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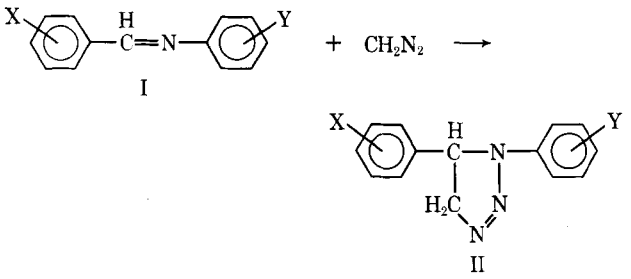
Triazolines VI: Evaluation of 1,5-Diaryl-Δ^2-1,2,3-triazolines and Arylidene Anilines for Herbicidal Activity

PANKAJA K. KADABA

Abstract □ A large number of 1,5-diaryl-Δ^2-1,2,3-triazolines and arylidene anilines (from which the triazolines are derived) have been examined for the first time for herbicidal activity. Although the majority of the compounds as a class showed no activity, those bearing 3 or 4 halogen substituents evinced slight activity in postemergence tests.

Keyphrases □ 1,5-Diaryl-Δ^2-1,2,3-triazolines—herbicidal activity □ Arylidene anilines—herbicidal activity □ Herbicidal activity—1,5-diaryl-Δ^2-1,2,3-triazolines, arylidene anilines

Studies in the author's laboratories on solvation effects and the role of protic–dipolar aprotic solvents in 1,3-cycloaddition reactions (1–5) have helped pave the way to the proper understanding and application of solvation energy to assist bimolecular cycloaddition reactions. Thus, the accelerating effect of water on the 1,3-cycloaddition of diazomethane to Schiff bases (arylidene anilines) (I) has led to a versatile general method for the synthesis of the rarely encountered Δ^2-1,2,3-triazolines (II) (3, 6) (Scheme I). By carrying out



Scheme I

the addition reaction in aqueous dioxane solutions, a variety of previously unknown 1,5-diaryl-1,2,3-triazolines have been obtained in good yields. Earlier methods of syntheses (7, 8) have either failed to give a triazoline adduct or have yielded only insignificant amounts of the products. As a result, there is no reference in the literature to any studies on the biological properties of this group of heterocyclic compounds. The cycloaddition reaction in aqueous dioxane solutions has now made a large number of 1,2,3-triazolines readily available in sufficient quantities to permit, for the first time, a detailed screening of these compounds for biological activity. In this paper, a brief report on the results of screening for herbicidal activity is presented.

About 30 1,5-diaryl-1,2,3-triazolines (II) bearing one or two substituent groups on the *C*-phenyl and/or the *N*-phenyl and the respective arylidene anilines (I), from which the triazolines are derived, were screened for preemergence, postemergence, and defoliant activities. Although the majority of the 1,2,3-triazolines and arylidene anilines showed no activity, compounds bearing 3 or 4 halogen substituents evinced slight activity. The latter compounds caused visible chlorosis, contact and formative effects, and necrosis in the broadleaf species in postemergence applications; the cereals, however, were unaffected. Both cereals and broadleaf species also were not affected in preemergence or defoliant tests.

EXPERIMENTAL

The 1,5-diaryl-1,2,3-triazolines and arylidene anilines containing such substituents as the nitro, chloro, bromo, methyl, methoxy, or carbalkoxy groups on the *C*-phenyl and/or the *N*-phenyl ring, in the *o*-, *m*-, or *p*-positions (with the exception of the carbalkoxy groups, which were present only in the *p*-position of the *N*-phenyl ring) were previously prepared in the author's laboratory (1–6). The *p*-aminobenzoic esters necessary for the preparation of the arylidene *p*-aminobenzoates were synthesized, in a convenient one-step reaction, by refluxing the *p*-aminobenzoic acid with excess alcohol in the presence of commercial boron trifluoride ethyl ether as the catalyst (9).

The test compounds were dissolved in acetone containing 0.5% polysorbate 20[1] and sprayed vertically onto potted seedlings aged 7 days from planting at the time of treatment. The spray volume used was 12 ml. directed evenly over 3 sq. ft. of area, and the spray rates were such that applications equivalent to 0.1 and 1 lb./acre were obtained. Each rate was applied to 12 pots simultaneously (two pots of each of the six species used). Observations were then made from four plants of each broadleaf species (two plants per pot) and 20 plants of each cereal species (10 plants per pot) at intervals of 1–2, 5, and 10–14 days for individual visual effects, the latter comprised of abscission, chlorosis, contact and formative effects, curvature, galling, killing, necrosis, abnormal pigmentation, quilling, adventitious root formation, and stunting.

Compounds bearing one or two halogen atoms, either alone or in conjunction with another group, showed little activity. Those bearing 3 or 4 halogen atoms, either alone or otherwise, produced visual effects, the tetrahalogen compounds being more powerful. Among those tested, 1-(3,4-dichlorophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline and 2,4-dichlorobenzylidene-3-chloroaniline appeared to be the most active and produced a greater variety of visual effects in a greater variety of crops than any of the other compounds.

[1] Tween 20, Atlas Chemical Industries, Wilmington, Del.

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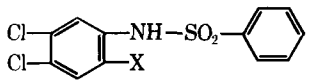
Preparation and Antitumor Activity of Some Schiff Bases of 2′-Amino-4′,5′-dichlorobenzenesulfonanilide and 2′-Amino-*p*-toluenesulfonanilide

JOHN H. BILLMAN and ROBERT L. SCHMIDGALL

Abstract □ Series of variously substituted salicylaldehyde Schiff bases and 2-substituted-*p*-[*N*,*N*-bis(2-chloroethyl)amino]benzaldehyde Schiff bases of 2′-amino-4′,5′-dichlorobenzenesulfonanilide and 2′-amino-*p*-toluenesulfonanilide have been prepared and screened for antitumor activity. None of the compounds showed appreciable activity against L-1210 leukemia.

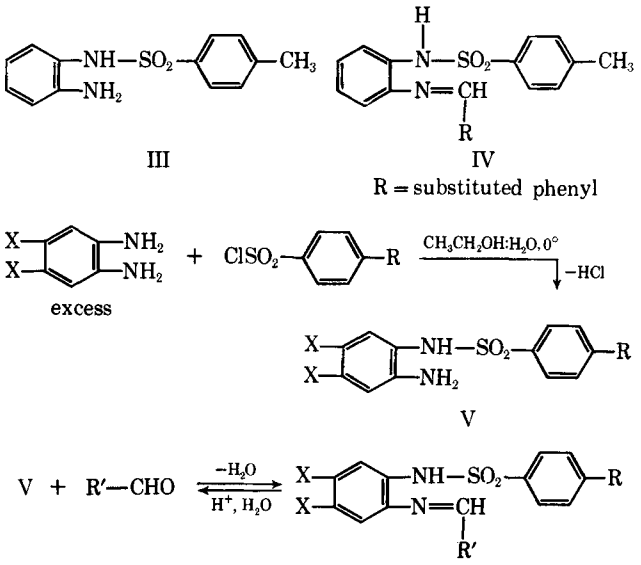
Keyphrases □ 2′-Amino-4′,5′-dichlorobenzenesulfonanilide, Schiff bases—synthesis, antitumor activity evaluation □ 2′-Amino-*p*-toluenesulfonanilide, Schiff bases—synthesis, antitumor activity evaluation □ Antitumor activity evaluation—2′-amino-4′,5′-dichlorobenzenesulfonanilide, 2′-amino-*p*-toluenesulfonanilide □ IR spectrophotometry—structure, analysis

Woolley *et al.* (1–3) have shown that 4′,5′-dichloro-2′-nitrobenzenesulfonanilide (I*a*) is effective in permanently curing some spontaneous mammary cancers of mice. Evidently the not very toxic I*a* functions as an antimetabolite of 1,2-dimethyl-4,5-diaminobenzene and inhibits the biosynthesis of vitamin B_{12}, which is synthesized by the spontaneous cancers but not by the hosts (4). 2′-Amino-4′,5′-dichlorobenzenesulfonanilide (I*b*) was also apparently active but much less potent than I*a*.



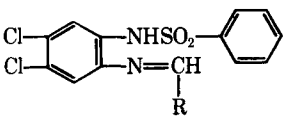
I*a*, X = —NO_2
I*b*, X = —NH_2

In view of the antitumor activity or at least accessibility to the tumor site of I*a* and I*b* plus the convenient handle of the primary amino group of I*b* for further structural modifications, it was decided to prepare some derivatives of Type II. Twelve of these derivatives (Table I) were conveniently synthesized (Scheme I) by condensing the desired aldehyde with I*b*, which was prepared from the corresponding *o*-phenylenediamine and arylsulfonyl chloride. The aldehydes employed were those substituted salicylaldehydes and 2-substituted-*p*-[*N*,*N*-bis(2-chloroethyl)amino]benzaldehydes which have previously shown antitumor activity



Scheme I

either in their own rights or in easily hydrolyzed derivatives (5–15). It was hoped that these new azomethine derivatives (II) would be even more potent antineoplastic drugs than either the active parent amine I*b* or the active aldehyde alone.



R = substituted phenyl
II

It is well known that a majority of tumors contain cells with a lower pH than cells in normal tissues. Fitch and Voegtlin (16) also have shown that the administration of glucose to tumor-bearing animals can produce an even lower pH value for the tumor cells. Since Schiff bases are one class of compounds that hydrolyze readily *in vitro* under mildly acidic conditions,