Thermally Induced Fragmentation of Some Azidopyrazole Derivatives[1]

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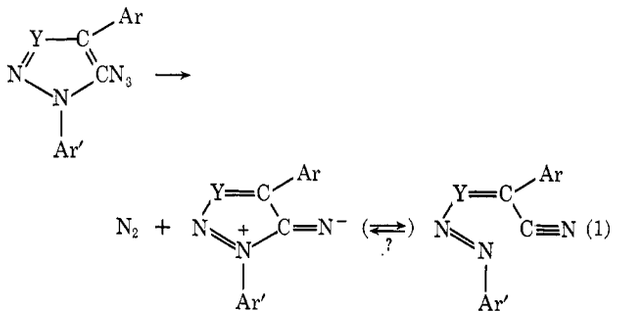
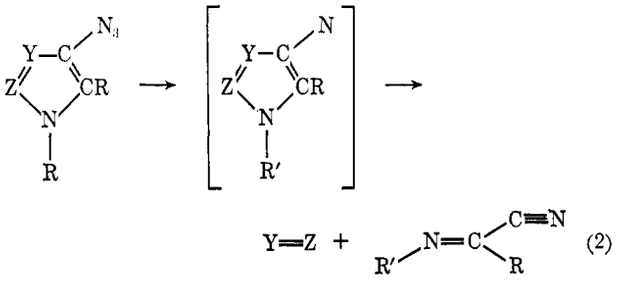
4-Azido-1,5-diphenyl-1,2,3-triazole thermolyzed at 110° into nitrogen and α-phenyliminophenylacetonitrile, as did a series of seven 4-azidopyrazoles bearing methyl and/or phenyl substituents between 40 and 80°, with fragmentation of the ring. The 3 substituent with the attached 3 carbon appeared as a nitrile, R^3CN, and the 1 and 5 substituents together with the 4 and 5 carbons appeared as an α-iminonitrile, $R^5C(CN)=NR^1$. When the 3 and 5 substituents were both phenyl, substantial amounts of the corresponding azopyrazole (formally a dimer of the nitrene) were formed as well. The ratio of dimeric to fragmentation product fell on dilution. Thermolysis of 1-methyl-3,5-diphenyl-4-azidopyrazole in the presence of *p*-anisyl azide gave the same products as in the absence of anisyl azide, and no unsymmetrical azo compound could be detected. Azo compounds are deduced not to arise from either dimerization of nitrene or attack of nitrene on azide. Photolysis of the azides or deoxygenation of the corresponding 4-nitrosopyrazoles gave similar products but in lower yields. 3,5-Dimethyl-4-azidopyrazole formed 4-phenylazo-3,5-dimethylpyrazole when thermolyzed in aniline, apparently through insertion of a pyrazoylylnitrene into an N-H bond. 3-Methyl-4-phenyl-5-azidopyrazole lost nitrogen slowly at 110° and formed the corresponding aminopyrazole (15 to 18%) and α-cyano-β-methylstyrene (38%).

Certain 5-azidopyrazoles and -triazoles have been found to lose nitrogen upon mild thermolysis and to produce a single fragmentation product, a conjugated nitrile, resulting from fission of the ring at the 1,5 bond (eq 1).[2] It is not known whether this is a concerted process, or whether a free nitrene intervenes, although there is some evidence that the conjugated nitriles may equilibrate with a very low concentration of the corresponding heterocyclic nitrene, whose energy content and reactivity are unusually low owing to electronic interaction with the ring.



The positionally isomeric 4-azidoazoles would give rise to a similarly stabilized nitrene (eq 2), but the option of a simple ring opening to form a conjugated nitrene isomeric with the nitrene is not available. If fragmentation occurs, two moieties must be formed, one derived from the 2 and 3 positions of the ring, the other from the 4, 5, and 1 positions. Nitrogen atoms as such are in principle not required at any of the ring positions. We have observed an example of this type of fragmentation in the triazole series: 1,5-diphenyl-4-azido-1,2,3-triazole fragments cleanly into two molecules of nitrogen and a molecule of α-phenyliminophenylacetonitrile when heated (Y = Z = N). Closely related examples in the pyrazole and pyrrole series have been reported: Wright found that 1,5-diphenyl-3-methyl-4-nitrosopyrazole fragments into acetonitrile and α-phenyliminophenylacetonitrile (Y = C, Z = N) when deoxygenated with triethyl phosphite,[3] and Irwin and Wibberley found that 7-nitroso-3,6-diphenylpyrrolo-[1,2-*c*]pyrimidine opens to 4-phenyl-6-(2-phenyl-2-cyano)vinylpyrimidine during catalytic hydrogenation.[4]



4-Azidopyrazoles.—The present work was undertaken to explore the generality of this type of fragmentation and to see if any evidence for an intermediate nitrene could be found. To this end, a group of 4-azidopyrazoles having methyl and/or phenyl substituents was prepared. The conventional route to such compounds would be through reaction of sodium azide with the diazotized amines,[5] which are obtained by reduction of the 4-nitro- or 4-nitrosopyrazoles. However, the general method for introducing nitrogen functionality into the 4 position of the pyrazole ring,[6] reaction of an α-oximino-β-dicarbonyl compound with a hydrazine to form a 4-nitrosopyrazole, gave only traces of 1,3,5-triphenyl-4-nitrosopyrazole and none of the desired product when applied to the synthesis of 1-methyl-3,5-diphenyl-4-nitrosopyrazole, evidently owing to rapid reaction of the desired product with the hydrazine.

Nitration of phenylpyrazoles is known to take place on the benzene ring and was thus not an alternative.[6] Although it has been stated[6] that "direct nitrosation of pyrazoles cannot be accomplished," we were able to effect the nitrosation of 1,3,5-triphenylpyrazole in 50% yield, using dinitrogen tetroxide in methylene chloride in the presence of sodium acetate. 1-Methyl-3,5-diphenyl-4-aminopyrazole was prepared by methylation of the known 3,5-diphenyl-4-aminopyrazole while the amino group was protected with a benzylidene group. 1,3-Diphenyl-4-amino-5-methylpyrazole was prepared from the known 4-carboethoxy compound through the Curtius reaction. Subsequent steps leading from these compounds to the 4-azidopyrazoles were unexceptional.

(1) From the doctoral dissertation of H. Dounchis, 1967.

(2) (a) P. A. S. Smith, W. Resemann, and L. O. Krbechek, *J. Amer. Chem. Soc.*, **86**, 2025 (1964); (b) P. A. S. Smith, G. J. W. Breen, M. K. Hajek, and D. C. V. Awang, *J. Org. Chem.*, **35**, 2215 (1970).

(3) J. B. Wright, *J. Org. Chem.*, **34**, 2474 (1969).

(4) W. J. Irwin and D. G. Wibberley, *Chem. Commun.*, 878 (1968).

(5) G. T. Morgan and I. Ackerman, *J. Chem. Soc.*, **123**, 1311 (1923).

(6) A. N. Kost and I. I. Grandberg, *Advan. Heterocycl. Chem.*, **6**, 347 (1966).

The 4-azidopyrazoles (*cf.* Table I) were obtained in a state of good purity (tlc, ir, nmr), in some instances

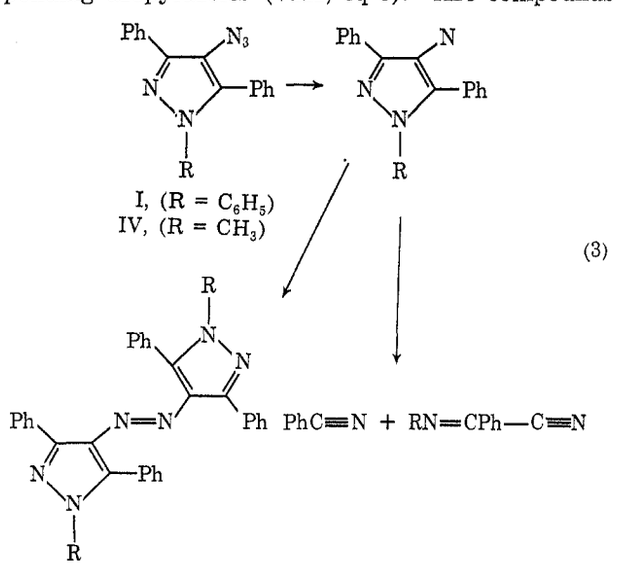
TABLE I
THERMOLYSIS OF 4-AZIDOPYRAZOLES (1-R′, 3-R³, 5-R⁵) IN CYCLOHEXANE SOLUTION

	Substituents			Yields, %[a]		
Compd	1-R¹	3-R³	5-R⁵	R³CN	R¹N=C-(CN)R⁵	Azopyrazole
I	Ph	Ph	Ph	Yes	21	14.5[b]
II	Ph	Ph	CH_3	54	75	None
III	Ph	CH_3	Ph	Yes	100	None
IV	CH_3	Ph	Ph	Yes	Yes	35
V	Ph	CH_3	CH_3	Yes	74	None
VI	CH_3	CH_3	CH_3	Yes	Yes	None
VII	H	CH_3	CH_3	Yes	?	None[c]

[a] Some tar was always formed. [b] 2% of benzanilide also formed. [c] Also formed were ~20% high-melting solid, and 7.5% X ($C_8H_{11}N_5$?): mp 172–174°; ir 3190 (NH), 1675, 1660 (C=N), 1635, 1340 cm^{-1}; nmr δ 1.48 (s, 1), 2.20 (s, 1), 2.23 ppm (s, 1); uv λ_{max} 222 nm (ε 3300), 257 (3400), 272 (3700), 337 (2300); *m/e* 177.

crystalline, but were unusually unstable for aryl azides, and decomposed slowly at ambient temperature and sometimes detonated during combustion, thus precluding meaningful analysis. In dilute solution in cyclohexane, nitrogen evolution was completed in ~30 min at reflux temperature (~80°). Although the products of the generalized fragmentation reaction were detected in each instance, they were usually accompanied by considerable amounts of polymeric material. The simple nitriles (acetonitrile or benzonitrile) were generally not isolated, but were detected by nmr or ir and by glc retention time. The α-iminonitriles bearing one or more phenyl groups were isolated in crystalline form when feasible; α-iminopropionitrile and α-methyliminopropionitrile, however, were too labile and presumably not solid at room temperature. Nmr signals attributable to the latter were obtained, but only presumed transformation products of the former could be detected. The results are collected in Table I.

In addition to the nitrilic fragmentation products, two of the azides, 1,3,5-triphenyl- (I) and 1-methyl-3,5-diphenyl-4-azidopyrazole (IV), produced the corresponding azopyrazoles (VIII, eq 3). Azo compounds



(3)

VIII

could not be detected among the products of the other azides even by thin layer chromatography (the azo compounds were synthesized from the nitroso pyrazoles for comparison). The formation of an azo compound indicates that fragmentation of the azido pyrazole is not a concerted process, but a nitrene is first formed by loss of nitrogen from the azido group in a discrete step. If the lifetime of the nitrene is long enough, reactions other than further fragmentation may compete. The two azidopyrazoles that gave rise to azo compounds are the only ones of those examined that have phenyl groups in the 3 and 5 positions, but it is not clear how such substitution brings about this effect.

The path from nitrenes to azo compounds in general is unlikely to be simple dimerization, although it has often been so represented.[7] Nitrenes are highly reactive intermediates, of unknown but assuredly short lifetimes, and their concentration at any moment in a decomposing azide solution must be very low; the probability that two nitrene molecules would collide before reacting in other ways (intramolecularly or with the medium) would be very small. Extensive kinetic measurements have shown that thermolysis of aryl azides is strictly first order, so that initial dimerization of the azide cannot be involved.[7] The likely alternatives are attack by nitrene on azide (eq 4) or processes involving hydrogenated intermediates, such as dimerization of amino radicals or insertion of nitrene into an N–H bond, followed by dehydrogenation of the resulting hydrazine (eq 5) by nitrene, amino radical, or air. In

$$RN + RN_3 \longrightarrow RN{=}NR + N_2 \qquad (4)$$

$$RN \xrightarrow{[H]} RNH\cdot \longrightarrow RNH_2 \xrightarrow{RN} RNHNHR \xrightarrow{-[H]} RN{=}NR \qquad (5)$$

either case, the proportion of azo compound to unimolecular fragmentation products or primary amine should decrease with dilution.

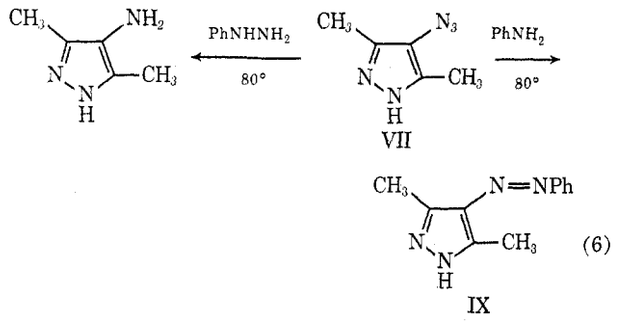
1,3,5-Triphenyl-4-azidopyrazole (I) has a generally low solubility, and thus did not lend itself to experiments over a range of concentrations. 1-Methyl-3,5-diphenyl-4-azidopyrazole (IV) is more soluble, and thermolyses were conducted at the concentrations of 0.40, 0.33, and 0.029 *M* in cyclohexane. The yield of azopyrazole was essentially the same (~35%) at the first two concentrations, but fell by one third (to 23%) at the higher dilution. This result is in qualitative agreement with expectation, but the quantitative significance is uncertain, owing to the extensive formation of intractable gums. Another experiment took advantage of the fact that the decomposition temperature of IV is much lower than that of *p*-anisyl azide, which is known to form *p,p′*-azoanisole on thermolysis. When IV, 0.14 *M* in cyclohexane, was thermolyzed in the presence of excess *p*-anisyl azide, which is stable at the reflux temperature of the solution, azopyrazole VIII was formed in normal yield (25%). No trace of the *p*-anisylazopyrazole which would have resulted from the attack of the pyrazole nitrene on anisyl azide could be detected.

This result is consistent with the observations of Abramovitch, Challand, and Scriven that phenyl azide

(7) P. A. S. Smith, in "Nitrenes," Lwowski, Ed., Wiley-Interscience, New York, N. Y., 1970, Chapter 4.

was unattacked when phenylnitrene was generated in its presence by deoxygenation of nitrobenzene with triethyl phosphite.[8] Such facts imply that eq 4 does not represent the path from azides to azo compounds, and eq 5 is therefore implicated.

There is precedent for insertion of arylnitrenes into N–H bonds to produce hydrazo or azo compounds in several independent reports.[9] Further evidence for this process and for eq 5 was obtained from 3,5-dimethyl-4-azidopyrazole (VII), which alone in benzene or toluene formed no detectable azopyrazole, but in a benzene solution of aniline formed the unsymmetrical azo compound, 3,5-dimethyl-4-phenylazopyrazole (IX), in 5.7% yield. In the presence of phenylhydrazine, a hydrogen donor much superior to benzene or aniline, the principal product was the aminopyrazole (42.6%) instead (eq 6). The formation of primary amine, fragmentation products, azo compounds, etc., would, of course be sensitively determined by influences of the medium and the structure of the azide on the relative rates of the steps in eq 5.



In the absence of aniline or phenylhydrazine, azide VII gave rise principally to a brown, amorphous material which could not be purified and which appeared to be polymeric. The other products were acetonitrile and, in 7% yield, a colorless, crystalline solid that decomposed slowly; the molecular formula was apparently $C_8H_{11}N_5$ (X). Its nmr spectrum showed three singlets, of equal intensity, corresponding to three methyl groups (the NH hydrogens could not be located, owing to extreme broadening of their signal, but their presence was confirmed in the ir). It corresponds to an adduct of the pyrazolylnitrene with α-iminopropionitrile, the other expected fragmentation product, although it cannot be said if it arose in that way. Its instability, the small quantities accessible, and its uncertain significance recommended that further investigation be deferred.

A sample of azide VII was thermolyzed by adding it in small portions to a boiling solution of maleic anhydride in benzene, in the hope of intercepting α-iminopropionitrile. The only product isolated was an unpurifiable and evidently polymeric solid, whose analysis corresponded roughly to a 1:1 adduct of α-iminopropionitrile with maleic anhydride, in ~85% yield; its poorly resolved ir spectrum showed both carbonyl and N–H stretching bands, but no discernible C≡N absorption.

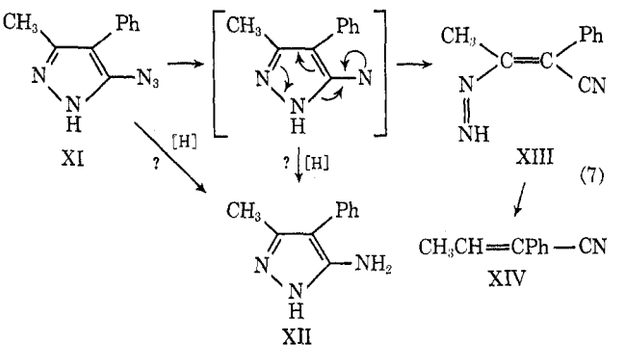
(8) R. A. Abramovitch, S. R. Challand, and E. F. V. Scriven, *J. Amer. Chem. Soc.*, **95**, 1374 (1972).

(9) R. A. Odum and M. Brenner, *J. Amer. Chem. Soc.*, **88**, 2074 (1966); R. Huisgen and K. von Frauenberg, *Tetrahedron Lett.*, 2595 (1969); R. E. Banks and A. Prakash, *ibid.*, 99 (1973); E. F. V. Scriven, H. Suschitzky, and G. V. Garner, *ibid.*, 103 (1973).

One example of a 4-azidopyrazole, IV, was decomposed by photolysis for comparison. The same products, benzonitrile, α-methyliminophenylacetonitrile, and the azopyrazole, were formed, but in lower yield. In addition to these and some tarry materials, an unstable solid photoproduct was isolated. Thin layer chromatography indicated one major and two minor components, but we could not purify them by either chromatography or recrystallization. Nitrile absorption showed in the ir spectrum of the mixture and nmr showed two *N*-methyl singlets and aromatic protons corresponding to a ratio of $CH_3:C_6H_5$ between 1:2 and 2:5. This ratio eliminates the possibility that the substance may have been derived from addition of the azide or nitrene to a fragmentation product, but that is all that can be said at this time.

4-Nitrosopyrazoles.—In two instances, the corresponding 4-nitrosopyrazoles were deoxygenated with triphenylphosphine. 1,5-Diphenyl-3-methyl-4-nitrosopyrazole (corresponding to azide III) gave acetonitrile and α-phenyliminophenylacetonitrile, as Wright obtained[4] by deoxygenation with triethyl phosphite, and as we obtained from the azide, but in lower yield. The yield of iminonitrile was sensitive to concentration, falling from 57% in 0.05 *M* solution to 38% in 0.37 *M* solution. 1,3,5-Triphenyl-4-nitrosopyrazole (corresponding to azide I) gave an intractable mixture on deoxygenation; no azopyrazole and only traces of iminonitrile could be detected by tlc.

5-Azidopyrazoles.—The behavior of the 4-azidopyrazoles, which indicates a role for nitrene intermediates in at least some cases, turned our attention to the possibility that nitrene intermediates might also be detectable from 5-azidopyrazoles. In the examples previously reported,[2b] the conjugated azoacrylonitrile produced according to eq 1 was considerably stabilized by the presence of aryl groups on the unsaturated carbon and nitrogen positions, a circumstance that might accelerate opening of the ring, and thus either bypass the nitrene (concerted fragmentation) or reduce its lifetime (or its equilibrium concentration). We therefore prepared and thermolyzed 3-methyl-4-phenylazidopyrazole (XI), the azoacrylonitrile from which would be stabilized by only one aryl group instead of three, and thus might not form so readily. This azide was considerably more stable than the 4-azidopyrazoles and than 1,3,4-triphenyl-5-azidopyrazole, which thermolyze at temperatures as low as 50°, and it decomposed at a reasonable rate only when heated to 110° (refluxing toluene). The products were the corresponding 5-aminopyrazole (XII, 20%) and α-phenylcrotonitrile (XIV, 38%) (eq 7). The azoacrylonitrile



derivative XIII was not detected directly, but its formation was inferred from the appearance of XIV and analogy to the behavior of other monosubstituted diazenes.[9]

The formation of an amine, a product of hydrogen abstraction, in substantial quantities distinguishes the behavior of XI from its 1,3,4-triaryl analogs. It is a reaction characteristic of nitrenes and would seem to imply that a nitrene intermediate in this instance has a long enough lifetime for other reactions to compete with the ring-opening path. However, bibenzyl, an expected product if the source of hydrogen were the toluene used as solvent, was detected in only trace amounts, and the same products were obtained when chlorobenzene was used as solvent instead. The most likely alternative source of hydrogen is the diazene XIII [diimide itself is known to be an effective donor of hydrogen, and phenyldiazene (phenyldiimide) is a very active reducing agent].[10]

If XIII is the source of hydrogen, it is more probable that it transfers hydrogen atoms to the azide XI[10] rather than the nitrene, for the latter would be present only at very low concentrations, and the concentration of XIII would also be low, owing to its depletion both by hydrogen transfer and by loss of nitrogen to form XIV. The product of dehydrogenation of XIII, a diazo free radical or the vinyl radical formed from it by loss of N_2, is a likely source of the tarry material formed. The stoichiometry of such a scheme is consistent with the observations, for the 20% yield of amine would require 40% of XIII for its formation, leaving 40% of the reaction mixture to be accounted for as XIV, compared to 38% actually obtained.

Experimental Section[11]

1,3,5-Triphenyl-4-nitrosopyrazole.—A solution of 8.0 g (27 mmol) of 1,3,5-triphenylpyrazole[12] [nmr δ 6.77 (s, 1), 7.3–7.4 (m, 13), 7.85–8.0 ppm (m, 2); ir 1600, 1495, 1365, 1215, 1175, etc., cm^{-1}] in 200 ml of methylene chloride in which 2.2 g of sodium acetate was suspended was cooled in an ice bath and stirred while 10 ml of dinitrogen tetroxide diluted with methylene chloride was added. The mixture was stirred for 6 hr while slowly attaining room temperature and was then washed with water and dried over magnesium sulfate. Evaporation left a green mass, which was recrystallized from 600 ml of ethanol to give 4.35 g (49.6%) of sparkling green crystals of the nitrosopyrazole: mp 184–186°; nmr δ 7.3–7.5 (m, 13), 7.85–8.0 ppm (m, 2); ir (Nujol) 1605, 1595, 1500, 1460 cm^{-1}.

Anal. Calcd for $C_{21}H_{15}N_3O$: C, 77.52; H, 4.65; N, 12.92. Found: C, 77.35; H, 4.76; N, 12.90.

Attempts to increase the yield by use of longer reaction times and excess dinitrogen tetroxide resulted in destruction of the nitroso compound and formation of unidentified orange-yellow substances. 1,3,5-Triphenyl-4-nitrosopyrazole was also prepared from the reaction of 1,3-diphenyl-1,2,3-propanetrione 2-oxime with phenylhydrazine, but in only 1.5% yield.

4-Amino-1,3-diphenyl-5-methylpyrazole.—A suspension of 11.2 g (36.6 mmol) of ethyl 1,3-diphenyl-5-methylpyrazole-4-carboxylate[13] in 24 ml of 95% hydrazine was refluxed with stirring for 5 hr and then poured into ice water. The resulting solid 4-carbohydrazide was washed with water, triturated with a small amount of ethanol, and dried in air: 10.17 g (95.2%); mp 181–183°; ir ($CHCl_3$) 3430, 3325 ($NHNH_2$), 1665–1650 cm^{-1} ($CONHNH_2$); nmr δ 2.53 (s, 3, 5-CH_3), 3.8 (broad, 2, NH_2), 6.9 (broad, 1, NH), 7.45 ppm (s, 10, aryl).

Anal. Calcd for $C_{17}H_{16}H_4O$: C, 69.84; H, 5.52, N, 19.17. Found: C, 69.70; H, 5.62; N, 19.21.

The entire yield of the foregoing hydrazide was quickly dissolved in a cold mixture of 50 ml of glacial acetic acid and 50 ml of 7% hydrochloric acid and treated with 2.4 g of sodium nitrite dissolved in a minimum of water. The gummy acyl azide that precipitated was separated by decantation and taken up in 100 ml of benzene. After one washing with water, the benzene solution was cautiously heated under reflux with 35 ml of concentrated hydrochloric acid. When gas evolution ceased (~1.5 hr), the mixture was filtered, and the aqueous phase was separated, neutralized with sodium bicarbonate, and extracted with chloroform. Attempts at crystallization having failed, the crude amine was converted to its benzylidene derivative by heating for several minutes with an equivalent quantity of benzaldehyde in 20 ml of ethanol; on cooling, 6.85 g (58.3%) of crystalline solid, mp 168–171°, separated. It was hydrolyzed by stirring overnight in a mixture of 50 ml of 5 *M* sulfuric acid and 50 ml of chloroform. The crystalline sulfate salt that separated was washed with chloroform and decomposed with aqueous sodium carbonate to give 2.5 g of 4-amino-1,3-diphenyl-5-methylpyrazole, mp 69–71°. Repeated crystallizations from cyclohexane gave an analytical sample: mp 70–71.5°; ir 3350, 3280, 1600 cm^{-1}; nmr δ 2.16 (s, 3, 5-CH_3), 2.84 (br, 2, NH_2), 7.2–7.5 (m, 8, aryl), 7.7–7.9 ppm (m, 2, *o*-aryl).

Anal. Calcd for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.86. Found: C, 77.03; H, 6.03; N, 17.06.

If the treatment of the acyl hydrazide with sodium nitrite was not done quickly, substantial amounts of *sym*-bis(1,3-diphenyl-5-methyl-4-carbonyl)hydrazine were formed: mp 236–237°; ir 3380, 3186, 1640, 1623 cm^{-1}.

Anal. Calcd for $C_{34}H_{28}N_6O_2$: C, 73.89; H, 5.11; N, 15.21. Found: C, 73.73; H, 5.20; N, 15.25.

4-Amino-3,5-diphenyl-1-methylpyrazole.—4-Amino-3,5-diphenylpyrazole[14] was converted to its pale yellow *N*-benzylidene derivative (mp 225–227°) by heating with an equivalent amount of benzaldehyde in ethanol. A suspension of 11.19 g (36.8 mmol) of the crude product in 200 ml of benzene was refluxed with 5.1 g (10% excess) of methyl sulfate for 16 hr. The cooled mixture was washed with three 100-ml portions of 10% sodium hydroxide solution and then with water and was then dried ($MgSO_4$), filtered, and evaporated. The crude, yellow residue, 9.53 g (77%), mp 130–140°, was recrystallized from ethanol to yield 5.89 g of 4-benzylidenamino-3,5-diphenyl-1-methylpyrazole: mp 145–146°; ir 1635 cm^{-1} (C=N); nmr δ 3.77 (s, 3, *N*-CH_3), 7.2–7.4 (m, 11, aryl), 7.5–7.7 ppm (m, 2, *o*-aryl).

Anal. Calcd for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68. Found: C, 81.72; H, 5.75.

The benzylidene group was removed by stirring a suspension of 2.05 g of the foregoing compound in a mixture of 40 ml of ether and 60 ml of 3 *M* sulfuric acid for ~12 hr. The precipitated salt was decomposed with sodium carbonate solution and the resulting oil was taken up in methylene chloride; crystallization took place slowly upon evaporation, giving 1.30 g (85.5%) of 4-amino-3,5-diphenyl-1-methylpyrazole, mp 83–85°. An analytical sample was obtained by repeated crystallization from cyclohexane: mp 85–86.5°; ir (CCl_4) 3420, 3350, 1610 cm^{-1}; nmr δ 3.02 (s, 2, NH_2), 3.75 (s, 3, *N*-CH_3), 7.3–7.5 (m, 8, aryl), 7.7–7.9 ppm (m, 2, *o*-aryl).

Anal. Calcd. for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.86. Found C, 77.08; H, 6.14; N, 16.90.

Preparation of Azidopyrazoles.—All of the azidopyrazoles were prepared by the reaction of the aminopyrazole with nitrous acid with only small variations according to solubilities. The procedure for 4-azido-1,3-diphenyl-5-methylpyrazole (II) is representative. A solution of 2.0 g (8.03 mmol) of amine in 6 ml of acetic acid and a solution of 0.55 g of sodium nitrite in 5 ml of water were added simultaneously to 10 ml of concentrated hydrochloric acid at 0° with stirring. The resulting solution was added after a few minutes to an ~20% excess of sodium azide dissolved in ice water. After 10 min the precipitated azide was filtered off, washed with water, and dried *in vacuo*: 1.90 g (86.1%); mp

(10) E. M. Kosower, *Accounts Chem. Res.*, **4**, 193 (1971); diimide is implicated in the reported reduction of phenyl azide by hydrazine in the presence of palladium.

(11) Analyses were done by Spang Microanalytical Laboratories, Ann Arbor, Mich. Ir spectra were taken on a Perkin-Elmer Model 237B instrument; Nujol mulls were used unless otherwise stated. Nmr spectra were taken on a Varian A-60 instrument, using tetramethylsilane as internal reference and deuteriochloroform for solvent, unless otherwise stated. Analyses for C, H, and N within 0.3% of calculated were obtained for all new compounds not explicitly described.

(12) L. Knorr and H. Laubmann, *Ber.*, **21**, 1205 (1888).

(13) L. Knorr and P. Duden, *Ber.*, **26**, 113 (1893).

(14) M. Ruccia, *Ann. Chim.* (*Rome*), **49**, 720 (1959).

TABLE II

AMINO- AND AZIDOPYRAZOLES

		Amino				Azido[a]		
Registry no.	Substituents	Source	Registry no.	Yield, %	Mp, °C	No.	Yield, %	Mp, °C
40697-39-0	1,3,5-Ph_3-4-	4-NO	40697-44-7	59[b]	163.5–165.5	I	High	78–80
40697-40-3	1,3-Ph_2-5-Me-4-	4-CO_2Et	7189-04-0	55[c]	70–71.5	II	86	62.5–65
40697-41-4	1,5-Ph_2-3-Me-4-	4-NO[d]	7171-64-4	69	106–107[e]	III	84	Oil
40697-42-5	3,5-Ph_2-1-Me-4-	4-N=CHPh	40697-47-0	85[f]	85–86.5	IV	85	64–66
21683-30-7	1-Ph-3,5-Me_2-4-	4-NO	715-99-1	53	60–63[g]	V	70	34–35
28466-21-9	1,3,5-Me_3-4-	4-NO	7171-70-2	35	99–101[h]	VI	58	36–38
5272-86-6	3,5-Me_2-4-	4-NO_2	14531-55-6	72	204–205[i]	VII	75	80–82[i]
31924-81-9	3-Me-4-Ph-5-	*j*	4468-48-8	35	138–140	XI	88	115–116

[a] Colorless to beige crystalline solids; elemental analyses not performed, owing to instability. Ir and nmr spectra were consistent with those of the corresponding amines; all showed ir absorption near 2120 cm^{-1} (N_3). [b] Reduction with zinc dust in ~1% solution in glacial acetic acid at 0–10°. This amine was also obtained in 53% yield by hydrogenation over platinum oxide in a 1:5:10 mixture of concentrated hydrochloric acid, chloroform, and ethanol. [c] By Curtius degradation. [d] G. Wittig, *Ber.*, **61**, 1142 (1928). [e] Reported[14] mp 104°. [f] 57% overall from 3,5-diphenyl-4-aminopyrazole. [g] Monohydrate. [h] Reported[16] mp 100–101°. [i] Reported mp 206° (amine) [reported[16] mp 65 and 81° (azide)]: G. T. Morgan and R. Reilly, *J. Chem. Soc.*, **105**, 441 (1914). [j] From 1-cyano-1-phenylacetone; reported[18] mp 140–142°.

62.5–65° with gas evolution; ir (Nujol) 2110 cm^{-1} (N_3); nmr δ 2.33 (s, 3, 5-CH_3), 7.2–7.5 (m, 8, aryl), 7.7–7.8 ppm (m, 2, *o*-aryl). The results are collected in Table II.

Thermolysis of 4-Azidopyrazoles.—The procedures used for the several azides varied somewhat, but principally in the work-up. The following examples are representative. A solution of 1.82 g (8.55 mmol) of 4-azido-1-phenyl-3,5-dimethylpyrazole (V) in 25 ml of cyclohexane was refluxed for 90 min. Monitoring by nmr showed the gradual disappearance of the two methyl singlets of V and the development of new singlets at positions corresponding to acetonitrile and pyruvonitrile anil. The resulting solution showed an ir band at 2220 cm^{-1} (C≡N) and none at 2120 cm^{-1} (N_3). The mixture was evaporated and then distilled, yielding 0.91 g (74%) of pyruvonitrile anil, a pale yellow oil, bp 78–80° (2 mm) [60–61° (0.25)]. On standing, it solidified: mp 44–46°; ir (neat) 3060, 3025, 2220 (C≡N), 1660, 1635 cm^{-1} (C=N); nmr δ 1.88 and 2.18 (s, total 3, ratio 1:3.4), 6.7–7.4 ppm (m, 5, aryl). The two high-field singlets correspond to the syn and anti configurations of the methyl group.

Anal. Calcd for $C_9H_8N_2$: C, 74.97; H, 5.59; N, 19.43. Found: C, 75.03; H, 5.69; N, 19.33.

A sample of pyruvonitrile anil (0.85 g) was warmed with phenylhydrazine in aqueous ethanol containing 2 ml of concentrated sulfuric acid. After cooling and dilution, the solution deposited 0.25 g (27%) of pyruvonitrile phenylhydrazone: mp 151–153° (reported[15] mp 150–151°); ir 3270 (NH), 2215 (C≡N), 1610 cm^{-1} (C=N); nmr δ 2.07 (s, 3), 7.0–7.4 ppm (5, aryl).

The tarry residue after distillation was examined by tlc on alumina; nothing with a retention time corresponding to authentic[14] 1,1′-diphenyl-3,3′,5,5′-tetramethyl-4,4′-azopyrazole could be detected.

A solution of 1.70 g (6.18 mmol) of 4-azido-1,3-diphenyl-5-methylpyrazole (II) in 16.4 ml of cyclohexane was refluxed for 1.25 hr; ir showed no azide frequency, but a doublet at 2120–2130 cm^{-1} indicated two cyano groups, and glc revealed two volatile components other than solvent. One component was deduced to be benzonitrile by retention time, peak enhancement and nmr (s, δ 7.5 ppm). The solvent was removed and the residue was distilled, bp 66–78° (0.5–1.0 mm). The distillate was collected in three fractions (0.20, 0.77, and 0.05 g). The first two were shown (glc, nmr) to be mixtures of benzonitrile and pyruvonitrile anil, and the last nearly pure pyruvonitrile anil (ir, nmr). Analysis by nmr showed the total distillate to contain 3.33 mmol (53.8%) of benzonitrile and 4.62 mmol (74.6%) of pyruvonitrile anil (the ratio of the *E* and *Z* isomers was 1:4) (some benzonitrile is believed to have been lost during evaporation). The undistilled residue weighed 70 mg (4.5%); tlc showed it to be a complex mixture, of which no single component appeared to be more than 1% of the starting material, thus establishing a maximum limit of azopyrazole, if, indeed, any was formed.

A solution of 4-azido-1,3,5-trimethylpyrazole (VI) in benzene was allowed to decompose at ambient temperature in an nmr tube. The initial peaks at δ 2.15, 2.23, and 3.65 ppm slowly decreased; after 1.5 hr, three new peaks appeared at δ 1.97 (s, CH_3CN), 2.12 (d), and 3.33 ppm (d). After 12 hr, the azide peaks had reached about half their original intensity, and after 6 days were completely gone. The two new doublets (δ 2.12 and 3.33 ppm), presumed to be due to pyruvonitrile methylimine, had increased after 12 hr, but decreased after 6 days in favor of two complex multiplets centered at δ 2.28 and 3.53 ppm. The resonances of 1,1′,3,3′,5,5′-hexamethyl-4,4′-azopyrazole were never seen. Attempts to isolate pyruvonitrile methylimine or the phenylhydrazone derived from it led only to red gums that tlc showed to be complex mixtures.

A solution of 1.65 g (6.0 mmol) of 4-azido-1-methyl-3,5-diphenylpyrazole (IV) in 15 ml of cyclohexane (0.40 *M*) ceased to evolve gas after 30 min at the bp. The solution was decanted from the red-black gum that had deposited; glc showed the presence of benzonitrile (peak enhancement by added authentic material) and a more strongly retained component, in similar amounts. Chromatography of the gum on alumina with benzene as eluant gave 404 mg of dark, amorphous material and 275 mg of 1,1′-dimethyl-3,3′,5,5′-tetraphenyl-4,4′-azopyrazole, mp 183–185°; another 319 mg was obtained by allowing the decantate to cool and stand. Evaporation of the decantate and chromatography yielded 43 mg more; the total yield was 35.8%. The presence of α-methyliminophenylacetonitrile in solution was inferred from the spectra (see below), but it could not be isolated in identifiable form, owing to decomposition.

The foregoing azopyrazole crystallized as a nonstoichiometric hydrate from ethyl acetate: red needles; mp 183–185°; ir 3550, 3345, 1415, 1250, 1200, 1180, 1050, 1030, 980 cm^{-1}.

Anal. Calcd for $C_{32}H_{26}N_6 \cdot H_2O$: C, 74.98; H, 5.51; N, 16.40. Found: C, 75.76; H, 5.62; N, 15.72.

Several recrystallization from cyclohexane gave canary yellow leaflets: mp 183–185°; ir 1415, 1180, 1030, 980 cm^{-1}; nmr δ 3.70 (s, 3), 7.3–7.5 ppm (m, 10).

Anal. Calcd for $C_{32}H_{26}N_6$: C, 77.71; H, 5.30; N, 16.99. Found: C, 77.63; H, 5.23; N, 17.00.

The anhydrous form reverted to the hydrate on exposure to moisture; a mixture showed no melting point depression. Reduction with zinc dust in acetic acid gave 4-amino-1-methyl-3,5-diphenylpyrazole in 95% yield.

A similar experiment in more dilute solution (0.95 g of IV in 118 ml of cyclohexane, 0.029 *M*) was handled similarly, except that the decantate was evaporatively distilled *in vacuo*. A pale yellow liquid (70 mg) was obtained: nmr δ 3.73 (s), 7.30–7.44 (m), 7.50 (s), 7.80–8.0 ppm (m). The 7.50-ppm resonance, identifiable as benzonitrile, had an intensity of <29% of the total of all signals; the other resonances were in the ratio 3:3:2, corresponding to the CH_3, *m,p*-C_6H_5, and *o*-C_6H_5 of α-methyliminophenylacetonitrile. The ir spectrum (CCl_4) showed, in addition to bands identifiable with benzonitrile, absorption at 3070, 2960, 2920, 2890, 2770, 2230 (C≡N), 1615 (C=N), 1580, 1405 cm^{-1}.

Chromatography of the original gum and the residue from distillation gave 196 mg (23%) of the azopyrazole.

Photolysis of a solution of 1.60 g of IV in 200 ml of cyclohexane at 5–10° using a Hanovia L-679A-36 immersion lamp with pyrex filter for 2.5 hr resulted in complete disappearance of the ir absorption at 2120 cm^{-1} (N_3). A beige, amorphous solid had precipitated: 0.31 g, mp 120–124° dec. Rapid recrystallization from benzene gave yellow crystals, mp 131–133° dec, but further

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recrystallization gave a product with a lower, wider melting point range. Tlc indicated one major component and two minor contaminants: ir 2220 (C≡N), 1645, 1615, 1595, 1560 cm^{-1}, etc.; nmr δ 3.76 (s, 3, N-CH_3), 4.25 (s, 3, N-CH_3), 7.32 ppm (24–25, aryl). The filtrate was shown by glc to contain benzonitrile and α-methyliminophenylacetonitrile in about equal amounts; chromatography on alumina (benzene eluent) gave 0.24 g (17.5%) of 1,1′-dimethyl-3,3′,5,5′-tetraphenyl-4,4′-azopyrazole, mp 182–185°.

1,1′,3,3′,5,5′-Hexamethyl-4,4′-azopyrazole.—A solution of 500 mg (3.6 mmol) of 1,3,5-trimethyl-4-nitrosopyrazole[16] in 4 ml of acetic acid containing 150 mg (3.8 mmol) of hydrazine hydrate was heated for 1 hr on a steam bath and then diluted with 2 ml of water. Upon cooling, 120 mg (28%) of the azopyrazole, mp 175–185°, deposited. Sublimation at 150° (0.05 mm) and chromatography on a short column of silica gel ($CHCl_3$ as eluent) gave yellow leaflets: mp 189–192°, raised to 196–197.5° by recrystallization from benzene; ir (Nujol) 1560, 1500, 1420 cm^{-1}; nmr δ 2.43 (s, 3), 2.46 (s, 3), 3.73 ppm (s, 3, N-CH_3).

Anal. Calcd for $C_{12}H_{18}N_6$: C, 58.51; H, 7.37; N, 34.12. Found: C, 58.53; H, 7.30; N, 34.09.

Deoxygenation of 4-Nitroso-3-methyl-1,5-diphenylpyrazole.—Solutions of the nitrosopyrazole in benzene containing a molar equivalent of triphenylphosphine were heated on a steam bath for 30 to 60 min and then chromatographed on alumina. Elution with petroleum ether (bp 30–60°) produced α-phenyliminophenylacetonitrile (38–57%), and elution with chloroform produced triphenylphosphine oxide (~40%) and small amounts of amorphous solid shown by tlc to be a complex mixture, which could not be purified or separated. Reactions conducted at higher dilutions (~0.05 *M*) gave the higher yields.

Thermolysis of 4-Azido-1-methyl-3,5-diphenylpyrazole (IV) in the Presence of *p*-Anisyl Azide.—A solution of 1.20 g (4.36 mmol) of freshly prepared IV in 30 ml of cyclohexane was added with stirring over a 15-min period to a refluxing solution of 3.64 g (23.7 mmol) of *p*-anisyl azide in 20 ml of cyclohexane. One hour after completion of the addition, the dark solution was filtered from some tar. After standing in the cold for several hours, the filtrate deposited a brown, amorphous solid, mp 100–110°, 90 mg, which tlc showed to be a complex mixture. The presence of a substantial quantity of α-methyliminophenylacetonitrile in the solution was detected by glc. Evaporation of the filtrate and trituration of the residue with petroleum ether (bp 30–60°) left 250 mg of red solid, which was chromatographed (alumina, benzene) to give 210 mg of 1,1′-dimethyl-3,3′,5,5′-tetraphenyl-4,4′-azopyrazole, mp 182–185° (mixture melting point undepressed, ir identical). The filtrate was distilled at 70–72° (0.8 mm) to remove *p*-anisyl azide and the residue was chromatographed, to yield an additional 58 mg of azopyrazole, total yield 24.8%. Elution of the column with chloroform removed more strongly retained material in the form of a brown, amorphous solid, which resisted further attempts at purification. Nothing corresponding to 4-*p*-anisylazo-1-methyl-3,5-diphenylpyrazole, which should have been less strongly retained than the symmetrical azopyrazole, could be detected.

Thermolysis of 4-Azido-3,5-dimethylpyrazole (VII) in the Presence of Phenylhydrazine.—The azide VII obtained from 4.0 g (21.7 mmol) of the corresponding amine dihydrochloride (thus ~16.3 mmol) was taken up in 30 ml of benzene and dried ($MgSO_4$); 5 ml of phenylhydrazine was added; and the solution was heated at 60–70° for 4 hr. On cooling, 1.01 g of a reddish solid, mp 198–203°, precipitated. It was identified as the aminopyrazole (ir, nmr, tlc), yield 42.6% based on 21.7 mmol of starting material. Concentration of the filtrate produced more of the same product, but in a less pure state; no other product could be identified. Experiments using lower proportions of phenylhydrazine gave mostly intractable tars. In otherwise identical experiments in the absence of phenylhydrazine, no aminopyrazole could be detected.

Thermolysis of VII in the Presence of Aniline.—A solution of 1.0 g of azide VII (7.5 mmol) in 25 ml of benzene and 15 ml of aniline was heated overnight on a steam bath. The dark mixture was then diluted with 40 ml of benzene and extracted with five portions of 1 *N* HCl. The resulting yellow benzene solution was washed with water, dried ($MgSO_4$), and evaporated. Crystallization of the residue from petroleum ether (bp 60–75°) gave 85 mg (5.7%) of golden needles: mp 138.5–140°, nmr δ 2.66 (s, 6), 7.5–7.7 ppm (m, 5). A recrystallized sample had mp 140–141°, undepressed by an authentic sample of 3,5-dimethyl-4-phenylazopyrazole (reported[17] mp 143°).

Neutralization of the acidic extracts gave only an intractable reddish block gum, which tlc showed to be a complex mixture.

Thermolysis of VII in the Presence of Maleic Anydride.—The damp azide prepared from 11.07 g of amine dihydrochloride (0.06 mol) was dissolved in 125 ml of benzene and dried ($MgSO_4$). The solution was added dropwise to a stirred, refluxing solution of 11.96 g (0.12 mol) of maleic anhydride in 200 ml of benzene over 75 min. After 1 hr more of refluxing, a beige, amorphous powder had precipitated: 8.61 g; mp >305°; insoluble in common solvents; ir 3200–3300 (br), 1600–1800 cm^{-1} (br), poorly resolved.

Anal. Calcd for $(C_6H_7N_2O_3)_x$: C, 50.60; H, 3.64; N, 16.86. Found: C, 50.01; H, 5.22; N, 17.20.

Thermolysis of 5-Azido-3-methyl-4-phenylpyrazole (XI). A. In Toluene.—Azide XI was freshly prepared from the corresponding amine[18] and showed ir 2120 cm^{-1} (N_3) and nmr δ 2.28 (s, 3) and 7.25 ppm (s, 5). A solution of 5.35 g (26.9 mmol) of XI in 200 ml of toluene was refluxed for 3 hr; tlc showed that all azide was gone, and only two significant spots, corresponding to the aminopyrazole and β-methylcinnamonitrile, were present. Glc also detected only small amouns of bibenzyl and showed only one substance of low volatility, with retention time identical with that of an authentic[19] sample of β-methylcinnamonitrile.

The mixture was extracted with three 50-ml portions of 12% hydrochloric acid, and the combined extracts were basified (NaOH) and extracted with methylene chloride. Evaporation of the dried ($MgSO_4$) extract left 1.44 g of solid, shown by tlc to consist mainly of aminopyrazole. Estimation by nmr indicated it to contain 0.92 g (19.7% yield) of amine; recrystallization from benzene gave 0.47 g of pure amine, mp 140–141°. The toluene phase was evaporated and distilled in a kugelrohr at 150–180° (0.5 mm) to give 1.45 g (37.6%) of pale yellow β-methylcinnamonitrile: ir (neat) 3060, 3030, 2975, 2915, 2220 (C≡N), 1625 cm^{-1}; nmr δ 2.18 (d, 3, J = 7 Hz), 6.8 (q, 1, J = 7 Hz), 7.2–7.5 ppm (m, 5).

No other products could be detected by chromatography, and the yields were reproducible within 2% in different experiments.

B. In Chlorobenzene.—In an otherwise similar experiment, using chlorobenzene in place of toluene, the yield of aminopyrazole fell to 15%, with no other significant change.

4-Azido-1,5-diphenyltriazole and Its Fragmentation.[20]—By the general method used for the other azidopyrazoles, 4-amino-1,5-diphenylpyrazole[21] was converted to the azide in 82% yield, mp 95°, ir 2120 cm^{-1} (N_3). An analytical sample recrystallized from chilled petroleum ether had mp 97°.

Anal. Calcd for $C_{14}H_{10}N_6$: C, 64.11; H, 3.84; N, 32.01. Found: C, 64.16; H, 4.00; N, 31.98.

A 0.6-g sample of the foregoing azide dissolved in 30 ml of toluene was refluxed for 8 hr, whereupon the mixture was evaporated to dryness and the residue was recrystallized from petroleum ether (bp 60–80°). Yellow crystals of α-phenyliminophenylacetonitrile deposited, 0.4 g (85%), mp 72° (undepressed by authentic material). The mother liquors appeared to contain only this same substance.

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Registry No.—I, 40697-50-5; II, 40697-51-6; III, 40697-52-7; IV, 40697-53-8; V, 40697-54-9; VI, 40697-55-0; VII, 40697-56-1; XI, 40697-57-2; 1,3,5-triphenylpyrazole, 2183-27-9; 1,3-diphenyl-5-methylpyrazole-4-carbohydrazide, 40697-58-3; 4-amino-3,5-diphenylpyrazole *N*-benzylidene derivatives, 40697-59-4; 4-amino-3,5-diphenylpyrazole, 5272-85-5; pyruvonitrile anil, syn, 40698-05-3; pyruvonitrile anil, anti, 40698-06-4; pyruvonitrile phenylhydrazone, 40697-35-6; 1,1′-dimethyl-3,3′,5,5′-tetraphenyl-4,4′-azopyrazole, 40697-36-7; 1,1′,3,3′,5,5′-hexamethyl-4,4′-azopyrazole, 40697-37-8; VII–maleic anhydride polymer, 40690-47-9; β-methylcinnamonitrile, 14368-40-2.

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(20) We are indebted to Dr. W. Resemann for carrying out this experiment.

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