Synthesis of 1-alkyl-1,2,4-triazolium 4-nitroimides by alkylation of 4-nitramino-1,2,4-triazole salts

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A method for the synthesis of 1-alkyl-1,2,4-triazolium 4-nitroimides was developed based on alkylation of 4-nitramino-1,2,4-triazole Na and Ag salts with halo- and dihaloalkanes.

Key words: 1-substituted 1,2,4-triazolium 4-nitroimides, 4-nitramino-1,2,4-triazole salts, alkylation.

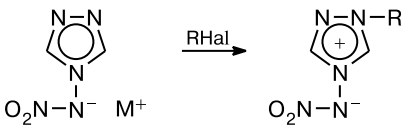
Earlier,[1,2] 1-alkyl-1,2,4-triazolium *N*-nitroimides were synthesized by nitration of 1-substituted 4-amino-1,2,4-triazolium nitrates.

Alternatively, 1-alkyl-1,2,4-triazolium 4-nitroimides can be obtained by alkylation of 4-nitramino-1,2,4-triazole salts. Alkylation of 4-nitramino-1,2,4-triazole Na salt (**1**) with methyl *p*-toluenesulfonate and benzyl bromide is known to afford the corresponding 1-substituted 1,2,4-triazolium *N*-nitroimides.[3,4] In the present work, we showed that this reaction is of general character and can be used in the preparation of various 1-substituted 1,2,4-triazolium 4-nitroimides (Table 1).

Results and Discussion

We studied reactions of 4-nitramino-1,2,4-triazole Na and Ag salts (**1** and **2**) with alkyl halides, α- and β-halogeno ethers, β- and γ-halogeno alcohols, chloroacetonitrile, bromoacetone, and ethyl bromoacetate. The reactions were carried out in dipolar aprotic solvents (DMF, MeCN, and DMSO); in some cases, phase-transfer catalysis was used.

Scheme 1



1, **2** **3**, **4**

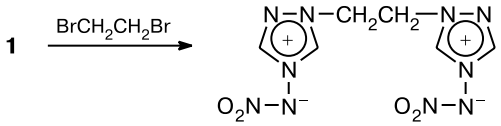
$M^+ = Na^+$ (**1**), Ag^+ (**2**)
R = Me (**3**), Et (**4**)

† Deceased.

It was found that MeI reacts with salts **1** and **2** in DMF even at room temperature to give 1-methyl-1,2,4-triazolium 4-nitroimide (**3**) (Scheme 1).

Other mono- and dihaloalkanes react with salts **1** and **2** under more drastic conditions. For instance, ethyl bromide reacts with salt **1** in DMSO or DMF at 50—60 °C to give 1-ethyl-1,2,4-triazolium 4-nitroimide (**4**). The reaction of salt **1** with $Br(CH_2)_2Br$ occurs only at 100 °C, affording bisalkylation product (**5**) in 28% yield (Scheme 2).

Scheme 2



5

The yield of compound **5** was increased to 40% by alkylation of salt **1** with 1,2-dibromoethane under conditions of phase-transfer catalysis ($H_2O/Br(CH_2)_2Br$, tetrabutylammonium iodide as a catalyst). Salt **1** proved to be inert to dibromomethane and diiodomethane under the conditions studied, which is probably due to a high stability of geminal dihaloalkanes[7].

α-Halogeno ethers are much more reactive in alkylation. Salts **1** and **2** react with chlorodimethyl, chloromethyl 2-fluoro-2,2-dinitroethyl, and bis(chloromethyl) ethers at 20 °C to give the corresponding alkylation products **6**—**8** (Scheme 3).

β- and γ-Halogeno ethers are less reactive toward salts **1** and **2**. The reaction of Na salt **1** with an excess of

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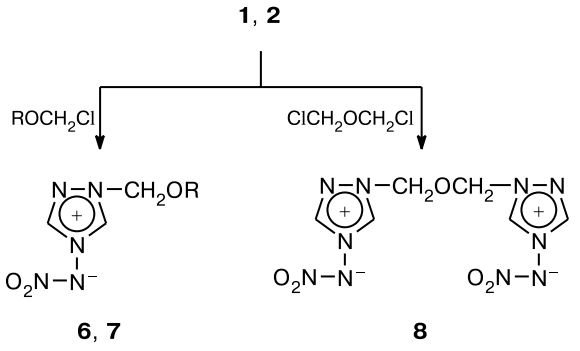
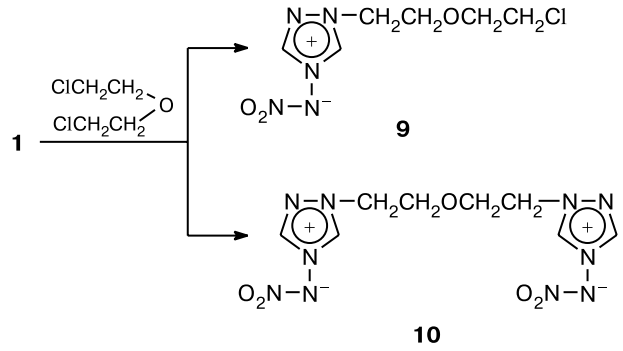
Scheme 3



M = Na (**1**), Ag (**2**)
R = Me (**6**), $CH_2C(NO_2)_2F$ (**7**)

2,2′-dichlorodiethyl ether at 90—100 °C predominantly gave monoalkylation product **9**; under these conditions, the yield of bisadduct **10** does not exceed 5% (Scheme 4).

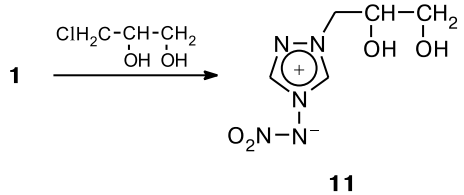
Scheme 4



The yield of bisadduct **10** was increased to 36% by carrying out the reaction at 150 °C.

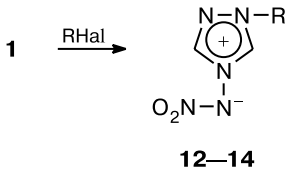
Alkylation of salt **1** with 3-chloropropane-1,2-diol at 110—120 °C afforded *N*-nitroimide **11** in 51% yield (Scheme 5).

Scheme 5



2,2-Bis(chloromethyl)propane-1,3-diol and 2-bromomethyl-2-hydroxymethylpropane-1,3-diol are inert under the conditions studied. The reactions of salt **1** with chloroacetonitrile, bromoacetone, and ethyl bromoacetate at 40—50 °C yielded the corresponding *N*-nitroimides **12**—**14** containing functionalized substituent R (Scheme 6).

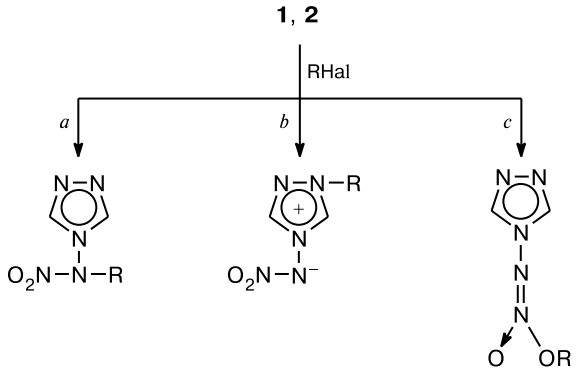
Scheme 6



R = CH_2CN (**12**), $CH_2C(O)Me$ (**13**), $CH_2C(O)OEt$ (**14**)

Theoretically, alkylation of ambident 4-nitramino-1,2,4-triazole anion can occur at three reaction centers, namely, (*a*) N atom of the amino group, (*b*) N atoms of the triazole ring, and (*c*) O atom of the nitro group (Scheme 7).

Scheme 7



In all the above examples, alkylation of both salts **1** and **2** selectively follows pathway *b*. The structures of the compounds obtained were determined from their IR and ^1H and ^{13}C NMR spectra. The structures of compounds **11** and **13** were confirmed by their independent syntheses.[2] The IR spectra of the compounds obtained contain absorption bands at 1280—1300 and 1390—1415 cm^{-1} characteristic of an *N*-nitroimido group bound to a heterocycle (Table 2).[4] Their spectra show no ν_{as} bands for the nitramino group at 1550—1620 cm^{-1}. In the ^1H NMR spectra of *N*-nitroimides **3**—**14** (Table 2), signals for the protons of the triazole ring are nonequivalent and shifted downfield ($\delta_{H(5)}$ 10.1—10.4, $\delta_{H(3)}$ 9.2—9.4) relative to signals for the protons in the starting salt (δ 8.33), which is evidence in favor of the imide structure. The same conclusion follows from the ^{13}C NMR data. In the compounds synthesized, the C(3) and C(5) atoms of the triazole ring are nonequivalent unlike the starting salt ($\delta_{C(3)} = \delta_{C(5)} = 142.00$, Table 2).

Table 1. Characteristics of 1,2,4-triazolium 4-nitroimides

Compound	Found / Calculated (%)			Molecular formula
	C	H	N	
3	—	—	—	$C_3H_5N_5O_2$
4	30.27 30.57	4.45 4.46	44.67 44.59	$C_4H_7N_5O_2$
5	25.35 25.40	2.82 2.70	49.30 49.39	$C_6H_8N_{10}O_4$
6	27.75 28.08	4.04 3.87	40.46 40.44	$C_4H_7N_5O_3$
7	20.34 21.18	2.03 2.33	33.22 33.33	$C_5H_6FN_7O_7$
8	24.00 24.11	2.67 2.58	46.87 46.25	$C_6H_8N_{10}O_5$
9	30.57 30.58	4.27 4.22	29.72 29.42	$C_6H_{10}ClN_5O_3$
10	29.27 29.23	3.66 3.63	42.68 42.77	$C_8H_{12}N_{10}O_5$
11	29.56 29.91	4.43 4.63	34.48 34.50	$C_5H_9N_5O_4$
12	28.55 28.57	2.35 2.38	50.44 50.00	$C_4H_4N_6O_2$
13	32.43 32.72	3.78 3.77	37.84 38.03	$C_4H_7N_5O_3$
14	33.01 33.48	4.09 4.19	32.41 32.56	$C_6H_9N_5O_4$

Note. Found/calculated (%): F, 6.44/6.51 (**7**); Cl, 15.07/14.26 (**9**).

Thus, the alkylation of 4-nitramino-1,2,4-triazole salts is a general method for the synthesis of various 1-substituted 1,2,4-triazolium 4-nitroimides.

Experimental

Melting points were determined on a Boetius microscope stage. ^1H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument; ^1H and ^{13}C chemical shifts are referenced to DMSO-d_6 (δ_H 2.5; δ_C 39.50). IR spectra were recorded on a UR-20 instrument (KBr pellets).

1-Methyl-1,2,4-triazolium 4-nitroimide (3). ***A.*** A suspension of salt **2** (0.30 g, 1.97 mmol) and MeI (1.50 mL, 10.5 mmol) in 5 mL of DMF was stirred at 20 °C for 4 h. The precipitate was filtered off and the filtrate was diluted with 50—70 mL of Et_2O. The precipitate that formed was filtered off to give product **3** (0.17 g, 93%), m.p. 169—170 °C (decomp., from water) (*cf.* Ref. 3: m.p. 171—172 °C (decomp., from water)). A mixture of compound **3** with an authentic sample did not depress the melting point.

B. A solution of salt **1** (0.50 g, 3 mmol) and MeI (0.19 mL, 3 mmol) in 3 mL of DMF (or DMSO) was left at 20 °C for 17 h and then concentrated *in vacuo*. Ethanol was added to the residue, and the precipitate (0.32 g) was filtered off and recrystallized from EtOH. The yield of compound **3** was 0.25 g (64%). The product was identical with that obtained by procedure ***A***.

1-Ethyl-1,2,4-triazolium 4-nitroimide (4). ***A.*** A solution of salt **1** (3.50 g, 20.7 mmol) and EtBr (1.60 mL, 20.7 mmol) in 25 mL of DMSO was stirred at 20 °C for 2 h and at 50—60 °C for 3 h and poured into a mixture of acetone (150 mL) and ether (30 mL). The precipitate of NaBr was filtered off. The filtrate

Table 2. IR and NMR (DMSO-d_6) data for 1,2,4-triazolium *N*-nitroimides

Compound	IR (KBr), ν/cm^{-1}		NMR, δ (*J*/Hz)					
	NO_2 [a]	Others	^1H			^{13}C		
			HC(3) (s, 1 H)	HC(5) (s, 1 H)	Other H atoms	C(3)	C(5)	Other C atoms
1	—	—	8.33	8.33	—	142.0 (dd, ^1J = 213.6, ^3J = 3.7)	142.0 (dd, ^1J = 213.6, ^3J = 3.7)	—
3	—	—	9.2	10.15	3.35 (s, 3 H, Me)	143.7 (dd, ^1J = 222.4, ^3J = 5.5)	141.6 (ddq, ^1J = 223.4, ^3J = 6.5, ^3J = 3.2)	38.8 (q, Me, J = 144.3)
4	1390, 1300		9.24	10.23	1.5 (t, 3 H, Me); 4.4 (q, 2 H, CH_2)	—	—	—
5	1414, 1297		9.25	10.20	4.95 (s, 4 H, $(CH_2)_2$)	—	—	—
6	1410, 1290		9.42	10.53	3.52 (s, 3 H, Me); 5.75 (s, 2 H, CH_2)	144.5 (dd, ^1J = 227.5, ^3J = 2.7)	142.5 (ddq, ^1J = 228.4, ^3J = 3.7, ^3J = 2.7)	57.6 (qt, Me, ^1J = 143.3±0.9, ^3J = 6.5)

(*to be continued*)

Table 2 (*continued*)

Compound	IR (KBr), ν/cm^{-1}		NMR, δ (*J*/Hz)					
	NO_2 [a]	Others	^{1}H			^{13}C		
			HC(3) (s, 1 H)	HC(5) (s, 1 H)	Other H atoms	C(3)	C(5)	Other C atoms
7	1405, 1280	1590, 1390, 1310 (NO_2)	9.34	10.32	5.17 (d, 2 H, CH_2C, $J_{H,F}$ = 18.0); 5.85 (s, 2 H, CH_2N)	144.5 (dd, ^1J = 229.3, ^3J = 6.5)	142.7 (dd, ^1J = 230.5, ^3J = 2.8)	67.0 (dtt, CH_2C, $^1J_{C,F}$ =18.5, ^1J = 155.4, ^3J = 6.5); 80.2 (tt, CH_2N, ^1J = 168.3, ^3J = 2.8); 120.2 (d, CF, $^1J_{C,F}$ = 291.0)
8	1400, 1290		9.27	10.43	5.93 (s, 4 H, CH_2)	144.6 (dd, ^1J = 229.3, ^3J = 6.5)	142.8 (ddt, ^1J = 229.3, ^3J = 1.8, ^3J = 3.7)	79.1 (tt, CH_2, ^1J = 168.3, ^3J = 6.5)
9	1410, 1285		9.23	10.20	3.67 (t, 4 H, CH_2CH_2); 3.90 (t, 2 H, CH_2); 4.53 (t, 2 H, CH_2)	—	—	—
10	1405, 1295		9.23	10.27	3.90, 4.47 (both t, 2 H each, CH_2)	143.7 (dd, ^1J = 221.9, ^3J = 5.5)	141.6 (dd, ^1J = 229.3, ^3J = 3.7)	57.1 (t, CH_2, J = 145.2); 66.7 (t, CH_2, J = 142.2)
11	1400, 1295		9.22	10.16	3.30—3.52 (m, 2 H, CH_2); 3.88 (m, 1 H, CH); 4.20—4.50 (m, 2 H, CH_2); 4.96 (t, 1 H, OH); 5.36 (d, 1 H, OH)	144.0 (dd, ^1J = 227.5, ^3J = 6.5)	141.9 (ddt, ^1J = 229.3, ^3J = 2.8, ^3J = 3.7)	55.7 (t, CH_2, ^1J = 142.4); 63.5 (t, CH_2, ^1J = 141.5); 69.1 (d, CHOH, ^1J = 142.4)
12	1415, 1300	2270 (C≡N)	9.38	10.30	5.83 (s, 2 H, CH_2)	144.4 (dd, ^1J = 229.3, ^3J = 5.5)	142.5 (br.d, J = 232.1)	39.5 (CH_2)[b]; 113.2 (t, C≡N, J = 7.0)
13	1400, 1290	1740 (C=O)	9.30	10.10	2.23 (s, 3 H, Me); 5.54 (s, 2 H, CH_2)	143.8 (dd, ^1J = 228.3, ^3J = 6.1)	142.6 (ddt, ^1J = 229.5, ^3J = 3.7, ^3J = 2.5)	27.0 (q, Me, J = 128.2); 60.3 (t, CH_2, J = 142.8); 199.1 (C=O)
14	1385, 1290	1750 (COO—)	9.30	10.23	1.22 (t, 3 H, Me); 4.20 (q, 2 H, CH_2) 5.45 (s, 2 H, CH_2)	143.9 (dd, (^1J = 228.4, ^3J = 6.5)	142.8 (dd, ^1J = 231.8, ^3J = 2.8)	13.8 (tq, Me, ^1J = 148.9, ^3J = 4.6); 52.5 (t, NCH_2, J = 147.0); 62.1 (tq, OCH_2, ^1J = 148.9, ^3J = 4.6); 165.7 (C=O)

[a] NO_2 of the nitroimido group.
[b] An apparent overlap with a signal for CD_3SOCD_3.

was concentrated *in vacuo*, and the residue was recrystallized from EtOH to give compound **4** (1.85 g, 56.3%), m.p. 139—140.5 °C.

B. A solution of salt **1** (0.50 g, 3 mmol) and EtBr (0.22 mL, 3 mmol) in 5 mL of DMF was stirred at 20 °C for 2 h and at 60—70 °C for 3 h. The precipitate of NaBr was filtered off. The filtrate was concentrated *in vacuo*, and the residue was recrystallized from EtOH to give compound **4** (0.27 g, 57%), m.p. 138—140 °C.

Bis(4-nitroimido-1,2,4-triazolium-1-yl)ethane (5). ***A.*** A solution of salt **1** (0.42 g, 2.42 mmol) and dibromoethane (0.94 g, 5.00 mmol) in 5 mL of DMF was stirred at 100 °C for 7 h, cooled, and poured into 30 mL of water. The precipitate that formed was filtered off and washed with EtOH and Et_2O. The yield of compound **5** was 0.10 g (28%), m.p. 266 °C (decomp., from water).

B. A mixture of salt **1** (4.00 g, 23.70 mmol) and TBAI (0.20 g, 0.64 mmol) was stirred in 20 mL of water and 20 mL

of dibromoethane at 75 °C for 24 h and cooled. The precipitate that formed was filtered off and washed with water, EtOH, and Et_2O. The yield of compound **5** was 1.34 g (40%). The product was identical with that obtained by procedure ***A***.

1-Methoxymethyl-1,2,4-triazolium 4-nitroimide (6). ***A.*** A mixture of salt **1** (1.69 g, 10.6 mmol) and chlorodimethyl ether (0.85 g, 10.6 mmol) was stirred in 5 mL of DMF at 20 °C for 20 h. The precipitate of NaCl was filtered off. The filtrate was diluted with 20 mL of acetone and 100 mL of Et_2O. The precipitate that formed was filtered off to give compound **6** (1.30 g, 75%), m.p. 117—117.5 °C (from EtOH).

B. A mixture of salt **2** (0.09 g, 0.38 mmol) and chlorodimethyl ether (0.10 g, 1.22 mmol) was stirred in 1 mL of DMF at 20 °C for 15 min. The precipitate of AgCl was filtered off. The filtrate was diluted with a mixture of acetone (5 mL) and Et_2O (40 mL). The precipitate that formed was filtered off to give compound **6** (0.07 g, 98%). The product was identical with that obtained by procedure ***A***.

1-(4-Fluoro-4,4-dinitro-2-oxabutyl)-1,2,4-triazolium 4-nitroimide (7). A suspension of salt **2** (0.47 g, 2.00 mmol) and chloromethyl 2-fluoro-2,2-dinitroethyl ether (0.41 g, 2.03 mmol) in 3 mL of DMF was stirred at 20 °C for 48 h. The precipitate of AgCl was filtered off, and the filtrate was concentrated *in vacuo* at 40—50 °C. The oily residue was diluted with EtOH (1—2 mL) and kept at 0 °C until crystallization started. The precipitate that formed was filtered off to give compound **7** (0.46 g, 78%), m.p. 128—128.5 °C (from EtOH).

1,3-Bis(4-nitroimido-1,2,4-triazolium-1-yl)-2-oxapropane (8). ***A.*** A solution of salt **1** (1.93 g, 13.00 mmol) and bis(chloromethyl) ether (0.65 g, 5.70 mmol) in 5 mL of DMF was stirred at 20 °C for 72 h. Acetone (40 mL) was added, and the precipitate that formed was filtered off and washed successively with water, EtOH, and Et_2O to give compound **8** (0.40 g, 24%), m.p. 213—215 °C (decomp., from water).

B. A solution of salt **2** (0.42 g, 1.78 mmol) and bis(chloromethyl) ether (0.10 g, 0.89 mmol) in 2 mL of DMF was stirred at 20 °C for 48 h. The precipitate of AgCl was filtered off. The filtrate was diluted with acetone (10 mL) and Et_2O (20 mL), and the precipitate that formed was filtered off to give compound **8** (0.16 g, 60%). The product was identical with that obtained by procedure ***A***.

1-(5-Chloro-3-oxapentyl)-1,2,4-triazolium 4-nitroimide (9). A solution of salt **1** (1.69 g, 10.00 mmol) and 2,2′-dichlorodiethyl ether (7.00 g, 49.40 mmol) in 5 mL of DMF was stirred at 100 °C for 10 h and cooled. The precipitate of NaCl was filtered off. The filtrate was concentrated *in vacuo*. A small amount of EtOH was added to the oily residue, and the mixture was kept at −70 °C for 1 h. Then the solvent was rapidly decanted, and the residue was crystallized by addition of an EtOH—acetone mixture. The yield of compound **9** was 1.00 g (43%), m.p. 77—78 °C (from EtOH).

1,5-Bis(4-nitroimido-1,2,4-triazolium-1-yl)-3-oxapentane (10). A solution of salt **1** (0.84 g, 5.00 mmol) and 2,2′-dichlorodiethyl ether (0.36 g, 2.50 mmol) in 5 mL of DMF was stirred at 148—150 °C for 4 h and cooled. Acetone (50 mL) was added, and the precipitate that formed was filtered off and successively washed with water, EtOH, and Et_2O. The yield of compound **10** was 0.30 g (36%), m.p. 189—190 °C (from EtOH—water).

1-(2,3-Dihydroxypropyl)-1,2,4-triazolium 4-nitroimide (11). A solution of salt **1** (3.38 g, 20.00 mmol) and 3-chloropropane-1,2-diol (3.50 g, 34.60 mmol) in 5 mL of DMF was stirred at 100—120 °C for 40 h and cooled. The precipitate of NaCl was filtered off. The filtrate was concentrated *in vacuo* to give an oily residue. Ethanol (10 mL) was added, and the product was precipitated with acetone (50 mL) and filtered off. The yield of compound **11** was 2.01 g (51%), m.p. 122—123 °C (from MeOH—Pr^iOH).

1-Cyanomethyl-1,2,4-triazolium 4-nitroimide (12). A solution of salt **1** (0.50 g, 2.96 mmol) in 1.40 mL of chloroacetonitrile was stirred at 95—98 °C for 24 h and cooled. The precipitate that formed was filtered off and successively washed with water, EtOH, and Et_2O. The yield of compound **12** was 0.43 g (87%), m.p. 174—175 °C (from EtOH—water).

1-(2-Oxopropyl)-1,2,4-triazolium 4-nitroimide (13). A solution of bromoacetone (1 g, 8.20 mmol) in 5 mL of MeCN was added dropwise at 20 °C to a stirred solution of salt **1** (1.12 g, 6.65 mmol) in 5 mL of MeCN. The reaction mixture was stirred at 20 °C for 16 h and at 50 °C for 10 h and cooled. The precipitate that formed was filtered off and washed with Et_2O. The product was extracted with boiling EtOH, and the solvent was evaporated. The yield of compound **13** was 1.17 g (96%), m.p. 153—154 °C (from EtOH).

1-Ethoxycarbonylmethyl-1,2,4-triazolium 4-nitroimide (14). A solution of salt **1** (1.00 g, 5.98 mmol) and ethyl bromoacetate (1.00 g, 6.00 mmol) in 7 mL of MeCN was stirred at 50 °C for 10 h and cooled. The precipitate that formed was filtered off and successively washed with water, EtOH, and Et_2O. The yield of compound **14** was 1.18 g (93%), m.p. 155—156 °C (from EtOH).

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