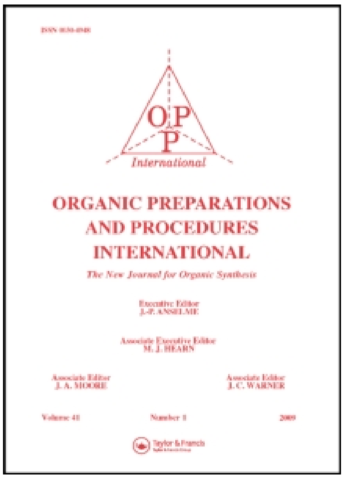

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SYNTHESIS OF DIAZOACETIC ESTERS AND AMIDES FROM CORRESPONDING ACETOACETIC ACID DERIVATIVES[1]

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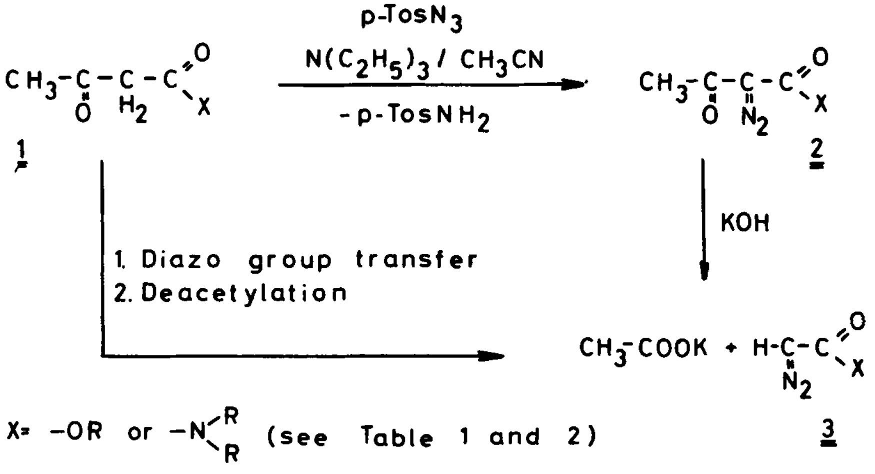

The present paper describes the conversion of acetoacetic esters and amides into diazoacetic esters and amides (1 → 3). In the first step, the diazo compounds 2 are prepared by diazo group transfer[3] onto the β-oxo esters and amides 1 with p-toluenesulfonyl azide in acetonitrile/

triethylamine[4]. The diazoacetoacetic acid derivatives **2** are then converted into the diazoacetic esters and amides **3** by deacetylation with potassium hydroxide in the same solvent[5]. Diazo group transfer and deacetylation may be accomplished in satisfactory yield by a "one-step procedure" (**1** → **3**) without isolation of **2**.

The results show (see Table 1 and 2), that this synthetic principle can compete with the usual diazotization of amines.

Experimental

1. Synthesis of diazoacetoacetic esters and amides (**2**) by diazo group transfer

Triethylamine (25.0 g, 0.25 mole) and 49.5 g (0.25 mole) p-toluenesulfonyl azide are added to a solution of 0.25 mole of the β-oxo carbonyl compound **1** in 300 ml anhydrous acetonitrile, whereby the temperature increases to about 30 - 50°. After 3 hrs. (diazoesters) or 24 hrs. (diazoamides) the solvent is removed at 35°/12 mm with a rotary evaporator. The residue is dissolved in 300 ml ether and washed successively with a solution of 14.0 g (0.25 mole) potassium hydroxide in 300 ml water and of 2.5 g potassium hydroxide in the same quantity of water. (Acidification of the aqueous potassium hydroxide phase with 6 N hydrochloric acid gives p-toluenesulfonyl amide, melting at 136°.) The yellow-orange ethereal phase is dried over anhydrous sodium sulfate and the solvent is evaporated at 35°/12 mm until the residue has attained a constant weight. For examples see Table 1. The preparation of ethyl and t-butyl diazoacetoacetate has already been described in[4].

2. Diazoacetic esters and amides (3)

a) From diazoacetoacetic esters and amides (2): To a solution of 0.25 mole of the diazo compound 2 in 350 ml acetonitrile is added 15.4 g (0.275 mole) potassium hydroxide in 250 ml water. The mixture is stirred 5 hrs. at room temperature and extracted three times with 200 ml ether. The ethereal phase is washed with 100 ml water and dried over anhydrous sodium sulfate. After removal of the solvent at 35 - 40°/100 mm[6] on the rotary evaporator the residual oil is distilled in vacuum[7] or recrystallized from ether at -70°. For examples see Table 2.

b) From acetoacetic esters and amides (1): 0.25 mole 1 is converted into 2 by diazo group transfer as described under 1.; the acetonitrile solution is directly mixed with 30.6 g (0.55 mole) potassium hydroxide in 250 ml water and stirred for 5 hrs. at room temperature. The isolation of the diazoacetic esters and amides (3) is the same as described under 2 a), except that the ethereal phase is washed with 2.5 g potassium hydroxide in 100 ml water instead of pure water. For examples see Table 2.

Table 1. Diazoacetoacetic esters and amides (**2**)

2, X =	Yield (%)	Formula (molar weight)		Analysis C %	H %	N %	IR (Liquid phase) $C=N_2$ (cm^{-1})
OCH_3 [8]	60	$C_5H_6N_2O_3$	Calcd.:	42.25	4.26	19.71	2135 2110 2222
		(142.11)	Found :	42.3	4.43	19.7	
OC_2H_5 [8]	84	analytical data see[4]					2141 2217
OC_3H_7 - n [8]	92	$C_7H_{10}N_2O_3$	Calcd.:	49.40	5.92	16.46	2137 2212
		(170.17)	Found :	49.9	6.15	15.7	
OC_4H_9 - n [9]	92	$C_8H_{12}N_2O_3$	Calcd.:	52.16	6.57	15.21	2132 2212
		(184.19)	Found :	52.0	6.76	15.1	
OC_4H_9 - t [8]	93	analytical data see[4]					2132 2212
Piperidino [9]	50	$C_9H_{13}N_3O_2$	Calcd.:	55.37	6.71	21.53	2103
		(195.22)	Found :	55.6	6.73	20.8	

Table 2, Diazoacetic esters and amides (3)

3, X =	Yield (%)[10] Procedure 2a	Yield (%)[10] Procedure 2b	Bp (^{o}C/mm)	Formula (molar weight)	Analysis	C %	H %	N %	IR (Liquid Phase) CN_2 (cm^{-1})
OCH_3	52	40	36/12	$C_3H_4N_2O_2$	Calcd.:	36.00	4.03	27.99	2110
				(100.08)	Found :	35.1	4.16	27.1	
OC_2H_5[11]	56	54	45/12		identified by IR-comparison with an authentic sample				2119
OC_3H_7 - n	55	-	60-61/12	$C_5H_8N_2O_2$	Calcd.:	46.87	6.29	21.87	2110
				(128.13)	Found :	46.4	6.30	21.1	
OC_4H_9 - n	-	64	79-80/13	$C_6H_{10}N_2O_2$	Calcd.:	50.69	7.09	19.71	2114
				(142.16)	Found :	50.4	7.14	19.6	
OC_4H_9 - t	60	48	51-53/12	$C_6H_{10}N_2O_2$	Calcd.:	50.69	7.09	19.71	2114
				(142.16)	Found :	50.7	7.23	19.8	
$N(C_2H_5)_2$[12]	-	68	85/0.4	$C_6H_{11}N_3O$	Calcd.:	51.04	7.85	29.77	2105
				(141.17)	Found:	50.6	7.88	29.9	
Piperidino[13]	86	70	123/1.2	$C_7H_{11}N_3O$	Calcd.:	54.88	7.24	27.43	2096
				(153.18)	Found :	53.8	7.17	26.9	

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1. Vth report on reactions of diazo compounds; IVth report: M. Regitz and H.-G. Adolph, Justus Liebigs Ann. Chem., in the press.

2. Diploma Thesis, Universität Saarbrücken, 1966; completed by further experiments.

3. Summary: M. Regitz, Angew. Chem. 79, 786 (1967); Angew. Chem. Int. Ed. Engl. 6, 733 (1967).

4. M. Regitz and A. Liedhegener, Chem. Ber. 99, 3128 (1966).

5. The analogous synthesis of t-butyl diazoacetate with sodium methylate as deacetylating reagent is described by us in Org. Syntheses 48 (in the press); cf. B. Eistert, M. Regitz, G. Heck and H. Schwall in Methoden der organ. Chemie (Houben-Weyl), 4. Edition, Vol. X/4, p. 588, Georg Thieme Verlag Stuttgart, 1968.

6. In the preparation of the more volatile methyl and ethyl diazoacetates, the solvent is distilled at 200 mm.

7. All distillations have been conducted taking the usual precautions; there have been no explosions up to the present time. The distillation residue consists of **2** and **3**.

8. Analyzed after recrystallization from ether at -70°; cf.[4].

9. The crude products were analyzed without further purification.

10. Referred to the product with constant bp.

11. Ethyl diazoacetate has also been prepared by diazo group transfer with deformylation: M. Regitz and F. Menz, Chem. Ber. 101, 2622 (1968).

12. For analysis, a distilled sample was recrystallized from ether at -70°; cf.[4].

13. The diazoamide is largely decomposed by distillation; it is purified by recrystallization from ether at -70°; cf.[4].

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