LITERATURE CITED

(1) Am. Soc. Testing Materials, Philadelphia, Pa., X-ray Powder Data Cards, 4-0836, 5-0661, 5-0727, 6-0615, 6-0696, 9-402, 9-418, 11-614, 13-534, 1963.
(2) Emmett, Paul H., "Catalysis," Vol. IV, p. 392, Reinhold, New York, 1956.
(3) Keely, W.M., Maynor, H.W., J. CHEM. ENG. DATA 8, 297 (1963).
(4) Kubaschewski, O., Evans, E.L., "International Series of Monographs on Metal Physics and Physical Metallurgy," Vol. I, "Metallurgical Thermochemistry," 3rd ed., p. 315, Pergamon Press, New York, 1958.
(5) Kuznetsov, A.N., Shestopavalova, A.A., Kulish, N.F., *Zh. Fiz. Khim.* **32**, 73-8 (1958).
(6) Lloyd, W.A., Amundson, N.R., *Ind. Eng. Chem.* **53**, 19-22 (1961).
(7) Mellor, J.W., "Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. **XII**, p. 768, Longmans, Green, New York, 1932.
(8) Pavlyuchenko, M.M., Rubenchek, Ya. S., *Zh. Prikl. Khim.* **24**, 666-70 (1951).

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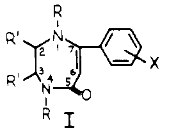
Synthesis of Some Substituted 7-Aryl-1,2,3,4-tetrahydro-1,4-diazepin-5-ones

C. M. HOFMANN, G. E. WIEGAND, and S. R. SAFIR
Lederle Laboratories, A Division of American Cyanamid Co., Pearl River, N. Y.

Seven 7-aryl-1,2,3,4-tetrahydro-1,4-diazepin-5-ones were prepared by the condensation of ethylenediamine with the appropriate ethyl aroylacetate. The 1,4-dimethyl- and 2,3-dimethyl-7-phenyltetrahydrodiazepinones were prepared by condensation of *N,N′*-dimethylethylenediamine and 2,3-diaminobutane with ethyl benzoylacetate. The preparation of the 3-ethyl-3,7-diphenyl analog is also described.

CONDENSATION of ethyl benzoylacetate with ethylenediamine to give 7-phenyl-1,2,3,4-tetrahydro-1,4-diazepin-5-one has been described (*2*). The present paper describes the preparation of several substituted diazepinones represented by formula I.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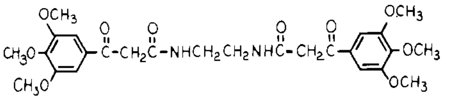
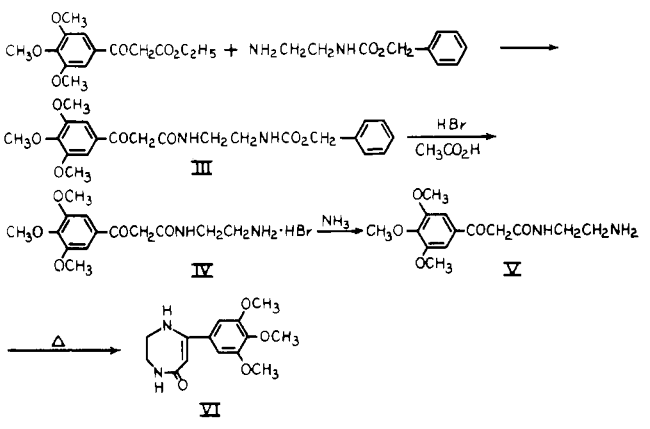
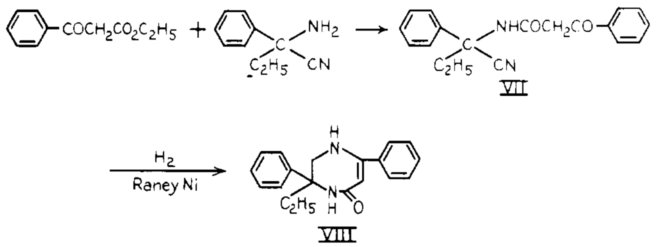

II

The 7-substituted phenyl derivatives, IX-XVI (Table I), were prepared in a manner similar to that described for the preparation of the parent compound (*2*)—i.e., condensation of an ethylenediamine with the requisite β-keto ester. This condensation, however, failed to give the desired product (VI) with ethyl 3,4,5-trimethoxybenzoylacetate, in which case the only isolable material was the linear amide II. The desired diazepinone VI was prepared as outlined below:



The 3-ethyl-3,7-diphenyl derivative VIII was prepared by the condensation of ethyl benzoylacetate with 2-amino-2-phenylbutyronitrile to give the acylated nitrile VII. Hydrogenation of VII in the presence of Raney nickel catalyst caused reductive cyclization to the desired product VIII.



The pertinent data for the diazepinones are listed in Table I.

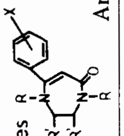
EXPERIMENTAL

All melting points and boiling points are uncorrected.

Ethyl Benzoylacetates. The required β-keto esters were prepared by a modification of the procedure of Perkin and Weizmann (*7*) as described by Burton and Ingold (*1*). The following esters were prepared: ethyl *m*-toluoylacetate, b.p. 98-100°/0.2 mm., copper salt, m.p. 188.5-190°; ethyl *p*-chlorobenzoylacetate (*1, 10*), ethyl *m*-chlorobenzoylacetate (*4*), ethyl *p*-toluoylacetate (*6*), ethyl *p*-anisoylacetate (*9*), ethyl *m*-α,α,α-trifluoromethylbenzoylacetate (*3*), and ethyl 3,4,5-trimethoxybenzoylacetate (*5*).

7-Aryl-1,2,3,4-tetrahydro-1,4-diazepin-5-ones (Table I). The procedure used to prepare these compounds is that reported by Hofmann and Safir (*2*) for the preparation of 7-phenyl-1,2,3,4-tetrahydro-1,4-diazepin-5-one. The pertinent data are listed in Table I.

Table I. 7-Substituted Phenyl Derivatives



	X	R	R'	M.P., °C. (Dec.)	Yield, %	Molecular Formula	Analysis Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Halogen Calcd.	Halogen Found	I.R., λ_{max}^{Nujol} μ	U.V., λ_{max}^{MeOH} mμ (ε)
IX[a]	H	CH_3	H	118.5-20[b]	20	$C_{13}H_{16}N_2O$	72.19	71.71 71.93	7.46	7.61 7.44	12.95	12.97	...	...	6.24[c]	230 (12,760) 302 (13,100)
X[d]	H	H	CH_3	263-8[e]	10	$C_{13}H_{16}N_2O$	72.19	71.86	7.46	7.54	12.95	12.75	...	...	6.15 6.46	229 (14,710) 302 (12,650)
XI[f]	4-Cl	H	H	266-7.5[g]	5	$C_{11}H_{11}ClN_2O$	59.33	59.34	4.98	5.14	12.58	12.51	15.92	16.04 15.87	6.07 6.18	298 (10,380) 237 (16,830)
XII[f]	3-Cl	H	H	258-9[g]	5	$C_{11}H_{11}ClN_2O$	59.33	58.90	4.98	4.79	12.58	13.06	15.92	16.03	6.08 6.15	310 (8,460) 235 (11,360)
XIII[f]	4-CH_3	H	H	267-9[g]	7.5	$C_{12}H_{14}N_2O$	71.26	71.18	6.98	7.11	13.85	14.03	...	...	6.15	294 (10,720) 237 (11,940)
XIV[f]	3-CH_3	H	H	254-5[h]	2	$C_{12}H_{14}N_2O$	71.26	70.83 70.92	6.98	7.11 7.58	13.85	13.82	...	...	6.13	295 (10,720) 236 (11,940)
XV[f]	4-CH_3O	H	H	264-5[h]	4	$C_{12}H_{14}N_2O_2$	66.03	65.82	6.47	6.47	12.84	12.77	...	...	6.17	300 (11,900) 262 (9,500)
XVI[f]	3-CF_3	H	H	262-3[h]	23	$C_{12}H_{11}F_3N_2O$	56.25	56.46	4.33	4.67	10.94	10.99	22.25	21.65 22.35 21.96	6.18	302 (6,920) 234 (10,250)

[a] 2,3-Diaminobutane purchased from Aldrich. [b] From benzene. [c] Chloroform. [d] *N,N'*-dimethylethylenediamine purchased from Aldrich. [e] From ethanol and propanol. [f] Ethylenediamine purchased from Aldrich. [g] From aqueous dimethylformamide. [h] From dimethylformamide.

Benzyl{2 - [2 - (3,4,5-trimethoxybenzoyl)acetamido]ethyl} carbamate (III). To a stirred refluxing solution of 2 grams (0.0075 mole) of ~75% benzyl (2-aminoethyl)carbamate (*2*) in 50 ml. of xylene was added a solution of 2 grams (0.0071 mole) of ethyl 3,4,5-trimethoxybenzoylacetate (*5*) in 75 ml. of xylene over 30 to 40 minutes. A water separator was placed between the flask and condenser and 75 ml. of distillate was collected. The reaction mixture was cooled to give a pale blue solid. The crude product was recrystallized from ethanol to give 2.2 grams (72%) of white crystals, m.p. 169.5-171°. A further recrystallization from chloroform-petroleum ether (30 to 60°) did not alter the melting point; infrared: $\lambda_{max}^{CHCl_3}$ 5.80 and 5.99 μ.

Anal. Calcd. for $C_{22}H_{26}N_2O_7$: C, 61.38; H, 6.09; N, 6.51. Found: C, 61.57; H, 6.27; N, 6.90, 6.56.

***N*-(2-Aminoethyl)-3,4,5-trimethoxybenzoylacetamide Hydrobromide (IV) and Base (V).** To 4.3 grams (0.01 mole) of III was added 55 ml. of 30% HBr in acetic acid, whereupon gas was evolved. The reaction solution was stirred at room temperature for 1.5 hours. A large volume of ether was added to the acid solution to give a sticky solid which crystallized on trituration with ethyl acetate. The crude hydrobromide was dried in vacuo over potassium hydroxide pellets and was then recrystallized from ethanol-ethyl acetate to give 2.3 grams (61%) of a white solid, m.p. 174-175.5° (dec.). The bulk of this material was used in the subsequent step; however, a small sample was recrystallized from ethanol to give the analytical sample, m.p. 174.5-175.5° (dec.).

Anal. Calcd. for $C_{14}H_{20}N_2O_5 \cdot HBr$: C, 44.57; H, 5.61; N, 7.43; Br, 21.18. Found: C, 44.43; H, 5.65; N, 7.40; Br, 20.72, 20.95, 20.83.

The base (V) was prepared from the hydrobromide with ammonia in chloroform, m.p. 119.5-121° (dec.), $\lambda_{max}^{CHCl_3}$ 2.95, 5.95-6.0 μ (broad).

7-(3,4,5-Trimethoxyphenyl)-1,2,3,4-tetrahydro-1,4 -diazepin-5-one (VI). A solution of 2.9 grams (0.01 mole) of V in 300 ml. of toluene was heated at reflux with stirring for 2 hours. A water separator was inserted, and 200 ml. of distillate was collected. The toluene solution was cooled to give 2.1 grams of a tan solid. Two recrystallizations from chloroform-petroleum ether (30 to 60°) gave 1.7 grams (63%) of an off-white powder, m.p. 245-247° (dec.)

An analytical sample was obtained by four recrystallizations from ethanol-petroleum ether (30 to 60°) to give a white crystalline solid, m.p. 249-250° (dec.). The compound showed $\lambda_{max}^{CHCl_3}$ 6.18 and 6.28 μ and λ_{max}^{MeOH} 303 mμ (ε15,300).

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.26; H, 6.65; N, 10.00.

2-Phenyl-2-benzoylacetamidobutyronitrile (VII). A solution of 51.2 grams (0.26 mole) of 2-amino-2-phenylbutyronitrile hydrochloride (*8*) in 400 ml. of water was neutralized with ammonium hydroxide, and the resulting solution was extracted with several portions of ether. The ether extracts were combined, dried over magnesium sulfate, filtered and evaporated to give 40.6 grams (0.25 mole) of 2-amino-2-phenylbutyronitrile as an oil. A solution of this nitrile in 500 ml. of xylene was stirred and refluxed as a solution of 48.8 grams (0.25 mole) of ethyl benzoylacetate in 50 ml. of xylene was added over a period of 45 minutes. A water separator was put in the system and 400 ml. of xylene was removed during 2 hours. The reaction solution was cooled and treated with petroleum ether. An oil separated. The mixture was allowed to stand for several hours and then the mother liquor was decanted and a small amount of alcohol was added to the oil. The oil solidified to a yellow solid. The crude product (28 grams) was recrystallized twice from absolute alcohol (250 to 300 ml.) to give 19.1 grams (25%) of VII, m.p. 160.5-161°; infrared, $\lambda_{max}^{CHCl_3}$ 5.93 and 5.99 μ (shoulder), no bands in the 4-5 μ region. An analytical sample which melted at 158-158.5° was obtained by sublimation at 150°/0.1 mm.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.14; H, 5.94; N, 9.22.

3-Ethyl-3, 7-diphenyl-1, 2, 3, 4-tetrahydro-1, 4-diazepin-5-one (VIII). A solution of 3 grams (0.01 mole) of VII in 200 ml. of absolute alcohol was hydrogenated at room temperature and 38.5 pounds pressure using ½ tsp. Raney nickel as the catalyst. The theoretical amount of hydrogen was absorbed within 24 hours. The mixture was filtered, and the filtrate was evaporated to dryness. The solid residue was recrystallized from alcohol, to give 1.1 grams (38%) of a white solid, m.p. 202–204°. The analytical sample melted at 203–205.5°, and showed bands in the infrared ($CHCl_3$) at 6.18 and 6.30 μ (shoulder), and absorbed in the ultraviolet region at λ_{max}^{MeOH} 228 (ϵ17,100) and 304 mμ (ϵ11,900); and $\lambda_{max}^{MeOH, HCl}$244 ($\epsilon$13,650) and 314 m$\mu$ (ϵ15,300).

Anal. Calcd. for for $C_{19}H_{20}N_20$: C, 78.05; H, 6.90; N, 9.58. Found: C, 77.50, 77.76; H, 6.59, 6.97; N, 9.56.

Hydrochloride. The hydrochloride of the above diazepinone was prepared in alcohol and recrystallized from alcohol-ether, m.p. 228–232° (dec.)

Anal. Calcd. for $C_{19}H_{21}N_2OCl$: C, 69.39; H, 6.44, N, 8.25; Cl, 10.78. Found: C, 68.96, 69.20; H, 6.86, 6.79; N, 8.29; Cl, 10.49.

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LITERATURE CITED

(1) Burton, H., Ingold, C.K., *J. Chem. Soc.* **1928**, p. 904.
(2) Hofmann, C.M., Safir, S.R., *J. Org. Chem.* **27**, 3565 (1962).
(3) Humphlett, W.J., Weiss, M.J., Hauser, C.R., *J. Am. Chem. Soc.* **70**, 4020 (1948).
(4) Khromov, N.V., Poraĭ-Koshits, A.E., *J. Gen. Chem. USSR* **17**, 1816 (1947); **42**, 4170 (1948).
(5) Koo, J., *J. Am. Chem. Soc.* **75**, 720 (1953).
(6) Marguery, F., *Bull. soc. chim.* **33**, 549 (1905).
(7) Perkin, W.H., Jr., Weizmann, C., *J. Chem. Soc.* **89**, 1649 (1906).
(8) Read, W.T., *J. Am. Chem. Soc.* **44**, 1746 (1922).
(9) Schoonjans, A., *Chem. Zentr.* **II**, 616 (1897).
(10) Thorp, L., Bruskill, E.R., *J. Am. Chem. Soc.* **37**, 1258 (1915).

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Reductive Desulfuration on Vanadium and Metalloporphyrin Contents of Fractions from Boscan Asphaltenes

JAMES M. SUGIHARA,[1] TOMIO OKADA,[2] and JAN F. BRANTHAVER
Department of Chemistry, University of Utah, Salt Lake City, Utah

Treatment of fractions derived from Boscan asphaltenes with lithium-ethylenediamine, with Raney nickel, and by electrolysis in lithium chloride–ethylenediamine effected reduction, desulfuration, decrease in vanadium and metalloporphyrin contents, and altered solubilities. Loss in vanadium correlated linearly with loss in metalloporphyrins. Correlation of extent of reduction and loss of vanadium and a similar relationship of extent of desulfuration and loss of vanadium were made. An association of nonporphyrin vanadium compounds with sulfur compounds was suggested.

THE USE of lithium metal in ethylenediamine (EDA) as a reducing agent has been demonstrated (*9*) to be effective in decreasing the sulfur content of coals. This finding suggested the application of this reagent to petroleum fractions to effect the same type of reductive desulfuration, but in addition follow the fate of vanadium metal and metalloporphyrins. Should any relationships emerge, such data could provide clues relating to the forms of occurrence of vanadium in crude oils.

Fractions derived from Boscan (Venezuela) crude oil were used in this investigation since the parent material is rich in vanadium, about 1200 p.p.m.

EXPERIMENTAL METHODS

Pentane asphaltenes, 30 grams, from Boscan crude oil was dispersed in 2625 ml. of pyridine by stirring for 1 hour, and the resulting solution was filtered through cotton to remove extraneous debris. (The rate of filtration through paper or sintered glass was very slow.) While the filtrate was being stirred, 26.5 ml. of water was added, and the resulting mixture was allowed to stand near 0° C. for 1 to 2 days. The suspension was filtered through cotton, and the filtrate was again passed through the same cotton mat. The solid on the cotton was collected and dried to provide about 8 grams of porphyrin-poor (Por-P) asphaltenes. More water, 1286 ml. (combined volume of water is ⅓ of the total volume of water and pyridine introduced), was added to the filtrate, and the resulting suspension was allowed to stand near 0° C. for 1 day. The mixture was again filtered twice through cotton, and the brown solid on the

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[1] Present address: College of Chemistry and Physics, North Dakota State University, Fargo, N. D.

[2] Present address: Maruzen Oil Co., Tokyo, Japan