6. S. E. Korostova, A. I. Mikhaleva, S. G. Shevchenko, V. V. Shcherbakov, R. N. Nesterenko, M. V. Sigalov, and B. A. Trofimov, *Zh. Org. Khim.* **22**, 2489 (1986).
7. M. V. Markova, A. I. Mikhaleva, M. V. Sigalov, L. V. Morozova, I. A. Aliev, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, No. 5, 604 (1989).
8. A. I. Mikhaleva, S. E. Korostova, A. N. Vasil'ev, L. N. Balabanova, N. P. Sokol'nikova, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, No. 12, 1636 (1977).
9. I. A. Aliev, A. I. Mikhaleva, S. Kh. Bairamova, and É. I. Akhmedov, *Zh. Org. Khim.* **22**, 489 (1986).
10. B. A. Trofimov, L. V. Morozova, M. V. Sigalov, A. I. Mikhaleva, and M. V. Markova, *Makromol. Chem.* **188**, 2251 (1987).

FIVE-MEMBERED 2,3-DIOXOHETEROCYCLES

15.* SYNTHESIS AND [1,3]-SIGMATROPIC REARRANGEMENT OF 1,5-DIARYL-3-DIPHENYLMETHOXY-4-ETHOXYCARBONYL-2,5-DIHYDROPYRROL-2-ONES

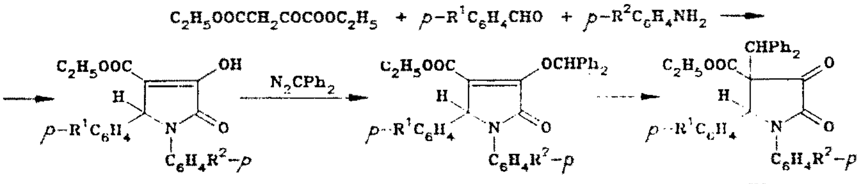
Yu. S. Andreichikov, V. L. Gein, and E. V. Shumilovskikh

UDC 547.745'749.04:543.422

Ethyl oxaloacetate reacts with a mixture of an aromatic aldehyde and an arylamine to give 1,5-diaryl-4-ethoxycarbonyltetrahydropyrrole-2,3-diones, which react with diphenyldiazomethane to give the O-alkylation products. On heating, the latter undergo suprafacial [1,3]-sigmatropic rearrangement to 1,5-diaryl-4-diphenylmethyl-4-ethoxycarbonyltetrahydropyrrole-2,3-diones. The effects of the type of migrating group on the rearrangement are discussed.

3-Diphenylmethoxy-substituted tetrahydrofuran- and tetrahydropyrrole-2,3-diones are convenient models for the study of [1,3]- and [1,5]-sigmatropic rearrangements in heterocyclic systems, in which the nature of the electron-acceptor group has a marked effect on the type of migration [2, 3].

In order to examine further the influence of the nature of the substituent in the 4-position of the heterocycle, we have obtained the 1,5-diaryl-4-ethoxycarbonyltetrahydropyrrole-2,3-diones (Ia, c-e) (Table 1), and examined their reactions with diphenyldiazomethane, and the thermal isomerization of the resulting O-alkyl derivatives (IIa-e).



Ia, c–e IIa–e IIIa–e

I—IIIa, e $R^1=H$, b $R^1=Br$, c $R^1=CH_3O$, d $R^1=NO_2$, a–d $R^2=H$, e $R^2=NO_2$

The IR spectra of (Ia, c-e) (Table 2) show absorption for the ester carbonyl at 1700-1721 cm^{-1}, lactam carbonyl at 1670-1687 cm^{-1}, the double bond at 1610-1655 cm^{-1}, and for the enol hydroxy at 3270-3310 cm^{-1}. In the PMR spectra, in addition to a multiplet for the aromatic protons at 6.98-7.55 ppm and signals for the ethoxy group, signals were observed for

---

*For Communication 14, see [1].

Perm State Institute of Pharmacy, Perm 614600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 753-757, June, 1990. Original article submitted November 24, 1987; revision submitted August 15, 1989.

0009-3122/90/2606-0627$12.50 ©1990 Plenum Publishing Corporation

TABLE 1. Reaction Conditions and Properties of (Ia, c-e), (II), and (IIIa-e)

Compound	Empirical formula	Reaction conditions		mp, °C	Yield, %
		T, °C*	time, h		
Ia	$C_{19}H_{17}NO_4$		48	174...176 (170 [5])	71
Ic	$C_{20}H_{19}NO_5$		72	148...150 (147 [6])	33
Id	$C_{19}H_{16}N_2O_6$		24	178...179	28
Ie	$C_{19}H_{16}N_2O_6$		240	185...187	30
IIa	$C_{32}H_{27}NO_4$		24	139...140	57
IIb	$C_{32}H_{26}BrNO_4$		24	135...136	86
IIc	$C_{33}H_{29}NO_5$		0,1	111...113	60
IId	$C_{32}H_{26}N_2O_6$		0,1	148...149	47
IIe	$C_{32}H_{26}N_2O_6$		0,1	200...201	88
IIIa	$C_{32}H_{27}NO_4$	198...200	0,5	271...272**	33
IIIb	$C_{32}H_{26}BrNO_4$	200...207	0,5	259...260**	43
IIIc	$C_{33}H_{29}NO_5$	200...207	0,58	245...246	45
IIId	$C_{32}H_{26}N_2O_6$	205...207	0,25	237...238**	54
IIIe	$C_{32}H_{26}N_2O_6$	207...213	1	252...254**	45

---

*Compounds (Ia, c-e) and (IIa-e) were obtained at room temperature.

**With decomposition.

TABLE 2. Spectral Properties of (I-III)

Compound	IR spectrum, ν, cm^{-1}					PMR spectrum, δ, ppm*			
	endocycl. C=C	lact. CO	ester CO	keton. CO	OH	H_{arom}, m	5-H, sec	C_2H_5	Ph_2CH, sec
Ia	1652	1680	1710	—	3295	7,35	5,65	1,1 t; 4,1 q	—
Ic	1610	1670	1700	—	3270	6,98	5,57	1,11 t; 4,08 q	—
Id	1652	1687	1721	—	3300	7,50	5,80	1,15 t; 4,08 q	—
Ie	1665	1718		—	3310	7,55	5,78	1,15 t; 4,17 q	—
IIa	1655	1692		—	—	7,18	5,55	1,17 t; 4,09 q	—
IIb	1655	1710		—	—	7,15	5,48	1,18 t; 4,05 q	—
IIc	1645	1700		—	—	7,21	5,48	1,20 t; 4,05 q	—
IId	1645	1700		—	—	7,25	5,63	1,22 t; 4,05 q	—
IIe	1650	1705		—	—	7,35	5,55	1,15 t; 4,05 q	—
IIIa	—	1760	1700		—	7,18	5,98	0,58 t; 3,20 q	5,25
IIIb	—	1770	1712		—	7,13	5,98	0,65 t; 3,17 q	5,20
IIIc	—	1755	1695		—	6,98	5,85	0,61 t; 3,13 q	5,15
IIId	—	1755	1735	1700	—	7,50	6,25	0,57 t; 3,10 q	5,28
IIIe	—	1760	1715		—	7,41	6,28	0,60 t; 3,27 q	5,30

---

*PMR spectrum, δ_{OH}: 8.45 s (Ia), 8.48 s (Ic), 8.75 ppm, (Id); δ_{CH_3O}: 3.63 s (Ic), 3.55 s (IIc), 3.58 ppm, s (IIIc).

the methine proton in the 5-position of the heterocycle at 5.43-5.80 ppm and for the enol hydroxy at 8.45-8.83 ppm. The spectral data show that (Ia, c-e) are, like 4-ethoxycarbonyltetrahydropyrrole-2,3-diones [4], enolized, existing in the 3-hydroxy-1,5-diaryl-4-ethoxycarbonyl-2,5-dihydropyrrole-2-one forms, as confirmed qualitatively by their reaction with alcoholic $FeCl_3$.

On treatment with diphenyldiazomethane, (Ia, c-e) are converted smoothly in dioxane at room temperature into 1,5-diaryl-3-diphenylmethoxy-4-ethoxycarbonyl-2,5-dihydropyrrole-2-ones (IIa-e). The reaction was followed by the disappearance of the color of diphenyldiazomethane. It is noteworthy that substituents in the para-position of the aryl radicals have little effect on the reaction rate, evidently as a result of the absence of conjugation of the substituent with the reaction center.

The 3-diphenylmethoxy compounds (IIa-e) were obtained as colorless, crystalline solids soluble in chloroform, the IR spectra showing absorption for the ester and lactam carbonyl conjugated with the double bond, and for the double bond. In the

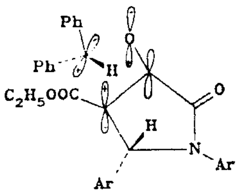
PMR spectra of (IIa-e), the signal for the methine proton of the diphenylmethoxy group overlapped the aromatic proton multiplet.

On heating (IIa-e) to 198-213°C, they rearranged to 1,5-diaryl-4-diphenylmethyl-4-ethoxycarbonyltetrahydropyrrole-2,3-diones (IIIa-e), the IR spectra of which showed no absorption for a double bond, but absorption was present for the ester group and the ketone and lactam carbonyls. The PMR spectrum contained, in addition to a multiplet for the aromatic protons and signals for the ethoxy-group, a signal for the methine proton in the 5-position of the heterocycle at 5.85-6.25 ppm, and for the proton of the diphenylmethyl radical at 5.15-5.28 ppm.

The mass spectrum of (IIIb) contained a molecular ion peak M$^+$, m/z 568, peaks corresponding to the ions [M – CHPh$_2$]$^+$ (m/z 401), [M – CHPh$_2$–COOC$_2$H$_5$]$^+$ (m/z 328), a strong peak for [Ph$_2$CH]$^+$ (m/z 167), and a peak for Ph$^+$ (m/z 77).

The formation of (IIIa-e), as in the case of 4-arylsulfonyl-3-diphenylmethoxy-2,5-dihydrofuran-2-ones [3], is due to [1,3]-suprafacial sigmatropic migration of the diphenylmethyl radical. The occurrence of a [1,3]-sigmatropic shift, rather than the [1,5]-sigmatropic rearrangement observed with 4-acyl-3-diphenylmethoxy-1,5-diphenyl-2,5-dihydropyrrole-2-ones [2], is due to the fact that the ethoxycarbonyl group is capable of participating in the formation of a cyclic transition state.

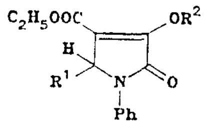
The rearrangement may be represented as occurring via the transition state:



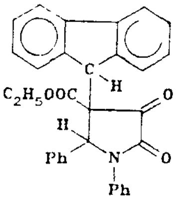
The fact that the yields of the rearrangement products (IIIa-e) are lower than those of 4-arylsulfonyl-4-diphenylmehyltetrahydrofuran-2,3-diones [3] is due to steric hindrance by the aryl radical in the 5-position in (IIa-e), and to the reduced electron-acceptor character of the ethoxycarbonyl group as compared with the sulfonyl group.

By analogy with the findings of Gilchrist et al. [7, 8], this rearrangement could be of a partially radical type.

In order to assess the influence of the migrating groups on the [1,3]-sigmatropic rearrangement, (Ia) was reacted with diazoalkanes to give 3-methoxy-, 3-benzyloxy-, and 3-(9-fluorenyloxy)-1,5-diphenyl-4-ethoxycarbonyl-2,5-dihydropyrrole-2-ones (IVa-c).



IVa-c



V

IV a R^1=p-BrC$_6$H$_4$, R^2=CH$_3$; b R^1=Ph, R^2=CH$_2$Ph; c R^1=Ph, R^2=9-fluorenyl

The reactions with diazomethane and benzoyldiazomethane occurred at room temperature. With diazofluorene, heating at 90-100°C or irradiation of the reaction mixture with UV was required, the yields of (IVc) by the thermal and photolytic routes being comparable, in accordance with the intermediate formation of fluorenylcarbene. On heating (IVa-c) at 165-212°C, only (IVc) underwent [1,3]-sigmatropic rearrangement to give the C-alkylation product (V) in 20% yield.

The nonoccurrence of a sigmatropic shift in the case of (IVa) and (IVb) confirms the partially radical nature of the transition state, and the participation of the phenyl substituents in the migrating group R^2 in the delocalization of the unpaired electron, and it also explains the decreased yield of the rearrangement product (IVc), which is in accordance with literature reports of the greater difficulty of formation of the fluorenyl radical, as compared with the diphenylmethyl radical [9, p. 193].

EXPERIMENTAL

IR spectra were obtained on a UR-20 instrument in Vaseline grease, and PMR spectra on an RYa-2310 (60 MHz) instrument, internal standard HMDS. The mass spectrum was obtained on an MKh-1320, ionizing irradiation energy 70 eV.

The elemental analyses for N and Hal were in agreement with the calculated values.

1,5-Diaryl-4-ethoxycarbonyltetrahydropyrrole-2,3-diones (Ia, c-e). To a solution of 15 mmoles of diethyl oxaloacetate in 5 ml of methanol was added a mixture of 15 mmoles of the appropriate aromatic aldehyde and 15 mmoles of the arylamine in 10 ml of ethanol. The mixture was kept at 20°C for 24-240 h, and the solid which separated was filtered off and recrystallized from toluene to give (Ia, c-e).

1,5-Diaryl-3-diphenylmethoxy-4-ethoxycarbonyl-2,5-dihydropyrrol-2-ones (IIa-e). To a solution of 10 mmoles of (Ia-e) in 20 ml of dioxane was added 11 mmoles of diphenyldiazomethane, dissolved in 10 ml of dioxane. The mixture was kept at 20°C for 0.1-24 h, until the solution became colorless. The solvent was removed, and the residue recrystallized from ethanol to give (IIa-e).

1,5-Diaryl-4-diphenylmethyl-4-ethoxycarbonyl Tetrahydropyrrole-2,3-diones (IIIa-e). The compound (IIa-e) (1.76 mmoles) was kept at 198-213°C for 15-60 min, cooled, treated with ethanol, and the solid filtered off and recrystallized from toluene to give (IIIa-e).

5-p-Bromophenyl-3-methoxy-1-phenyl-4-ethoxycarbonyl-2,5-dihydropyrrol-2-one (IVa, $C_{20}H_{18}BrNO_4$). To a solution of 2.01 g (5 mmoles) of (Ib) in 10 ml of dioxane was added 15 ml (10 mmoles) of a solution of diazomethane in ether. When evolution of gas ceased, the solvent was removed, and the residue recrystallized from heptane to give 0.96 g (46%) of (IVa), mp 88-89°C. IR spectrum: 1660 (C=C), 1700 cm^{-1} (CON and COO). PMR spectrum ($CDCl_3$): 1.10 (3H, t, $COOCH_2CH_3$); 4.03 (2H, q, $COOCH_2CH_3$); 4.23 (3H, s, CH_3O); 5.43 (1H, s, 5-H), and 7.05 ppm (m, 9H arom.).

1,5-Diphenyl-3-benzyloxy-4-ethoxycarbonyl-2,5-dihydropyrrol-2-one (IVb, $C_{26}H_{23}NO_4$). To a solution of 1.61 g (5 mmoles) of (Ia) in 20 ml of dioxane was added slowly 2.45 g (21 mmoles) of phenyldiazomethane, until a yellowish-orange coloration was obtained. When gas evolution had ceased, the solvent was removed, and the residue recrystallized from methanol to give 1.0 g (50%) of (IVb), mp 114-115°C. IR spectrum: 1640 (C=C), 1690 cm^{-1} (CON and COO). PMR spectrum ($CDCl_3$): 1.08 (3H, t, $COOCH_2CH_3$); 3.98 (2H, q, $COOCH_2CH_3$); 5.58 (1H, s, 5-H); 5.75 (2H, s, $PhCH_2O$), and 7.15 ppm (m, 15H arom.).

1,5-Diphenyl-3-(9-fluorenyloxy)-4-ethoxycarbonyl-2,5-dihydropyrrol-2-one (IVc, $C_{32}H_{25}NO_4$). A. To a solution of 1.97 g (6 mmoles) of (Ia) in 20 ml of dioxane was added 1.17 g (6 mmoles) of diazofluorene dissolved in 10 ml of dioxane. The mixture was heated on a water bath for 4 h, until the solution had become colorless. After removal of the solvent, the residue was recrystallized from toluene to give 1.27 g (43%) of (IVc), mp 197-198°C.

B. To a solution of 1.97 g (6 mmoles) of (Ia) in 20 ml of dioxane was added 1.17 g (6 mmoles) of diazofluorene, dissolved in 10 ml of dioxane. The mixture was irradiated with an OKN-11 quartz-mercury lamp for 2 h, until the solution had become colorless. After removal of the solvent, the residue was recrystallized from toluene to give 1.33 g (44%) of (IVc), mp 197-198°C. IR spectrum: 1633 (C=C), 1690 cm^{-1} (CON and COO). PMR spectrum ($CDCl_3$): 0.81 (3H, t, $COOCH_2CH_3$); 3.81 (2H, q, $COOCH_2CH_3$); 5.48 (1H, s, 5-H), and 7.21 ppm (m, 18H arom.).

1,5-Diphenyl-4-(9-fluorenyl)-4-ethoxycarbonyltetrahydropyrrole-2,3-dione (V, $C_{32}H_{25}NO_4$). The compound (IVc) (1.0 g, 2 mmoles) was kept at 203-211°C for 1 h. After cooling, the product was recrystallized from carbon tetrachloride to give 0.2 g (20%) of (V), mp 215-217°C. IR spectrum: 1715 (COO and CO), 1745 cm^{-1} (CON). PMR spectrum (DMSO-D_6): 0.85 (3H, t, $COOCH_2CH_3$); 3.65 (2H, q, $COOCH_2CH_3$); 4.51 ($C_{12}H_8CH$); 5.02 (1H, s, 5-H), and 7.00 ppm (m, 18 H arom.).

LITERATURE CITED

1. V. V. Zalesov, N. A. Pulina, and Yu. S. Andreichikov, *Zh. Org. Khim.* (1989) (in press).
2. Yu. S. Andreichikov, V. L. Gein, and I. N. Anikina, *Khim. Geterotsikl. Soedin.*, No. 5, 625 (1987).
3. Yu. S. Andreichikov, V. L. Gein, and I. N. Anikina, *Khim. Geterotsikl. Soedin.*, No.10, 1428 (1985).
4. I. J. Simon and A. Conduche, *Ann. Chim.* **12**, 5 (1907).
5. R. Schiff and C. Bertini, *Ber. Chem. Ges.* 30, 601 (1897)
6. J. R. Merchant and V. Srinavasan, *Rec. Trav. Chim.* **81**, 144 (1962).
7. T. Gilchrist and R. Storr, *Organic Reactions and Orbital Symmetry* [Russian translation], Mir, Moscow (1976), p. 279.
8. I. E. Baldwin and J. E. Brown, *J. Am. Chem. Soc.* 91, 3647 (1969).
9. A. S. Dneprovskii and T. I. Temnikova, *The Theoretical Foundations of Organic Chemistry* [in Russian], Khimiya, Leningrad (1979).