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Synthesis and Some Transformations of New Acetophenone Derivatives Containing a Carbamate Moiety

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Abstract—The acylation of methyl phenylcarbamate, 2-(morpholin-4-yl)ethyl phenylcarbamate, and 2-(pyridin-2-yl)ethyl phenylcarbamate with acetic anhydride in polyphosphoric acid at 50–55°C (3 h) involved the *para* position with respect to the carbamate group with the formation of the corresponding acetophenones. Methyl 2-methoxyphenylcarbamate was acylated under similar conditions to give methyl 5-acetyl-2-methoxyphenylcarbamate. Methyl 4- and 2-acetylphenylcarbamates reacted with *N*-bromosuccinimide in the presence of copper(II) acetate and DMF at 80°C and with HCl and HBr in the presence of DMSO in ethyl acetate at 30–33°C to afford methyl [4(2)-(2-dimethylamino-2-oxoacetyl)phenyl]carbamates and methyl [4(2)-(2-bromo-2-chloroacetyl)phenyl]carbamates, respectively. The condensation of 2-(morpholin-4-yl)ethyl and 2-(pyridin-2-yl)ethyl (4-acetylphenyl)carbamates with 4-methoxybenzaldehyde in methanolic potassium hydroxide furnished the corresponding chalcones.

Keywords: aromatic carbamates, 1-arylethan-1-ones, acylation, acetic anhydride, polyphosphoric acid, [(2-dimethylamino-2-oxoacetyl)phenyl]carbamates, [(2-bromo-2-chloroacetyl)phenyl]carbamates, chalcones

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INTRODUCTION

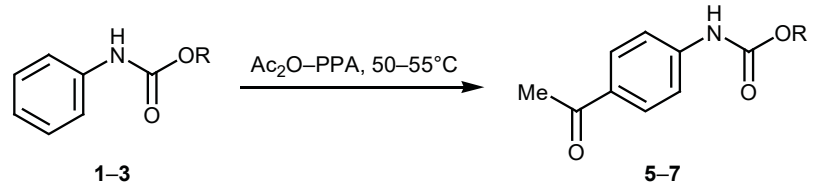
We previously studied amination, amidation, and acetamidation of phenylcarbamates substituted at the benzene ring in polyphosphoric acid (PPA) using sodium azide and nitroalkanes [1]. In continuation of these studies, we tried to use PPA for the synthesis of 1-arylethan-1-ones (acetophenones) with a carbamate functionality.

Due to the presence of an acetyl group, acetophenones are widely used in the synthesis of various organic compounds. Acetophenones are capable of undergoing various transformations leading to the formation of chalcones [2, 3], functionalized acetophenones [4–6], and heterocyclic compounds [2, 7–12]. The interest in acetophenones is determined by the fact that, depending on the reagent used, their reactions can involve the carbonyl [13–15] of methyl group [2, 4, 5, 16] or both these [17–19]. The primary transformation products of the acyl group can participate in further reactions [20]. Therefore, the development of new synthetic approaches to functionally substituted acetophenones and study of their transformations represent an important problem.

RESULTS AND DISCUSSION

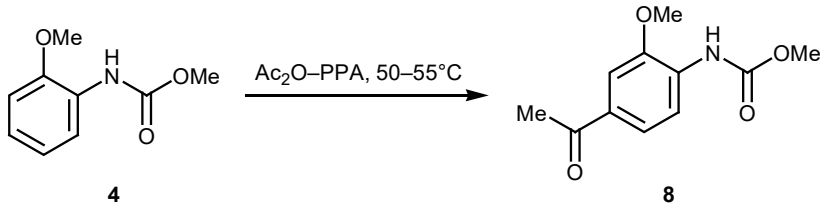
We studied the acylation of methyl phenylcarbamate (**1**), 2-(morpholin-4-yl)ethyl phenylcarbamate (**2**), 2-(pyridin-2-yl)ethyl phenylcarbamate (**3**), and methyl 2-methoxyphenylcarbamate (**4**) with acetic anhydride in PPA on heating at 50–55°C for 3 h. The acylation of **1**–**4** under these conditions was regioselective, and the acetyl group entered the *para* position of the benzene ring of carbamates **1**–**3** to give acetophenones **5**–**7** (Scheme 1). In the case of carbamate **4**, the reaction occurred at the *para* position with respect to the methoxy group with the formation of acetophenone **8** (Scheme 2). Compounds **6** and **7** were isolated by treatment of the reaction mixture with ice water, followed by neutralization with ammonia and extraction with diethyl ether.

Scheme 1.



1, **5**, R = Me; **2**, **6**, R = 2-(morpholin-4-yl)ethyl; **3**, **7**, R = 2-(pyridin-2-yl)ethyl.

Scheme 2.

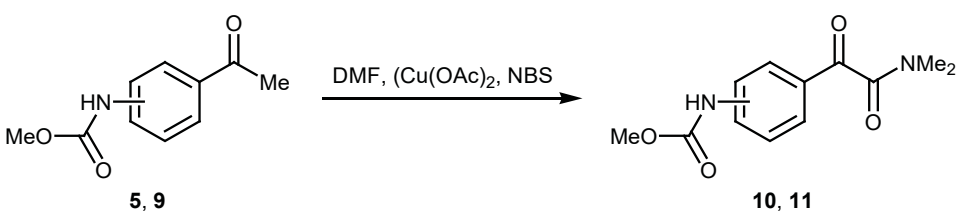


The product structure was confirmed by ^{1}H NMR. In the ^{1}H NMR spectra of **5**–**7**, the four aromatic protons resonated as two doublets at δ 7.76–7.79 and 7.92–7.94 ppm. The ^{1}H NMR spectrum of **8** showed a singlet at δ 8.54 ppm and two doublets at δ 7.06 and 7.56 ppm (one-proton each). The position of the acetyl group in the *para* position with respect to the methoxy group was confirmed by the HMQC spectrum which showed correlations between the 3-H and 4-H protons (δ 7.06 and 7.56 ppm) with C^3 and C^4 (δ_C 115.21 and 124.32 ppm), respectively, and between C^6 (δ_C 117.28 ppm) and 6-H (δ 8.54 ppm, s).

With the goal of obtaining new functionally substituted alkyl phenylcarbamates, acetophenones **5** and **9** were reacted with *N*-bromosuccinimide in the presence of copper(II) acetate and DMF at 80°C under vigorous stirring for 12 h. As a result, we isolated the corresponding methyl {2(3,4)-[2-(dimethylamino)-2-oxoacetyl]phenyl}carbamates **10** and **11** in 76–78% yields (Scheme 3). The ^{1}H NMR spectra of **10** and **11** showed singlets at δ 2.96 (3) and 3.12 ppm (3H) due to protons of the dimethylamino group. A probable mechanism of this transformation is outlined in Scheme 4 [4]. Preliminarily, dimethylformamide in the presence of copper(II) acetate undergoes hydrolysis into dimethylamine and formic acid, while acetophenone **5** or **9** reacts with *N*-bromosuccinimide (NBS) to give ω-bromoacetophenone **A**. Nucleophilic substitution of bromine in **A** by the action of dimethylamine produces intermediate **B** which is oxidized with copper(II) acetate to iminium ion **C**, and hydrolysis of the latter produces 2-(dimethylamino)-2-hydroxy-1-phenylethan-1-one **D**. Finally, the oxidation of **D** with copper(II) acetate yields methyl 4(2)-(2-dimethylamino-2-oxoacetyl)phenylcarbamate **10** or **11**.

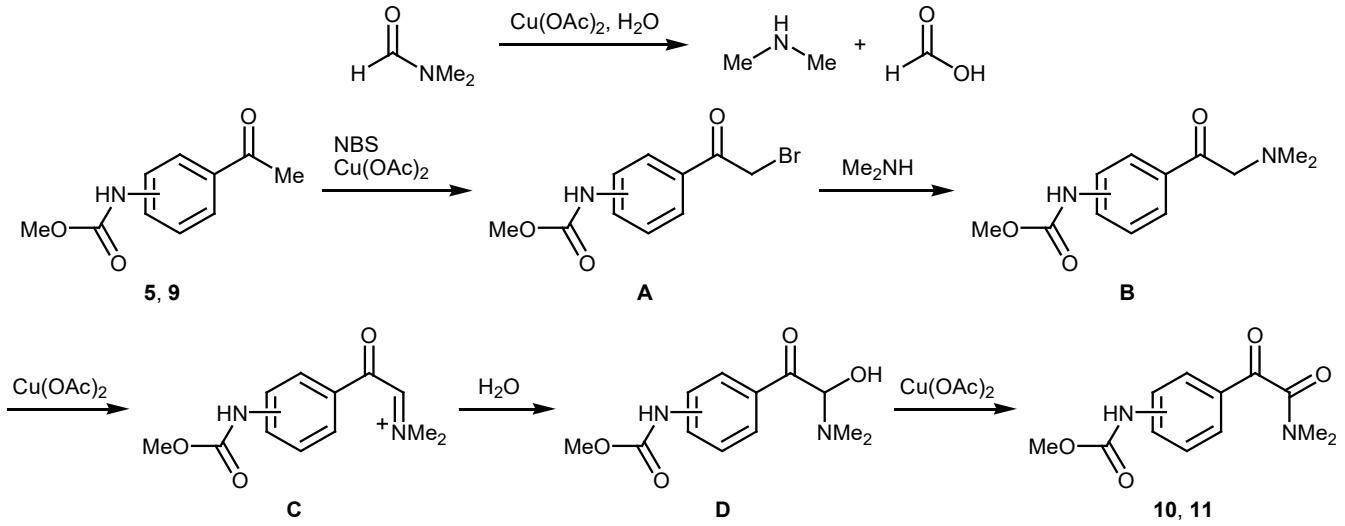
Kędziora et al. [21] synthesized ω,ω-dichloroacetophenones by the reaction of the corresponding acetophenones with *N*-chlorosuccinimide in the presence of *p*-toluenesulfonic acid in acetonitrile at 50°C, and the products were then used to obtain racemic dichlorohydrins by the action of sodium tetrahydridoborate in methanol [21]. It was shown [5] that treatment of acetophenones in ethyl acetate with a mixture of HCl and HBr in the presence of DMSO led to substitution of two methyl hydrogen atoms by chlorine and bromine atoms. We made an attempt to perform a similar functionalization of methyl [4(2)-acetylphenyl]carbamates **5** and **9**. In fact, the reaction of **5** and **9** with HBr–HCl–DMSO in ethyl acetate at 30°C (15 h) afforded 70–72% of the corresponding 2-bromo-

Scheme 3.



5, **10**, 4-$NHCO_2Me$; **9**, **11**, 2-$NHCO_2Me$.

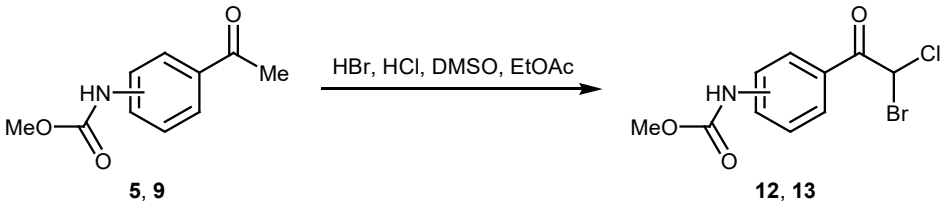
Scheme 4.



2-chloroacetyl derivatives **12** and **13** (Scheme 5). The structure of **12** and **13** was confirmed by ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectra of these compounds, the CHBrCl proton resonated as a downfield singlet at δ 6.73–6.74 ppm, and the corresponding carbon signal was located in the ^{13}C NMR spectra at δ_C 54.28–54.32 ppm. The carbon signal of analogous geminal dibromides is observed at about δ_C 40 ppm, and the signal of similar dichloride appears at a lower field (δ_C ~68 ppm) [5].

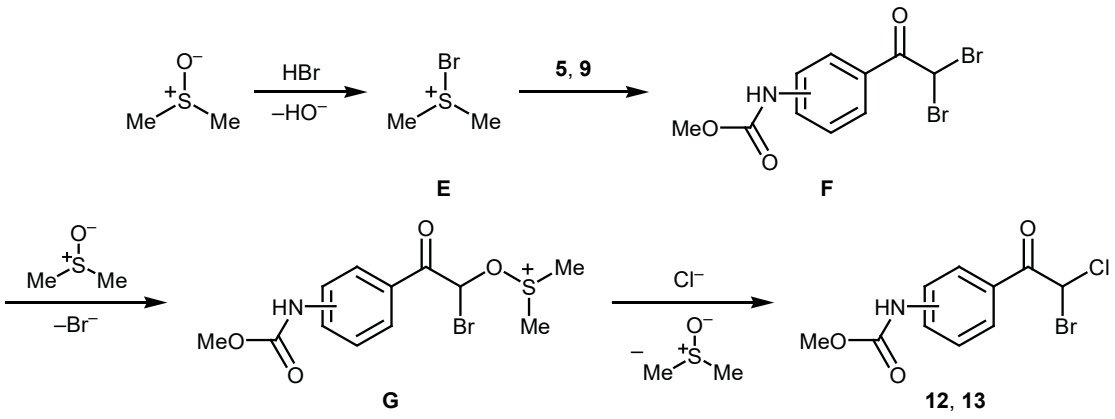
Scheme 6 illustrates a probable reaction mechanism [5]. In the first stage, the reaction of dimethyl sulfoxide with hydrogen bromide generates bromosulfonium intermediate **E** which reacts with acetophenone **5** or **9** to produce dibromoacetyl derivative **F**. Nucleophilic attack by the oxygen atom of DMSO [5, 22] on the dibromomethyl group of **F** leads to the formation of intermediate **G** via elimination of bromide ion. In the final stage, dimethyl sulfoxide fragment in **G** is replaced by chlorine as a result of nucleophilic attack

Scheme 5.

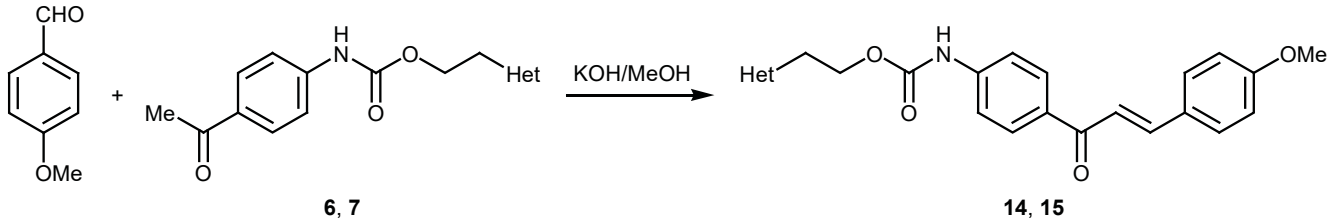


5, **12**, R = 4-$NHCO_2Me$; **9**, **13**, R = 2-$NHCO_2Me$.

Scheme 6.



Scheme 7.



6, **7** **14**, **15**

6, **14**, Het = 2-(morpholin-4-yl)ethyl; **7**, **15**, Het = 2-(pyridin-2-yl)ethyl.

of chloride ions whose concentration in solution remains fairly high.

The condensation of (acetylphenyl)carbamates **6** and **7** containing heterocyclic amine fragments with 4-methoxybenzaldehyde in methanolic potassium hydroxide afforded chalcones **14**–**15** (Scheme 7) in good yields (74–76%). The structure of 2-(morpholin-4-yl)-ethyl {4-[(*E*)-3-(4-methoxyphenyl)prop-2-enoyl]-phenyl}carbamate (**14**) and 2-(pyridin-2-yl)ethyl {4-[(*E*)-3-(4-methoxyphenyl)prop-2-enoyl]phenyl}-carbamate (**15**) was confirmed by IR and ^{1}H NMR spectra. The *E* configuration of the C=C double bond in molecules **14** and **15** followed from the ^{1}H NMR spectra, in which the CH=CH protons resonated at δ 7.25–7.29 and 7.41–7.42 ppm as doublets with coupling constants of 15.4 and 15.3 Hz.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra (including HMQC experiments) were recorded on a Bruker DRX 500 spectrometer (USA) at 500 and 126 MHz, respectively, using DMSO-d_6 as solvent; the ^{13}C NMR spectra were measured with complete decoupling from protons. The IR spectra were recorded in the range 4000–400 cm^{-1} on an InfraLUM FT-02 FTIR spectrometer (Russia) from samples prepared as KBr discs. The purity of the isolated compounds was checked by TLC on Silufol UV-254 plates (Chemapol, Czechia); visualization was done by treatment with iodine vapor. Elemental analysis was performed on a Perkin Elmer 2400 Series II analyzer (USA). Commercially available regents from Aldrich and Alfa Aesar (USA) were used.

Methyl (4-acetylphenyl)carbamate (5). Methyl phenylcarbamate (**1**), 1.51 g (0.01 mol), and acetic anhydride, 0.56 mL (0.0059 mol), were added to 15 g of PPA, and the mixture was stirred at 50–55°C for 3 h. After cooling to room temperature, the red mixture was transferred into 60 mL of ice water and extracted with diethyl ether (3×15 mL). The organic extract was washed with 5% aqueous sodium hydrogen carbonate and water and dried over anhydrous sodium sulfate, and the solvent was removed. Yield 0.97 g (85%), colorless crystals, mp 167–168°C; published data [23]: mp 167.5–168.0°C. IR spectrum, ν, cm^{-1}: 3310 (NH), 1710, 1680 (C=O), 1610, 1575, 1565 (C=C$_{arom}$). Found, %: C 62.09; H 5.46; N 7.08. $C_{10}H_{11}NO_3$. Calculated, %: C 62.18; H 5.70; N 7.25.

Acetophenones **6** and **7** were synthesized in a similar way by the reactions of 1.25 g (5 mmol) of carbamate **2** or 1.21 g (5 mmol) of **3** with 0.28 mL of acetic anhydride in 7.5 g of PPA. The reaction mixture was diluted with water, treated with 30% aqueous ammonia to pH 7.0–7.5, and extracted with diethyl ether.

2-(Morpholin-4-yl)ethyl (4-acetylphenyl)carbamate (6). Yield 0.72 g (84%), colorless crystals, mp 109–111°C (Al_2O_3, eluent chloroform). IR spectrum, ν, cm^{-1}: 3315 (NH), 1710, 1675 (C=O), 1610, 1580, 1575 (C=C$_{arom}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.73 s (3H, $COCH_3$), 2.22–2.37 m (4H, CH_2NCH_2), 2.97 d.d (2H, CH_2, J = 5.8, 11.0 Hz), 3.52–3.66 m (4H, CH_2OCH_2), 4.15 d.d [2H, C(O)OCH_2, J = 5.8, 11.5 Hz], 7.12 d (2H, H$_{arom}$, J = 8.6 Hz), 7.98 d (2H, H$_{arom}$, J = 8.6 Hz), 9.54 br.s (1H, NH). Found, %: C 61.39; H 6.73; N 9.27. $C_{15}H_{20}N_2O_4$. Calculated, %: C 61.64; H 6.85; N 9.59.

2-(Pyridin-2-yl)ethyl (4-acetylphenyl)carbamate (7). Yield 0.70 g (85%), colorless crystals, mp 83–85°C (neutral Al_2O_3, eluent chloroform). IR spectrum, ν, cm^{-1}: 3310 (NH), 1708, 1680 (C=O), 1612, 1585, 1575 (C=C$_{arom}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.73 s (3H, $COCH_3$), 3.11 d.d (2H, CH_2, J = 6.7, 14.6 Hz), 4.35 d.d [2H, C(O)CH_2, J = 5.8, 14.9 Hz], 7.05 t (1H, H$_{arom}$, J = 4.8 Hz), 7.17 d (1H, H$_{arom}$, J = 7.4 Hz), 7.23 d (2H, H$_{arom}$, J = 8.6 Hz), 7.45 t (1H, H$_{arom}$, J = 7.4 Hz), 7.99 d (2H, H$_{arom}$, J = 8.6 Hz), 8.44 d (1H, H$_{arom}$, J = 4.8 Hz), 9.58 br.s (1H, NH). Found, %: C 67.33; H 5.62; N 9.75. $C_{16}H_{16}N_2O_3$. Calculated, %: C 67.61; H 5.63; N 9.86.

Methyl (5-acetyl-2-methoxyphenyl)carbamate (8) was synthesized as described above for compound

5 from 0.597 g (3.3 mmol) of carbamate **4**. Yield 0.65 g (88%), colorless crystals, mp 68–70°C (from $CHCl_3$). IR spectrum, ν, cm^{-1}: 3313 (NH), 1714, 1670 (C=O), 1610, 1580, 1565 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.72 s (3H, $COCH_3$), 3.71 s (3H, $NHCO_2$**Me**), 4.13 s (3H, OCH_3), 7.09 d (1H, H_{arom}, J = 8.3 Hz), 7.87 d (1H, H_{arom}, J = 8.3 Hz), 8.16 s (1H, H_{arom}), 9.60 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 26.78 (CO**Me**), 52.60 ($NHCO_2$**Me**), 56.20 (OMe), 115.21(C^3), 117.28 (C^6), 124.32 (C^4), 128.02 (C^1), 135.04 (C^5), 146.18 (C^2), 154.12 (NH**C**O_2Me), 200.54 (**C**OMe). Found, %: C 58.94; H 5.54; N 6.09. $C_{11}H_{13}NO_4$. Calculated, %: C 59.19; H 5.83; N 6.28.

Methyl {4-[2-(dimethylamino)-2-oxoacetyl]-phenyl}carbamate (10). *N*-Bromosuccinimide (NBS), 0.213 g (1.2 mmol), was added with shaking to a solution of 0.193 g (1 mmol) of methyl (4-acetylphenyl)-carbamate (**5**) and 0.218 g (1.2 mmol) of copper(II) acetate in 2 mL of DMF. The mixture was stirred at 80°C for 12 h, cooled to room temperature, poured into 50 mL of water, and extracted with methylene chloride (3×10 mL). The combined extracts were washed with water (2×25 mL), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure, and the residue was purified by column chromatography on Silica gel 60 (0.040–0.063 mm) using petroleum ether–ethyl acetate (2:1) as eluent. Yield 0.19 g (76%), colorless crystals, mp 143–145°C. IR spectrum, ν, cm^{-1}: 3310 (NH), 1710, 1660 (C=O), 1610, 1580, 1565 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.96 s and 3.12 s (3H each, NMe_2), 3.70 s (3H, $NHCO_2$**Me**), 7.26 d (2H, H_{arom}, J = 8.6 Hz), 7.78 d (2H, H_{arom}, J = 8.6 Hz), 9.65 br.s (1H, NH). Found, %: C 57.39; H 5.43; N 11.08. $C_{12}H_{14}N_2O_4$. Calculated, %: C 57.60; H 5.60; N 11.20.

Methyl {2-[2-(dimethylamino)-2-oxoacetyl]-phenyl}carbamate (11) was synthesized in a similar way from 0.193 g (1 mmol) of carbamate **9**. Yield 0.18 g (73%), colorless crystals, mp 70–72°C. IR spectrum, ν, cm^{-1}: 3310 (NH), 1710, 1666 (C=O), 1610, 1587, 1575 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.96 s and 3.12 s (3H each, NMe_2), 3.71 s (3H, $NHCO_2$**Me**), 7.18 t (1H, H_{arom}, J = 7.2 Hz), 7.50 t (1H, H_{arom}, J = 7.2 Hz), 7.74 d (1H, H_{arom}, J = 7.2 Hz), 8.75 d (1H, H_{arom}, J = 7.2 Hz), 9.59 br.s (1H, NH). Found, %: C 57.53; H 5.32; N 10.95. $C_{12}H_{14}N_2O_4$. Calculated, %: C 57.60; H 5.60; N 11.20.

Methyl [4-(2-bromo-2-chloroacetyl)phenyl]-carbamate (12). Methyl (4-acetylphenyl)carbamate (**5**), 0.193 g (1 mmol), was dissolved in 0.2 mL (3 mmol) of DMSO, and a solution of 0.12 mL (4 mmol) of 38% aqueous HCl and 0.15 mL (1 mmol) of 40% aqueous HBr in 3 mL of ethyl acetate was added. The mixture was stirred at 30–33°C for 15 h, treated with anhydrous magnesium sulfate, and filtered, the filtrate was concentrated on a rotary evaporator under reduced pressure (10 mm Hg), and the residue was purified by column chromatography on Silica gel 60 (0.040–0.063 mm) using petroleum ether–ethyl acetate (3:1) as eluent. Yield 0.22 g (72%), light yellow crystals, mp 135–137°C. IR spectrum, ν, cm^{-1}: 3325 (NH), 1680, 1714 (C=O), 1610, 1584, 1570 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.70 s (3H, $NHCO_2$**Me**), 6.73 s (1H, CHBrCl), 7.34 d (2H, H_{arom}, J = 9.0 Hz), 7.99 d (2H, H_{arom}, J = 8.9 Hz), 9.58 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 52.65 ($NHCO_2$**Me**), 54.28 (CHBrCl), 120.18, 124.62, 129.11, 138.14 (C_{arom}), 154.82 (NH**C**O_2Me), 185.62 (C=O). Found, %: C 66.37; H 5.23; N 4.83. $C_{10}H_9BrClNO_3$. Calculated, %: C 66.67; H 5.38; N 5.02.

Methyl [2-(2-bromo-2-chloroacetyl)phenyl]carbamate (13) was synthesized as described above for **12** from 0.234 g (3 mmol) of carbamate **9**. Yield 0.21 g (70%), light yellow crystals, mp 88–90°C. IR spectrum, ν, cm^{-1}: 3324 (NH), 1680, 1710 (C=O), 1612, 1580, 1575 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.71 s (3H, $NHCO_2$**Me**), 6.74 s (1H, CHBrCl), 7.30 t (1H, H_{arom}, J = 7.2 Hz), 7.58 t (1H, H_{arom}, J = 7.2 Hz), 8.20 d (1H, H_{arom}, J = 7.2 Hz), 8.90 d (1H, H_{arom}, J = 7.2 Hz), 9.54 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 52.64 ($NHCO_2$**Me**), 54.32 (CHBrCl), 121.61, 124.55, 126.31, 127.37, 134.29, 138.03 (C_{arom}), 154.48 (NH**C**O_2Me), 183.65 (C=O). Found, %: C 66.42; H 5.19; N 4.74. $C_{10}H_9BrClNO_3$. Calculated, %: C 66.67; H 5.38; N 5.02.

2-(Morpholin-4-yl)ethyl {4-[(*E*)-3-(4-methoxyphenyl)prop-2-enoyl]phenyl}carbamate (14). A mixture of 0.292 g (1 mmol) of carbamate **6** and 0.12 mL (1 mol) of 4-methoxybenzaldehyde in 5 mL of methanol was stirred for 30 min, 0.3 mL of a 10% solution of potassium hydroxide in methanol was added over a period of 30 min, and the mixture was stirred at 35°C for 4 h and left to stand at room temperature for 24 h. The mixture was poured into 100 mL of water and carefully acidified with dilute (1:1 by volume) aqueous HCl, and the precipitate was filtered off, washed on a filter with 20 mL of water, dried, and recrystallized from chloroform. Yield 0.30 g (74%), light yellow crystals, mp 140–143°C. IR spectrum, ν,

cm^{-1}: 3315 (NH), 1665, 1710 (C=O), 1610, 1584, 1565 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.22–2.36 m (4H, CH_2NCH_2), 2.95 d.d (2H, CH_2, J = 5.8, 11.0 Hz), 3.52–3.65 m (4H, CH_2OCH_2), 3.93 s (3H, OCH_3), 4.15 d.d [2H, $(CO)OCH_2$, J = 5.8, 11.0 Hz], 6.90 d (2H, H_{arom}, J = 8.7 Hz), 7.22 d (2H, H_{arom}, J = 8.6 Hz), 7.29 d [1H, C(O)C**H**=CH, J = 15.4 Hz], 7.41 d [1H, C(O)CH=C**H**, J = 15.4 Hz], 7.56 d (2H, H_{arom}, J = 8.7 Hz), 7.95 d (2H, H_{arom}, J = 8.6 Hz), 9.57 br.s (1H, NH). Found, %: C 67.18; H 5.99; N 6.53. $C_{23}H_{26}N_2O_5$. Calculated, %: C 67.32; H 6.34; N 6.83.

2-(Pyridin-2-yl)ethyl {4-[(*E*)-3-(4-methoxyphenyl)prop-2-enoyl]phenyl}carbamate (15) was synthesized as described above for compound **14** from 0.284 g (1 mmol) of carbamate **7**. Yield 0.31 g (76%), light yellow crystals, mp 109–111°C. IR spectrum, ν, cm^{-1}: 3315 (NH), 1711, 1665 (C=O), 1608, 1585, 1570, 1565 (C=C_{arom}). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.10 d.d (2H, CH_2, J = 6.9, 14.8 Hz), 3.92 s (3H, OCH_3), 4.34 d.d [2H, $(CO)OCH_2$, J = 6.9, 10.4 Hz], 6.92 d (2H, H_{arom}, J = 8.8 Hz), 7.06 t (1H, H_{arom}, J = 4.8 Hz), 7.17 d (1H, H_{arom}, J = 7.6 Hz), 7.25 d [1H, C(O)C**H**=CH, J = 15.3 Hz], 7.30 d (2H, H_{arom}, J = 8.6 Hz), 7.42 d [1H, C(O)CH=C**H**, J = 15.3 Hz], 7.47 t (1H, H_{arom}, J = 7.6 Hz), 7.54 d (2H, H_{arom}, J = 8.8 Hz), 7.98 d (2H, H_{arom}, J = 8.6 Hz), 8.44 d (1H, H_{arom}, J = 4.8 Hz), 9.56 br.s (1H, NH). Found, %: C 71.58; H 5.21; N 6.65. $C_{24}H_{22}N_2O_4$. Calculated, %: C 71.64; H 5.47; N 6.97.

CONCLUSIONS

The acylation of methyl phenylcarbamate, 2-(morpholin-4-yl)ethyl phenylcarbamate, 2-(pyridin-2-yl)-ethyl phenylcarbamate, and methyl (2-methoxyphenyl)-carbamate with acetic anhydride in polyphosphoric acid occurs regioselectively at the *para* position with respect to the carbamate or methoxy groups. New functionalize acetophenone derivatives, namely methyl {2(4)-[2-(dimethylamino)-2-oxoacetyl]phenyl}carbamates, methyl [(2-bromo-2-chloroacetyl)phenyl]carbamates, and chalcones containing heterocyclic amine fragments, have been synthesized.

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CONFLICT OF INTEREST

The authors declare the absence of conflict of interest.

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