($CDCl_3$) δ 1.22 (br s, exchanges with D_2O, 2), 3.32 (br d, J = 6 Hz, 2), 5.60–7.05 (m, 4), 7.33 (m, 5); IR (film) 3622, 3352, 3165, 3015, 2900, 2836, 1635, 1592, 1488, 1447, 1379, 1297, 1070, 987, 850, 744, 690 cm^{-1}.

(*E*)-3-(*p*-Chlorophenyl)-2-propenylamine, 7 (R = *p*-ClC_6H_4), was obtained, as above, via hydrazine cleavage of the phthalimide, in 78% overall yield. In this instance, the crude phthalimide was used directly for the preparation. The allyl amine was sensitive to air, light, and atmospheric carbon dioxide which slowly transformed the oily product into a carbonate salt. However, freshly prepared amine could be spectroscopically characterized; ^1H NMR ($CDCl_3$) δ 1.50 (br s, 2), 3.50 (br s, 2), 6.32–6.72 (m, 2), 7.30 (s, 4). The broad singlet at δ 1.50 exchanged with D_2O.

(*E*)-3-(2-Furyl)-2-propenylamine, 7 (R = 2-furyl). The crude phthalimide **6** (R = 2-furyl) was dissolved in 50 mL of THF and 40 mL water and cooled to 0 °C in an ice bath. After 2.0 g of $Na_2S{\cdot}H_2O$ was added and the solution was stirred at 0 °C for 2 h, the mixture was made alkaline by addition of 3 mL of 50% sodium hydroxide. Extraction with ether (salt was added to facilitate the separation of layers) and discarding the ether wash gave an aqueous solution which was acidified (pH 1) with concentrated hydrochloric acid and extracted with dichloromethane. The organic phase was dried ($MgSO_4$) and concentrated to leave a yellow solid (phthalamic acid).[11] The solid was dissolved in 70 mL of methanol and then 9 mL of saturated oxalic acid was added and the solution heated to reflux for 8 h. The cooled solution was acidified with 3 mL of concentrated hydrochloric acid and washed with dichloromethane. The aqueous layer was made alkaline with 50% sodium hydroxide (with cooling) and extracted with ether. After the solution was dried (Na_2SO_4), the solvent was removed, leaving a light yellow oil that was pure by ^1H NMR (78% yield). Kugelrohr distillation (110–120 °C, 20 torr) gave a colorless oil: ^1H NMR ($CDCl_3$) δ 2.45 (s, 2), 3.38 (d, J = 4 Hz, 2), 6.0–6.4 (m, 4), 7.25 (s, 1); IR (film) 3450, 1600 cm^{-1}. The product rapidly forms (~0.5 h) a solid when exposed to the atmosphere (carbonate salt).

Acknowledgment. We thank the National Institutes of Allergic and Infectious Diseases for financial support of this work. D.C. acknowledges a National Research Service Award (NIH) for a postdoctoral fellowship. Special thanks are also due the Colorado State University Regional NMR Center, funded by National Science Foundation Grant No. CHE 78-18581.

Registry No. (*E*)-**6** (R = Ph), 17480-07-8; (*Z*)-**6** (R = Ph), 4335-61-9; (*E*)-**6** (R = *p*-ClPh), 22621-98-3; (*Z*)-**6** (R = *p*-ClPh), 77629-04-0; (*E,E*)-**6** (R = PhCH=CH), 77629-05-1; (*E,Z*)-**6** (R = PhCH=CH), 77629-06-2; (*E*)-**6** (R = 1-naphthyl), 77629-07-3; (*Z*)-**6** (R = 1-naphthyl), 77629-08-4; (*E*)-**6** (R = *p*-$MeOC_6H_4$), 77629-09-5; (*Z*)-**6** (R = *p*-$MeOC_6H_4$), 77629-10-8; (*E*)-**6** (R = 2-furyl), 77629-11-9; (*Z*)-**6** (R = 2-furyl), 77629-12-0; (*E*)-**6** (R = 2-pyridyl, 77629-13-1; (*E*)-**6** (R = 2-phenethyl), 77629-14-2; (*Z*)-**6** (R = 2-phenethyl), 77629-15-3; (*E*)-**7** (R = Ph), 4335-60-8; (*E*)-**7** (R = *p*-ClPh), 60691-88-5; (*E,E*)-**7** (R = PhCH=CH), 77629-16-4; (*E*)-**7** (R = 2-furyl), 77629-17-5; **8**, 1883-19-8; 4-(5-phthalimidopentadienyl)-2-phenyl-1,3-dioxane, 77629-18-6; vinyltriphenylphosphonium bromide, 5044-52-0; benzaldehyde, 100-52-7; *p*-chlorobenzaldehyde, 104-88-1; (*E*)-3-phenyl-2-propenal, 14371-10-9; phthalimide sodium salt, 33081-78-6; phthalimide lithium salt, 51501-57-6; phthalimide potassium salt, 1074-82-4; 1-naphthalenecarboxaldehyde, 66-77-3; 2-furancarboxaldehyde, 98-01-1; 2-pyridinecarboxaldehyde, 1121-60-4; benzenepropanal, 104-53-0; 4-methoxybenzaldehyde, 123-11-5; 3-(2-phenyl-1,3-dioxan-4-yl)-2-propenal, 77629-19-7; phthalimide, 85-41-6.

Notes

New Synthesis of *s*-Triazolo[1,5-*a*]pyridines and *s*-Triazolo[5,1-*a*]isoquinoline

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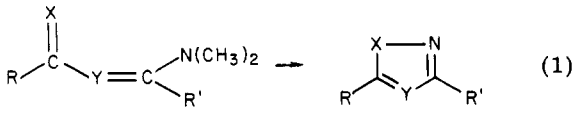
Received January 14, 1981

In previous publications,[1,2] we described a general method for the synthesis of 1,2,4-thiadiazoles **4**, isoxazoles **5**, and isothiazoles **6** (eq 1) in which the (dimethylamino)-

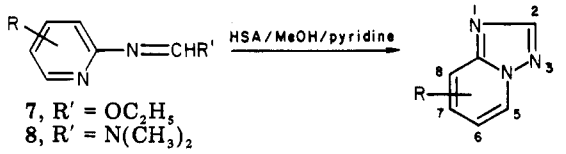


(1)

1, X = S; Y = N
2, X = O; Y = CH
3, X = S; Y = CH

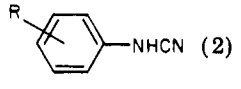
4, X = S; Y = N
5, X = O; Y = CH
6, X = S; Y = CH

alkylidene moiety was utilized as a masked acyl function.[1-6] The method involved the reaction of *N'*-(thioaroyl)-*N,N*-dimethylamidines **1**, enaminones **2**, and thioenaminones **3** with hydroxylamine-*O*-sulfonic acid (HSA) to give 1,2,4-thiadiazoles **4**, isoxazoles **5**, and isothiazoles **6** in excellent yields. We now report the extension of the method to the synthesis of *s*-triazolo[1,5-*a*]pyridines **9** and *s*-triazolo[5,1-*a*]isoquinoline (**12**) by the reaction of ethyl formimidates **7** and *N',N'*-dimethylformamidines **8** and **11** with HSA (eq 2 and 3).



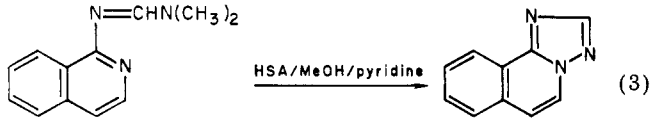
7, R' = OC_2H_5
8, R' = $N(CH_3)_2$

9



(2)

10



(3)

11 12

Ethyl formimidates **7**[7] and *N',N'*-dimethylformamidines **8** and **11**[8] were prepared in excellent yields by reported

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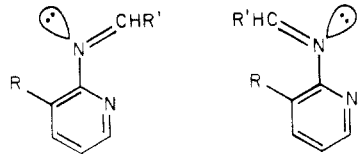
Table I. *s*-Triazolo[1,5-*a*]pyridines and *s*-Triazolo[5,1-*a*]isoquinoline

compd	R	yield, % from 7	yield, % from 8 or 11	mp, °C	formula
9a	8-CH_3	84	87	50-52[a]	$C_7H_7N_3$
9b	7-CH_3	38	26	77-79[b]	$C_7H_7N_3$
9c	6-CH_3	54	35	66-69[c]	$C_7H_7N_3$
9d	H	34		103-104.5[d]	$C_6H_5N_3$
12			83	93-95[e]	$C_{10}H_7N_3$

[a] Lit.[11] mp 51 °C. [b] Lit.[11] mp 79 °C. [c] Lit.[11] mp 57-58 °C. [d] Lit.[11] mp 102-103 °C. [e] Lit.[14] mp 95-96.5 °C.

methods. The formimidates **7** and formamidines **8** and **11** then reacted with HSA in methanol in the presence of pyridine to give *s*-triazolo[1,5-*a*]pyridines **9** and *s*-triazolo[5,1-*a*]isoquinoline (**12**) in 26–87% yields. Formimidate **7a** and formamidines **8a** and **11** gave *s*-triazolo[1,5-*a*]pyridine (**9a**) and *s*-triazolo[5,1-*a*]isoquinoline (**12**) in excellent yields (83–87%). Other formimidates (**7b–d**) and formamidines (**8b–c**) gave *s*-triazolo[1,5-*a*]pyridines **9b–d** in lower yields (26–54%) due to a concomitant formation of 2-pyridinecarbamonitriles **10**[9] which were removed by treating the crude product with sodium hydroxide solution. Because of the predominance of geometrical isomer A over B for **7a**, **8a**, and **11**, a smaller



A B

decrease in entropy of activation (ΔS^*), relative to the parent system, for the formation of *s*-triazoloazines **9a** and **12** completely eliminates the competing side reaction for the formation of cyanamides. Presumably, the reaction proceeds by replacing the dimethylamino or ethoxyl moiety with HSA followed by cyclization.

2-Unsubstituted *s*-triazolo[1,5-*a*]pyridines have been synthesized by the following methods: (1) amination of 2-aminopyridine with HSA, followed by ring-closure with formic acid in ~30% overall yield;[10,11] (2) reaction of 2-aminopyridine with DMF dimethyl acetal, followed by reaction with hydroxylamine and cyclization with polyphosphoric acid in 54% overall yield;[12] (3) reaction of *N*-iminopyridine with liquid hydrogen cyanide in 2% yield;[10] (4) rearrangement of *s*-triazolo[4,3-*a*]pyridine with base in 65% yield.[13] *s*-Triazolo[5,1-*a*]isoquinoline has been prepared by rearrangement of *s*-triazolo[3,4-*a*]isoquinoline under basic conditions in 37% yield.[14]

Our new synthetic method provides a useful alternative to literature methods and is particularly effective for the synthesis of 8-methyl-*s*-triazolo[1,5-*a*]pyridine (**9a**) and *s*-triazolo[5,1-*a*]isoquinoline (**12**) (see Table I).

Experimental Section

All melting points were taken on a Mel-Temp apparatus. Samples for elemental analyses were dried over phosphorus pentoxide under high vacuum for 1–10 h. IR spectra were measured on a Perkin-Elmer spectrophotometer (Model 21). NMR spectra were determined with a Varian Model HA-100 spectrometer; chemical shifts (δ) are in parts per million relative to internal tetramethylsilane. Mass spectra were recorded on AEI MS 902. Ethyl formimidates **7**[7] and *N',N'*-dimethylformamidines **8** and **11**[8] were synthesized by the reported methods.

8-Methyl-*s*-triazolo[1,5-*a*]pyridine (9a). The following is a typical procedure for **9a–d** and **12** except that in the case of **9b–d** the dichloromethane solution of the crude product was washed with 30 mL of 1 N sodium hydroxide solution to remove the 2-pyridinecarbamonitrile. To a solution of 6.52 g (0.040 mol) of **8a** in a mixture of absolute methanol (60 mL) and pyridine (6.4 mL) at 0 °C was added rapidly a solution of 4.96 g (0.044 mol) of hydroxylamine-*O*-sulfonic acid in 40 mL of absolute methanol. After the mixture was stirred at room temperature for 1 h, the solvents were removed under reduced pressure at room temperature to leave a residue which was partitioned between 150 mL of dichloromethane and 30 mL of cold 3 N sodium hydroxide solution. The aqueous layer was extracted with another 50 mL of dichloromethane. The combined dichloromethane solution was washed with 30 mL of water and dried over sodium sulfate. After removal of the dichloromethane, the colorless residue (4.95 g, 93%; mp 48–51 °C) was recrystallized from hexane to give 4.6 g (87%) of **9a** as colorless crystals: mp 50–52 °C (lit.[11] mp 51 °C); ^{1}H NMR ($CDCl_3$) δ 2.66 (s, 3 H), 6.94 (t, J = 7.0 Hz, 1 H), 7.30 (d, J = 7.0 Hz, 1 H), 8.34 (s, 1 H), 8.46 (d, J = 7.0 Hz, 1 H); IR (KBr) 1630, 1500, 1345, 1310, 1260, 1200, 760 cm^{-1}; mass spectrum, m/e 133 (M^+; calcd for $C_7H_7N_3$ m/e 133.15).

Acknowledgment. The authors thank Dr. W. Gore and Mr. G. Morton and staff for the measurement and interpretation of spectral data and Mr. L. Brancone and staff for microanalyses.

Registry No. 7a, 3189-28-4; **7b**, 33842-51-2; **7c**, 65258-06-2; **7d**, 33842-49-8; **8a**, 36172-55-1; **8b**, 36172-54-0; **8c**, 36172-53-9; **8d**, 17175-39-2; **9a**, 4931-18-4; **9b**, 4999-42-2; **9c**, 4931-24-2; **9d**, 274-85-1; **11**, 76999-01-4; **12**, 234-75-3.

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(9) In addition to **9d**, the reaction of **7d** with HSA gave 2-pyridinecarbamonitrile as colorless crystals: mp 161–162 °C (lit.[15] mp 163 °C); ^{1}H NMR (Me_2SO-d_6) δ 6.69 (t, J = 6.0 Hz, 1 H), 7.02 (d, J = 9.0 Hz, 1 H), 7.6–7.9 (m, 2 H); IR (KBr) 2150 cm^{-1} (NC≡N).
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Efficient Synthesis of the Gossypol Binaphthyl Backbone[1]

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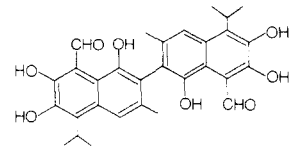
Received December 17, 1980

The polyphenolic binaphthyl gossypol (**1**) is well-known



Gossypol, 1

as a major constituent of cottonseed pigment. The elegant synthetic and degradative studies of Adams and Edwards, in particular the total synthesis by the latter, remain the most significant efforts in this area.[2] Interest in this

(1) Contribution No. 574 from the Syntex Research Institute of Organic Chemistry.

0022-3263/81/1946-3124$01.25/0