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Received May 24, 1985

The title compounds were prepared from benzoxepino-, benzothiepine- or benzocycloheptaioxazolones which in turn were synthesized from simple materials.

J. Heterocyclic Chem., **22**, 1659 (1985).

We previously reported on the regiospecific synthesis and structures of isomeric 3-methyl-4*H*,10*H*[1]benzoxepino or benzothiepine[4,3-*d*]isoxazol-4-one (**6a**) or (**10a**) and 3-methyl-4*H*,10*H*[1]benzoxepino or benzothiepine[3,4-*c*]isoxazol-4-one (**7a**) or (**11a**) from 5- or 3-(phenoxyethyl or phenylthiomethyl)isoxazole-4 carboxylic acids [1]. The isoxazole moiety may be seen as a masked 1,3-diketone and these tricyclic compounds could be considered as useful precursors for the synthesis of 4-acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzoxepino or benzothiepine (**12**) or (**14**). 2,3-Dihydro[1]benzoxepino-4-carboxaldehyde was the only parent compound reported in the literature [2]. In this paper we describe an alternate more simple synthetic scheme leading to mixtures of isomeric tricyclic compounds **6-11** and their conversion to the bicyclic β,β' -triketones **12-16**.

The previously unreported ethyl 2-acyl-3-methylamino-2-butenates (**3**) (X = O, CH₂ or S) prepared by the Benary's method [3] were the appropriate precursors for elaboration of the intermediate isoxazoles (scheme A). Treatment of compounds **3** with hydroxylamine hydrochloride and subsequent alkaline hydrolysis afforded a mixture of isomeric isoxazole 4-carboxylic acids **4** + **5** in which the acid **4** was the main product (> 90%). Cyclization of the acids **4** + **5** led to isomeric tricyclic compounds **6** + **7**, **8** + **9** or **10** + **11**. Structural

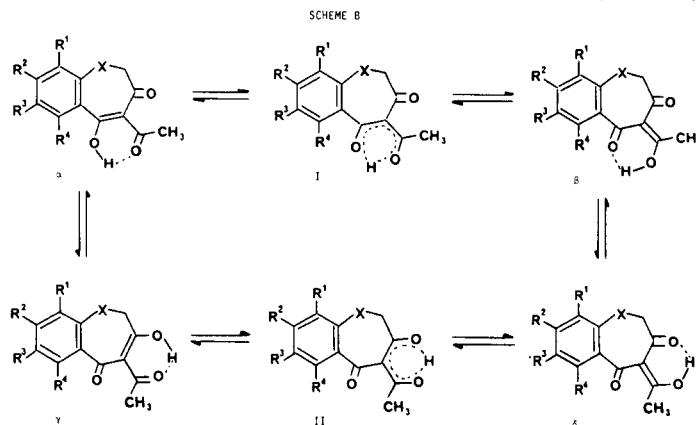
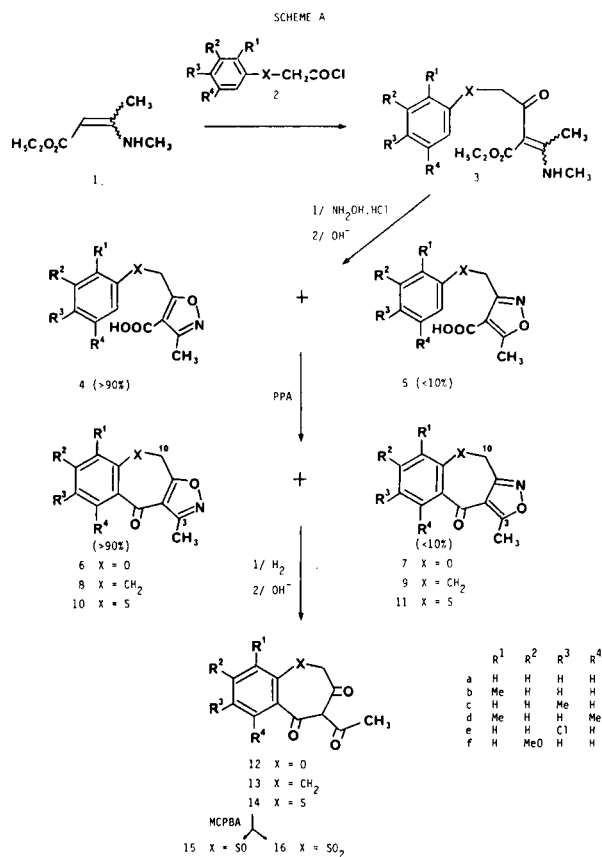


Table 1

Physical Data for 4*H*,10*H*[1]Benzoxepino[4,3-*d*] or [3,4-*c*]isoxazol-4-ones **6** + **7**, 9,10-Dihydro-4*H*-benzo[4,5]cyclohepta[2,1-*d*] or [1,2-*c*]isoxazol-4-one (**8** + **9**) and 4*H*,10*H*[1]Benzothiepiro[4,3-*d*] or [3,4-*c*]isoxazol-4-one (**10** + **11**).

Compound No.	Yield %	Molecular Formula	Analyses %					Pertinent ¹ H-NMR Spectral Data (CDCl ₃) δ6/δ7, δ8/δ9 or δ10/δ11 ³ C-CH ₃ (s)
			Calcd./Found	C	H	N	S	
6a + 7a	45	C ₁₂ H ₉ NO ₃	66.97	4.22	6.51			2.60/2.83
			67.17	4.21	6.52			
6b + 7b	45	C ₁₃ H ₁₁ NO ₃	68.11	4.84	6.11			2.60/2.84
			67.71	4.83	6.04			
6c + 7c	40	C ₁₃ H ₁₁ NO ₃	68.11	4.84	6.11			2.60/2.83
			68.18	4.68	6.05			
6d + 7d	50	C ₁₄ H ₁₃ NO ₃	69.12	5.39	5.76			2.58/2.80
			69.18	5.41	5.75			
6e + 7e	45	C ₁₂ H ₈ NO ₃ Cl	57.73	3.23	5.61		14.20	2.60/2.81
			57.59	3.13	5.55		14.41	
6f + 7f	60	C ₁₃ H ₁₁ NO ₄	63.67	4.52	5.71			2.61/2.84
			63.66	4.63	5.89			
8a + 9a	50	C ₁₃ H ₁₁ NO ₂	73.22	5.20	6.57			2.55/2.81
			73.30	5.20	6.50			
10a + 11a	60	C ₁₂ H ₉ NO ₂ S	62.32	3.92	6.06		13.86	2.58/2.82
			62.23	3.87	6.17		13.65	

Table 2

Physical Data for Compounds **12-16**

Compound No.	Yield %	Mp (°C) Solvent	Molecular Formula	Analyse %				IR (cm ⁻¹)	UV λ max nm
				Calcd./Found	C	H	S		
12a	80	71 hexane	C ₁₂ H ₁₀ O ₄	66.05	4.62			1660, 1610, 1590	306 (13000)
				66.09	4.38				
12b	60	90 hexane	C ₁₃ H ₁₂ O ₄	67.23	5.21			1665, 1600, 1590	308 (14500)
				67.12	5.17				
12c	70	93 hexane	C ₁₃ H ₁₂ O ₄	67.23	5.21			1660, 1615, 1590	306 (12500)
				67.38	5.12				
12d	55	111 hexane	C ₁₄ H ₁₄ O ₄	68.28	5.73			1675, 1580	306 (13500)
				68.12	5.71				
12e	65	121 hexane	C ₁₂ H ₉ O ₄ Cl	57.04	3.59			1665, 1605, 1585	300 (11500)
				57.07	3.62				
12f	65	110 hexane	C ₁₃ H ₁₂ O ₅	62.90	4.87			1650, 1610, 1585	332 (19500)
				62.60	4.91				
13a	85	67 hexane	C ₁₃ H ₁₂ O ₃	72.21	5.59			1660, 1600, 1585	304 (13500)
				72.48	5.78				
14a	65	60 hexane	C ₁₂ H ₁₀ O ₃ S	61.52	4.30			1640, 1590	296 (9000)
				61.56	4.29	13.69 13.72			
15a	57	134 [a]	C ₁₂ H ₁₀ O ₄ S	57.59	4.03			1675, 1600, 1075, 1040	304 (11500)
				57.62	3.96	12.81 12.38			
16a	60	140 [a]	C ₁₂ H ₁₀ O ₅ S	54.13	3.79			1680, 1600, 1340, 1175, 1130	308 (9200)
				54.33	3.81	11.72			

[a] Purified by column chromatography.

assignments for compounds **6-11** were derived from nmr spectral data (Table 1) on the basis of our previous findings concerning the structures of the model compounds **6a/7a** and **10a/11a** [1].

The mixtures of tricyclic compounds served well as the precursors for the bicyclic β,β'-triketones **12-14**. Hydrogenolytic fission of the labile N-O linkage by catalytic hydrogenation followed by hydrolysis of the intermediate

enaminodiketones resulted in the formation of 4-acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzoxepines or benzothiepine or 6-acetyl-5,7-dioxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**12a-f**), (**14a**) and (**13a**) respectively. Oxidation of compound **14a** by means of *m*-chloroperbenzoic acid afforded either 4-acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzothiepin 1-oxide (**15a**) or 4-acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzothiepin 1,1-dioxide (**16a**) according to the reac-

Table 3

Proton Magnetic Resonance Parameters of Compounds **12-16** in Deuteriochloroform

Compound No.	I:II ratio	δ , J
12a	90:10	2.50 (s, 0.3H), 2.59 (s, 2.7H), 4.64 (s, 1.8H), 4.71 (s, 0.2H), 7.05-7.68 (m, 3H), 7.90-8.23 (m, 1H), 17.55 (s, 0.1H exchangeable with deuterium oxide), 18.73 (s, 0.9H exchangeable)
12b	91:9	2.34 (s, 3H), 2.50 (s, 0.27H), 2.59 (s, 2.73H), 4.64 (s, 1.82H), 4.76 (s, 0.18H), 7.09-7.63 (m, 2H), 7.63-8.00 (m, 1H), 17.5 (br, 0.09H exchangeable), 18.68 (s, 0.91H exchangeable)
12c	92:8	2.40 (s, 3H), 2.53 (s, 0.24H), 2.59 (s, 2.76H), 4.63 (s, 1.84H), 4.71 (s, 0.16H), 6.94-7.48 (m, 2H), 7.74-8.05 (m, 1H), 17.6 (br, 0.08H exchangeable), 18.70 (s, 0.92H exchangeable)
12d	89:11	2.29 (s, 3H), 2.45 (s, 3H), 2.50 (s, 3H), 4.53 (s, 1.78H), 4.70 (s, 0.22H), 7.02, 7.25 (2d, 2H, AB system, $J_{AB} = 8$ Hz), 18.0 (br, 0.11H exchangeable), 18.62 (s, 0.89H exchangeable)
12e	88:12	2.53 (s, 0.36H), 2.61 (s, 2.64H), 4.65 (s, 1.76H), 4.74 (s, 0.24H), 7.00-7.65 (m, 2H), 7.98-8.23 (m, 1H), 17.7 (br, 0.12H exchangeable), 18.73 (s, 0.88H)
12f	85:15	2.49 (s, 0.45H), 2.60 (s, 2.55H), 3.89 (s, 3H), 4.63 (s, 1.7H), 4.70 (s, 0.3H), 6.64 (d, 1H, $J = 3$ Hz), 6.83 (dd, 1H, $J = 9$ Hz, $J = 3$ Hz), 8.01 (d, 1H, $J = 9$ Hz), 17.5 (br, 0.15H exchangeable), 18.81 (s, 0.85H exchangeable)
13a	>95: <5	2.41 (s, >2.85H), 2.48 (s, <0.15H), 2.74-3.16 (m, 4H), 7.15-7.50 (m, 3H), 7.75-7.88 (m, 1H), 18.0 (s, <0.05H exchangeable), 18.12 (s, >0.95H exchangeable)
14a	50:50	2.27 (s, 1.5H), 2.49 (s, 1.5H), 3.61 (s, 1H), 3.70 (s, 1H), 7.40-7.70 (m, 3H), 7.85-8.15 (m, 1H), 16.9 (br, 0.5H exchangeable), 18.3 (br, 0.5H exchangeable)
15a	100:0	2.45 (s, 3H), 4.09, 4.32 (2d, 2H, AB system, $J_{AB} = 17$ Hz), 7.55-8.13 (m, 4H), 18.03 (s, 1H exchangeable)
16a	90:10	2.41 (s, 2.7H), 2.55 (s, 0.3H), 4.48 (s, 1.8H), 4.53 (s, 0.2H), 7.60-8.28 (m, 4H), 18.2 (br, 1H exchangeable)

tion conditions.

The structure of compounds **12-16** was demonstrated by the analytical and spectral data (Tables 2 and 3). In deuteriochloroform solution, these compounds exist in an equilibrium mixture of external tautomers $\alpha, \beta \rightleftharpoons \gamma, \delta$ (scheme B) as evidenced by their $^1\text{H-NMR}$ spectra which display two different methyl signals. The equilibria between the internal tautomers $\alpha = \beta, \gamma = \delta$ are expected to be fast with regard to spectra averaging. Because of extensive electron delocalization in the conjugated chelate ring, the tautomeric pairs α, β and γ, δ may be described as resonance hybrids I and II respectively. The resulting very strong intramolecular hydrogen-bond is evidenced by the two very low-field hydroxyl resonance. The I:II ratio

appears to depend on the nature of X as outlined in Table 3. When X = O, CH_2 , SO or SO_2 , the ultraviolet spectra of compounds **12, 13, 15** and **16** are largely similar to those of aroylacetonates [4,5], thus indicating that these systems exist mainly as the enol form I. These results are in close analogy with the proposed structure for 5-hydroxy-3-oxo-2,3-dihydro[1]benzoxepin-4-carboxaldehyde [2]. When X = S, an equivalent amount of the two forms is detected.

EXPERIMENTAL

All melting points were determined on a Kofler block apparatus and are uncorrected. The infrared spectra were determined on a Beckman aculab 2 spectrometer in deuteriochloroform. The ultraviolet spectra were obtained on a Beckman DB spectrometer in ethanol. The proton nmr spectra were recorded using a Brücker WP80 spectrometer. The chemical shifts reported are in parts per million with respect to TMS. Elemental analyses were performed by Microanalytical laboratory, Centre National de la Recherche Scientifique, 69390 Vernaison, France. Ethyl 3-methylamino-2-butenate (**1**) was prepared as previously described [6]. The acyl chlorides **2** were obtained from the corresponding acids (commercially available or prepared as previously described [7]) by current methods using thionyl chloride (**2a-e**, X = O; **2a**, X = CH_2 ; **2a**, X = S) or phosphorus pentachloride (**2f**, X = O) (Yields, 80-95%).

4*H*,10*H*[1]Benzoxepino[4,3-*d*] or [3,4-*c*]isoxazol-4-ones (**6 + 7**), 9,10-dihydro-4*H*-benzo[4,5]cyclohepta[2,1-*d*] or [1,2-*c*]isoxazol-4-one (**8 + 9**) and 4*H*,10*H*[1]benzothiepine[4,3-*d*] or [3,4-*c*]isoxazol-4-one (**10 + 11**).

To a stirred solution, cooled in a water-ice bath, of ethyl 3-methylamino-2-butenate (**1**) (0.05 mole) and pyridine (4 ml, 0.05 mole) in anhydrous ethyl ether (100 ml) was added dropwise a solution of acyl chloride **2** (0.05 mole) in anhydrous ethyl ether (20 ml). The resulting mixture was refluxed for 5 hours, cooled and poured into 5% hydrochloric acid. The ethereal solution was dried and the solvent evaporated to yield the crude compound **3** which was dissolved in ethanol (250 ml). Hydroxylamine hydrochloride (5.2 g, 0.075 mole) was added to the ethanolic solution and the mixture was refluxed for 1 hour. Ethanol was evaporated *in vacuo* and ethyl ether added to the residue. The solution was washed with water and dried. Ethyl ether was evaporated. To the residue was added 2*N* ethanolic potassium hydroxide (100 ml) and the solution was refluxed for 3 hours. After evaporation of ethanol, water was added. The aqueous layer was extracted with ethyl ether and then acidified with concentrated hydrochloric acid. The mixture of crude acids **4 + 5** was collected by filtration or by extractive work-up with ethyl acetate. The mixture of crude acids **4 + 5** and polyphosphoric acid (phosphoric acid/phosphorus pentoxide, 1/1, 150 g) was stirred at 100° (10 mn for **4f + 5f**, X = O; 2 hours for **4a + 5a**, X = CH_2 or S and 4 hours for **4a-e + 5a-e**, X = O). The resultant mixture was poured into crushed ice and extracted with methylene chloride. The extracts were dried and the solvent evaporated under reduced pressure.

Work-up Procedure for Products **6a-f + 7a-f**.

The residue was column chromatographed on silica gel (50 g) eluting with methylene chloride (**a, c, e**) or ethyl ether (**b, d, f**). Analytical samples were obtained by recrystallization from cyclohexane (**a, b** and **d**); acetonitrile (**c** and **e**) or hexane/ethyl acetate 4:1 (**b**) (Table 1).

Work-up Procedure for Products **8a + 9a** and **10a + 11a**.

The residue was recrystallized from hexane (**8a + 9a**) or acetonitrile (**10a + 11a**) (Table 1).

4-Acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzoxepine (**12**), 6-Acetyl-5,7-dioxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**13**) and 4-Acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzothiepine (**14**). General Procedure.

A solution of the mixture of tricyclic compounds (0.01 mole) in ethyl

acetate (100 ml) (**6 + 7** or **8 + 9**) or in ethanol (100 ml) (**10 + 11**) was hydrogenated with 5% palladium on carbon (1 g) (**6 + 7** or **8 + 9**) or with W4 Raney Nickel (0.5 g) (**10 + 11**) at room temperature using a low pressure (ca. 1 atmosphere) hydrogenation apparatus. After uptake of the calculated amount of hydrogen, the catalyst was filtered off and the solvent evaporated under reduced pressure. The residue was refluxed for 3 mn (**a**) or 10 mn (**b-f**) in 0.5 aqueous potassium hydroxide (100 ml). After cooling and filtration, the solution was acidified with 10% sulfuric acid. Pure bicyclic β,β' -triketones were obtained by filtration (**12a-e**), or by extractive work-up with ethyl ether (**12f**, **13a** and **14a**) followed by recrystallization from hexane (Tables 2 and 3).

4-Acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzothiepine 1-Oxide (**15a**).

A solution of *m*-chloroperbenzoic acid (1.2 g, 7 mmoles) in methylene chloride (25 ml) was added dropwise under nitrogen to a solution of compound **14a** (1.64 g, 7 mmoles) in methylene chloride (25 ml) at -10° . The reaction mixture was stirred for 15 mn at -10° and then washed with 5% sodium hydrogenocarbonate and water. The solution was dried and the solvent evaporated *in vacuo*. The residual product was column chromatographed on silica gel (50 g) eluting with ethyl acetate to yield compound **15a**, 1 g. An analytical sample was obtained by recrystallization from ethanol (Tables 2 and 3).

4-Acetyl-3,5-dioxo-2,3,4,5-tetrahydro[1]benzothiepine 1,1-Dioxide (**16a**).

A solution of *m*-chloroperbenzoic acid (2.17 g, 1.26 mmoles in methylene chloride (50 ml) was added dropwise under nitrogen to a solution of compound **14a** (1.47 g, 6.3 mmoles) in methylene chloride (25 ml) at 0° . The reaction mixture was stirred overnight at room temperature and then washed with 5% sodium hydrogenocarbonate and water. The solution was dried and the solvent evaporated *in vacuo*. The residual product was column chromatographed on silica gel (50 g) eluting with hexane/ethyl acetate 1:1 to yield compound **16a**, 1 g. An analytical sample was obtained by recrystallization from ethanol (Tables 2 and 3).

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