48. A. Hassner, S. Burke, and J. Cheng-fan, J. Am. Chem. Soc., 97, 4692 (1975).
49. A. V. Eremeev, R. S. Él'kinson, and V. A. Imuns, Khim. Geterotsikl. Soedin., No. 5, 643 (1981).
50. E. Schaumann, E. Kausch, and W. Walter, Chem. Ber., 108, 2500 (1975).
51. O. C. Dermer and G. E. Ham, Ethyleneimine and Other Aziridines, Academic Press, New York (1969).
52. P. Chandrasekhar, H. Heimgartner, and H. Schmid, Helv. Chim. Acta, 60, 2270 (1977).
53. N. J. Leonard and B. Zwanenburg, J. Am. Chem. Soc., 89, 4456 (1967).
54. N. J. Leonard, E. F. Muth, and V. Nair, J. Org. Chem., 33, 827 (1968).
55. H. Bader and H.-J. Hansen, Helv. Chim. Acta, 61, 286 (1978).
56. A. Kakehi, S. Ito, and T. Manabe, J. Org. Chem., 40, 544 (1975).
57. P. W. Neber and A. Burgard, Ann. Chem., 493, 281 (1932).
58. R. F. Parcell, Chem. Ind., No. 33, 1396 (1963).
59. D. F. Morrow, M. E. Butler, and E. C. J. Huang, J. Org. Chem., 30, 579 (1965).
60. D. F. Morrow and M. E. Butler, J. Heterocycl. Chem., 1, 53 (1964).
61. G. Alverne, E. Kozlowska-Gramsz, S. Lacomb-Bar, and A. Laurent, Tetrahedron Lett., No. 52, 5203 (1978).
62. G. Alverne, S. Lacomb, and A. Laurent, Tetrahedron Lett., No. 21, 1437 (1980).
63. T. Wade and R. Kheribet, J. Org. Chem., 45, 5333 (1980).
64. T. Wade and R. Guedj, Tetrahedron Lett., No. 41, 3953 (1979).
65. J. S. Meeck and J. S. Fowler, J. Org. Chem., 33, 985 (1968).
66. D. Black and J. Doyle, Austral. J. Chem., 31, 2313 (1978).
67. P. Vittorelli, H. Heimgartner, H. Schmid, P. Hoet, and L. Ghosez, Tetrahedron, 30, 3737 (1974).
68. P. Chandrasekhar, U. Schmid, R. Schmid, H. Heimgartner, and H. Schmid, Helv. Chim. Acta, 58, 1191 (1975).
69. A. V. Eremeev, R. S. Él'kinson, and V. A. Imuns, Khim. Geterotsikl. Soedin., No. 1, 124 (1981).

RESEARCH ON UNSATURATED LACTONES.

91.* SELECTIVE OXIDATION OF THE BROMOMETHYL GROUP IN SUBSTITUTED 2-BUTEN-4-OLIDES

A. A. Avetisyan, V. V. Ovsepyan, and G. G. Tokmadzhyan

UDC 547.314:547.323+547.38:547.388

The selective oxidation of the bromomethyl group to a formyl group was realized by the direct action of dimethyl sulfoxide on 2-ethoxycarbonyl-3-bromomethyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olides.

The production of aldehydes by the oxidation of a bromomethyl group by dimethyl sulfoxide (DMSO) was realized for the first time in 1957 [2] in a series of p-substituted bromomethyl aryl ketones. The reaction was subsequently extended to alkyl halides, and it was ascertained that in this case chlorides and bromides are oxidized by DMSO only through the corresponding tosylates and that aldehydes are obtained only from alkyl iodides by direct oxidation with DMSO [3, 4].

We have for the first time realized the similar oxidation of the bromomethyl group in a number of unsaturated γ-lactones by the direct action of DMSO on 2-ethoxycarbonyl-3-bromomethyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olides.

*See [1] for communication 90.

Erevan State University, Erevan 375049. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 740-743, June, 1984. Original article submitted July 25, 1983; revision submitted November 23, 1983.

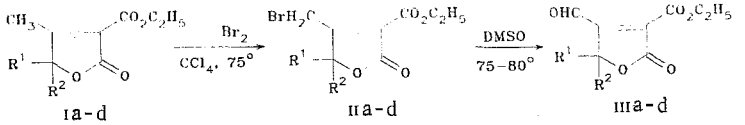
 0009-3122/84/2006-0594$08.50

TABLE 1. 2-Ethoxycarbonyl-3-bromomethyl-4,4-dialkyl-2-buten-4-olides (IIa-d)

Compound	mp, °C	R_f[a]	IR spectrum, cm^{-1}	PMR spectrum (in CCl_4), δ, ppm (J, Hz)	Found, % C	Found, % H	Found, % Br	Empirical formula	Calc., % C	Calc., % H	Calc., % Br	Yield, %
IIa	80—81	0,87	650, 1645, 1730, 1760	1,45 (3H, t, J=7,5); 1,65 (6H, s); 4,20—4,65 (4H, m)	43,4	4,7	28,3	$C_{10}H_{13}BrO_4$	43,3	4,8	28,6	97
IIb	87—88	0,80	670, 1650, 1735, 1760	0,72 (3H, t, J=7,5); 1,35 (3H, t, J=7,5); 1,50 (3H, s); 1,88 (2H, q, J=7,5); 4,32 (2H, q, J=7,5); 4,40 (2H, s)	45,5	5,1	27,1	$C_{11}H_{15}BrO_4$	45,4	5,2	27,5	83
IIc	98—99	0,73	665, 1655, 1725, 1765	1,32 (3H, t, J=7,5); 1,70—2,20 (8H, m); 4,32 (2H, q, J=7,5); 4,55 (2H, s)	47,2	5,2	26,1	$C_{12}H_{15}BrO_4$	47,5	4,9	26,4	50
IId	119—121	0,56	660, 1650, 1735, 1765	1,20 (3H, t, J=7,5); 1,45—1,80 (10H; m); 4,25 (2H, q, J=7,5); 4,50 (2H, s)	49,3	5,6	25,0	$C_{13}H_{17}BrO_4$	49,2	5,4	25,2	84

[a]Acetone—benzene—hexane (3:1:1).

In a continuation of our research on the radical bromination of 2-functionally substituted 3,4,4-trimethyl-2-buten-4-olides we have accomplished the bromination of 2-ethoxycarbonyl-3-methyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olides (Ia-d), which led to the corresponding 3-bromomethyl derivatives (IIa-d), evidence for the structure of which is provided by the results of elementary analysis and the IR and PMR spectral data presented in Table 1.



Ia-d IIa-d IIIa-d

I—III a $R^1=R^2=CH_3$; b $R^1=CH_3$, $R^2=C_2H_5$; c $R^1R^2=(CH_2)_4$; d $R^1R^2=(CH_2)_5$

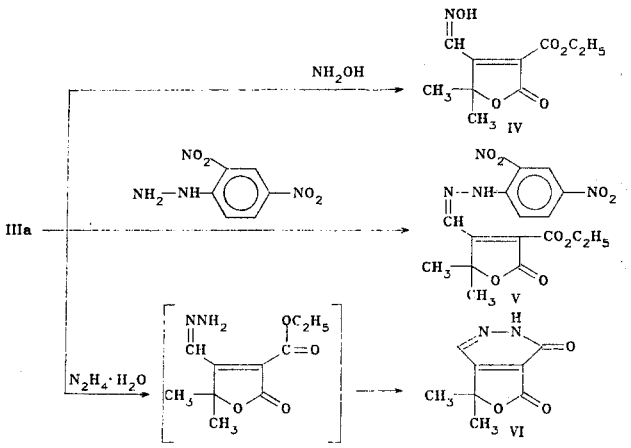
Compounds IIa-d were then oxidized to 3-formyl-substituted derivatives IIIa-d by the direct action of DMSO at 75-80°C.

The structures of the compounds obtained were proved by data from the IR and PMR spectra (Table 2); in the case of IIIa we accomplished alternative synthesis by oxidation of 2-ethoxycarbonyl-3,4,4-trimethyl-2-buten-4-olide (Ia) with selenium dioxide by the method in [5].

Compound IIIa was also subjected to a number of transformations that identify the aldehyde group, viz., reactions with hydroxylamine, 2,4-dinitrophenylhydrazine, and hydrazine hydrate. Whereas the expected oxime IV and 2,4-dinitrophenylhydrazone V were obtained in the first two cases, the reaction with hydrazine hydrate did not stop with the formation of the hydrazone, which underwent ring closing to give 6,7-dioxo-4,4-dimethyl-1,4,6,7-tetrahydrofuro[4,3-d]pyridazine (VI) due to reaction of the terminal amino and ethoxy groups; this was confirmed by data from the IR, PMR, and mass spectra (Table 3). (See reaction on next page.)

EXPERIMENTAL

The IR spectra of mineral oil suspensions and solutions of the compounds in CCl_4 were recorded with a UR-20 spectrometer. The PMR spectra of solutions in carbon tetrachloride, d_6-acetone, and d_6-DMSO were recorded with a Perkin-Elmer R-12B spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at an ionization energy of 30 eV. Thin-layer chromatography (TLC) was accomplished on Silufol UV-254 plates with development in UV light and with iodine vapors.



2-Ethoxycarbonyl-3-bromomethyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olides (IIa-d). A 6.4-g (0.04 mole) sample of bromine was added to a solution of 0.04 mole of 2-ethoxycarbonyl-3-methyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olide (Ia-d) in 50 ml of dry carbon tetrachloride, and the mixture was stirred and heated at the boiling point of the solvent until hydrogen bromide evolution ceased (8-10 h). The bulk of the solvent was removed by distillation, and the precipitated crystals were removed by filtration and recrystallized from carbon tetrachloride (Table 1).

2-Ethoxycarbonyl-3-formyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olides (IIIa-d). A solution of 0.014 mole of 2-ethoxycarbonyl-3-bromomethyl-4,4-dialkyl(cycloalkyl)-2-buten-4-olide (IIa-d) in 20 ml of DMSO was heated on a water bath at 75-80°C for 15-20 h, after which the contents of the flask were poured into 50 ml of ice water, and the aqueous mixture was extracted with ether. The ether extracts were dried over magnesium sulfate, the solvent was removed by distillation, and the residue was distilled *in vacuo* (Table 2).

Preparation of 2-Ethoxycarbonyl-3-formyl-4,4-dimethyl-2-buten-4-olide (IIIa) by the Reaction of Ia with Selenium Dioxide. A 7-g (0.035 mole) sample of Ia was added with stirring to a heated (to 55-60°C) solution of 3.88 g (0.035 mole) of freshly activated selenium dioxide in 26 ml of aqueous dioxane (1 ml of water), and the mixture was refluxed for 13-14 h. The liquid was removed from the precipitate (selenium metal) by decantation and extracted with ether. A 25-ml sample of a 40% aqueous solution of sodium bisulfite was added to the ether

TABLE 2. 2-Ethoxycarbonyl-3-formyl-4,4-dialkyl-2-buten-4-olides (IIIa-d)

Compound	bp, °C (2 mm) (mp)	R_f[a], (n_D^{20})	IR spectrum, cm^{-1}	PMR spectrum (in CCl_4), δ, ppm (J, Hz)	Found, % C	Found, % H	Empirical formula	Calc. % C	Calc. % H	Yield, %
IIIa	127—128	0,85 (1,4900)	1650 (C=C), 1690 (CHO), 1730 (C=O), 1785 (C=O)	0,87 (3H, t, J=7,5); 1,10 (6H, s); 3,95 (2H, q, J=7,5); 10,00 (1H, s)	56,9	5,1	$C_{10}H_{12}O_5$	56,6	5,7	70
IIIb	120—121	0,83 (1,4850)	1650 (C=C), 1695 (CHO), 1730 (C=O), 1785 (C=O)	0,82 (3H, t, J=7,5); 1,40 (3H, t, J=7,5); 1,60 (3H, s); 1,98 (2H, q, J=7,5); 10,32 (1H, s)	58,5	6,2	$C_{11}H_{14}O_5$	58,4	6,2	63
IIIc	148—149 (55—56)	0,80	1650 (C=C), 1700 (CHO), 1730 (C=O), 1780 (C=O)	1,38 (3H, t, J=7,5); 1,78—2,30 (8H, m); 4,40 (2H, q, J=7,5); 10,38 (1H, s)	60,3	6,0	$C_{12}H_{14}O_5$	60,5	5,9	60
IIId	152—153 (69—70)	0,80	1650 (C=C), 1700 (CHO), 1735 (C=O), 1780 (C=O)	1,40 (3H, t, J=7,5); 1,55—2,10 (10H, m); 4,40 (2H, q, J=7,5); 10,32 (1H, s)	61,6	6,7	$C_{13}H_{16}O_5$	61,9	6,3	72

[a]Acetone—benzene (1:2).

TABLE 3. Compounds IV-VI

Compound	R_f	IR spectrum, cm^{-1}	PMR spectrum, δ, ppm (J, Hz)	Mass spectrum, m/z (relative intensity, %)	Found, %			Empirical formula	Calc., %		
					C	H	N		C	H	N
IV	0,50[a]	1620 (C=C), 1670 (C=N), 1760 (C=O), 3300 (OH)	1,30 (3H, t, J=7,5[b]); 1,50 (6H, s); 4,20 (2H, q, J=7,5); 8,50 (1H, s)	227 (4,7), 211 (13), 210 (100), 182 (97), 181 (21), 166 (96), 165 (16), 164 (97), 140 (23), 139 (22), 138 (53), 122 (19), 96 (9), 92 (13), 65 (9), 53 (9), 45 (56)	53,2	6,0	6,2	$C_{10}H_{13}NO_5$	52,8	5,7	6,2
V	0,75[a]	1605 (Ph), 1640 (C=C), 1730 (C=O), 1765 (C=O), 3270 (NH)	1,20 (3H, t, J=7,5[c]); 1,50 (6H, s); 4,25 (2H, q, J=7,5); 7,75 (A part, d, 1H); 8,20 (B part, q, 1H, J=3, J_{AB}=10,5); 8,65 (1H, d, J=3), 8,70 (1H, s)		56,9	3,9	11,8	$C_{16}H_{16}N_4O_8$	56,8	3,4	12,1
VI	0,50[d]	1610 (C=C), 1680 (C=O), 1775 (C=O), 3185 (NH)	1,45 (6H, s)[c]; 7,90 (1H, s)	176 (43), 164 (83), 141 (20), 140 (100), 122 (97), 120 (10), 95 (47), 93 (11), 65 (8), 62 (31), 53 (14)	54,5	4,9	15,7	$C_8H_8N_2O_3$	54,5	4,5	15,9

[a]Acetone–benzene (1:2). [b]$(CD_3)_2O$. [c]$(CD_3)_2CO$. [d]Acetone–benzene–hexane (3:1:1).

extract, and the mixture was stirred vigorously for 1 h. The resulting precipitate was removed by filtration and dissolved in 40 ml of 2 N sulfuric acid, and the solution was heated at 40-45°C until sulfur dioxide evolution ceased. The solution was extracted with ether, and the ether extract was washed with sodium carbonate solution and dried over magnesium sulfate. The solvent was removed by distillation, and the residue was distilled *in vacuo* to give 4.4 g (60%) of aldehyde IIIa with bp 127-128°C (2.66 hPa) and R_f 0.84. IR spectrum: 1650 (C=C), 1690 (CHO), 1730 (ester C=O), and 1785 cm^{-1} (lactone C=O). PMR spectrum (in CCl_4): 0.85 (3H, t, J = 7.5 Hz, CH_3–CH_2), 1.10 (6H, s), 3.92 (2H, q, J = 7.5 Hz, CH_3–CH_2), and 10.10 ppm (1H, s, CHO). Found: C 56.3; H 5.3%. $C_{10}H_{12}O_5$. Calculated: C 56.6; H 5.7%.

2-Ethoxycarbonyl-3-formyl-4,4-dimethyl-2-buten-4-olide Oxime (IV). A 0.14-g (2 mmole) sample of hydroxylamine hydrochloride and 0.2 g (2 mmole) of sodium carbonate dissolved in 8 ml of 50% aqueous ethanol were added to a solution of 0.5 g (2 mmole) of aldehyde IIIa in 5 ml of ethanol. The precipitated crystals were removed by filtration and recrystallized from ethanol to give 0.4 g (93.3%) of oxime IV with mp 240-242°C (Table 3).

2-Ethoxycarbonyl-3-formyl-4,4-dimethyl-2,buten-4-olide 2,4-Dinitrophenylhydrazone (V). A solution of 0.39 g (2 mmole) of 2,4-dinitrophenylhydrazine in 5 ml of 20% aqueous ethanol and one to two drops of concentrated H_2SO_4 were added to a solution of 0.5 g (2 mmole) of aldehyde IIIa in 10 ml of 20% aqueous ethanol, and the yellow crystals that formed immediately were removed by filtration and recrystallized from alcohol to give 0.81 g (90%) of hydrazone V with mp 179-180°C (Table 3).

6,7-Dioxo-4,4-dimethyl-1,4,6,7-tetrahydrofuro[4,3-d]pyridazine (VI). A solution of 0.5 g (2 mmole) of aldehyde IIIa in 3 ml of absolute ethanol was added to a solution of 1.2 g (2 mmole) of hydrazine hydrate in 5 ml of absolute ethanol. The crystals that precipitated after 10-15 min were removed by filtration and recrystallized from alcohol to give 0.25 g (74%) of VI with mp 190°C (dec.).

LITERATURE CITED

1. A. Avetisyan, A. A. V. Galstyan, G. S. Melikyan, and M. T. Dangyan, Armyansk. Khim. Zh., 35, 468 (1982).
2. N. Kornblum, W. Powers, and J. W. Jones, J. Am. Chem. Soc., 79, 6562 (1957).
3. N. Kornblum, J. W. Jones, and G. J. Anderson, J. Am. Chem. Soc., 81, 4113 (1959).
4. A. P. Jonson and A. Pelter, J. Chem. Soc., 520 (1964).
5. L. Fieser and M. Fieser, Reagents for Organic Synthesis, Vol. 3, Wiley.