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Reactions of Aliphatic Diazo Compounds: III.* Reaction of Ethyl Diazoacetate with 1,3-Diarylpropenones**

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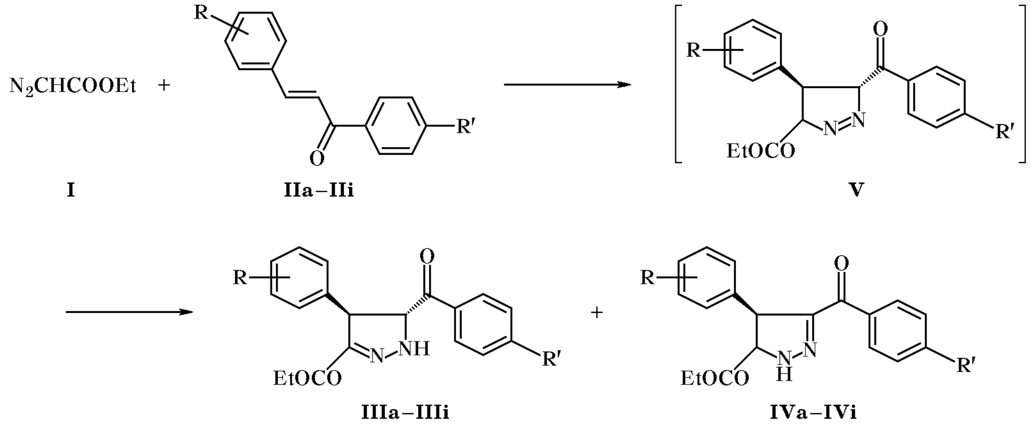
Abstract—Ethyl diazoacetate adds to 1,3-diarylpropenones in a regioselective fashion to give intermediate 4,5-dihydro-3*H*-pyrazole derivative; 1,3-hydride shift in the latter leads to formation of isomeric ethyl 4-aryl-5-aroyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate and ethyl 4-aryl-3-aroyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate at a ratio of 5 : 1. Thermolysis of these products is not stereospecific; as a result, three isomeric substituted ethyl cyclopropanecarboxylates and 2-pyranone derivative are formed.

Although 1,3-dipolar cycloaddition reactions of diazo compounds with unsaturated compounds possessing electron-acceptor groups were known for a long time, in some cases the structure of the adducts was not established unambiguously [2]. For example, Kohler and Steele [3] showed that the reaction of ethyl diazoacetate (**I**) with 1,3-diphenylpropenone (**IIa**) yields ethyl 5-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate, whereas in the more recent study [4] the same product was assigned the structure of ethyl 3-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate.

We have examined the reactions of ester **I** with 1,3-diarylpropenones **IIa**–**IIi**. By heating of a mixture of ethyl diazoacetate (**I**) with 1,3-diphenylpropenone (**IIa**) in heptane for 7 h at 75°C we obtained isomeric dihydropyrazoles **IIIa** and **IVa** which were isolated in 36 and 8% yield, respectively (Scheme 1). The structure of the products was determined on the basis of their elemental compositions (Table 1) and spectral

Scheme 1.



II–**IV**, R = R′ = H (**a**); R′ = H, R = 4-Me (**b**), 4-MeO (**c**), 3-Br (**d**), 4-Br (**e**), 2-Cl (**f**); R = H, R′ = 4-MeO (**g**); R = 4-MeO, R′ = 4-Cl (**h**); R = 3-Br, R′ = 4-Cl (**i**).

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[*] For communication II, see [1].

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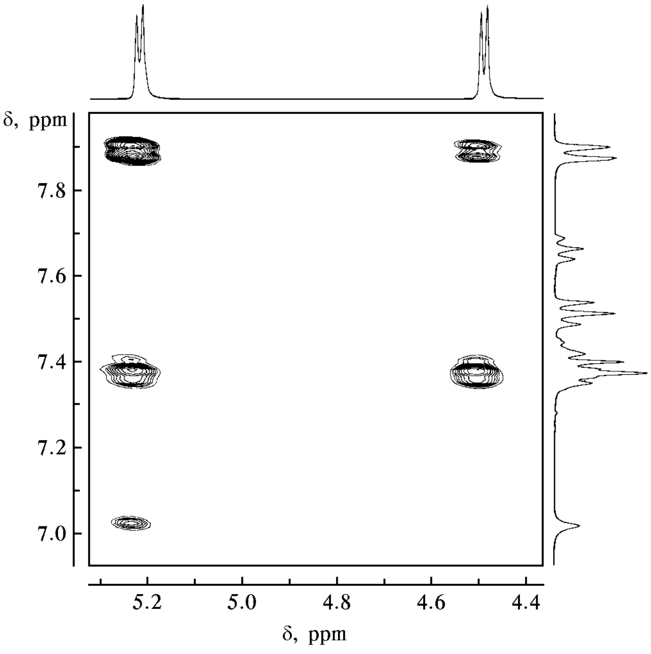


Fig. 1. ^1H–^1H NOESY spectrum of ethyl 5-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**IIIa**).

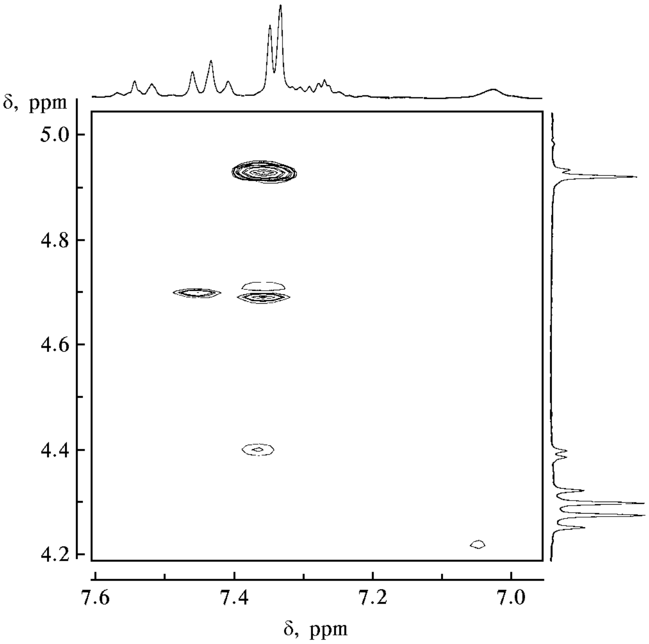
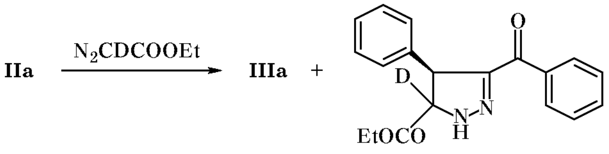


Fig. 2. ^1H–^1H NOESY spectrum of ethyl 3-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate (**IVa**).

data (Table 2). In the IR spectra of **IIIa** and **IVa** we observed absorption bands typical of NH (3400 cm^{-1}) and C=O groups (1700 and 1740 cm^{-1}). The absorption maxima in the UV spectrum of **IVa** are displaced to the long-wave region as compared to those observed for compound **IIIa**: λ_{max} 260 and 326 nm for **IVa** and 248 and 290 nm for **IIIa**. This indicates a more extended conjugation chain in molecule **IVa**. The ^1H NMR spectrum of pyrazole **IIIa** contains two doublets at δ 4.49 and 5.22 ppm (*J* = 4 Hz). In the spectrum of **IVa** the pyrazole ring protons give two doublets at δ 4.40 and 4.95 ppm (*J* = 4 Hz); also, signals from the ethyl group, aromatic rings, and NH group are present. The ^{13}C NMR spectra of **IIIa** and **IVa** are consistent with the assumed structures.

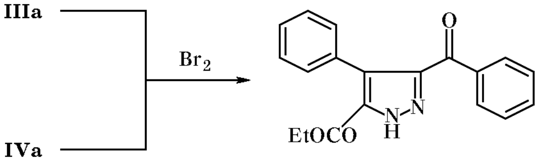
In order to prove the structure of products **IIIa** and **IVa** more rigorously, diphenylpropenone **IIa** was brought into reaction with ethyl diazoacetate-*d* [5]. The reaction afforded two products, one of which had physical properties and spectral parameters similar to those of **IIIa**. The other product showed in the ^1H NMR spectrum a singlet from 4-H of the pyrazole ring, indicating the presence of deuterium on the neighboring carbon atom to which the ester group is attached. This means that the second product has structure **VI**:



VI

The ^1H–^1H NOESY spectrum of isomer **IIIa** (Fig. 1) displayed a cross peak due to coupling of the NH proton with C**H**COPh. In the ^1H–^1H NOESY spectrum of isomer **IVa** (Fig. 2) we observed cross peaks corresponding to coupling between C**H**CO_2Et and NH protons and between the former and *ortho*-protons of the phenyl (but not benzoyl) group. These data allowed us to rule out alternative structures of ethyl 4-benzoyl-5-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate and ethyl 4-benzoyl-3-phenyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate.

The oxidation of compounds **IIIa** and **IVa** with bromine gave ethyl 3-benzoyl-4-phenylpyrazole-5-carboxylate (**VII**) whose structure was established on the basis of its spectral parameters and published data [4]:



VII

Table 1. Yields, melting points, and elemental analyses of compounds **IIIa–IIIi**, **IVa**, **VIII**, **IXa**, **IXb**, and **XIIb**

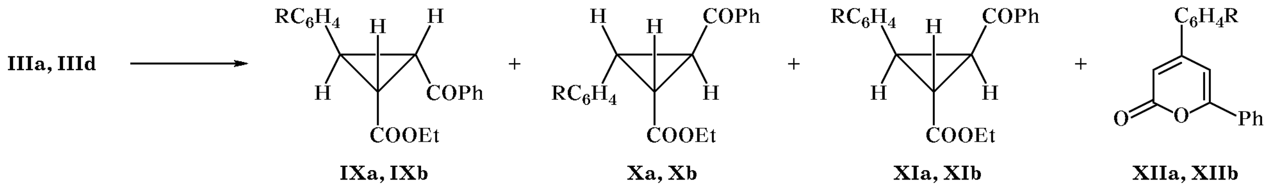
Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	36	142	70.66	5.76	8.66	$C_{19}H_{18}N_2O_3$	70.80	5.59	8.69
IIIb	47	147	71.32	6.02	8.33	$C_{20}H_{20}N_2O_3$	71.43	5.95	8.33
IIIc	15	158	68.23	5.65	7.87	$C_{20}H_{20}N_2O_4$	68.18	5.68	7.95
IIId	62	175	56.85	4.46	6.89	$C_{19}H_{17}BrN_2O_3$	56.86	4.24	6.98
IIIe	16	131	56.89	4.30	6.87	$C_{19}H_{17}BrN_2O_3$	56.86	4.24	6.98
IIIf	11	124	63.83	4.68	7.77	$C_{19}H_{17}ClN_2O_3$	63.90	4.77	7.80
IIIg	49	149	62.20	5.71	7.95	$C_{20}H_{20}N_2O_4$	68.18	5.68	7.95
IIIh	27	137	62.03	5.01	7.28	$C_{20}H_{19}ClN_2O_4$	62.09	4.95	7.24
IIIi	46	151	52.41	3.70	6.38	$C_{19}H_{16}BrClN_2O_3$	52.35	3.67	6.43
IVa	8	102	70.76	5.62	8.72	$C_{19}H_{18}N_2O_3$	70.80	5.59	8.69
VIII	20	181	64.07	4.37	7.72	$C_{19}H_{15}ClN_2O_3$	64.31	4.23	7.89
IXa	11	86	81.42	6.15	–	$C_{19}H_{18}O_3$	81.63	6.12	–
IXb	16	94	64.23	4.60	–	$C_{19}H_{17}BrO_3$	64.34	4.55	–
XIIb	9	119	62.28	3.41	–	$C_{17}H_{11}BrO_2$	62.38	3.36	–

Thus, the reaction of ethyl diazoacetate with 1,3-diphenylpropenone follows the Auwers pattern and regioselectively yields 4,5-dihydro-3*H*-pyrazole (**V**); 1,3-hydride shift in the latter leads to formation of isomeric 4,5-dihydro-1*H*-pyrazole derivatives **IIIa** and **IVa** at a ratio of 5 : 1. In the reactions of ester **I** with 1,3-diarylpropenones **Ib**–**Ii** we succeeded in isolating only the major products, pyrazoles **IIIb**–**IIIi**. Their structure was established on the basis of their elemental compositions (Table 1) and spectral parameters (Table 2). Compounds **IIIb**–**IIIi** showed in the ^{1}H NMR spectra doublet signals at δ 4.40–4.48 and 5.13–5.22 ppm ($CDCl_3$), J = 4 Hz, from protons at C^4 and C^5 of the pyrazole ring, which are arranged *trans* with respect to each other. The ^{1}H NMR spectra of the reaction mixtures obtained from ethyl diazoacetate and 1,3-diarylpropenones also contained signals from 4-H and 5-H of isomeric pyrazoles **IVb**–**IVi** at δ 4.40 and 5.00 ppm (J = 4 Hz). The signal positions and isomer ratios **III** : **IV** are given in Experimental. In the reaction of ethyl diazoacetate with 3-(2-chlorophenyl)-1-phenylpropenone (**IIf**), apart from products **IIIf** and **IVf**, 20% of ethyl 3-benzoyl-4-(2-chlorophenyl)pyrazole-5-carboxylate (**VIII**) was isolated.

It is known that thermolysis of dihydropyrazoles is a method for preparation of cyclopropane derivatives [6]. According to the data of [3, 7], thermolysis of compound **IIIa** leads to formation of substituted 2-pyranone **XIIa** and ethyl 2-benzoyl-3-phenylcyclopropanecarboxylate whose steric structure was not established. By heating of dihydropyrazoles **IIIa** and **IIId** for 75 min at 220°C, followed by separation of the reaction mixture by column chromatography, we isolated cyclopropanecarboxylates **IXa**, **IXb**, and **Xa** and 2-pyranones **XIIa** and **XIIb** (Scheme 2).

The ^{1}H NMR spectrum of **IXa** contained three signals from the cyclopropane ring ptotons at δ 2.65 (J_1 = 6, J_2 = 10 Hz), 3.11 (J_1 = 6, J_2 = 10 Hz), and 3.39 ppm (J_1 = 6, J_2 = 7 Hz). Compound **Xa** showed in the spectrum signals at δ 2.89 (J_1 = 5, J_2 = 10 Hz),

Scheme 2.



R = H (**a**), 3-Br (**b**).

Table 2. IR and ^{1}H NMR spectra of compounds **IIIa–IIIi**, **IVa**, **VI**, **VIII**, **IXa**, **IXb**, **Xa**, and **XIIb**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum,[a] δ, ppm (J, Hz)
IIIa[b]	1130, 1250, 1350, 1580, 1690, 1710, 3040, 3370	1.25 t (3H, 7), 4.11 q (2H, 7), 4.49 d (1H, 4), 5.22 d (1H, 4), 7.03 s (1H), 7.31–7.72 (8H), 7.92 d (2H, 7)
IIIb	1130, 1250, 1350, 1580, 1690, 1710, 3040, 3370	1.09 t (3H, 7), 4.02 q (2H, 7), 4.31 d (1H, 4), 5.42 d (1H, 4), 7.07 d (2H, 8), 7.18 d (2H, 8), 7.55 m (2H), 7.70 m (1H), 7.90 m (2H), 8.91 s (1H)
IIIc	1120, 1190, 1260, 1330 1600, 1690, 1710, 3040, 3370	1.10 t (3H, 7), 3.72 s (3H), 4.00 q (2H, 7), 4.30 d (1H, 4), 5.40 d (1H, 4), 6.93 d (2H, 8), 7.11 d (2H, 8), 7.53–7.70 (3H), 7.90 m (2H), 8.83 s (1H)
IIId	1130, 1250, 1350, 1580, 1690, 1710, 3040, 337	1.08 t (3H, 7), 4.04 q (2H, 7), 4.44 d (1H, 4), 5.58 d (1H, 4), 7.12–7.78 (7H), 7.90 d (2H, 7), 9.07 s (1H)
IIIe	1130, 1250, 1350, 1580, 1690, 1710, 3040, 3370	1.20 t (3H, 7), 4.11 q (2H, 7), 4.45 d (1H, 4), 5.18 (1H, 4), 7.03 s (1H), 7.20–7.71 (7H), 7.80 d (2H, 7)
IIIf	1130, 1260, 1350, 1590, 1690, 1710, 3040, 3370	1.24 t (3H, 7), 4.20 q (2H, 7), 4.45 d (1H, 4), 5.10 d (1H, 4), 7.03–7.60 (7H), 8.00 d (2H, 7), 9.68 s (1H)
IIIg	1120, 1190, 1260, 1330, 1600, 1690, 1710, 3040, 3370	1.08 t (3H, 7), 3.86 s (3H), 4.00 q (2H, 7), 4.35 d (1H, 4), 5.42 d (1H, 4), 7.08 d (2H, 7), 7.30–7.45 (3H), 7.87 d (2H, 8), 8.91 s (1H)
IIIh	1100, 1190, 1260, 1340, 1590, 1690, 1710, 3040, 3370	1.24 t (3H, 7), 3.82 s (1H), 4.16 q (2H, 7), 4.40 d (1H, 4), 5.13 d (1H, 4), 6.93 d (2H, 8), 6.95 s (1H), 7.28 d (2H, 8), 7.49 d (2H, 8), 7.82 d (2H, 8)
IIIi	1130, 1250, 1350, 1580, 1690, 1710, 3040, 3370	1.21 t (3H, 7), 4.18 q (2H, 7), 4.41 d (1H, 4), 5.18 d (1H, 4), 7.00 s (1H), 7.20–7.60 (6H), 7.81 d (2H, 7)
IVa[c]	1110, 1280, 1410, 1650, 1735, 3050, 3380	1.35 t (3H, 7), 4.28 q (2H, 7), 4.40 d (1H, 4), 4.95 d (1H, 4), 7.01 s (1H), 7.24–7.59 (8H), 8.13 d (2H, 7)
VI	1110, 1280, 1410, 1650, 1735, 3050, 3380	1.35 t (3H, 7), 4.28 q (2H, 7), 4.40 d (0.1H, 4), 4.95 s (1H), 7.01 s (1H), 7.30–7.60 (8H), 8.13 d (2H, 7)
VIII	1130, 1250, 1350, 1690, 1710, 3040, 3370	1.12 t (3H, 7), 4.18 q (2H, 7), 7.30–8.10 (9H), 14.80 br.s (1H)
IXa	1220, 1310, 1450, 1730	1.14 t (3H, 7), 2.66 d.d (1H, 10, 6), 3.11 d.d (1H, 10, 6), 3.39 d.d (1H, 7, 6), 4.10 q (2H, 7), 7.18–7.65 (8H), 8.06 d (2H, 7)
IXb	1220, 1310, 1450, 1680, 1730	1.14 t (3H, 7), 2.65 d.d (1H, 10, 6), 3.10 d.d (1H, 10, 6), 3.36 d.d (1H, 7, 6), 4.10 q (2H, 7), 7.10–7.70 (7H), 8.07 d (2H, 7)
Xa		1.08 t (3H, 7), 2.89 d.d (1H, 10, 5), 3.29 d.d (1H, 10, 6), 3.87 d.d (1H, 6, 5), 4.02 q (2H, 7), 7.10–7.70 (8H), 8.16 d (2H, 7)
XIIb	1540, 1630, 1720, 3040	6.47 s (1H), 6.92 s (1H), 7.34–7.75 (9H)

[a] The ^{1}H NMR spectra of compounds **IIIb**, **IIIc**, **IIId**, **IIIf**, and **IIIg** were recorded in DMSO-d_6, and of the others, in $CDCl_3$.

[b] ^{13}C NMR spectrum, δ_C, ppm: 14.0 (CH_3), 54.7 (CH), 61.2 (CH_2), 73.5 (CH), 127.5, 128.0, 128.9, 129.0, 129.3, 132.7, 134.1, 139.1, 161.2 (C=O), 195.6 (C=O); UV spectrum, λ_{max}, nm (log ε): 248 (4.17), 290 (4.01).

[c] ^{13}C NMR spectrum, δ_C, ppm: 13.9 (CH_3), 53.4 (CH), 62.1 (CH_2), 69.4 (CH), 127.0, 127.4, 127.9, 128.8, 129.2, 136.7, 139.4, 171.1 (C=O), 186.4 (C=O); UV spectrum, λ_{max}, nm (log ε): 260 (3.89), 326 (4.08).

3.29 (J_1 = 6, J_2 = 10 Hz), and 3.87 ppm (J_1 = 5, J_2 = 6 Hz). The spectral data coincide with those reported for the corresponding methyl esters [8]. In the ^{1}H NMR spectrum of the product mixture obtained by thermolysis of compound **IIIa** we also observed CH signals from one more isomeric cyclopropane ester **XI**, δ, ppm (J, Hz): 3.23 (5, 6), 3.35 (6, 10), 3.57 (5, 10); by analogy with the spectrum of methyl *t*-2-benzoyl-*t*-3-phenylcyclopropanecarboxylate [9], product **XI** was assigned the *trans,trans*-configuration. Analogous cyclopropane proton signals were also observed in the ^{1}H NMR spectrum of the thermolysis products of dihydropyrazole **IIId**. In both cases the ratio **IX** : **X** : **XI** : **XII** was 2 : 1 : 1 : 1. Thus the thermolysis of compounds **III** is not stereospecific.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from 2% solutions in chloroform. The ^{1}H NMR spectra were obtained on a Bruker DPX-300 instrument (300 MHz) from 2% solutions in $CDCl_3$

or DMSO-d_6. The UV spectra were measured on a Specord UV-Vis spectrophotometer.

Ethyl 5-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (IIIa). 1,3-Diphenylpropenone (**IIa**), 10 g (0.05 mol), was dissolved in 30 ml of heptane, and 10.9 g (0.1 mol) of ethyl diazoacetate (**I**) was added. The mixture was heated for 7 h at 75°C, and the solvent was distilled off. By fractional crystallization of the residue from alcohol we isolated 5.75 g (36%) of compound **IIIa** and 1.2 g (8%) of ethyl 3-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate (**IVa**).

Ethyl 5-benzoyl-4-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazole-3-carboxylate (IIIb) was synthesized in a similar way from 4.44 g (0.02 mol) of 3-(4-methylphenyl)-1-phenylpropenone and 4.56 g (0.04 mol) of ester **I**. Yield 3.2 g.

Ethyl 5-benzoyl-4-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole-3-carboxylate (IIIc) was synthesized in a similar way from 1 g (4 mmol) of 3-(4-methoxyphenyl)-1-phenylpropenone (**IIc**) in 10 ml of toluene and 0.95 g (8.4 mmol) of ester **I**. Recrystallization of the product gave 0.22 g of compound **IIIc**.

Pyrazoles **IIIe**–**IIIi** were obtained in a similar way.

Ethyl 5-deutero-3-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate (VI). 1,3-Diphenylpropenone, 10 g (48 mmol), was dissolved in 30 ml of heptane, and 8.5 g (74 mmol) of ethyl diazoacetate-*d* was added. The mixture was heated for 7 h at 75°C and evaporated. By fractional crystallization from alcohol we isolated 0.55 g (4%) of pyrazole **VI**, mp 103°C, and 3.5 g (22%) of compound **IIIa**.

Ethyl 3-benzoyl-4-phenyl-1*H*-pyrazole-5-carboxylate (VII). Compound **IVa**, 1 g (31 mmol), was dissolved in 30 ml of acetic acid, and 1 ml of bromine was added. After 45 min, the mixture was poured into 100 ml of water, and the precipitate was filtered off and recrystallized from ethanol. Yield 0.5 g (50%), mp 98°C [4]. Following the same procedure, from 1 g (3.1 mmol) of a mixture of dihydropyrazoles **IVa** and **Va**, 0.76 g (76%) of compound **VII** was obtained.

Thermolysis of ethyl 5-benzoyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (IIIa). Compound **IIIa**, 2 g, was heated for 75 min at 210–220°C. The mixture was cooled, and the product was recrystallized from alcohol. Yield of ethyl *c*-2-benzoyl-*t*-3-phenylcyclopropanecarboxylate (**IXa**) 0.2 g (11%), mp 86°C. The residue was subjected to column chromatography on Al_2O_3 using hexane–ether (1 : 1, by volume) as eluent to isolate 20 mg of ethyl *t*-2-benzoyl-*c*-3-phenylcyclopropanecarboxylate (**Xa**).

Thermolysis of ethyl 5-benzoyl-4-(3-bromophenyl)-4,5-dihydro-1*H*-pyrazole (IIId). Compound **IIId**, 2 g, was heated for 75 min at 210–220°C. After cooling, the resulting material was subjected to column chromatography on Al_2O_3 using hexane–ether, (1 : 1, by volume) as eluent to isolate 0.3 g (16%) of ethyl *c*-2-benzoyl-*t*-3-(3-bromophenyl)cyclopropanecarboxylate (**IXb**), mp 94°C, and 0.15 g (9%) of 4-(3-bromophenyl)-6-phenyl-2*H*-2-pyranone (**XIIb**), mp 119°C.

The ratio of isomeric dihydropyrazoles **III** and **IV** was determined from the ^{1}H NMR spectra of the reaction mixtures. Below are given compound no., chemical shifts of the 4-H and 5-H protons (δ, ppm), and **III** : **IV** isomer ratios: **IIIa**, 5.22, 4.48, **IVa**, –, 4.91, 5; **IIIb**, 5.19, 4.46, **IVb**, 4.38, 4.88, 4; **IIIc**, 5.17, 4.44, **IVc**, 4.36, 4.87, 2; **IIId**, 5.21, 4.46, **IVd**, 4.38, 4.88, 5; **IIIe**, 5.19, 4.47, **IVe**, 4.38, 4.89, 3; **IIIf**, 5.49, 5.02, **IVf**, 4.46, 5.12, 3; **IIIg**, 5.18, 4.49, **IVg**, 4.38, 4.94, 4; **IIIh**, 5.14, 4.40, **IVh**, 4.38, 4.86, 5; **IIIi**, 5.18, 4.42, **IVi**, –, 4.85, 2.

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