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Synthesis of Indole from Aniline and Ethylene Glycol with Pb(II) Catalysts

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Synopsis. Various catalysts for the direct synthesis of indole from ethylene glycol and aniline have been reported. It was found that in Pb(II) catalysts, the selectivities of indole are greatly influenced by the ligands; some of these, such as PbI_2–KI and PbI_2–BaI_2, provide indole in high yields. The catalytic activities of lead halides and binary systems were investigated regarding the effects of the ligands of Pb(II); recycling of the catalyst was tested.

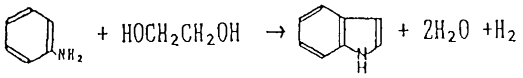
Indole is an industrially important substance as a raw material of tryptophan (amino acid) and of indigo dye. There have been many methods for producing indole, namely syntheses from *o*-ethylaniline,[1)] from 2-(*o*-aminophenyl)ethanol,[2)] from phenylhydrazine and paraldehyde (Fischer method),[3)] from aniline and acetaldehyde[4)] and so on. In the latter method the yield of indole is less than 20%. In the former three methods the starting materials are expensive and not very available on an industrial scale. On the other hand, a synthesis from ethylene glycol (EG) and aniline is relatively new. Since it is direct and simple from aniline to indole, and utilizes inexpensive starting materials, a low-cost process on the industrial scale could be possible. For more than one decade, various catalysts for the new synthesis have been developed.[5—8)] We have found that some lead halides, such as PbI_2, and binary catalysts, such as PbI_2–KI, PbI_2–SrI_2, and PbI_2–BaI_2, provide indole in high yields.[7,9,10)] The catalytic characteristics in gas- and liquid-phase reactions were somewhat systematically investigated while referring to the effects of the ligands of Pb(II) compounds or complexes. A recycling of the PbI_2–KI catalyst was tested in order to clarify its catalytic life.

Experimental

A reaction in the gas–solid phase was conducted under atmospheric pressure with a flow-type reactor having a bed volume of 50 ml. Aniline and EG were passed through a reactor containing a catalyst bed, and were then cooled at 3 to 5 °C. The condensed products were analyzed by gas chromatography (GC) (column, fused silica/OV-1 capilary column); (1) H_2, CO, and CH_4 and (2) CO_2, C_2H_4, and C_2H_6 of uncondensed gas were analyzed by GC (column, molecular sieve 13X) and GC (column, PORAPAK QS), respectively. A reaction in the liquid phase was conducted in an autoclave with a catalyst, aniline and EG (mole ratio=10) at a content of 50 to 100 ml under a pressure of 30 to 70 $\mathrm{kg\,cm^{-2}}$. After the reaction, the autoclave was cooled to room temperature and the contents of the gas and liquid phases were analyzed by the above-mentioned GC. Aniline and EG (Wako pure chemical, high grade) were used as reactants, and market metal halide was used as a catalyst or its component.

Results and Discussion

The indole synthesis from aniline and ethylene glycol comprises dehydration and dehydrogenation:



(1)

In our catalytic tests of many metal compounds (oxides, metals, sulfates, sulfides, halides, and others) some lead and cadmium compounds exhibiting high yield were found. In the case of Pb(II) and Cd(II) catalysts, various by-products were observed: *N*-ethylaniline (EA), 4-methylquinoline (MQ), 1,2-dianilinoethane (DAE), *N*-ethylindole (EI), and decomposition products (DE) of EG itself (C_2H_5OH, C_2H_4, CO, and CO_2). Table 1 shows the result of gas-phase reactions with lead halides and cadmium halides. The main by-products with these catalysts were, respectively, DE, MQ, EA, and DAE for PbI_2; DE for $PbBr_2$; DE and MQ for $PbCl_2$ and PbF_2; and DE, MQ, EA, and EI for all of the cadmium halides. In the case of Pb(II), the indole selectivity drastically changed in the following order: I(62.1%)>Br>Cl>F-(2.5%). $PbCl_2$ and PbF_2 mainly decomposed EG, itself, and PbI_2 provided the maximum indole yield. On the other hand, in the case of Cd(II), the differences in the selectivity between halogens were comparatively small, within about 19%.

Figure 1 shows the effect of adding KI to PbI_2. In a liquid-phase reaction the yield of indole with the PbI_2

Table 1. Activities of Indole Syntheses of Lead and Cadmium Halides in Gas–Solid Phase Reactions

Catalyst[a)]	Temp	EG conv.	Indole select.
	°C	%	%
PbI_2^*	350	88.2	62.1
$PbBr_2$	300	88.5	41.1
$PbCl_2$	405	47.0	17.0
PbF_2	382	31.0	2.5
CdI_2	300	92.1	55.0
$CdBr_2$	350	87.7	58.2
$CdCl_2$	350	92.8	39.3
CdF_2	315	99.7	47.1

a) Aniline/EG mole ratio=10, L.H.S.V=0.1 h^{-1} (except * 0.2), catalyst=50 ml.

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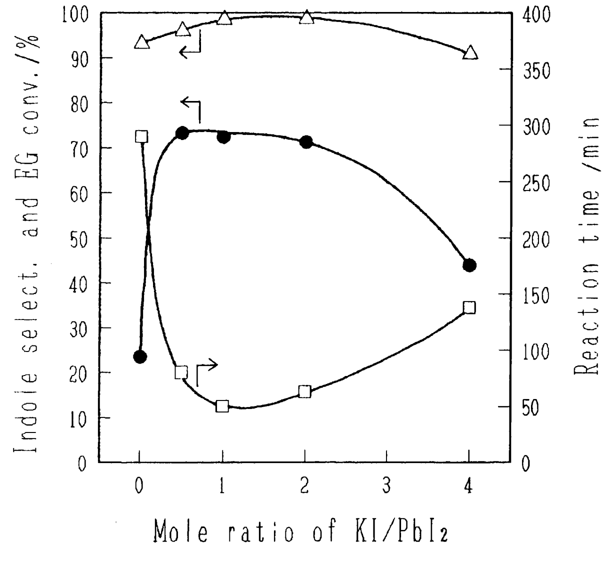

Fig. 1. Effect of an addition of KI to PbI_2 in a liquid phase reaction. $EG/PbI_2=5.9$, $H_2=15$ kg cm^{-2}, □: time, △: conv., ●: select.

catalyst was low. With an addition of KI, the yield and reaction rate remarkably increased, and a yield of more than 70% was attained. Too much KI additives caused a decrease in both the yield and the rate.

Table 2 shows the effect of adding alkali metal iodides, alkali earth metal iodides and pyridines to PbI_2. In the case of alkali metal iodides, compared with KI, over LiI and NaI, the rate wasn't much changed and the selectivity was slightly low; over RbI and CsI both the rate and selectivity were low. In the case of alkali earth metal iodides the rate was very high and the reaction temperature could be lowered to 15~40 °C compared with KI. Over SrI_2 or BaI_2, high selectivity was attained and over PbI_2–BaI_2 a maximum yield of 76.0% was attained. In the case of pyridines the rate was not so different from that of the non-additive case, though the selectivity increased.

Table 2. Effect of Additions of Alkali and Alkali Earth Metal Iodides and Pyridines to PbI_2

Additive[a]	Temp °C	Time min	EG conv. %	Indole select. %
LiI	330	50	91.9	56.9
NaI	330	40	89.7	69.5
KI	330	50	98.4	72.4
RbI	330	80	33.0	43.1
CsI	330	95	39.7	43.9
MgI_2	310	67	97.5	25.2
CaI_2	314	40	96.9	55.0
SrI_2	308	50	95.4	73.4
BaI_2*	290	70	99.2	76.6
py	320	260	99.1	55.0
2-Mepy	330	480	96.3	39.7
4-Mepy	330	460	98.5	47.9
4-(Me)$_2$Npy	320	160	97.3	42.1
cf. None	330	290	93.1	23.5

a) Aniline/EG = 10, $EG/PbI_2 = 5.9$ (except * 5.2), $MI/PbI_2=1$, $MI_2/PbI_2=0.5$, pyridines/$PbI_2=1$, $H_2=15$ kg cm^{-2}.

A mixture of KI and PbI_2 with a mp of 402 °C can form a 1 : 1 compound with a mp of 342 °C and a 2 : 1 compound with a mp of 370 °C.[11] The existence of $M_n[PbX_{n+2}]$ (MX: alkali metal halide, n: 1, 2, 4) is known, a typical one of which is $K[PbI_3]$.[12,13] According to an observation of the reaction in a glass autoclave, the dissolution of PbI_2 or PbI_2–KI into aniline–EG reactants until 240 °C seemed to hardly occur. It is conceivable that during the reaction at least part of the PbI_2 formed a complex with KI, and the complex subsequently contributed to indole formation, perhaps in a dissolved state due to the reaction temperature being just below its melting point. In PbX_2–KY and PbX_2–$0.5BaY_2$ catalysts (X, Y: halogen, Temp=330 °C) large effects of not only X, but also Y, on indole formation were observed as follows: PbI_2–KI (Sel: 72.4%), PbI_2–KBr (40.0%), $PbBr_2$–KI (36.4%), $PbBr_2$–KBr (31.0%). PbI_2–BaI_2 (76.0%), PbI_2–$BaBr_2$ (42.1%), $PbBr_2$–BaI_2 (45.3%), $PbBr_2$–$BaBr_2$ (34.9%).

Figure 2 shows the result of recycling the PbI_2–KI catalyst. After the reaction the content was evaporated and the residue was reused as a catalyst in the next reaction. The yield decreased about 10% at the initial stage, but a yield of about 60% was maintained from the 2nd on. By an X-ray diffraction analysis, Pb(OH)I other than PbI_2 and KI was detected in the residue. As shown in Fig. 2, by an elementary analysis the ratio of I combined with Pb decreased by about 17% at the beginning, but was kept from the 3rd on. The reason

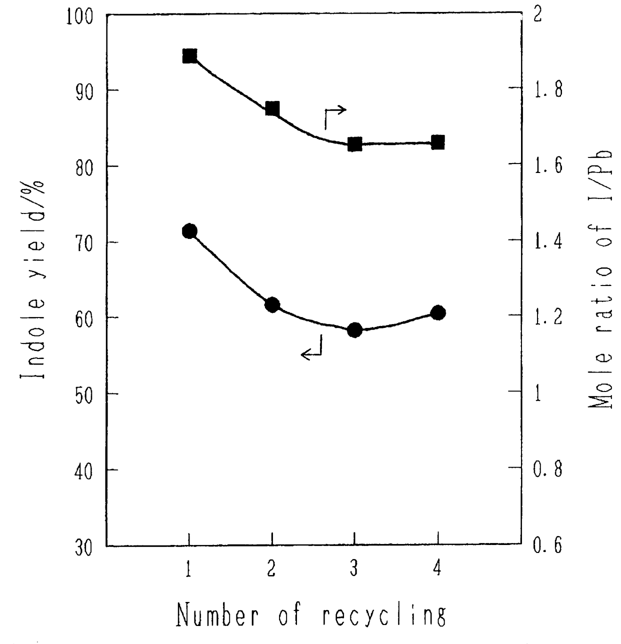

Fig. 2. Recycling of PbI_2–KI catalyst. $PbI_2/KI=1$, $EG/PbI_2=5.9$, 330 °C, From the left point conv. (%) and time (min) are 98.4, 50, 83.2, 50, 82.2, 49, 95.6, and 38 respectively.

why the formation of Pb(OH)I stopped and the yield was maintained after a few reactions may have been due to equilibrium being established between a group of PbI_2, water and aniline and a group of Pb(OH)I and hydriodic acid of aniline.

In conclusion, in a Pb(II) catalyst, ligands of Pb(II) have a large effect on indole formation; a binary system, such as PbI_2–KI or PbI_2–BaI_2, in a liquid phase exhibits a high yield and makes a new and industrially advantageous process of indole possible. However, further experiments are necessary in order to clarify the reaction with the Pb(II) catalyst, including its mechanism.

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