Synthesis and Antimicrobial Activity of Some Novel Heterocycles. Azolo-*as*-triazines[1]

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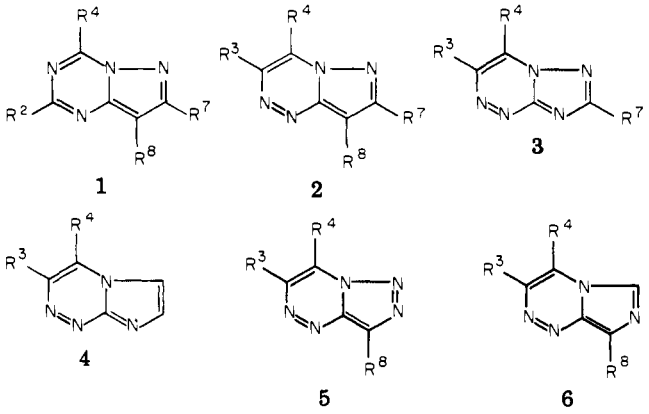
A general method for the preparation of substituted azolo-*as*-triazines is reported. The various α-aminoazoles (3-aminopyrazole, 3-amino-*s*-triazole, 5-amino-*v*-triazole, 2-aminoimidazole, 4(5)-aminoimidazole, and their substituted derivatives) were diazotized and coupled with active methylene reagents (β-diketones, β-keto esters, β-keto acids, ethyl cyanoacetate and malononitrile) to afford intermediates which were then cyclized in methanol, acetic acid, or benzene. The cyclized products were the corresponding pyrazolo[2,3-*c*]- (**2**), *s*-triazolo[2,3-*c*]- (**3**), imidazo[3,4-*c*]- (**4**), *v*-triazolo[1,2-*c*]- (**5**), and imidazo[3,4-*c*]-*as*-triazines (**6**) with substituents such as amino, alkyl (or hydrogen), ester, ketone, or nitrile, depending on the methylene reagent used. Of the 28 compounds synthesized (representative of the five heterocycles) six, with various substituents, exhibited specific in vitro antimicrobial activity. Compounds **2b** and **2d** inhibited the gram-negative bacterium *Pseudomonas*, **3a**, and **5a** inhibited the gram-positive *Staphylococcus*, **2h** inhibited the dermatophyte *Trichophyton*, and **2c** inhibited the yeast *Candida* in the MIC (minimum inhibitory concentration) range of 0.40–0.16 μmol/ml.

Our recent work on the synthesis of 2,4-dialkylpyrazolo[1,5-*a*]-1,3,5-*s*-triazines[2] (**1**) as nitrogen bridgehead analogues of the purines suggested the synthesis and antimicrobial testing of the isomeric pyrazolo[2,3-*c*]-1,-3,4-*as*-triazines (**2**).

Since only a few derivatives of this fused *as*-triazine ring system (**2**) were known,[3] a logical extension of this work was to synthesize additional related ring systems, such as the triazolo[2,3-*c*]-*as*-triazines (**3**), the imidazo[1,2-*c*]-



as-triazines (**4**), the *v*-triazolo[3,4-*c*]-*as*-triazines (**5**), and the imidazo[3,4-*c*]-*as*-triazines (**6**).

Chemistry. Earlier literature methods employed substituted 3-amino-*as*-triazines as the basis of synthesizing these fused rings. For example, 3-amino-5,6-dimethyl-1,3,4-triazine has been condensed with bromoacetaldehyde to afford 3,4-dimethylimidazo[1,2-*c*]-*as*-triazine[4] (**4**, $R^2 = R^3 = CH_3$). Such a method has limitations dependent on the availability of appropriate 3-amino-5,6-disubstituted *as*-triazines.

A more logical approach was taken, in which azole diazonium salts,[5] prepared from the appropriate α-aminoazoles (3-aminopyrazoles,[6,7] 3-amino-*s*-triazoles,[8] 2-aminoimidazoles,[9] 5-amino-*v*-triazoles,[10,11] and 5-aminoimidazoles[12]), were coupled with active methylene reagents, followed by cyclization of the intermediates to the fused ring systems. For example, 3-amino-4-(*p*-chloro)-phenylpyrazole was diazotized and coupled in an aqueous, buffered (sodium acetate) solution with nonane-4,6-dione to give an intermediate, which upon thermal cyclization (in methanol, acetic acid, or benzene) gave 3-*n*-butyryl-8-(*p*-chloro)phenyl-4-propylpyrazolo[2,3-*c*]-*as*-triazine (**2b**). All of the azole (pyrazole, triazole, imidazole) diazonium salts coupled smoothly with β-diketones (pentane-2,4-dione, heptane-3,5-dione, and nonane-4,6-dione) to give intermediates which were then cyclized. The fused *as*-triazines (**2–6**) appeared to be stable to oxidizing reagents. Thus, 7-benzylsulfonyl-3-*n*-butyryl-4-*n*-propyl-*s*-triazolo[2,3-*c*]-*as*-triazine (**3b**) was prepared from the corresponding 7-benzylthio precursor (**3a**) with *p*-chloroperbenzoic acid in chloroform. As an alternate method of synthesis, ring closure of the diazotized and coupled 3-amino-5-benzylsulfonyl-*s*-triazole (prepared by oxidation of 3-amino-5-benzylthio-*s*-triazole[13]) also gave **3b** (Scheme I).

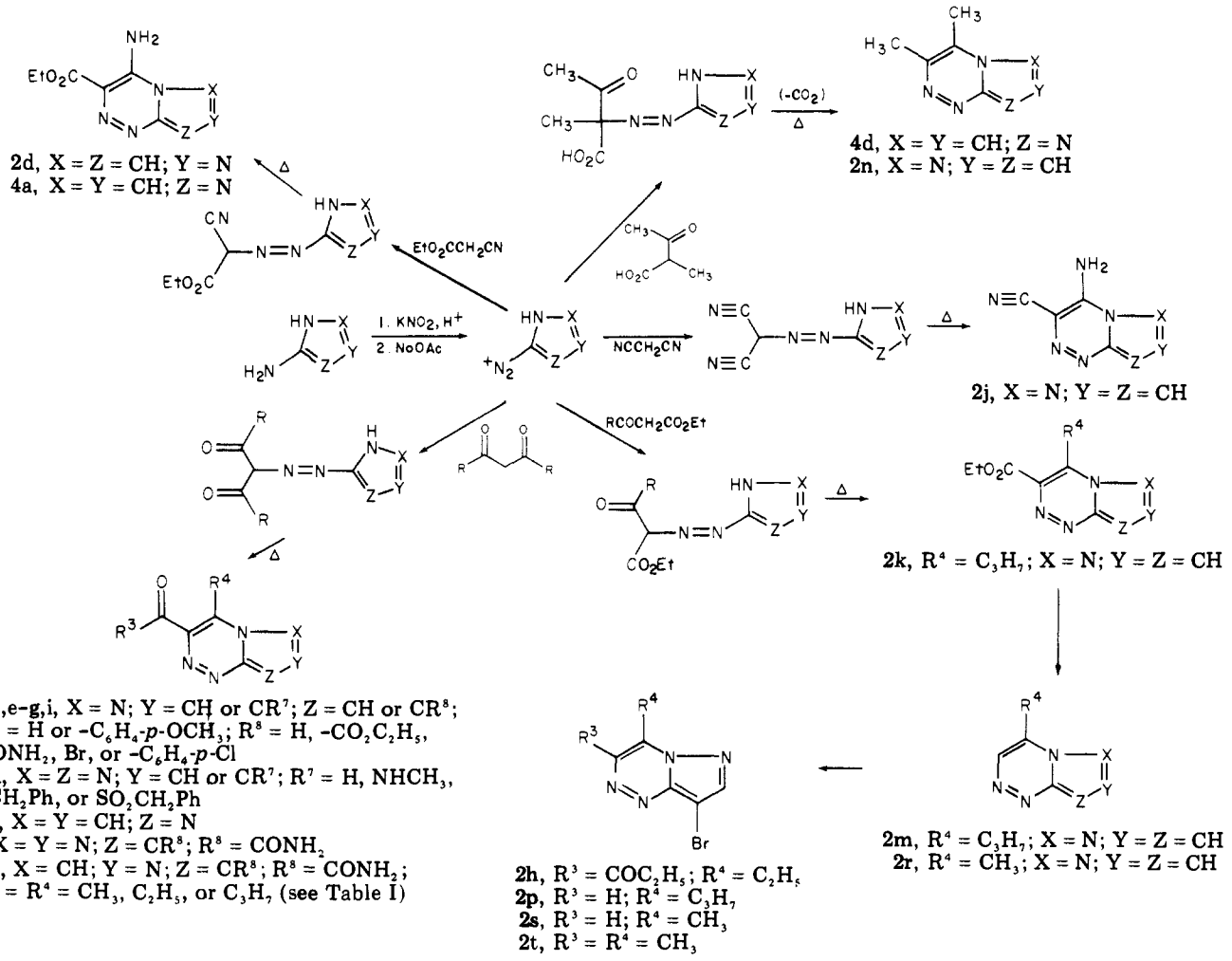
The coupling of ethyl cyanoacetate with a diazotized amine, such as imidazole-2-diazonium chloride, buffered with sodium acetate, gave an intermediate which was cyclized, in this case, to ethyl 4-aminoimidazo[1,2-*c*]-*as*-triazine-3-carboxylate (**4a**). When malononitrile was substituted for ethyl cyanoacetate, cyclization of the intermediate from pyrazole-3-diazonium chloride gave 4-amino-3-cyanopyrazolo[2,3-*c*]-*as*-triazine (**2j**). In a similar fashion, ethyl butyrylacetate furnished ethyl 4-*n*-propylpyrazolo[2,3-*c*]-*as*-triazine-3-carboxylate (**2k**) from the appropriate intermediate.

Saponification of the ester group, followed by acidification and decarboxylation of **2k**, gave 4-*n*-propylpyrazolo[2,3-*c*]-*as*-triazine (**2m**). An alternate method of synthesis of **2m** employed the condensation of pyrazole-3-diazonium chloride with butyrylacetic acid, prepared in situ by saponification of ethyl 2-butyrylacetate at 0°. The synthesis of dialkyl-substituted azolo-*as*-triazines was accomplished by condensing, for example, 2-methylacetoacetic acid (prepared in situ) with imidazole-2-diazonium chloride in aqueous sodium acetate. Cyclization of this intermediate was accompanied by spontaneous decarboxylation, giving 3,4-dimethylimidazo[1,2-*c*]-*as*-triazine (**4d**).

Electrophilic attack took place in the 8 position of the pyrazole ring of **2**, which might be expected on the basis of our previous work on the chemistry of the pyrazolo-[1,5-*a*]pyrimidines.[14] Thus, 4-ethyl-3-propionylpyrazolo[2,3-*c*]-*as*-triazine (**2g**) gave the corresponding 8-bromo analogue **2h**.

Microbiology. The in vitro antibacterial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* and also antifungal activity against *Candida albicans* and *Trichophyton mentagrophytes* were quantitatively determined by broth dilution assay.[15] All microorganisms were clinical isolates. Serial dilutions of each compound were prepared in chemically defined medium from 0.4 to 0.005 μmol/ml. The minimal inhibitory concentration (MIC) was recorded as the highest dilution of compound which prevented visible growth of

Scheme I



the microorganism. MIC data of the bacteria and yeasts were determined following 24-h incubation at 25°. *Trichophyton* inhibition was determined after 48-h incubation at 30°.

Results and Discussion

The in vitro antibacterial and antifungal activity of the 28 compounds screened is summarized in Table I. Among the variously substituted derivatives of the five azolo-*as*-triazines studied, six had antimicrobial activity. In the pyrazolo[2,3-*c*]-*as*-triazines, the 3-*n*-butyryl-4-*n*-propyl-8-(*p*-chloro)phenyl derivative **2b** and the ethyl 4-amino-3-carboxylate (**2d**) inhibited *Pseudomonas*. It is of interest that several *p*-chlorophenyl-*as*-triazines have shown activity against *Plasmodium gallinaceum*.[16-18]

Ethyl 3-propionyl-4-*n*-propylpyrazolo[2,3-*c*]-*as*-triazine-8-carboxylate (**2c**) had activity against the yeast *C. albicans*. In this same ring system, the activity of the ethyl 8-bromo-4-ethyl-3-carboxylate analogue **2h** was specific for *T. mentagrophytes*, a mycelial fungus.

In the triazolo[2,3-*c*]-*as*-triazine system, the 7-benzylthio-3-*n*-butyryl-4-*n*-propyl derivative **3a** inhibited *S. aureus*. This activity was lost on oxidation to the 7-benzyl sulfone **3b**. Finally, 3-*n*-butyryl-4-*n*-propyl-*v*-triazolo-[3,4-*c*]-*as*-triazine (**5a**) had anti *S. aureus* activity.

The in vitro antimicrobial activity of the six most active compounds, unfortunately, was deemed insufficient to warrant further evaluation. Although a structure–activity relationship is not immediately evident, it can be noted that some specific antimicrobial properties (albeit marginal) appear to be inherent in these novel heterocyclic rings themselves (cf. **2d** and **2h**) rather than in common toxic functional groups (cf. **2b**). The synthetic route outlined here is useful as a general method for the preparation of substituted azolo-*as*-triazines.

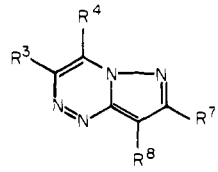
Experimental Section

All of the compounds reported were analyzed by Galbraith Laboratories of Knoxville, Tenn., and were found to be within ±0.4% of the calculated values of C, H, and N. Ir spectra of all solids were taken in KBr disks on a Perkin-Elmer 257 instrument. All uv spectra were taken in MeOH on both Cary 15 and Perkin-Elmer 202 instruments. NMR spectra were recorded in either Me_2SO-d_6, $CDCl_3$ (Me_4Si internal standard for both), D_2O (DDS internal standard), or trifluoroacetic acid (TFAA; DDS internal standard), according to solubility, on a Hitachi Perkin-Elmer R-20A high-resolution instrument. Melting points were taken on a Thomas-Hoover (capillary tube) apparatus and are uncorrected.

Diazotization of α-Aminoazoles. The diazotization of 3-aminopyrazole, 3-amino-*s*-triazole, and 2-aminoimidazole was described elsewhere[5] as this manuscript was in preparation. Substituted 3-amino-5-aryl-[6] and -4-arylpyrazoles[7] were synthesized according to known synthetic methods. The examples given below are representative of all the compounds listed in Table I.

General Method A. Reactions of α-Aminoazoles with β-Diketones. 3-*n*-Butyryl-4-*n*-propylimidazo[3,4-*c*]-*as*-triazine-8-carboxamide (6a). To a freshly prepared suspension of 5.24 g (0.03 mol) of 5-diazoimidazole-4-carboxamide[19] in MeOH (30 ml) was added 4.7 g (0.03 mol) of nonane-4,6-dione, immediately followed by 10.0 g (excess) of sodium acetate trihydrate in water (20 ml), at a temperature maintained below 5°. The mixture was allowed to stand at 10° for 24 h. The yellow precipitate of **4(5)-azo(5-nonane-4,6-dionyl)imidazole-5(4)-**

Table I. Antimicrobial and Physical Properties of Azolo-*as*-triazines



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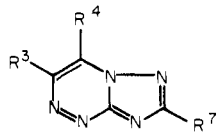

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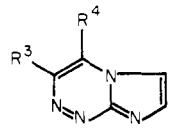

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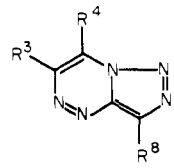

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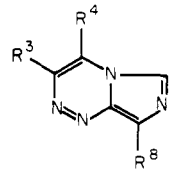

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No.	R^3	R^4	R^7	R^8	In vitro act.[a]	Mp, °C	Yield, %	Recrystn solvent[b]	Emp formula (mol wt)
2a	$COCH_3$	CH_3	H	H	NA[c]	88-89	70	EtOH	$C_8H_8N_4O$ (176)
2b	COC_3H_7	C_3H_7	H	$-C_6H_4$-*p*-Cl	0.4 (*Pa*)[d]	137-138	80	EtOH	$C_{18}H_{19}NOCl$ (342.8)
2c	COC_3H_7	C_3H_7	H	$CO_2C_2H_5$	0.4 (*Ca*)[e]	129-130	85	MeOH	$C_{15}H_{20}N_4O_3$ (304)
2d	$CO_2C_2H_5$	NH_2	H	H	0.16 (*Pa*)	147-148	80	EtOH	$C_8H_9N_5O_2 \cdot 0.5H_2O$ (207)
2e	COC_3H_7	C_3H_7	H	$CONH_2$	NA	191-192	66	MeOH	$C_{13}H_{17}N_5O_2$ (275)
2f	COC_2H_5	C_2H_5	H	$CONH_2$	NA	237-238	92	HOAc	$C_{11}H_{13}N_5O_2$ (247)
2g	COC_2H_5	C_2H_5	H	H	NA	57-58	70	PE	$C_{10}H_{12}N_4O$ (204)
2h	COC_2H_5	C_2H_5	H	Br	0.16 (*Tm*)[f]	85-86	80	PE	$C_{10}H_{11}N_4OBr$ (283)
2i	COC_2H_5	C_2H_5	$-C_6H_4$-*p*-OCH_3	H	NA	142-143	65	PhH	$C_{17}H_{18}N_4O_2$ (310)
2j	CN	NH_2	H	H	NA	275-276	80	HOAc	$C_6H_4N_6$ (160)
2k	$CO_2C_2H_5$	C_3H_7	H	H	NA	74-75	75	Et_2O	$C_{11}H_{14}N_4O_2$ (234)
2m	H	C_3H_7	H	H	NA	54-56	35	PE	$C_8H_{10}N_4$ (162)
2n	CH_3	CH_3	H	H	NA	104-105	11.7	PhH-PE	$C_7H_8N_4$ (148)
2p	H	C_3H_7	H	Br	NA	93-95	32	PE	$C_8H_9N_4Br$ (241)
2r	H	CH_3	H	H	NA	98-100	25	EtOH	$C_6H_6N_4$ (134)
2s	H	CH_3	H	Br	NA	127-128	40	EtOH	$C_6H_5N_4Br$ (213)
2t	CH_3	CH_3	H	Br	NA	134-135	56	EtOH	$C_7H_7N_4Br$ (227)
3a	COC_3H_7	C_3H_7	SCH_2Ph		0.4 (*Sa*)[g]	54-55	45	MeOH	$C_{18}H_{21}N_5OS$ (355)
3b	COC_3H_7	C_3H_7	SO_2CH_2Ph		NA	200-201	53	MeOH	$C_{18}H_{21}N_5O_3S$ (387)
3c	COC_3H_7	C_3H_7	H		NA	143-144	37	Et_2O	$C_{11}H_{15}N_5O$ (233)
3d	COC_3H_7	C_3H_7	$NHCH_3$		NA	168-169	14	EtOH	$C_{12}H_{18}N_6O$ (262)
4a	$CO_2C_2H_5$	NH_2	H		NA	253-255	82.1	EtOH	$C_8H_9N_5O_2$ (207)
4b	COC_3H_7	C_3H_7	H		NA	87-88	85	Et_2O	$C_{12}H_{16}N_4O$ (232)
4c	COC_2H_5	C_2H_5	H		NA	93-94	75	PhH	$C_{10}H_{12}N_4O$ (204)
4d	CH_3	CH_3	H		NA	144-146	55	$CHCl_3$-PE	$C_7H_8N_4$ (148)
5a	COC_3H_7	C_3H_7		$CONH_2$	0.4 (*Sa*)	181-182	25	MeOH	$C_{12}H_{16}N_6O_2$ (276)
6a	COC_3H_7	C_3H_7		$CONH_2$	NA	182-183	54.3	MeOH	$C_{13}H_{17}N_5O_2$ (275)
6b	COC_2H_5	C_2H_5		$CONH_2$	NA	215-216	47	MeOH	$C_{11}H_{13}N_5O_2$ (247)
6c	$COCH_3$	CH_3		$CONH_2$	NA	226-227	25	MeOH	$C_9H_9N_5O_2$ (219)

[a] MIC (minimum inhibitory concentration) in μmol/ml. [b] PhH = benzene, PE = petroleum ether, bp 30-60°. [c] Not active; MIC >0.40 μmol/ml for all microorganisms. [d] *Pseudomonas aeruginosa*. [e] *Candida albicans*. [f] *Trichophyton mentagrophytes*. [g] *Staphylococcus aureus*.

carboxamide, which was formed, was filtered and used without subsequent purification for the next step. Recrystallization from EtOH gave yellow plates: mp 146–147°; 88% yield. Anal. C, H, N. The crude intermediate was suspended in HOAc (20 ml) and refluxed for 10 h. After distillation of the solvent in vacuo, the oily residue was recrystallized from MeOH to yield 4.0 g (54.3%) of **6a** as yellowish buff colored platelets: mp 182–183°. Anal. C, H, N (see Table I).

In the same fashion, **2a** and **6c** were prepared from acetylacetone, while **2f–i**, **4c**, and **6b** were synthesized from heptane-3,5-dione and **2b,c,e**, **3a–d**, **4b**, and **5a** were obtained from nonane-4,6-dione.

General Method B. Reactions of α-Aminoazoles with Ethyl Cyanoacetate. Ethyl 4-Aminoimidazo[1,2-*c*]-*as*-triazine-3-carboxylate (4a). A stirred solution of 1.32 g (10 mmol) of 2-aminoimidazole hemisulfate in 1 N HCl (50 ml) was cooled to 0° and a cold solution of 0.8 g (11 mol) of sodium nitrite in water (10 ml) was added dropwise over a 5-min period, maintaining the temperature below 5°. Then 1.2 g (10 mmol) of ethyl cyanoacetate and 5.0 g of sodium acetate trihydrate (excess) were added in one portion. The mixture was stirred for 4 h at 25° and then the precipitate was filtered and washed with water to yield 0.8 g (40%) of yellow **ethyl 2-(imidazol-2-yl)azocyanoacetate** (mp 246–247° from MeOH. Anal. C, H, N) which was cyclized in acetic acid, as described for **6a**. The yield of **4a** was 82%, mp 253–255° (pale yellow needles) from EtOH.

The preparation of the isomeric **ethyl 4-aminopyrazolo-[2,3-*c*]-*as*-triazine-3-carboxylate (2d)** was similar: mp 129–130° from benzene.

General Method C. Reactions of α-Aminoazoles with Malononitrile. 4-Amino-3-cyanopyrazolo[2,3-*c*]-*as*-triazine (2j). The diazonium salt obtained from 5.0 g (60 mmol) of 3-aminopyrazole in 14 ml of concentrated HCl (12 N) and 4.2 g (65 mmol) of sodium nitrite in 20 ml of H_2O was treated with 4.0 g of malononitrile and 7.0 g (excess) of sodium acetate trihydrate at 0°. The suspension was filtered after stirring for 1 h at 25°. The filtered precipitate, upon recrystallization from DMF–MeOH, and then HOAc, gave 7.0 g (80%) of yellow needles, mp 275–276° dec, which was identified as the product by ir (CN at 2220 cm^{-1} and NH_2 at 3240 cm^{-1}) and by analysis. Anal. C, H, N.

General Method D. Reactions of α-Aminoazoles with 2-Methylacetoacetic Acid. 3,4-Dimethylimidazo[1,2-*c*]-*as*-triazine (4d). Ethyl 2-methylacetoacetate (7.2 g, 0.05 ml) was stirred with 4.2 g of KOH (pellets) in 30 ml of H_2O at 0° for 24 h. The solution was cautiously adjusted to pH 6 with cold 12 N HCl, and then a cold solution of the diazonium salt prepared in situ from 6.6 g (0.05 mol) of 2-aminoimidazole hemisulfate and 3.8 g (0.051 mol) of sodium nitrite (in 30 ml of water) was run in below the surface of this solution. Sodium acetate trihydrate (21 g, large excess) was immediately added to the mixture. Stirring was continued for 1 h and then the deep red mixture was extracted with 4 × 50 ml of chloroform. The $CHCl_3$ extract was dried (Na_2SO_4) and chromatographed on alumina (Woelm, neutral, activity grade I), with ~200 ml of fresh $CHCl_3$. The residual yellow oil obtained on evaporation of the eluent was taken up in hot benzene and diluted with petroleum ether to afford 3.0 g (55%) of **4d** as stocky, yellowish needles: mp 144–146° (recrystallized from chloroform–petroleum ether). Anal. C, H, N.

The preparation of the isomeric 3,4-dimethylpyrazolo[2,3-*c*]-*as*-triazine (**2n**) was similar.

General Method E. Reactions of α-Aminoazoles with *n*-Butyrylacetic Acid (and Related β-Keto Acids). 4-*n*-Propylpyrazolo[3,2-*c*]-*as*-triazine (2m). A solution of *n*-butyrylacetic acid was prepared in situ from ethyl butyrylacetate

(17.0 g, 0.11 mol) and KOH (7.0 g) in H_2O (50 ml) at 0°, following the procedure described for **4d**. The aqueous diazonium salt obtained from 8.4 g (0.1 mol) of 3-aminopyrazole, 25 ml of concentrated HCl (12 N), and 7.0 g of sodium nitrite (in 50 ml of H_2O) was added below the surface of the aqueous *n*-butyrylacetic acid solution at 0°.

The black, tarry material obtained after stirring the reaction mixture for 2 h at 10° was extracted with 5 × 50 ml of $CHCl_3$. The $CHCl_3$ was dried ($MgSO_4$) and chromatographed on neutral alumina with fresh $CHCl_3$ (~200 ml). The eluent was evaporated to yield an oily, yellowish solid which was recrystallized from petroleum ether, giving 4.0 g (55%) of yellow needles: mp 54–56°. The structure was confirmed via ^1H NMR (in $CDCl_3$), analysis, and hydrolysis–decarboxylation of **2k** (general method F, below).

General Method F. Reactions of α-Aminoazoles with Ethyl *n*-Butyrylacetate (and Related β-Keto Esters). Ethyl 4-*n*-Propylpyrazolo[2,3-*c*]-*as*-triazine-3-carboxylate (2k). A solution of pyrazole-3-diazonium chloride (from 11.0 g, 0.13 mol of 3-aminopyrazole, 30 ml of concentrated HCl, and 10.0 g of sodium nitrite) was allowed to react with ethyl *n*-butyrylacetate (16.0 g, 0.13 mol) and sodium acetate trihydrate (30.0 g, large excess) at 0°, employing a method similar to the preceding examples. A $CHCl_3$ extract of the dark, aqueous mixture was dried ($MgSO_4$) and chromatographed on neutral alumina ($CHCl_3$). The crude residual intermediate was cyclized directly to the product **2k** by refluxing with MeOH. Evaporation of the MeOH was followed by recrystallization of the residue from $CHCl_3$ diluted with petroleum ether. The product was obtained as long yellow needles (7.5 g, 25%): mp 74–75° from EtOH–petroleum ether. The structure was confirmed by ^1H NMR ($CDCl_3$) and analysis. Anal. C, H, N.

Saponification of 3.0 g of **2k** with 2.0 g of KOH in MeOH (20 ml) at 50°, followed by neutralization (6 N HCl) and recrystallization of the residue (after evaporation of the MeOH and removal of KCl) from petroleum ether, gave 1.7 g (65%) of **2m**, mp 54–56°, which was identical (mixture melting point) with the sample prepared by the preceding method (method E).

General Method G. Electrophilic Halogenation of the Azolo-*as*-triazines. 8-Bromo-4-*n*-propylpyrazolo[2,3-*c*]-*as*-triazine (2p). A solution of 2.0 g of **2m** in 70.0 ml of $CHCl_3$ was treated with 2.5 g of *N*-bromosuccinimide at 25°, and then the solution was refluxed for 30 min. The solution was washed with aqueous $NaHCO_3$ and the organic layer was dried ($MgSO_4$), concentrated to a volume of 10 ml, and chromatographed on neutral alumina ($CHCl_3$). Upon evaporation of the eluent, a solid was obtained and recrystallization of this material from petroleum ether gave 0.95 g (40%) of yellowish needles: mp 93–95°. The position of bromination was confirmed via ^1H NMR ($CDCl_3$) and analysis, as discussed in two of our earlier publications.[2,14] Anal. C, H, N.

The other 8-bromo derivatives, **2h** and **2s**, were prepared in similar fashion from the appropriate heterocycles, **2g** and **2r**, respectively.

7-Benzylsulfonyl-3-*n*-butyryl-4-*n*-propyl-*s*-triazolo[1,5-*a*]-*as*-triazine (3b). A solution of 3.6 g (0.01 mol) of **7-benzylthio-3-*n*-butyryl-4-*n*-propyl-*s*-triazolo[1,5-*a*]-*as*-triazine (3a**, prepared from the diazotization of 3-amino-5-benzylthio-*s*-triazole[13] followed by coupling with nonane-4,6-dione and cyclization in acetic acid, as described in general method A) in 50 ml of $CHCl_3$ was cooled to 0° and 5 g (slight excess over 0.02 mol) of 85% *m*-chloroperbenzoic acid was added in small portions. The mixture was stirred 0.5 h at 0° and then allowed to stand at 25° for 24 h. The dark solution thus obtained was then washed with cold, aqueous 10% Na_2CO_3 and the organic layer was separated, dried ($MgSO_4$), and chromatographed on neutral alumina ($CHCl_3$). Evaporation of the first fraction ($CHCl_3$) gave a solid which was recrystallized from MeOH to afford 2.0 g (55%) of buff colored needles: mp 200–201°. Anal. C, H, N.

As an alternative method of synthesis, 12.6 g (0.63 mol) of 3-amino-5-benzylthio-*s*-triazole[13] was dissolved in 250 ml of $CHCl_3$ and treated with 26.0 g of 85% *m*-chloroperbenzoic acid at 0° for 24 h. The resulting precipitate was filtered, suspended in 200 ml of ether, and stirred at 20° for 1 h. The insoluble material was filtered, washed with ether, and recrystallized from EtOH to give 5.2 g (29%) of **3(5)-amino-5(3)-benzylsulfonyl-*s*-triazole**: mp 206–208°. Anal. C, H, N.

Diazotization of the above (2.4 g, 0.01 mol) and coupling with nonane-4,6-dione (1.6 g, 0.01 mol) in the presence of sodium acetate trihydrate (4 g) gave an aqueous insoluble precipitate of **3(5)-azo(nonane-4,6-dion-5-yl)-5(3)-benzylsulfonyl-*s*-triazole**: 3.8 g (95%); mp 154–155° as white needles from benzene. Anal. C, H, N.

The material was then cyclized by refluxing in 50 ml of HOAc for 12 h. The **3b** crystallized from the HOAc when the solution cooled to room temperature. The material was of sufficient purity for elemental analysis after filtration, washing with a few milliliters of ether, and drying in vacuo: yield 1.2 g (52.2%); mp 200–201°. Further recrystallization from MeOH did not change the melting point.

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References and Notes

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