The Synthesis of Electron Donor-acceptor Substituted Pyrazoles

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A variety of 1,3- and 1,5-donor-acceptor substituted pyrazole derivatives have been synthesized by the cyclocondensation of α,β-ethynyl ketones with substituted phenyl hydrazines. The regioselectivity of the cyclization depends on the reaction conditions in a manner consistent with competitive 1,2- and 1,4-addition followed by ring closure. 1,4-Disubstituted derivatives can be prepared from the corresponding 4-iodopyrazole using palladium catalyzed carbon-carbon bond forming reactions. The pyrazole chromophores are expected to show interesting nonlinear optical properties.

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Introduction.

Five-membered heterocyclic azole derivatives comprise a much studied class of thermally and environmentally stable compounds with interesting chemical, spectroscopic and biological properities [1,2]. Within this class, the pyrazole ring system represents a thermally stable, quasi-aromatic ring system which resists ring opening and undergoes a variety of regioselective ring substitution reactions upon treatment with electrophilic reagents. Although very few pyrazole derivatives occur naturally, many are pharmacologically active and the class has received widespread attention [1]. Moreover, the substantial second order molecular hyperpolarizabilities of a number of simple derivatives [3] have suggested possible utility for a variety of nonlinear optical (NLO) applications [4]. It is the interesting NLO properties of this class which have led us to study new synthetic procedures for the preparation of donor-acceptor substituted, conjugation-extended pyrazole derivatives.

Although there are a plethora of synthetic methods applicable to the synthesis of pyrazole derivatives [1,2], the vast majority of techniques utilize the cyclocondensation of substituted hydrazines with a wide variety of β-dicarbonyl derivatives. However, since we were interested in the synthesis of unsymmetrical donor-acceptor substituted derivatives, ideally containing substituents which extend the conjugation path, the classical techniques often required inaccessible starting materials and/or suffered from poor regioselectivity upon ring closure. For example, although styryl substitution provides a common approach for conjugation extension, there are relatively few reports of styryl substituted pyrazoles [5-12]. For these reasons, we chose to study the cyclocondensation of aryl and substituted cinnamoyl α,β acetylenic ketones with hydrazines as a method for preparing donor-acceptor substituted, conjugation-extended pyrazoles.

Table I

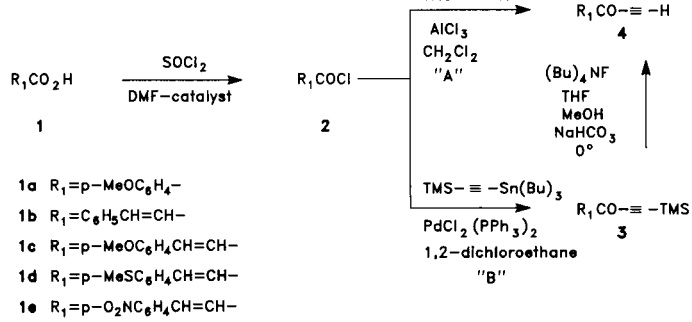
Preparation of α,β-Acetylenic Ketones

$R_1COCl \longrightarrow R_1CO{-}{\equiv}{-}H$
2 4

2		3		4		
2a	R_1=p-$MeOC_6H_4$-	3a	(70)	4a	-- [a]	70(B) [b]
2b	$R_1=C_6H_5CH=CH-$	--		4b	60(A) [a]	--
2c	R_1=p-$MeOC_6H_4CH=CH-$	3c	(66)	4c	50(A)	70(B)
2d	R_1=p-$MeSC_6H_4CH=CH-$	3d	(70)	4d	0(A)	68(B)
2e	R_1=p-$O_2NC_6H_4CH=CH-$	3e	(61)	4e	17(A)	65(B)

[a] Isolated yield using method A, Scheme I. [b] Isolated yield using method B, Scheme I.

Scheme I

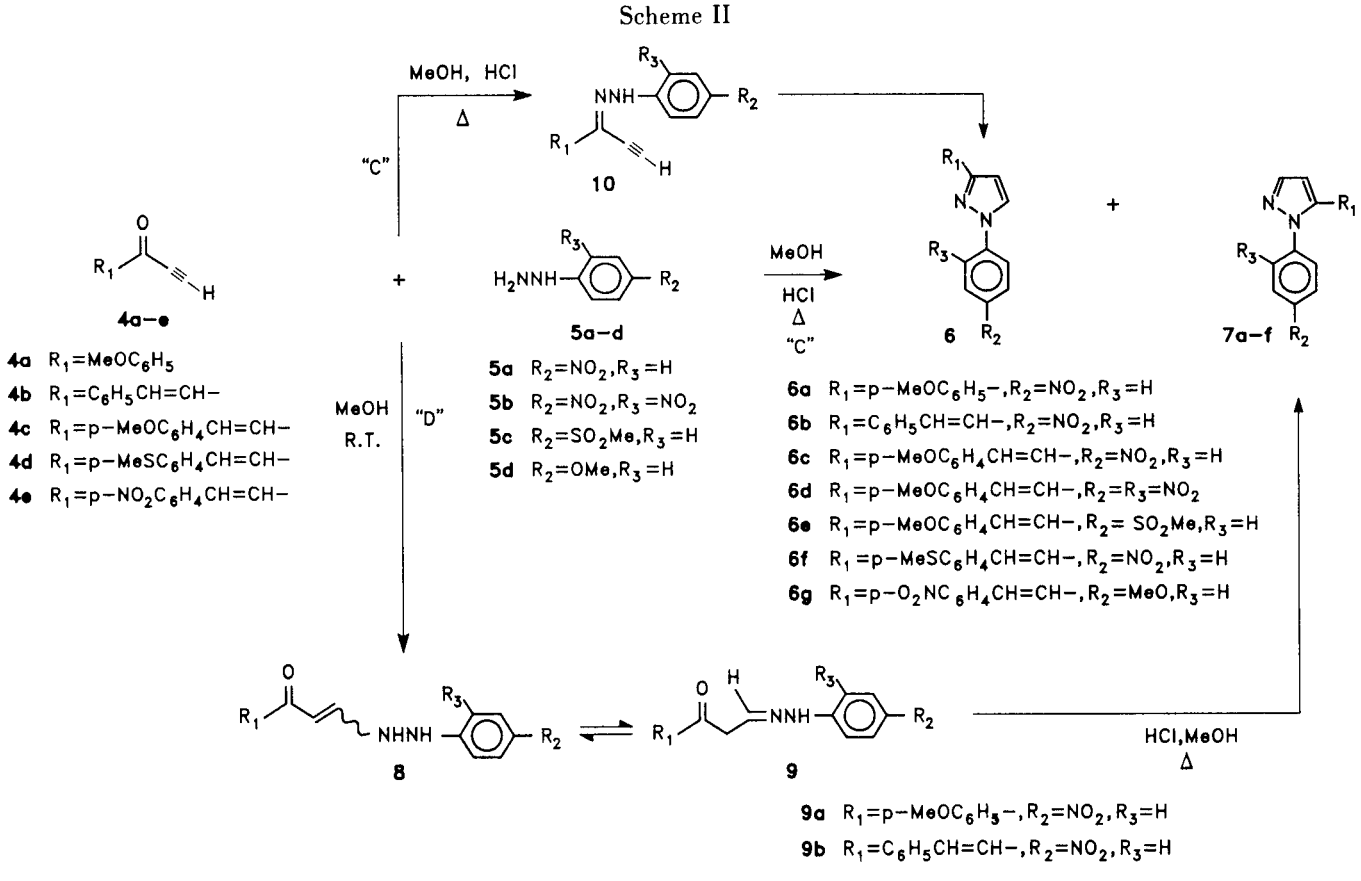


Results and Discussion.

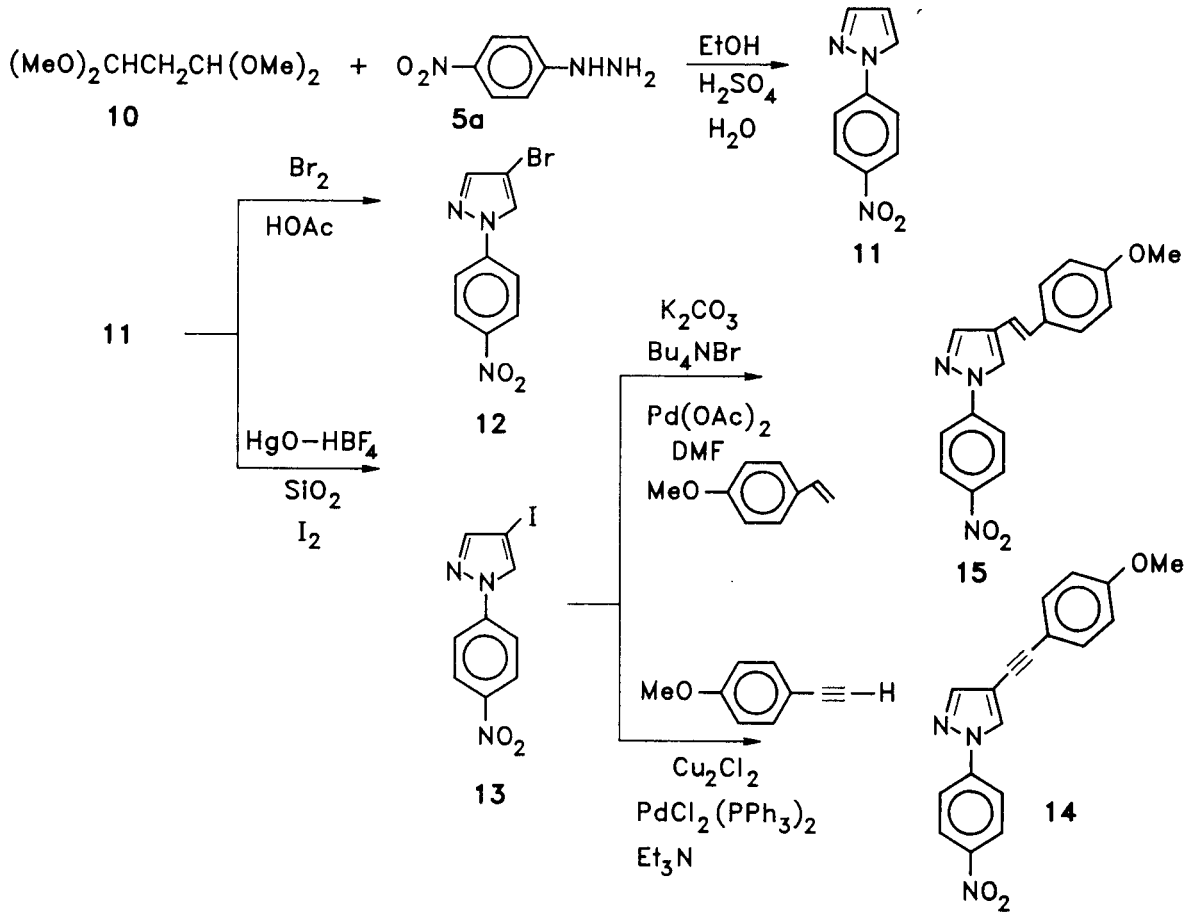
The reaction of α,β-acetylenic ketones with hydrazine derivatives produces hydrazones and pyrazoles [13]. The nature of the products generated vary with the type and position of the substituents and the reaction conditions employed. In our case, we have employed terminal acetylenic derivatives in an effort to better control the regioselectivity and to facilitate the ring closure. The desired acetylenic starting materials were prepared as shown in Scheme I and the results are tabulated in Table I. Since the electrophilic desilylation of bistrimethylsilylacetylene by acid chlorides in the presence of aluminum chloride to produce acyltrimethylsilylacetylenes has been described previously [14], we have extended this procedure using trimethylsilylacetylene to produce the unprotected terminal acetylenes directly (Method A). The yields are often moderate, but the procedure is simple and straightforward. In certain cases, however, this procedure either works poorly, **4e**, or not at all, **4d**. For these examples, changing the order of reagent addition (aluminum chloride added to the acetylene and acid chloride *vs* the acetylene added to the acid chloride-aluminum chloride) or the reaction temperature had little effect. Fortunately, Method B involving the palladium catalyzed coupling of the acid chloride with tributylstannyltrimethylsilylacetylene to produce first the silylated acetylene [15] followed by deprotection offers a viable alternative. Although this requires two synthetic steps, the yields are respectable for each transformation. The silylated ketones are easily deprotected using dilute base [15,16] or tetrabutylammonium fluoride with a bicarbonate buffer. In every case that we examined, Method B represented a viable synthetic alternative to direct electrophilic desilylation.

The condensation of the acetylenic ketones **4** with a variety of substituted phenylhydrazine derivatives produces pyrazoles in fair to good yield. The substituent pattern in the pyrazoles depended on the nature of substituents in the starting materials and particularly on the reaction conditions employed (see Scheme II and Table II). When the reactants are dissolved in a solvent such as methanol and stirred at room temperature for some time prior to the addition of acid and the application of heat (Method D), 1,5-disubstituted pyrazoles are the major products. If, however, acid is present and heat applied from the onset (Method C), a mixture of 1,3- and 1,5-substituted pyrazoles results. The isomers are easily separated by flash column chromatography [17] using methylene chloride as an eluant. With this solvent, the 1,3-derivatives always have a higher R_f value than the 1,5-substituted materials. The use of ethyl acetate and hexane as the

Scheme II



Scheme III

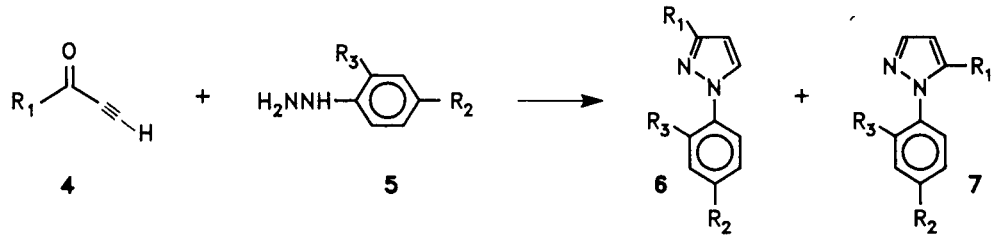


eluant leads to poor separation between the isomers. The individual pyrazole isomers are stable under the reaction conditions employed in Method D and no equilibration is observed.

The structures of the pyrazole derivatives are secured by their spectral and analytical data. The structure of **6c** was also verified by single crystal X-ray analysis [18]. From this data, it was confirmed that the molecule is practically planar and the confirguration around the external double bond was *E*. In the ^{1}H nmr spectra, the two five-membered pyrazole ring protons are distinctive and appear as doublets (J = 1.7-2.5 Hz). In both the 1,3- and 1,5-substituted derivatives, these resonances, are widely separated (8.1-8.8 *vs* 6.5-6.8 ppm) and within each isomeric pair, the pyrazole ring protons for the 1,3-derivatives are slightly downfield (δ = 0.05-0.35) relative to the comparable protons of the 1,5-isomers. For those materials containing styryl substituents (*i.e.*, **2b-e, 3c-e, 4b-e, 6b-g,** and **7b-f**), the *E* configuration of the double bond is indicated by the large proton coupling constants (J = 16-16.5 Hz). The uv spectra of the 1,3- and 1,5-derivatives are also remarkably different, with the long wavelength absorption maxima of the former consistently red-shifted by 50-60 nm relative to the corresponding 1,5-isomers (see Table III). This is presumably caused by substantial twisting of the substituents in the 1,5-derivatives to relieve unfavorable steric interactions [19,20], a hypothesis which is also supported by MM2 and MOPAC geometry calculations.

The variation in isomer composition with the reaction conditions is rationalized in Scheme II. Not surprisingly, in each case the terminal acetylene is selected over the internal olefin in the cyclization. In the absence of acid, the initial reaction apparently involves Michael addition of the more basic terminal nitrogen of the hydrazine derivative to the terminal acetylenic carbon to yield an enamine **8** which is expected to be in tautomeric equilibrium with the isomeric hydrazone **9**. Cyclization of this hydrazone in the presence of acid added subsequently yields exclusively the 1,5-substituted pyrazoles **7**. Insoluble intermediates with the hydrazone structure **9** were isolated and spectrally characterized in the reaction of **4a** and **4b** with *p*-nitrophenylhydrazine with no acid present. Similar intermediates have been reported by Baddar *et al.* [21] in the reaction of diarylacetylenic ketones (ArC≡CCOAr') with carboalkoxyhydrazine derivatives. Under our conditions, the

Table II
Preparation of Substituted Pyrazoles by Cyclocondensation



4 5 6 7

Entry	R_1	R_2	R_3	Reaction Conditions	Pyrazole Yield (%)	Products	
1a	$MeOC_6H_4-$	$-NO_2$	H	Method C [a]	84	**6a** (50) [c]	**7a** (50) [c]
1b				Method D [b]	74	**7a** (100)	
2a	$C_6H_5CH=CH-$	$-NO_2$	H	Method C	76	**6b** (39)	**7b** (61)
2b				Method D	86	**7b** (100)	
3a	$p-MeOC_6H_4CH=CH-$	$-NO_2$	H	Method C	60	**6c** (63)	**7c** (37)
3b				Method D	74	**7c** (100)	
4	$p-MeOC_6H_4CH=CH-$	$-NO_2$	$-NO_2$	Method C	55	**6d** (59)	**7d** (41)
5	$p-MeOC_6H_4CH=CH-$	SO_2Me	H	Method C	56	**6e** (83)	**7e** (17)
6a	$p-MeSC_6H_4CH=CH-$	$-NO_2$	H	Method C	60	**6f** (43)	**7f** (57)
6b				Method D	65	**7f** (100)	
7	$p-O_2NC_6H_4CH=CH-$	-OMe	H	Method C	45	**6g** (100)	

[a] Methanol, HCl, Δ, 15h. [b] Methanol, RT, 15h–HCl, Δ, 2h. [c] Pyrazole isomeric distribution.

hydrazones **9a** and **9b** cleanly produced the 1,5-substituted pyrazoles **7a** and **7b**, respectively upon treatment with acid with no trace of the corresponding 1,3-substituted pyrazoles. When acid is present from the onset, hydrazone formation apparently competes with the Michael addition and the hydrazone cyclizes to the corresponding 1,3-disubstituted pyrazole **6**. A similar pathway has been proposed by Coispeau and Elguero [22] to explain the pyrazole product distribution from the reaction of 1,3-diphenylprop-2-yn-1-one with 2,4-dinitrophenylhydrazine.

Consistently, a small amount of red solid which precipitates early in the reaction of **4d** with *p*-nitrophenylhydrazine in methanol containing a drop of hydrochloric acid was tentatively identified as the corresponding hydrazone formed by 1,2-addition to the carbonyl followed by dehydration (ir, ^1H nmr and ^{13}C nmr indicated the presence of NH, $-C\equiv CH$ and $C=N-$). This material was subsequently converted under the reaction conditions to **6f** (none of the 1,5-isomer **7f** was detected by tlc), although the transformation was not as clean overall as observed for the reaction of **9a** and **9b** to the corresponding pyrazoles **7a** and **7b**. The cyclization of the hydrazone to **6f** is accompanied by the formation of a small amount of a unidentified yellow material with a slightly higher R_f (methylene chloride) than the pyrazole **6f**.

Table III
Solution UV Spectra Data of Substituted Pyrazoles

Pyrazole	λ_{max} (nm) [a]	Pyrazole	λ_{max} (nm) [a]
6a	352 [b]	**7a**	296 [b]
6b	356	**7b**	300
6c	364 [c]	**7c**	302 [c]
6d	375 [c]	**7d**	306
6e	328 [c]	**7e**	326
6f	365	**7f**	312,333 (sh)
6g	370 [c]	14	340
		15	362

[a] Measured in p-dioxane unless otherwise noted. [b] Ethanol. [c] Acetonitrile.

While the pathways described in Scheme II seem reasonable and are supported by experimental evidence, our results are somewhat different than those reported by Engelmann and Kirmse [23] for the reaction of 1-phenyl-2-propyn-1-one with phenylhydrazine. These authors report the initial Michael addition of the anilino nitrogen in neutral media and subsequent acid-catalyzed cyclization to 1,3-diphenylpyrazole. Perhaps it is the strongly electron donating and attracting substituents present in our systems which alter the reaction pathway.

Finally, the 1-nitrophenyl-4-substituted pyrazoles **14** and **15** could be prepared as described in Scheme III. 1-Nitrophenylpyrazole **11** was regioselectively halogenated with bromine [24] to yield the respective 4-bromo derivative **12**. Attempts to halogenate **11** directly with iodine were unsuccessful. However, the use of iodine in the presence of mercuric tetrafluoroborate adsorbed on silica gel [25] produced the iodide **13** regioselectively and in good yield. The desired acetylenic and styrenyl substituted derivatives **14** and **15** could be prepared from **13** using standard palladium catalyzed carbon-carbon bond forming reactions [26-28] (see Scheme III). The bromide **12** was unreactive under these conditions.

In summary, a variety of donor-acceptor substituted, conjugation-extended pyrazole derivatives have been prepared. 1,3- and 1,5-disubstituted pyrazoles can be prepared directly from the corresponding α,β-acetylenic ketones by condensation with substituted phenyl hydrazine derivatives. The ratio of 1,3- to 1,5-substituted products can be controlled by varying the reaction conditions in a manner consistent with the proposal of competitive 1,2- *vs* 1,4-addition of the substituted phenyl hydrazine reactant prior to cyclization. 1,4-Substituted pyrazoles can be prepared from the 4-iodopyrazoles by palladium-catalyzed ethynylation or olefination. The donor-acceptor substituted pyrazole derivatives are expected to show enhanced nonlinear second order hyperpolarizabilities and other interesting NLO effects. These studies are currently in progress.

EXPERIMENTAL

All nuclear magnetic resonance (nmr) spectra were recorded on an IBM-Bruker AF-250 machine operating at 250 MHz for proton and 62.9 MHz for carbon and are referenced relative to tetramethylsilane as a standard. Infrared (ir) spectra were taken on an IBM Instruments IR-32 FT machine. Ultraviolet (uv) spectra were recorded using a Hewlett-Packard 8550A diode array instrument. Solvents were routinely dried prior to use. The substituted cinnamoyl chlorides were prepared from the respective cinnamic acids by treatment with thionyl chloride and a catalytic amount of dry DMF. The crude acid chlorides were purified by recrystallization before use.

Preparation of α,β-Acetylenic Ketones.

General Procedure: Method A (Scheme I).

Into a flask under nitrogen was placed 133.4 mg (1 mmole) of aluminum chloride and 10 ml of dry methylene chloride. To this slurry cooled to $-40°$, was added a mixture of 1 mmole of the corresponding acid chloride dissolved in 10-15 ml of methylene chloride over a period of 0.5 hour. The reaction mixture was maintained at this temperature with stirring for 1 hour and allowed to warm slowly to $-10°$ over 3 hours. At this point, 10 g of ice was added, the reaction mixture was diluted with additional methylene chloride, and the organic phase washed successively with 10% hydrochloric acid, saturated sodium bicarbonate and dried over sodium sulfate. After removal of the solvent, the crude product was purified by flash column chromatography [17] on silica gel and recrystallized.

p-Methoxyphenylethynyl Ketone (**4a**).

This material was isolated in 46% yield as colorless crystals, 75 mg, mp 85-87°, lit 82-83° [27]; ir (chloroform) 3299, 2843, 1645, 1597, 1575, 1257 and 1167 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.15 (d, J = 8.8 Hz, 2H), 7.0 (d, J = 8.8 Hz, 2H), 3.92 (s, 3H), 3.40 (s, 1H); ^{13}C nmr (chloroform-d_1): δ 176.6, 164.7, 132.1, 129.5, 80.3, 79.9 and 55.5.

5-Phenylpent-4-(*E*)-en-1-yn-3-one (**4b**).

This material was isolated in 60% yield as colorless crystals (94 mg) by flash chromatography using 10% ethyl acetate-hexane as the eluant, mp 64.5-66.5°, lit 64° [14]; ir (chloroform): 3298, 2103, 1638, 1599, 1242 and 977 cm^{-1}; ^1H nmr (chloroform-d_1): δ 7.91 (d, J = 16.2 Hz, 1H), 7.58-7.69 (m, 2H), 7.40-7.50 (m, 3H), 6.82 (d, J = 16.2 Hz, 1H), 3.37 (s, 1H); ^{13}C nmr (chloroform-d_1): δ 177.5, 149.6, 133.7, 131.3, 129.0, 128.7, 127.9, 79.8 and 79.2.

5-(4'-Methoxyphenyl)pent-4-(*E*)-en-1-yn-3-one (**4c**).

This material was isolated in 50% yield (93 mg) by flash chromatography using 20% ethyl acetate-hexane as colorless crystals, mp 92-95°; ir (chloroform): 3300, 2101, 1645, 1597, 1574, 1258 and 1167 cm^{-1}; ^1H nmr (chloroform-d_1): δ 7.85 (d, J = 15.8 Hz, 1H), 7.53 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.70 (d, J = 15.8 Hz, 1H), 3.86 (s, 3H) and 3.27 (s, 1H); ^{13}C nmr (chloroform-d_1): δ 177.7, 162.4, 149.6, 130.7, 126.6, 125.5, 114.6, 80.1, 78.9 and 55.4.

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.25; H, 5.52.

5-(4'-Nitrophenyl)pent-4-(*E*)-en-1-yn-3-one (**4e**).

This material was isolated by flash column chromatography using methylene chloride-hexane (1:1) as the eluant in 17% yield (34 mg) as pale yellow crystals, mp 110-114°; ^1H nmr (chloroform-d_1): δ 8.02 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 15.8 Hz, 1H), 6.89 (d, J = 15.8 Hz, 1H) and 3.40 (s, 1H); ^{13}C nmr (chloroform-d_1): δ 176.7, 149.0, 145.7, 139.8, 131.2, 129.2, 124.3, 80.2, 79.7; hrms: Calcd. for $C_{11}H_7NO_3$: 201.0426. Found: 201.0432.

Anal. Calcd. for $C_{11}H_7NO_3$: C, 65.67; H, 3.51. Found: C, 65.67; H, 3.84.

Coupling of Acid Chlorides with 1-Trimethylsilyl-2-tributylstannylacetylene.

General Procedure: Method B (Scheme I).

Into a three-necked flask under argon was placed 10 mmoles of the acid chloride, 10 mmoles of 1-trimethylsilyl-2-tributylstannylacetylene, 50 ml of 1,2-dichloroethane and 100 mg of palladium chloride bistriphenylphosphine. The homogeneous reaction mixture was refluxed for 3 hours, cooled and diluted with 200 ml of

ether. The organic layer was stirred vigorously with 30 ml of saturated, aqueous potassium fluoride, filtered through Celite, washed with water and dried over sodium sulfate. After stripping the solvent, the crude products were purified by flash column chromatography (silica gel, ethyl acetate-hexane).

1-Trimethylsilyl-5-(4'-methoxyphenyl)pent-4-(*E*)-en-1-yn-3-one (**3c**).

This material was isolated as a colorless oil in 66% yield (1.7 g) by flash column chromatography using 10% ethyl acetate-hexane as the eluant; ir (neat): 1627, 1601, 1572, 1513, 1251, 1240, 1171, 873, 859, 846 and 828 cm^{-1}; ^1H nmr (chloroform-d_1): δ 7.74 (d, J = 16 Hz, 1H), 7.48 (d, J = 9.7 Hz, 2H), 6.88 (d, J = 9.7 Hz, 2H), 6.6 (d, J = 16 Hz, 1H), 3.8 (s, 3H) and 0.22 (s, 9H); ^{13}C nmr (chloroform-d_1): δ 177.8, 162.1, 148.8, 130.5, 126.5, 125.9, 114.5, 100.7, 97.9, 55.3 and −0.70.

Anal. Calcd. for $C_{15}H_{18}O_2Si$: C, 69.73; H, 7.02. Found: C, 69.56; H, 7.38.

1-Trimethylsilyl-5-(4'-thiomethylphenyl)pent-4-(*E*)-en-1-yn-3-one (**3d**).

This material was isolated in 70% yield (1.9 g) by flash column chromatography using 15% ethyl acetate-hexane as the eluant, mp 76.5-77.5°; ir (chloroform): 2150, 1622, 1589, 1254, 1093, 874 and 849 cm^{-1}; ^1H nmr (chloroform-d_1): δ 7.79 (d, J = 15 Hz, 1H), 7.49 (d, J = 7.7 Hz, 2H), 7.25 (d, J = 7.7 Hz, 2H), 6.73 (d, J = 15 Hz, 1H), 2.51 (s, 3H) and 0.30 (s, 9H); ^{13}C nmr (chloroform-d_1): δ 177.8, 148.3, 143.4, 130.2, 128.9, 127.1, 125.7, 106.6, 98.4, 14.9 and −0.73; hrms: Calcd. for $C_{15}H_{18}OSSi$: 274.0848. Found: 274.0856.

Anal. Calcd. for $C_{15}H_{18}OSSi$: C, 65.65; H, 6.61; S, 11.68. Found: C, 65.52; H, 6.67; S, 12.08.

1-Trimethylsilyl-5-(4'-nitrophenyl)pent-4-(*E*)-en-1-yn-3-one (**3e**).

This material was isolated in 61% yield (1.68 g) by flash column chromatography using 15% ethyl acetate-hexane as the eluant, mp 108-111.5°; ir (chloroform): 2964, 2158, 1634, 1599, 1526, 1348, 873 and 847 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.27 (d, J = 8.8 Hz, 2H), 7.81 (d, J = 16 Hz, 1H), 7.71 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 16 Hz, 1H) and 0.32 (s, 9H); ^{13}C nmr (chloroform-d_1): δ 1770.0, 148.8, 144.8, 139.9, 131.3, 129.1, 124.1, 100.2, 100.0 and −0.80; hrms: Calcd. for $C_{14}H_{15}NO_3Si$: 273.0821. Found: 273.0812.

Anal. Calcd. for $C_{14}H_{15}NO_3Si$: C, 61.51; H, 5.53. Found: C, 61.31; H, 5.18.

Preparation of α,β-Acetylenic Ketones.

General Procedure: Method B (Scheme I).

Into a flask was placed 10 mmoles of the trimethylsilylacetylenic ketone, 25 ml of tetrahydrofuran, 1.7 ml of methanol and 1.72 g of sodium bicarbonate. After cooling to 0°, 12.3 ml of a 1.0 *M* solution of tetrabutylammonium fluoride in tetrahydrofuran was added, and the reaction was stirred for 5 minutes. At this point, 100 ml of ether was added and the organic layer was washed with water and dried over sodium sulfate. The crude products were purified by flash column chromatography (hexane-ethyl acetate).

5-(4'-Thiomethylphenyl)pent-4-(*E*)-en-1-yn-3-one (**4d**).

This material was isolated in 68% yield (1.37 g) by flash column chromatography using 15% ethyl acetate-hexane as the eluant, mp 102-103°; ir (chloroform): 3298, 2927, 2103, 1631, 1590 and 1093 cm^{-1}; ^1H nmr (chloroform-d_1): δ 7.82 (d, J = 16 Hz, 1H), 7.5 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 6.75 (d, J = 16 Hz, 1H), 3.32 (s, 1H) and 2.5 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 177.4, 149.0, 143.8, 130.1, 129.0, 126.8, 125.7, 79.9, 79.1 and 14.8.

Anal. Calcd. for $C_{12}H_{10}OS$: C, 71.26; H, 4.98. Found: C, 71.08; H, 5.01.

Preparation of the Substituted Pyrazoles.

General Procedure: Method C (Scheme II).

Into a flask under nitrogen was placed 1 mmole of the acetylenic ketone, 1 mmole of the substituted phenylhydrazine, 5-10 ml of methanol and 2 drops of concentrated hydrochloric acid. The slurry was stirred 2 hours at room temperature. At this point, two more drops of concentrated hydrochloric acid were added and the mixture refluxed for 2 hours. After cooling, any precipitate was filtered and the filtrate evaporated. The residue was purified by flash column chromatography over silica gel using methylene chloride as the eluant and the combined fractions recrystallized. Similarly, the precipitated solid was purified by flash column chromatography if necesary.

1-(4'-Nitrophenyl)-3-(*p*-methoxyphenyl)pyrazole (**6a**).

This material was isolated in 42% yield (124 mg) by flash column chromatography using methylene chloride as the eluant, mp 197-198.2°; ir (chloroform): 2938, 2839, 1613, 1599, 1514, 1338 and 854 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.38 (d, J = 9.2 Hz, 2H), 8.08 (d, J = 2.6 Hz, 1H), 7.97 (d, J = 9.2 Hz, 2H), 7.89 (d, J = 9.1 Hz, 2H), 7.01 (d, J = 9.1 Hz, 2H), 6.82 (d, J = 2.6 Hz, 1H) and 3.89 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 160.0, 154.2, 144.8, 144.3, 128.1, 127.2, 125.3, 124.8, 118.6, 114.1, 106.4 and 55.2; uv (ethanol): λ max (ϵ) 237 (843), 267 (10,434), 270 (10, 227), 298 (4246) and 352 (16, 736) nm.

Anal. Calcd. for $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.44; N, 14.23. Found: C, 64.74; H, 4.34; N, 13.87.

1-(4'-Nitrophenyl)-5-(*p*-methoxyphenyl)pyrazole (**7a**).

This material was isolated in 42% yield (124 mg) by flash column chromatography using methylene chloride as the eluant, mp 101-103°; ir (chloroform): 1620, 1590, 1539, 1500, 1340, 1250 and 860 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.19 (d, J = 9.0 Hz, 2H), 7.78 (d, J = 1.9 Hz, 1H), 7.50 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 6.5 (d, J = 1.9 Hz, 1H) and 3.83 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 160.0, 145.7, 144.9, 143.4, 141.6, 130.1, 124.5, 124.3, 122.1, 114.2, 109.1 and 55.2; uv (ethanol): λ max (ϵ) 246 (11, 666), 296 (9750) nm: hrms: Calcd. for $C_{16}H_{13}N_3O_3$: 295.0957. Found: 295.0950.

Anal. Calcd. for $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.44; N, 14.23. Found: C, 64.82; H, 4.55; N, 14.56.

1-(4'-Nitrophenyl)-3-(β-styryl)pyrazole (**6b**).

This material was isolated in 30% yield (187 mg) by flash column chromatography using methylene chloride, mp 184-186°; ir (chloroform): 1598, 1521, 1506, 1340, 1113, 1048, 945 and 855 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.34 (d, J = 9.2 Hz, 2H), 7.99 (d, J = 2.8 Hz, 1H), 7.88 (d, J = 9.2 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.16-7.47 (m, 5H) and 6.78 (d, J = 2.8 Hz, 1H); ^{13}C nmr (chloroform-d_1): δ 153.7, 144.9, 143.7, 136.6, 132.3, 128.6, 128.0, 127.8, 126.5, 125.2, 119.4, 117.9 and 106.6; uv (dioxane): λ max (ϵ) 226 (23, 487), 289 (18, 621), 309 (15, 757) and 356 (32, 720) nm.

Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.08; H, 4.50; N, 14.43. Found: C, 69.60; H, 4.46; N, 14.37.

1-(4'-Nitrophenyl)-5-(β-styryl)pyrazole (**7b**).

This material was isolated in 46% yield (136 mg) by flash column chromatography using methylene chloride as the eluant, mp 138-140°; ir (chloroform): 2999, 1610, 1598, 1522, 1502, 1389, 1346, 1111, 1093 and 860 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.40 (d, J = 9.2 Hz, 2H), 7.65-8.77 (m, 3H), 7.29-7.51 (m, 5H), 7.18 (d, J = 16.2 Hz, 1H), 6.92 (d, J = 16.2 Hz, 1H) and 6.71 (d, J = 1.8 Hz, 1H); ^{13}C nmr (chloroform-d_1): δ 146.3, 144.5, 141.7, 141.6, 135.8, 133.5, 128.8, 128.7, 126.7, 124.8, 124.9, 114.7 and 105.9; uv (dioxane): λ max (ε) 223 (16, 858) and 300 (28, 142) nm; hrms: Calcd. for $C_{17}H_{13}N_3O_2$: 291.1008. Found: 291.1013.

Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.08; H, 4.50; N, 14.43. Found: C, 69.64; H, 4.48; N, 14.08.

1-(4'-Nitrophenyl)-3-(*p*-methoxy-β-styryl)pyrazole (**6c**).

This material was isolated in 38% yield (122 mg) by flash column chromatography using methylene chloride as the eluant, mp 178-180°; ir (potassium bromide): 1595, 1528, 1506, 1503, 1383, 1336, 1324, 1307, 1294, 1254, 1178, 1111, 1084, 1045, 1027, 941, 854, 852 and 749 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.33 (d, J = 8.9 Hz, 2H), 7.98 (d, J = 8.9 Hz, 2H), 7.98 (d, J = 2.7 Hz, 1H), 7.48 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 7.18 (d, J = 16.2 Hz, 1H), 7.05 (d, J = 16.2 Hz, 1H), 6.73 (d, J = 2.7 Hz, 1H), and 3.84 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 159.8, 152.2, 145.0, 144.3, 132.1, 129.3, 128.1, 128.0, 125.4, 118.0, 117.4, 114.2, 106.7 and 55.3; uv (acetonitrile): λ max (ε) 295 (30, 800) and 364 (34, 900) nm.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.70; N, 13.07. Found: C, 67.07; H, 4.79; N, 13.09.

1-(4'-Nitrophenyl)-5-(*p*-methoxy-β-styryl)pyrazole (**7c**).

This material was isolated in 23% yield (74 mg) by flash column chromatography using methylene chloride as the eluant, mp 154-156°; ir (chloroform): 1600, 1523, 1512, 1502, 1345, 1255, 1160, 1080 and 1020 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.35 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 1.8 Hz, 1H), 7.34 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 16.1 Hz, 1H), 6.73 (d, J = 16.1 Hz, 1H), 6.63 (d, J = 1.8 Hz, 1H) and 3.84 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 159.8, 146.2, 144.7, 142.0, 141.6, 133.2, 128.6, 128.0, 124.8, 124.7, 114.3, 112.5, 105.5 and 55.3; uv (dioxane): λ max (ε) 211 (17, 311) and 302 (28, 819) nm; hrms: Calcd. for $C_{18}H_{15}N_3O_3$: 321.1113. Found: 321.1078.

1-(2',4'-Dinitrophenyl)-3-(*p*-methoxy-β-styryl)pyrazole (**6d**).

This material was isolated in 33% yield (121 mg) by flash column chromatography using methylene chloride as the eluant, mp 178.5-180.5°; ir (potassium bromide): 3131, 3087, 1606, 1574, 1522, 1389, 1347, 1304, 1258, 1240, 1175, 1153, 1071, 1027, 965, 943, 913, 831, 762 and 745 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.33 (ABX, δ_A = 8.48, δ_B = 7.85, δ_X = 8.65, J_{AB} = 8.9 Hz, J_{AX} = 2.4 Hz, 3H), 7.72 (d, J = 2.7 Hz, 1H), 7.44 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.9 Hz, 2H), 7.13 (d, J = 16.8 Hz, 1H), 6.96 (d, J = 16.8 Hz, 1H), 6.74 (d, J = 2.7 Hz, 1H) and 3.83 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 159.9, 155.4, 144.9, 142.4, 137.1, 132.1, 130.4, 129.1, 128.1, 127.4, 125.0, 121.2, 116.8, 114.2, 107.4 and 55.3; uv (acetonitrile): λ max (ε) 294 (32, 285) and 375 (19, 286) nm.

Anal. Calcd. for $C_{18}H_{14}N_4O_5$: C, 59.02; H, 3.85; N, 15.29. Found: C, 59.07; H, 3.92; N, 15.38.

1-(2',4'-Dinitrophenyl)-5-(*p*-methoxy-β-styryl)pyrazole (**7d**).

This material was isolated in 23% yield (84 mg) using flash column chromatography using methylene chloride as the eluant, mp 171-173°; ir (potassium bromide): 1606, 1535, 1513, 1389, 1347, 1307, 1302, 1294, 1253, 1177, 1027, 967, 934, 927, 914, 852, 834, 820, 797 and 744 cm^{-1}; ^1H nmr (chloroform-d_1): δ (ABX, δ_A = 8.57, δ_B = 7.78, δ_X = 8.82, J_{AB} = 8.8 Hz, J_{AX} = 2.5 Hz, 3H), 7.72 (d, J = 1.8 Hz, 1H), 7.33 (d, J = 8.9 Hz, 2H), 6.86 (d, J = 8.9 Hz, 2H), 7.08 (d, J = 16.2 Hz, 1H), 6.56 (d, J = 16.2 Hz, 1H), 6.68 (d, J = 1.8 Hz, 1H) and 3.81 (s, 3H); ^{13}C nmr (acetone-d_6): δ 161.0, 147.6, 146.6, 143.8, 143.1, 137.8, 134.5, 130.9, 129.5, 129.0, 128.7, 121.8, 114.8, 112.0, 105.3 and 55.4; uv (dioxane): λ max (ε) 306 (28, 867) nm.

Anal. Calcd. for $C_{18}H_{14}N_4O_5$: C, 59.02; H, 3.85; N, 15.29. Found: C, 58.62; H, 3.79; N, 15.21.

1-(4'-Methylsulfonylphenyl)-3-(*p*-methoxy-β-styryl)pyrazole (**6e**).

This material was isolated in 47% yield (166 mg) by flash chromatography using methylene chloride as the eluant, mp 233-235°; ^1H nmr (chloroform-d_1): δ 8.02 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 8.8 Hz, 2H), 7.94 (d, J = 2.7 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 16.2 Hz, 1H), 7.02 (d, J = 16.2 Hz, 1H), 6.91 (d, J = 8.5 Hz, 2H, 6.73 (d, J = 2.7 Hz, 1H), 3.84 (s, 3H) and 3.09 (s, 3H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 159.4, 153.3, 142.9, 137.4, 131.7, 129.7, 129.2, 128.9, 128.1, 118.0, 117.6, 114.3, 106.4, 55.2 and 43.7; uv (acetonitrile): λ max (ε) 281 sh (11, 797) and 328 (33, 706) nm; hrms: Calcd. for $C_{19}H_{18}N_2O_3S$: 354.1038. Found: 354.1058.

Anal. Calcd. for $C_{19}H_{18}N_2O_3S$: C, 64.39; H, 5.12; N, 7.90. Found: C, 64.49; H, 5.18; N, 7.93.

1-(4'-Methylsulfonylphenyl)-5-(*p*-methoxy-β-styryl)pyrazole (**7e**).

This material was isolated in 10% yield (35 mg) by flash column chromatography using methylene chloride as the eluant, mp 179-181.5°; ir (potassium bromide): 1606, 1599, 1596, 1512, 1497, 1389, 1310, 1298, 1290, 1259, 1176, 1150, 970, 925, 823, 779, 565 and 539 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.09 (d, J = 7.3 Hz, 2H), 7.77 (d, J = 7.3 Hz, 2H), 7.70 (d, J = 1.8 Hz, 1H), 7.38 (d, J = 8.8 Hz, 2H), 7.10 (d, J = 16.3 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 16.3 Hz, 1H), 6.65 (d, J = 1.8 Hz, 1H), 3.82 (s, 3H) and 3.11 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 160.0, 143.9, 141.9, 141.5, 139.0, 133.0, 128.6, 128.0, 125.3, 114.2, 112.5, 105.0, 55.3 and 44.5; uv (dioxane): λ max (ε) 230 (8, 838), 280 (19, 198) and 326 (21, 962) nm.

Anal. Calcd. for $C_{19}H_{18}N_2O_3S$: C, 64.39; H, 5.12; N, 7.91; S, 9.03. Found: C, 64.16; H, 5.25; N, 7.83; S, 8.86.

1-(4'-Nitrophenyl)-3-(*p*-methylthio-β-styryl)pyrazole (**6f**).

This material was isolated in 26% yield (88 mg) by flash column chromatography using methylene chloride as the eluant, mp 150-153°; ir (chloroform): 2298, 2926, 1597, 1522, 1502, 1388, 1345, 1112, 965, 924 and 858 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.32 (d, J = 9.2 Hz, 2H), 8.01 (d, J = 2.8 Hz, 1H), 7.86 (d, J = 9.2 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.15 (s, 2H), 6.77 (d, J = 2.8 Hz, 1H), 6.76 (d, J = 8.5 Hz, 2H) and 2.15 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 153.9, 145.1, 144.2, 138.8, 133.3, 131.8, 128.0, 127.0, 126.4, 125.4, 118.8, 118.0, 106.8 and 15.6; uv (dioxane): λ max (ε) 306 (19, 489), 332 (19, 808) and 365 (31, 373) nm.

Anal. Calcd. for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45; S, 9.50. Found: C, 63.64; H, 4.71; N, 12.29; S, 9.80.

1-(4'-Nitrophenyl)-5-(*p*-methylthio-β-styryl)pyrazole (**7f**).

This material was isolated in 34% yield (115 mg) by flash column chromatography using methylene chloride as the eluant, mp

176-179°; ir (chloroform): 3089, 2859, 1598, 1524, 1502, 1389, 1345, 1090 and 860 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.38 (d, J = 8.8 Hz, 2H), 7.64-7.86 (m, 3H), 7.37 (d, J = 8.7 Hz, 2H), 7.21 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 16.2 Hz, 1H), 6.84 (d, J = 16.2 Hz, 1H), 6.67 (d, J = 1.5 Hz, 1H) and 2.50 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 158.5, 146.0, 144.5, 141.7, 139.7, 132.9, 132.5, 127.0, 126.3, 124.8, 124.7, 113.8, 105.7 and 15.4; uv (dioxane): λ max (ε) 312 (31, 719) and 333 sh (28, 906) nm; hrms: Calcd. for $C_{18}H_{15}N_3O_2S$: 337.0885. Found: 337.0889.

Anal. Calcd. for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45; S, 9.50. Found: C, 63.74; H, 4.55; N, 12.19; S, 9.57.

1-(4'-Methoxyphenyl)-3-(*p*-nitro-β-styryl)pyrazole (**6g**).

This material was isolated in 45% yield (144 mg) by flash column chromatography using methylene chloride as the eluant, mp 158-161°; ^1H nmr (chloroform-d_1): δ 8.22 (d, J = 8.6 Hz, 2H), 7.83 (d, J = 2.5 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 9.1 Hz, 2H), 6.99 (d, J = 9.1 Hz, 2H), 7.38 (d, J = 16.5 Hz, 1H), 7.20 (d, J = 16.5 Hz, 1H), 6.70 (d, J = 2.5 Hz, 1H) and 3.86 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 158.5, 150.6, 146.8, 143.7, 133.5, 128.3, 127.9, 126.8, 125.0, 124.2, 120.8, 114.6, 105.4 and 55.6; uv (acetonitrile): λ max (ε) 277 (17, 250) and 370 (26, 688) nm; hrms: Calcd. for $C_{18}H_{15}N_3O_3$: 321.1113. Found: 321.1081.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.70; N, 13.08. Found: C, 67.37; H, 4.93; N, 13.20.

General Procedure for the Preparation of 1,5-Disubstituted Pyrazoles: Method D (Scheme II).

Into a flask under nitrogen was placed 1 mmole of the acetylenic ketone, 1 mmole of a substituted phenylhydrazine and 5-10 ml of methanol. The reaction mixture was stirred vigorously at room temperature for 15 hours. At this point, 2-3 drops of concentrated hydrochloric acid was added and the reaction mixture was refluxed for 3-6 hours. The methanol was removed under vacuum and the residue dissolved in methylene chloride. The organic solution was washed with saturated sodium bicarbonate and dried over sodium sulfate. Examination (tlc) of the reaction mixture (methylene chloride) showed that very little 1,3-disubstituted pyrazole was produced using this procedure with the major product being the 1,5-disubstituted pyrazole derivatives. Further purification was effected by flash column chromatography using methylene chloride. Depending on the starting material, a precipitate was often present after the room temperature reaction. These materials were clearly precursors to the corresponding 1,5-disubstituted pyrazoles upon treatment with acid. In a number of cases these intermediates were actually isolated and identified as hydrazone derivatives.

2-(*p*-Methoxybenzoylacetaldehyde)-*p*-nitrophenylhydrazone (**9a**).

A 50 ml flask was charged with 67.5 mg (0.42 mmole) of *p*-methoxybenzoylacetylene, 71.6 mg (0.42 mmole, 98% pure) *p*-nitrophenylhydrazine and 5 ml of methanol. The mixture was stirred for 12 hours at room temperature and the precipitate filtered and washed with methylene chloride (58 mg), 50% yield, mp 152-154° dec; ir (potassium bromide): 3287, 1655, 1605, 1579, 1546, 1487, 1423, 1328, 1273, 1225, 1220, 1181, 1125, 1111, 1089, 992, 836, 835, 751 cm^{-1}; ^1H nmr (tetrahydrofuran-d_8): δ 9.40 (s, 1H), 7.93 (d, J = 9.2, 16.5 Hz, 4H), 7.41 (t, J = 5.5 Hz, 1H), 6.90 (d, J = 9.2 Hz, 4H), 3.91 (d, J = 5.5 Hz, 2H), 3.78 (s, 3H); ^{13}C nmr (tetrahydrofuran-d_8): δ 195.0, 164.9, 151.9, 140.8, 140.2, 131.1, 130.4, 126.5, 114.5, 111.4, 55.7, 42.1; hrms: Calcd. for $C_{16}H_{15}N_3O_4$: 313.1063. Found: 295.0952 (P-H_2O, $C_{16}H_{13}N_3O_3$).

Anal. Calcd. for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 14.41. Found: C, 60.89; H, 4.91; N, 14.30.

2-Cinnamoylacetaldehyde-*p*-nitrophenylhydrazone (**9b**).

A flask was charged with 156.2 mg (1 mmole) of cinnamoyl acetylene, 153 mg (1 mmole) *p*-nitrophenylhydrazine and 5 ml of methanol. The mixture was stirred 12 hours at 25° and filtered (216 mg, 70% yield, orange solid), mp 160-162° dec; ir (potassium bromide): 3268, 1650, 1626, 1601, 1576, 1550, 1501, 1482, 1385, 1344, 1309, 1320, 1278, 1183 and 1113 cm^{-1}; ^1H nmr (tetrahydrofuran-d_8): δ 9.96 (s, 1H), 8.08 (d, J = 9.2 Hz, 2H), 7.77-7.59 (m, 3H), 7.50-7.30 (m, 4H), 7.00 (d, J = 9.2 Hz, 2H), 6.87 (d, J = 16.2 Hz, 1H) and 3.78 (d, J = 5.8 Hz, 2H); ^{13}C nmr (tetrahydrofuran-d_8): δ 196.0, 161.5, 151.7, 143.7, 140.2, 135.7, 131.2, 129.7, 129.1, 125.7, 126.4, 114.4 and 44.3; hrms: Calcd. for $C_{17}H_{15}N_3O_3$: 309.1113. Found: 291.1025 (P-H_2O, $C_{17}H_{13}N_3O_2$).

Anal. Calcd. for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.59. Found: C, 65.82; H, 4.83; N, 13.42.

Preparation of 1-*p*-Nitrophenyl-4-iodopyrazole (**13**).

Mercuric tetrafluoroborate on silica gel was prepared by adding 5.02 g of 35% fluoroboric acid and 2.16 g (10 mmoles) of yellow mercuric oxide to 2.16 g of silica gel [25]. The flask was rotated on the rotary evaporator at 50° for 1 hour and the water removed *in vacuo*. Into a flask was placed 656 mg (4 mmoles) of 1-nitrophenylpyrazole, **11**, and 30 ml of 1,2-dichloroethane. The coated silica gel (1.74 g) was added with stirring, followed by 586 mg (2.3 mmoles) of iodine. The mixture was stirred for 1 hour and filtered. The filtrate was washed with 10% sodium thiosulfate, water and dried over sodium sulfate. Evaporation of the solvent gave 972 mg of an off-white solid. Analysis (tlc) (80/20 methylene chloride-hexane) showed a single spot of higher R_f than the starting pyrazole.

The pyrazole **13** (967 mg) was isolated in 77% yield, mp 193.6-194.6°; ir (potassium bromide): 1594, 1525, 1523, 1511, 1509, 1396, 1384, 1382, 1378, 1340, 1328, 1193, 1112, 1025, 945, 940, 864 and 750 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.38 (d, J = 6.8 Hz, 2H), 8.12 (s, 1H), 7.88 (d, J = 6.8 Hz, 2H) and 7.81 (s, 1H); ^{13}C nmr (acetone-d_6) δ 148.0, 146.5, 144.3, 138.4, 133.5, 125.9, 119.3; hrms: Calcd. for $C_9H_6N_3O_2I$: 314.9505. Found: 314.9506.

Anal. Calcd. for $C_9H_6N_3O_2I$: C, 34.31; H, 1.92; N, 13.34. Found: C, 34.26; H, 1.92; N, 13.02.

1-*p*-Nitrophenyl-4-(*p*-methoxyphenylethynyl)pyrazole (**14**).

A 50 ml flask was charged with 315 mg (1 mmole) of the iodide **13**, 5 ml of dioxane, and 1.53 ml of distilled triethylamine. The mixture was heated to 70° for 10 minutes degassing with argon and 35 mg of bis(triphenylphosphine)palladium dichloride and 20 mg of cuprous chloride were added. A degassed solution of 145 mg (1.1 mmoles) of *p*-methoxyphenylacetylene in 2 ml of dioxane was added at 70° and the mixture stirred for 1.5 hours. The reaction mixture was cooled, diluted with methylene chloride and washed with 2% hydrochloric acid, water and dried over sodium sulfate. Evaporation yielded 270 mg of a orange solid (single spot by tlc analysis, 80/20 methylene chloride-hexane), 84% yield, mp 170-172°; ir (chloroform): 2218 (vw), 1600, 1527, 1510, 1466, 1439, 1403, 1372, 1341, 1303, 1292, 1250, 1185, 1174, 1112, 948, 867 and 833 cm^{-1}; ^1H nmr (chloroform-d_1): δ 8.38 (d, J = 9.3 Hz, 2H), 8.18 (s, 1H), 7.98-7.82 (m, 3H), 7.44 (d, J = 7 Hz, 2H), 6.91 (d, J = 7 Hz, 2H), 3.84 (s, 3H); ^{13}C nmr (chloroform-d_1): δ 159.6,

155.5, 144.7, 143.6, 132.8, 128.8, 125.3, 121.8, 118.6, 114.7, 114.0, 107.0, 91.5, 55.2; uv (dioxane): λ max (ε) 276 (20, 887), 292 (19, 098) and 340 (21, 267) nm; hrms: Calcd. for $C_{18}H_{13}N_3O_3$: 319.0957. Found: 319.0952.

Anal. Calcd. for $C_{18}H_{13}N_3O_3$: C, 67.71; H, 4.10; N, 13.16. Found: C, 68.10; H, 4.39; N, 13.08.

1-Nitrophenyl-4-(*p*-methoxy-β-styryl)pyrazole (**15**).

A screw-capped bottle was charged with 315 mg (1 mmole) of **13**, 268 mg (2 mmoles) of *p*-vinylanisole, 322 mg (1 mmole) tetrabutylammonium bromide, 350 mg (2.5 mmoles) potassium carbonate and 10 ml of dimethylformamide. After degassing. 75 mg of palladium acetate was added and the mixture was heated with stirring at 70° for 18 hours. The reaction mixture was cooled, diluted with methylene chloride and washed five times with 50 ml of water. After drying (sodium sulfate), the crude product was chromatographed using methylene chloride to yield 475 mg of product **15**, 74% yield, mp 230-232°; ir (potassium bromide): 1607, 1595, 1512, 1405, 1340, 1306, 1303, 1250, 1199, 1180, 1130, 1021, 959, 946, 855, 853, 849, 815, 750 cm^{-1}; ^1H nmr (tetrahydrofuran-d_8): δ 8.38 (s, 1H), 8.23 (d, J = 9.3 Hz, 2H), 7.94 (d, J = 9.3 Hz, 2H), 7.90 (s, 1H), 7.31 (d, J = 8.5 Hz, 2H), 6.88 (AB_q, J = 16.3 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 3.67 (s, 3H); ^{13}C nmr (tetrahydrofuran-d_8): δ 160.4, 146.5, 145.5, 141.4, 130.4, 129.4, 128.0, 125.9, 125.5, 125.2, 118.7, 116.0, 114.8, 55.3; uv (dioxane): λ max (ε), 212 (18, 356), 218 (17, 476), 298 (24, 264), 325 sh (17, 782) and 362 (21, 434) nm; hrms: Calcd. for $C_{18}H_{15}N_3O_3$: 321.1095. Found: 321.1104.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.70; N, 13.08. Found: C, 66.73; H, 4.68; N, 12.90.

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