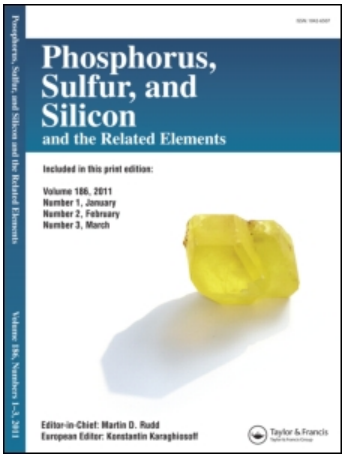

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SULFENAMIDES AND SULFINAMIDES VI.† REACTIONS OF ARYL SULFENAMIDES WITH DIPHENYLPICRYLHYDRAZYL FREE RADICAL

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Hydrogen abstraction may be postulated as the first step in reactions of aryl sulfenamides with the stable diphenylpicrylhydrazyl free radical. Differences in the reactivity of the sulfenamides are controlled by steric and electronic effects of the substituents, with attention drawn to the capacity of the divalent sulfur atom to relay these effects. Origins of decomposition products are discussed.

Key words: Sulfenamides, diphenylpicrylhydrazyl free radical, sulfenyl-nitrogen bond, radical stability.

Stable diphenylpicrylhydrazyl (**1**), prepared over sixty years ago[1] is noteworthy as the first free radical for which hyperfine structure was observed in electron spin resonance studies[2] and as a reagent for studies of free radical hydrogen abstraction reactions. In addition **1** has itself acted as a substrate for reaction with nitrogen dioxide, halogens and other free radicals leading to substitution at one or both para positions of the phenyl rings with transfer of hydrogen to nitrogen to give mono- or disubstituted hydrazines.

Study by others of hydrogen abstractions by **1** has had an initial, but as events have revealed, a superficial attraction of simplicity with rates of reaction being followed by loss of absorption of the radical at 515–520 nm. Determinations of reaction constants have not fallen into a consistent pattern and expressions of first,[3] second[4,5] and third order[4] rate constants have been observed.

Although **1** has not generally been regarded as a powerful dehydrogenating agent, it has displayed strong capability for removal of hydrogen attached to nitrogen in a variety of compounds, exemplified by the quantitative recovery of nitrogen and diphenylpicrylhydrazine (**18**) from reactions with ammonia or hydrazine.[6,7] Hydrogen abstraction from primary aliphatic[4] and secondary aromatic amines[5] has been established. Abstraction from primary aromatic amines is subject to substituent influence. Whereas electron donating groups enhance reactivity, para substitution with nitro, cyano and benzoyl groups deactivates the system to a very slow reaction in the dark, but in these instances photoactivation leads to a ready reaction.[4]

Higher temperatures, about 80–90°C, are required for reactions with hydroaromatics, even with a substrate as active as 9,10-dihydroanthracene. The difference in reactivity, well shown by comparison of dibenzyl, which is unreactive, with its aza analogue *N*-(benzyl)-aniline, which is rapidly converted to benzylidene aniline,[6]

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has been attributed to the greater readiness with which nitrogen can pass from a tetrahedral to a planar trigonal configuration (planarity at a carbon atom will be established only concurrently with fission of the C—H bond). Only at an advanced stage of the dehydrogenation will any resonance stabilization of the resulting intermediate become effective. Resonance stabilization assists fission of the N—H bond well before the transition state is reached with consequent lowering of the energy of activation.

Present work concerns the extents to which these factors apply to N—H bond fission in the sulfenamides (ArSNHAr), where the group is subject to the further influence of directly linked sulfur atoms. Thus present concern is with reactions whose first step may be nominally expressed as:

$$\text{ArSNHAr}' + \mathbf{1} \text{ — } \text{ArS}\dot{\text{N}}\text{Ar}' + \mathbf{18} \qquad (1)$$

RESULTS AND DISCUSSION

Figure 1 provides an initial comparison of reaction rates and leads to the following major conclusions: (i) reactions of the sulfenamides are enhanced by electron donating substituents. (ii) polar and steric factors are important in the reaction.

Structure and rate of reaction

The disposition of curves (Figure 1) above or below that of the parent **2** is indicative of steric and electronic influences exercized by substituents. In the first instance

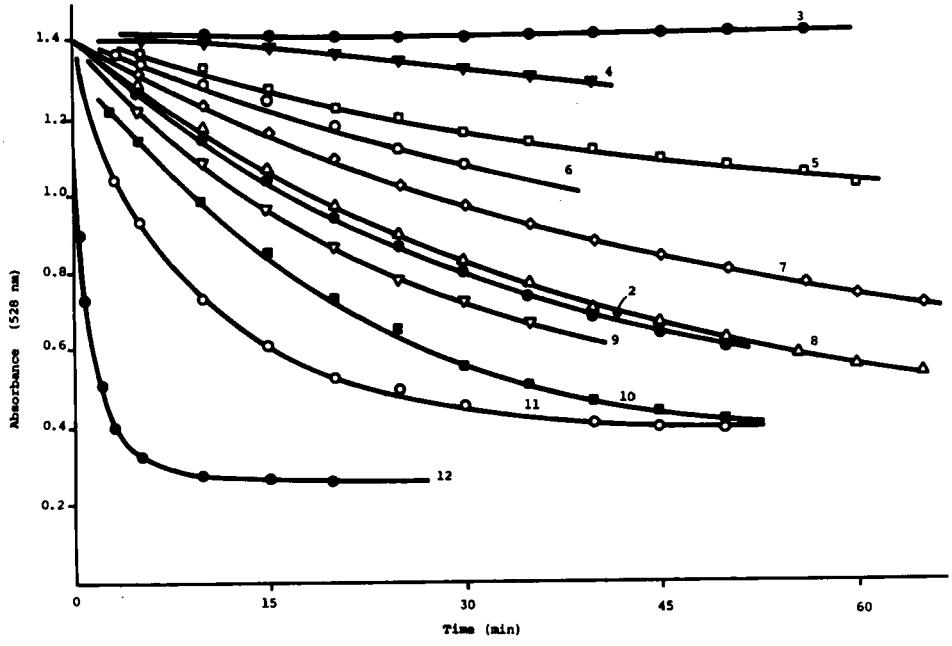


FIGURE 1 Substituent influence on the reaction of sulfenamides with diphenylpicrylhydrazyl. **2**, Ph-S-NH-Ph; **3**, Ph-S-NH-C_6H_4-(2)-Cl; **4**, Ph-S-NH-C_6H_4-(2)-CH_3; **5**, (2)-Cl-C_6H_4-S-NH-Ph; **6**, Ph-S-NH-C_6H_4-(2)-O-CH_3; **7**, (4)-Cl-C_6H_4-S-NH-Ph; **8**, Ph-S-NH-C_6H_4-(4)-Cl; **9**, (2)-CH_3-C_6H_4-S-NH-Ph; **10**, (4)-CH_3-C_6H_4-S-NH-Ph; **11**, Ph-S-NH-C_6H_4-(4)-CH_3; **12**, Ph-S-NH-C_6H_4-(4)-O-CH_3.

4-substitution with chlorine in the N-aromatic ring (**8**) had very little effect, giving only marginal retardation. By contrast, the extent of inhibition imposed by a 2-chlorine in the same ring (**3**) is remarkable in completely blocking reaction. In view of the absence of influence from the 4-position, which would be better favored for electronic influence, the inhibition from the 2-position must be attributed completely to steric hindrance.

Retardation by chloro substitution in the S-aromatic ring (**5, 7**) may be attributed to an electronic influence enhancing the withdrawing effect of the phenylthio group and more markedly from the 4-position (**7**). The importance of the environment of the N—H group is reinforced by the variously substituted methyl derivatives (**4, 9, 10, 11**) since the chlorine and methyl groups are about equal size. The influence on the reaction of 2-methyl substitution in the N-aromatic ring (**4**) must again be due to a combination of steric and electronic effects. The fact that the reaction is not completely inhibited must mean that the methyl group is promoting the reaction slightly through a hyperconjugative effect. By contrast, a methyl group in the 4-position of the N-aromatic ring (**11**) produces considerable acceleration. Not unexpectedly, the accelerating influence of a methyl group in the 4-position of the S-aromatic ring (**10**) in opposing the withdrawing effect of the phenylthio-group is greater than from the 2-position. In accordance with these principles, substitution with a 2-methoxyl group in the N-aromatic ring (**6**) produces steric retardation but its greater mesomeric effect gives a rate faster than that of the equivalent methyl derivative. Methoxyl substitution in the 4-position (**12**) gives the fastest reacting sulfenamide.

The effects of substituents on reactions of **1** with sulfenamides were compared with effects on a series of aromatic amines, which, after a set reaction time of 90 min gave the relative extents of reaction: 4-anisidine (Δ 1.04; pKa 5.31) > 2-anisidine (Δ 0.83; pKa 4.52) > 4-toluidine (Δ 0.67; pKa 5.10) > 2-toluidine (Δ 0.39; pKa 4.39) > aniline (Δ 0.33; pKa 4.33) where "Δ" is the extent of loss of absorbance of **1**. It may be noted that the order of reaction of amines with **1** does not follow that of the pKa values.[8,9] This order of reactivities, together with the fact that the parent sulfenamide (**2**) has a pKa of 2.82,[10] illustrate again problems encountered in attempts to correlate physical properties with structure.

Overall, the results provide another instance of the capacity of a divalent sulfur atom to relay substituent effects to a reaction center.

The unusual counterpoised effects on the rate of reaction given by methyl substitution in the N-aromatic ring, accelerating from the 4-position but inhibiting from the 2-position, provide a contrast with the common accelerating effect from both positions in the reaction with phenols,[11] thus drawing attention to the easier access of **1** to the structurally simpler phenolic group.

Hydrogen abstraction from the substrate has been proposed as a rate determining step in reactions of **1**. A transition state similar to that suggested for the peroxy radical/antioxidant reaction, through which polar influences are exerted,[12,13] may also be considered for the sulfenamide reactions, subject further to consideration of emergent radical stability.

$$\begin{array}{l} \text{Ar-S} \\ \quad | \\ \text{Ar-NH} \end{array} + \begin{array}{l} \text{C}_6\text{H}_2(\text{NO}_2)_3 \\ \quad | \\ \cdot\text{N-N}(\text{C}_6\text{H}_5)_2 \end{array} \rightleftharpoons \left[\begin{array}{l} \text{Ar-S} \qquad \text{C}_6\text{H}_2(\text{NO}_2)_3 \\ \quad | \qquad\quad | \\ \text{Ar-N---H---N-N}(\text{C}_6\text{H}_5)_2 \end{array} \right] \rightleftharpoons \begin{array}{l} \text{Ar-S} \\ \quad | \\ \text{Ar-N}\cdot \end{array} + \begin{array}{l} \text{C}_6\text{H}_2(\text{NO}_2)_3 \\ \quad | \\ \text{HN-N}(\text{C}_6\text{H}_5)_2 \end{array}$$

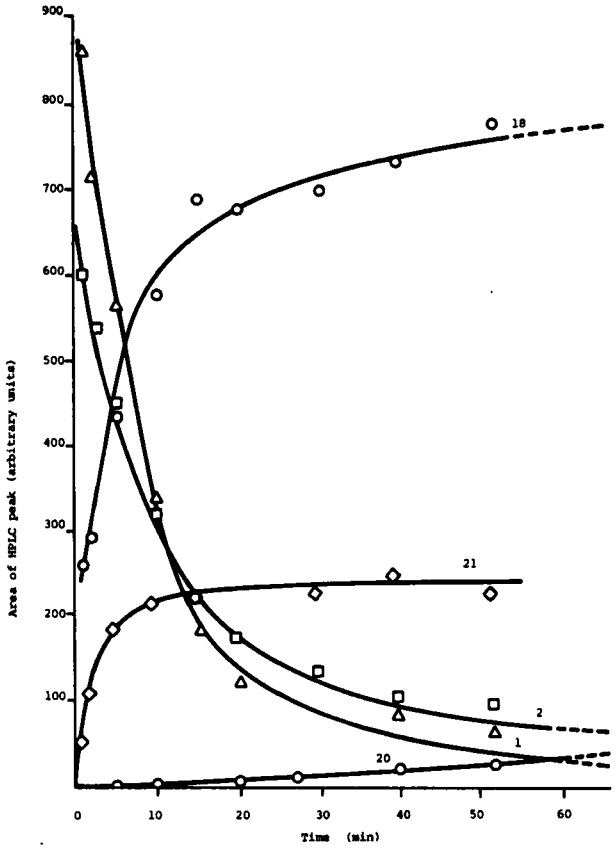


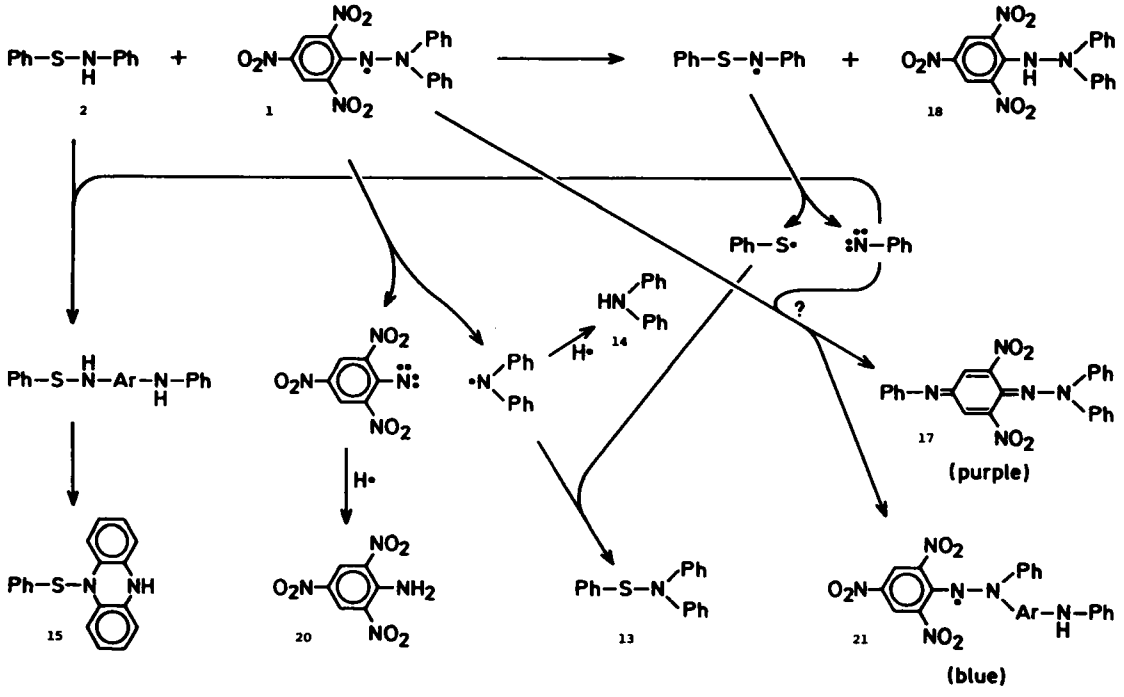
FIGURE 2 Reaction of diphenylpicrylhydrazyl (**1**) with *N*-(phenyl)benzenesulfenamide (**2**). Changes in concentration of reactants and products with time. **18**, diphenylpicrylhydrazine; **20**, Picramide; **21**, *N*-phenyl-*N*-(4-anilinophenyl)-picrylhydrazyl.

Thus, the more stable the ArSṄAr radical is, the more rapid will be the reaction. Supporting this expression, Figure 2 shows that in the reaction of **1** with **2**, the rates of loss of substrate and reagent are closely related and are equally conversely matched by the formation of **18** over the first 60 min to almost complete loss of reactants. A superimposed instability of the first formed products is shown by the very early appearance of fragments.

Since the reaction of **1** with **2** (Figure 1) is considerably faster than that of **1** with aniline (see above), the phenylthio group must contribute strongly to the stabilization of ArSṄAr, probably by a sharing of the unpaired electron between the sulfur and nitrogen atoms. Additional stabilization of the radical, and therefore more rapid reaction, is achieved by the hyperconjugative effect of the 4-methyl group on the N-aromatic ring and, even more so, by the electron-donating effects of the 4-methoxyl group.

Products of reaction of **1** *with* **2**

Scheme 1 provides the basis for discussion of secondary reactions but does not imply any quantitative relationships. The majority of compounds isolated were derived from **1** with only compounds **13** and **15** containing sulfur.



SCHEME 1 Possible course of reaction between diphenylpicrylhydrazyl (**1**) and *N*-(phenyl)benzenesulfenamide (**2**).

Compound **15** appears to have been formed by addition of an anilino radical or phenyl nitrene to **2** and subsequent oxidation. Other isomeric amino sulfide structures have been rejected as they would have been formed by addition of the anilino radical or phenyl nitrene to a 2- or 4-aminodiphenyl sulfide. Neither of these two isomers was noted in the reaction mixture despite the fact that both are readily formed under free radical[14] and ionic conditions[15,16] by rearrangement of **2** and both are much more stable than **2**. Decomposition of **1** or **18** also results in the formation of the diphenylamino radical ($Ph_2N\cdot$) which may combine with PhS· to form **13**.

Strong fragmentation peaks at m/z 169 (Ph_2NH) and 168 suggest that compound **16** (Table I) has been derived from diphenylamine and it has been assigned the structure of *N,N'*-diphenyl-2-phenylenediamine on the basis of its yellow color.[17] However since this compound and its other possible isomers are all aromatic amines

TABLE I

Products of reaction between diphenylpicrylhydrazyl (**1**) and *N*-(phenyl) benzenesulfenamide (**2**)

Products	No.	R_f TLC	Compared with Standard	Color	CI (methane) mass spectral data—main peaks
N,N-(diphenyl) benzene sulfenamide	**13**	0.91	*	colorless	278[M + 1]$^+$ (100), 277(63), 196(10), 168(70)
diphenylamine	**14**	0.82	*	colorless	170[M + 1]$^+$ (100)
N-(phenylsulfenyl) phenazine or isomer	**15**	0.69		yellow	291[M + 1]$^+$ (100), 290(22), 257(11), 213(9), 201(8), 185(48), 184(29), 183(33), 139(13), 126(10), 111(44)
N,N'-(diphenyl)-2-phenylenediamine or isomer	**16**	0.62		yellow	261[M + 1]$^+$ (43), 260(35), 259(43), 197(10), 169(82), 168(100), 126(12)
N-(diphenylamino) *N'*-(phenyl)-2,6-dinitro-benzo-quinonediimine	**17**	0.52		purple	440[M + 1]$^+$ (100), 439(34), 423(11), 393(11), 303(11), 275(91), 257(11), 210(7), 198(28), 184(14), 170(100), 169(69), 168(89)
diphenylpicryl-hydrazine	**18**	0.46	*	brown	396[M + 1]$^+$ (37), 229(18), 169(100)
unknown	**19**	0.31		green	
picramide	**20**	0.26	*	yellow	229[M + 1]$^+$ (100), 213(3), 199(4), 183(1), 169(2)
N-(phenyl)- *N*-4-(anilinophenyl)-picrylhydrazyl	**21**	0.22		blue	307(4), 287(5), 279(14), 269(4), 261(28), 260(19), 259(24), 229(100)

which tend to be oxidized spontaneously, a small amount of impurity in any of them could produce a yellow color.

Compound **17** (purple) gave what appeared to be a strong $[M+1]^+$ ion at m/z 440 and equally strong fragment ions at m/z 275, 170 and 168. Fragmentation between the N—N bond of **17** would give diphenylamine (m/z 170, $[M+1]^+$), which could be oxidized to carbazole m/z 168 ($[M+1]^+$), and a quinone diimine which could be reduced to m/z 275, **17**-Ph_2N + 4H, ($[M+1]^+$) at the expense of diphenylamine.

Compound **21** was the main component responsible for the blue color observed and was the second major product amounting to about 26% of the total weight of the reactants. The mass spectrum did not appear to give a molecular ion, but two major peaks, namely m/z 229, which probably corresponds to the $[M+1]^+$ ion of picramide (**20**), and m/z 261 which could be the $[M+1]^+$ ion of structure Ph-NH_2^+-C_6H_4-NH-Ph.

Compound **21** appeared to be somewhat unstable. It was noted during purification, that **20** was almost always present as an impurity despite repeated purification steps. Solutions of **21** in chloroform reacted within 30 min with aniline, thiophenol and **2**, turning brown. A solution of **21** in chloroform-acetone gradually changed from blue to brown over a two-week period, and analysis of the discolored mixture showed the presence of **18**. The observed high reactivity of the compound resembled that of **1**, and suggested that it might be a stable free radical. The possible structure (**21**) for this compound is equivalent to a molecule of **1** having an anilino group substituted onto the 4-position of one of the phenyl rings. Adduct formation of this type has been proposed and in some cases adducts have been isolated.[18,19] Furthermore, aniline reacted with **1** to produce a blue compound which had retention behaviour and reactivity identical to **21**. A blue coloration was observed with all sulfenamides when they were reacted with **1**. HPLC analysis of these reaction mixtures showed slightly different retention times for the blue compound formed, depending on the substitution of the sulfenamide (Table II). Within experimental error, the sulfenamides containing the same substituent on the nitrogen moiety gave blue compounds having the same retention time regardless of the substitution on the sulfur moiety.

TABLE II

Blue compounds formed by sulfenamides with diphenylpicrylhydrazyl (**1**)

Sulfenamide (Ar-S-NH-Ar') Ar	Ar'	Amine	HPLC retention time (relative to **18**)
Ph	Ph		1.19
4-Cl-C_6H_4	Ph		1.20
2-Cl-C_6H_4	Ph		1.19
Ph	4-Cl-C_6H_4		1.27
4-Cl-C_6H_4	4-Cl-C_6H_4		1.27
Ph	2-Cl-C_6H_4		1.24
Ph	2-CH_3-C_6H_4		1.34
		aniline	1.20
		4-bromoaniline	1.29

The formation of these compounds may be explained as follows. Compound **1** abstracts a hydrogen atom from **2** to form **18** which builds up rapidly (Figure 2). The other product of this first step is the sulfenamido radical (PhSṄPh) which may in turn break down into a sulfenyl radical (PhS·) and a phenyl nitrene (PhN:). The phenyl nitrene may add to **1** to form **21,** which also builds up rapidly (Figure 2), or it may displace NO_2 from **1** to form **17.** The phenyl nitrene may also add to the *N*-aromatic ring of **2** and subsequent oxidation could produce **15.** Formation of **20** takes place slowly (Figure 2), is clearly a secondary reaction and probably results from the decomposition of **1** or **18.**

EXPERIMENTAL

Instrumentation and Materials. UV-Visible spectra were determined on a Pye Unicam SP1800 spectrometer and ^{1}H NMR spectra ($CDCl_3$) were taken on a JEOL FX100 spectrometer. Electron impact (EI) mass spectra were recorded on an A.E.I MS12 or an A.E.I MS902 mass spectrometer. GC-Chemical Ionization (GC-CI) mass spectra were obtained using a Finnigan 3200 quadrupole GC-MS system interfaced to an Incos 2300 data system. High pressure liquid chromatography (HPLC) was performed on a Waters Associates instrument equipped with two 6000A pumps, U6K injector, 440 UV detector, 730 data module and 720 system controller. Products were separated on a μ-Porasil column using ethyl acetate/light petroleum (1:19) as eluent at a flow rate of 3 ml/min. All reagents were of analytical grade and used without further purification.

Sulfenamides **(2–12), 20** and **18** were prepared by standard methods[20,21,22] and gave satisfactory elemental analyses. *N,N*-Diphenylbenzenesulfenamide **(13)** was prepared by the general method.[20] The EI mass spectrum of the product purified by chromatography showed a molecular weight 277 and a major fragment at m/z 168 (Ph_2N^+). The ^{1}H NMR spectrum had only one multiplet at δ 7.20–7.50.

Light petroleum refers to the fraction b.p. 40–60°C.

Procedures

(*i*) *Rates of reaction.* A typical reaction was as follows: To a solution of sulfenamide (6.25 μmol) in chloroform (4.5 ml) was added **1** (12.5 μmol) in chloroform (0.5 ml), the reaction allowed to proceed at room temperature and the absorbance monitored at 528 nm (λ_{max} of **1** in chloroform). Results are recorded in Figure 1.

(*ii*) *Products of reaction of* **1** *with* **2.** A solution of **1** (0.394 g, 1 mmol) and **2** (0.1 g, 0.5 mmol) in chloroform (20 ml) was allowed to stand in the dark for 3 hr. Solvent was removed in vacuo and the residue, chromatographed on a column of silica gel using ethyl acetate/light petroleum as developing solvent, gave nine fractions distinguished by color. TLC on Kieselgel G plates using the same solvent system showed that the fractions consisted of mixtures. Purification of these fractions by HPLC gave nine compounds (Table I). Products were characterized by comparisons of R_f values on TLC and C.I. mass spectra with known materials where possible. Structures of compounds **13, 14, 18** and **20** (Table I; c.f. Scheme 1 for structures) were established by having HPLC retention data and mass spectral fragmentation identical with those of authentic materials. Other identifications, as discussed earlier, are tentative due to the limited amounts of material available.

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