *syn* methyl group between the two isomers, **7c** and **8c** ($\Delta\delta$=0.11 ppm). The assignment of the chemical shifts to each isomer is based upon the assumption that the *syn* methyl group with the closer nitro substituent (isomer **8c**) will suffer a more shielding effect than that in the other isomer, **7c**. The ratio, thus determined by NMR, is 1.44 (by VPC, the ratio is 1.50). The same adducts were not obtained from the reaction of **2c**[8] because the diazotization of the corresponding 3-nitroanthranilic acid by isopentyl nitrite in the presence of hydrochloric acid caused an unusual nucleophilic substitution of the nitro group[9] by the chloride anion to produce 6-chlorobenzenediazonium-2-carboxylate (**2e**).

The assignment of the NMR spectra of the isomers, **7d** and **8d**, which were obtained as mixtures from both precursors, **2d** and **4d**, was carried out by the aid of the lanthanoid-shift reagent. The reagent facilitated the separation of the chemical shifts of the aromatic protons situated beta to the nitro substituent, *i.e.*, β_7-H in **7d** and β_8-H in **8d**. Here, the principal assumption is that β_8-H, that locates in closer proximity to the carbonyl group, is shifted to a lower field than β_7-H because of the complexation of the shift reagent with the carbonyl group.[10] The isomer ratio, **7d**/**8d**, determined therefrom, are 0.99 in the reaction of **2d** and 1.00 in that of **4d**. The ratios determined by a VPC analysis are 1.07 in both reactions. These two isomers, **7d** and **8d**, were separated by recrystallization from methanol; **7d**, with a less crowded structure, has a higher mp (158.5—159.5 °C) than that of **8d** (126—128 °C).

The two isomeric adducts, **7e** and **8e**, that were obtained from **2e**, can be separated; the isomer with a higher mp (107—108 °C) was assigned to **7e**, while the one with a lower mp (93—94 °C) to **8e**, on the basis of the mp as well as of the NMR chemical shift of the *syn*-*gem*-methyl groups. The isomer ratio (**7e**/**8e**) determined from the NMR integrations of *syn*-methyls ($\Delta\delta$=0.10 ppm) is 1.09, while it is 1.11 when determined by VPC.

In the adducts mentioned above, it is anticipated that the isomer with an intramolecularly more crowded

Table 2. Melting points of some benzyne-adducts (°C)

Substituents		Adducts	
o-	*m*-	Type **7**	Type **8**
H	NO_2	158.5—159.5	126—128
Cl	H	107—108	93—94
CH_3	CH_3	154—156.5	127—130

structure will have a lower mp than the one with a less crowded structure. In fact, some isomers which were separated and structurally assigned support this hypothesis (see Table 2). This finding must be useful for the structure assignment of isomeric benzyne-adducts by a comparison of their melting points.

Table 3. Substituent effects on the isomer ratios **7**/**8**[a]

Run	Benzynes		Diazonium carboxylates	
	o-X	*m*-Y	**2**	**4**
1	CH_3	H	1.73 (2.03)	1.75 (2.11)
2	NO_2	H		1.44 (1.50)
3	Cl	H	1.09 (1.11)	
4	H	CH_3	1.01	1.00
5	H	NO_2	0.99 (1.07)	1.00 (1.07)
6	CH_3	CH_3		1.71

a) The numbers in parentheses are the ratios determined by VPC.

The Interrelation between Substituent Effects and the Structure of Arynes. The isomer ratios (**7**/**8**) in the addition products are listed in Table 3. There it is evident that the isomer ratios are the same in both adducts obtained from the precursors of Type **2** and Type **4**, though the dispositions of their ion-pairs are inverse to each other. Thus, the identity of the arynes generated from both precursors is established, ruling out any possibility of intervening ionic memory effect inheritable from the starting-diazonium salts. The reason for the predominant formation of the isomer of Type **7** over **8** will be presented below.

In the general reaction procedure, 1,2-dichloroethane was employed as the solvent. This solvent, however, is non-polar and shows a poor dissolving power to benzenediazonium-2-carboxylate hydrochlorides. In this solvent the polar interaction, if any, between dienone **6** and aryne precursors (**2** and **4**) in or prior to the transition state will be exerted less than that in polar solvents. Therefore, the effect of the increasing solubility of **2** and **4** in such polar solvents as acetonitrile, *N*-methylformamide, and dienone itself, in which all reactants are soluble, was examined. The results are shown in Table 4. No appreciable difference was observed in the **7a**/**8a** isomer ratio between the starting compounds **2** and **4**, although, in polar solvents, the ratios are inclined to increase somewhat more than those in less polar solvents. Thus again, the memory effect was not observed even in these polar solvents. The increased isomer ratio observed in polar solvents seems to be ascribable mainly to the lower temperature of the decomposition of the aryne precursors in these solvents.

Table 4. Isomer ratios **7a**/**8a** in various solvents

Solvent	Diazonium carboxylates	
	2a	**4a**
CH_2ClCH_2Cl	1.73	1.75
CH_2ClCH_2Cl[a]	1.69	
CH_3CN	1.88	1.89
CH_3NHCHO	2.05	2.08
Dienone **6**[a]	1.90	1.97

a) The diazonium salts, **2a′** and **4a′** were used without PO.

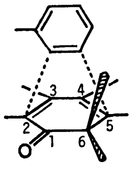
Table 5. Isomer ratios **7a**/**8a** at various temperatures[a]

Temp (°C)	Diazonium carboxylates	
	2a	**4a**
80	1.72	1.70
70	1.71	1.72
60		1.70
50	1.77	1.79
40	1.76	1.80

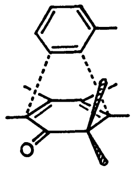
a) Butene-1-oxide was used instead of PO.

The effect of the reaction temperature on the isomer ratios was also examined, especially in an attempt to know whether it is different between the two starting compounds (**2** and **4**). It has been calculated that the ion-pair structure, **1c**, has a higher free energy than that of **1a** or **1b**,[2] hence, a temperature effect will be anticipated if any function of **1c** is involved in or prior to the transition state. The results in Table 5, however, give a negative evidence to this hypothesis, because no appreciable difference is observable in the isomer ratios obtained from the two aryne precursors, **2** and **4**. The slightly enhanced formation of the **7a** isomer over **8a** at lower temperatures, as shown in this table, seems to indicate that the energy of activation for the formation of **7** is slightly lower than that for **8**. This difference, $\Delta E_a = E_a(\mathbf{8a}) - E_a(\mathbf{7a})$, was determined by the Arrhenius plotting of the isomer ratios in Table 5. Thus, we found that $\Delta E_a = 0.26 \pm 0.04$ kcal/mol, and $A(\mathbf{7a})/A(\mathbf{8a}) = 1.18 \pm 0.07$.

Although the possibility of the participation of the memory effect was thus completely ruled out, the substituent effects that determine the isomer ratios in the benzyne adducts still remain unclarified. Table 3 clearly indicates that the steric interaction between the *gem*-dimethyl groups of **6** and the substituent, X, in the transition state seems to be the sole factor controlling the isomer ratios. Thus, the ratios decrease as the Van-der-Waals radius of the X substituent diminishes, and accordingly, the effect of the β-substituent, Y, is negligible.[11] In the case of 3-methylbenzyne, that gave the largest isomer ratio (1.7—1.8) among those examined, the difference in kinetic parameters between the two sterically different transition states, *i.e.*, $\Delta E_a = 0.26$ kcal/mol, and especially the ratio of the frequency factors $A(\mathbf{7a})/A(\mathbf{8a}) = 1.18$, indicates that the steric course leading to the adduct of Type **7** is slightly, but apparently, favored over that of Type **8**. A framework diagnosis of possible transition states (*e.g.*, **A** and **B**) also supports this. These framework are constructed on the supposition that benzyne approaches vertically to the 2- and 5-positions of the planar dienone, keeping the two bonding distances equal. Then, when Type **B** is concerned, the overlapping of Var-der-Waals radii between *gem*-dimethyl and aryne methyl groups becomes substantial in the range of bonding distances shorter than 2.8 Å, about twice the bond length in the adduct.



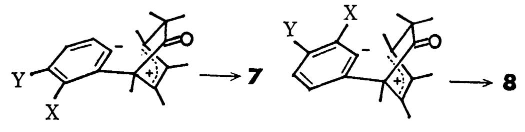
A



B

(The interaction between the aryne methyl and 5- methyl of the dienone in Type **B** is also substantial, but is cancelled out by the similar interaction in Type **A** between aryne methyl and 2-methyl of the dienone when **A**/**B** is considered).

Other substituent effects that seem to be involved in determining the isomer ratio are: *a*) the dipole-dipole interaction between the carbonyl group of the **6** dienone and the X substituent, or/and *b*) the inductive effect of X. In the case of nitrobenzynes, if the former effect operates between the nitro group and the carbonyl group, then the product, **8c** (or **8d**), should be the predominant product in Run 2 (or Run 5) in Table 3. However, the ratios are **7c**/**8c**=1.44 and **7d**/**8d**=1.00; thus, the possibility of *a* is ruled out. As for the latter effect, *b*, if it contributes to the polar structure of arynes, then the adduct of Type **8** should favorably be formed in Runs 1, 4, and 6, and Type **7**, in Runs 2, 3, and 5.



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Alternatively, recent studies of aryne reactions[12] have led us to suspect that the inductive effect of the X substituent (or/and Y) operates in the transition state of a two-stage addition reaction, so that a zwitter-ion, **9** or **10**, can be stabilized. According to this hypothesis, the adduct of Type 7 should be obtained predominantly from methyl-substituted benzynes, and Type **8**, from nitro- or chloro-benzynes. However, this was not the case. Therefore, the inductive effect is not likely to be involved, and, even when be involved, its magnitude is too small to overcome the steric effects.

Recently, Newman and Kannan reported that, in the reaction of 2-substituted furans with the aryne precursors analogous to Types **2a** and **4a**, where the steric interaction was expected to be more substantial than in our system, the isomer ratios found were smaller than 1.8.[19] Comparing our results with those, it should be noticed that the interaction of the X substituent with the *gem*-methyl group of **6** that is located at the 5-position of a cyclic 1,3-diene is almost as large as that of X with the substituent at the 1- or 4-position.

Experimental

General. The NMR spectra were measured in CCl_4 solutions, and the chemical shifts are given in δ-units. The VPC analyses were performed on a chromatograph equipped with a FID. Below, the experimental description will be divided into three sections: 1) methylbenzynes, 2) nitrobenzynes, and 3) chlorobenzyne. The combustion analysis was performed by the Elemental Analysis Laboratory of the Institute for Chemical Research of Kyoto University. The analyses of isomeric mixtures of benzyne-adducts agreed well (within an error of 0.30%) with the corresponding calculated values for the methylbenzyne- and nitrobenzyne adducts, and fairly well (within an error of 0.80%) for the chlorobenzyne adduct.

1. Preparation and Reaction of Methylbenzynes. *1-a) 6-Methylbenzenediazonium-2-carboxylate Hydrochloride (**2a**)*: This compound, **2a**, was prepared from 3-methylanthranilic acid (**11**)[5] by a procedure analogous to that previously reported.[13] Yield, 97%; mp 112.5—113.5 °C (dec); IR ν(N≡N) 2230 cm^{-1} (Nujol).

*1-a') Free 6-Methylbenzenediazonium-2-carboxylate (**2a'**)*: Compound **2a'** was prepared by a procedure analogous to that employed above (see *1-a*), except that HCl was not added to the initial ethanolic solution. Yield, 43%; mp 98—99 °C; IR ν(N≡N) 2230 cm^{-1}.

*1-b) 1,2,3,4,6,10,10-Heptamethyl-1,4-dihydro-1,4-ethanonaphthalene-9-one (**7a**) and Its 1,2,3,4,7,10,10-Heptamethyl Isomer (**8a**) by the Reaction of **2a** with 2,3,4,5,6,6-Hexamethylcyclohexa-2,4-dien-1-one (**6**)*: The experimental conditions of seven runs are tabulated below. The first three runs were carried out in order to examine the solvent effects, and the last four runs, to examine the temperature effects. For the isomer ratios, see Tables 3,4, and 5. The experimental procedure for Run 1 is described below as the standard procedure, which will be refered to in the procedures following.

Run	Base	Solvent	Temp (°C)	Time (min)	Yield (%)
1	PO	CH_2ClCH_2Cl	60	70	95
2	PO	CH_3CN	60	70	26
3	PO	CH_3NHCHO	60	70	17
4	EB	CH_2ClCH_2Cl	40	480	100
5	EB	CH_2ClCH_2Cl	50	180	100
6	EB	CH_2ClCH_2Cl	70	60	100
7	EB	CH_2ClCH_2Cl	80	60	100

EB: 1,2-epoxybutane.

Run 1. Into a suspension of **2a** (0.50 g, 2.5 mmol) in 1,2-dichloroethane (6.3 ml), **6** (0.45 g, 2.5 mmol) and propylene oxide (0.8 ml, abbreviated as PO) were added. The mixture was then immediately heated under the standard conditions; *i.e.*, the temperature was raised at the rate of 2.5 °C/min from 25 to 60 °C. After additional stirring at 60 °C for 70 min, the dark brown solution was cooled. (These conditions were employed in the other runs that were carried out with the purpose of obtaining the adduct-isomer ratios.) After a vacuum evaporation, the residue was redissolved in Et_2O, and the solution was washed four times with 5 ml of 5% aq NaOH and again four times with water, and then dried ($MgSO_4$). The subsequent evaporation of the solvent gave a mixture of **7a** and **8a**; 0.64 g (95%). These isomers could not be separated satisfactorily by column chromatography ($CHCl_3$, silica gel). NMR **7a**: *gem*-Me 0.54 and 1.02 (3H each; Me's *syn* and *anti* to the benzene ring respectively), Ar–Me 2.47 (3H), allylic Me 1.65—1.75 (6H), bridge-head Me 1.55 and 1.78 (3H each), Ar–H 6.7—7.1 (3H) ppm. **8a**: *gem*-Me 0.61 and 0.99 (3H each; Me's *syn* and *anti* to the benzene ring respectively), Ar–Me 2.52 (3H), allylic Me 1.65—1.75 (6H), bridge-head Me 1.55 and 1.78 (3H each), Ar–H 6.7—7.1 (3H) ppm; $P^+(m/e)$ 268. The isomer ratio, **7a**/**8a**, determined by a comparison of the NMR-integration, was 1.73. A VPC analysis (PEG-succinate, 2 m at 175 °C), though not achieving a satisfactory isomer separation, also gave the isomer ratio of 2.03.

Runs 4—7. Instead of PO, 1,2-epoxybutane (0.44 ml; abbreviated as EB) was added to a mixture of **2a** and **6** in 1,2-dichloroethane; the mixture was immediately heated at 80-, 70-, 50-, or 40±0.2 °C for the periods listed in the table. For the work-up, see the details in Run 1. Yield (**7a**+**8a**), *ca.* 100% in all runs. For the isomer ratios, see Table 5.

1-c) 7a and 8a by the Reaction of 2a′ with 6: Two runs were performed in order to examine the effect of free diazonium carboxylate, **2a′**, on the isomer ratio: Run 1, without PO in CH_2ClCH_2Cl; yield, 37%; Run 2, without PO, but in an excess amount of **6**; yield, 54%. The other reaction conditions were the same as in *1-b*. For the isomer ratios, see Table 4.

1-d) 3-Methylbenzenediazonium-2-carboxylate Hydrochloride (4a). From 6-Mcthylanthranilic Acid (12): For the preparative procedure, see *1-a*. Yield, 84%; mp 110.5—111 °C (dec); IR ν(N≡N) 2210 cm^{-1} (Nujol).

1-e) 3-Methylbenzenediazonium-2-carboxylate (4a′): See the procedure *1-a′*. Yield 4%; mp 68—70 °C (dec); IR ν(N≡N) 2250 cm^{-1}.

1-f) 7a and 8a by the Reaction of 4a with 6: For the procedure, see *1-b*. The reaction conditions and the results of eight runs are tabulated below. The first three runs were carried out in order to examine the solvent effects, and the last five runs, to examine the temperature effects. For the isomer ratios, see Tables 3, 4, and 5.

Run	Base	Solvent	Temp (°C)	Time (min)	Yield (%)
1	PO	CH_2ClCH_2Cl	60	70	83
2	PO	CH_3CN	60	70	13
3	PO	CH_3NHCHO	60	70	13
4	EB	CH_2ClCH_2Cl	40	560	100
5	EB	CH_2ClCH_2Cl	50	180	98
6	EB	CH_2ClCH_2Cl	60	70	100
7	EB	CH_2ClCH_2Cl	70	60	98
8	EB	CH_2ClCH_2Cl	80	60	100

1-g) 7a and 8a by the Reaction of 4a′ with 6: Refer to the *1-c* procedure. See also Table 4. Yield (**7a**+**8a**), 36%.

1-h) 5- and 4-Methylbenzenediazonium-2-carboxylate Hydrochloride (2b and 4b): Diazonium salts, **2b** and **4b**, were prepared from the corresponding anthranilic acids by the same method as in *1-a*. Yields, 89% (**2b**) and 84% (**4b**).

1-i) 1,2,3,4,6,10,10-Heptamethyl-1,4-dihydro-1,4-ethanonaphthalen-9-one (7b) and Its 1,2,3,4,7,10,10-Heptamethyl Isomer (8b): See the *1-b* procedure, Run 1. The same mixture of the **7b**+**8b** adducts were obtained from either precursor **2b** or **4b**. Yields, 75—77%. The isomers could not be separated. $P^+(m/e)$ 268; NMR **7b**: *gem*-Me 0.48 and 1.03 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–Me 2.29 (3H), allylic Me 1.65—1.76 (6H), bridgehead Me 1.56 (6H), Ar–H 6.85—7.1 (3H) ppm. **8b**: all the chemical shifts, except that of Ar–Me at 2.31, are the same as those of **7b.** The **7b**/**8b** isomer ratios determined by the NMR integration (see the text) were 1.01 and 1.00 from **2b** and **4b** respectively.

2. Preparation and Reactions of Nitrobenzynes. The procedure reported in old literature[14–16] on the preparation of nitroanthranilic acids was insufficient to reproduce the same results reported therein. The present authors employed the following modified procedure, that gave the acids in better yields than those previously reported.

2-a) 6-Nitroanthranilic Acid (14) from 6-Nitrophthalamic Acid (13): Acid **13** (5.69 g, 27.1 mmol)[15] was slowly added to a NaOCl solution which had been prepared by mixing 17.6 g of a commercial grade NaOCl-solution containing 10% active Cl, 2.0 g of NaOH, and 10 ml water at 0 °C. The mixture was warmed at 82 °C for 30 min (gas evolution was observed), cooled, and acidified with HCl. "After removing the solids that precipitated at pH 4, the filtrate was evaporated. The residue was extracted with Et_2O to give **14**. The extraction residue was redissolved in dil NaOH, and the solution was acidified." The above procedure in quotation marks "—" was repeated three times. Yield, 1.68 g (34%); mp 185.5—189.5 °C.[17]

2-b) 3-Nitrobenzenediazonium-2-carboxylate Hydrochloride (4c) from 14: See the *1-a* procedure. **4c**: yellow-orange powder; yield, 69%; mp 110.5—111 °C (dec); IR ν(N≡N) 2190 cm^{-1} (Nujol). Avoid unnecessary impact by hammering or heating; otherwise, it detonates!

2-c) 1,2,3,4,10,10-Hexamethyl-5-nitro-1,4-dihydro-1,4-ethanonaphthalen-9-one (7c) and Its 8-Nitro Isomer (8c): See the *1-b* procedure. A mixture of **7c** and **8c** was obtained. They were purified through a silica gel column (benzene), but could not be separated. NMR **7c**: *gem*-Me 0.68 and 1.04 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 6.91—7.38 (3H), bridge-head Me 1.59 and 1.62 (3H each), allylic Me 1.71—1.84 (6H) ppm. **8c**: *gem*-Me 0.57 and 1.08 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 6.91—7.38 (3H), bridge-head Me 1.54 and 1.64 (3H each), allylic Me 1.71—1.84 (6H) ppm. **7c**/**8c** isomer ratio =1.44 (NMR), 1.50 (VPC). $P^+(m/e)$ 299; IR ν(C=O) 1730 and (NO_2) 1355 cm^{-1} (for both isomers in CCl_4); yield, 1.69 g (44%) after column chromatography.

2-d) 4-Nitro- and 5-Nitroanthranilic Acid (17 and 18): A mixture of 4- and 5-nitrophthalamic acid (**15** and **16**)[14] was treated with the NaOCl solution by the same method as in *2-a*. Cooling the reaction mixture separated needle-like precipitates. They were dissolved in water and acidified with HCl to pH 3—4, and the separated solid was washed with water, dried, and extracted with xylene by means of a Soxhlet apparatus for two days. The insoluble residue was recrystallized from aq EtOH ($EtOH/H_2O=1.0$ v/v) to give glistening yellow-green needles of **18** (48%): mp 275—283 °C (dec). The xylene solution was then evaporated to give **17** (32%) contaminated by **18**.

2-e) 5-Nitrobenzenediazonium-2-carboxylate Hydrochloride (2d): See the *2-b* procedure. Commercially available acid **17** was used. Here also caution should be taken when handling the dried powder of **2d**: yield, 90%; mp 128—130 °C (dec); IR ν(N≡N) 2230 cm^{-1}.

2-f) 1,2,3,4,10,10-Hexamethyl-6-nitro-1,4-dihydro-1,4-ethanonaphthalen-9-one (7d) and Its 7-Nitro Isomer (8d): See the *1-b* procedure. Yield (**7d**+**8d**), 61% after recrystallization from MeOH. The two isomers were separated mannually by the aid of a magnifying glass and recrystallized independently. **7d**: mp 158.5—159.5 °C; NMR *gem* Me 0.52 and 1.10 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 7.90—8.12 (2H, α to NO_2) 7.29 (H, β to NO_2), other Me's 1.64—1.80 (12H) ppm; IR ν(C=O, NO_2) 1730 and 1355 cm^{-1} (CCl_4); $P^+(m/e)$ 299. **8d**: mp 126—128 °C; NMR *gem*-Me 0.53 and 1.10 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 7.90—8.12 (2H, α to NO_2), 7.26 (H, β to NO_2), other Me's 1.64—1.80 (12H) ppm; the IR and $P^+(m/e)$ were the same as those of **7d**. For the isomer ratio, see Table 3.

*2-g) 4-Nitrobenzenediazonium-2-carboxylate Hydrochloride (**4d**)*: See *1-b*. Caution should be taken when handling **4d**. Yield, 67%; mp 119.5—120 °C (dec); IR $\nu(N{\equiv}N)$ 2210 cm^{-1}(Nujol).

*2-h) **7d** and **8d** by the Reaction of **4d** with **6***: See *1-b*, Run 1. Yield (**7d**+**8d**), 69%. For the isomer ratio, see Table 3.

3. Preparation and Reaction of 3-Chlorobenzyne.

*3-a) 6-Chlorobenzenediazonium-2-carboxylate Hydrochloride (**2e**) from 3-Chloroanthranilic Acid (**19**)*: Acid **19** was prepared from *o*-chloroaniline.[18,5] For the preparation of the diazonium salt **2e**, see *1-a*, Run 1. Yield, 92%; mp 146—148 °C; IR $\nu(N{\equiv}N)$ 2230 cm^{-1}.

*3-b) 1,2,3,4,10,10-Hexamethyl-5-chloro-1,4-dihydro-1,4-ethanonaphthalen-9-one (**7e**) and Its 8-Chloro Isomer (**8e**)*: A mixture of **7e** and **8e** was obtained by the method described in *1-b*. The two isomers were separated by column chromatography (silica gel; cyclohexane for **7e** and benzene for **8e**). The separated isomers were recrystallized independently from MeOH (the rate of crystallization of **8e** was slower than that of **7e**). Yield (**7e**+**8e**), 89%; isomer ratio, see Table 3. **7e**: mp 107—108 °C; NMR *gem*-Me 0.67 and 1.03 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 7.00—7.15 (3H), allylic Me 1.7—1.9 (6H), bridge-head Me 1.59 and 1.98 (3H each) ppm; $P^+(m/e)$ 289; IR $\nu(C{=}O)$ 1725 cm^{-1} (CCl_4). **8e**: mp 93—94 °C; NMR *gem*-Me 0.57 and 1.06 (3H each, Me's *syn* and *anti* to the benzene ring respectively), Ar–H 7.0—7.15 (3H), allylic Me 1.77 (6H), bridge-head Me 1.59 and 1.91 (3H each) ppm; the $P^+(m/e)$ and IR were the same as those of **7e**.

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